RESEARCH STUDY PROTOCOL

Optimization of antibiotic use and control of infections at the community level through a package of behavior-targeted interventions in Burkina Faso

CABU-B

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Declaration of compliance

This protocol contains the information necessary to conduct this research study. By signing this document, the Investigator agrees to conduct the study in accordance with the protocol, applicable ethical guidelines such as the Declaration of Helsinki, the European General Data Protection Regulation (GDPR), the ESF/ALLEA Code of Conduct for Research Integrity, as well as in accordance with international scientific standards and all applicable regulatory requirements. The Investigator will also make every reasonable effort to complete the study within the designated time frame.

Once the protocol has been published and signed by the Investigator(s) and authorized signatories, it cannot be modified informally. Amendments to the protocol have the same legal status and must go through the mandatory review and approval steps before being implemented.

Principal Investigator

Title, name: Prof. Halidou Tinto Date: February 4, 2022

Signed: 

Coordinating Investigator

Title, name: Prof. Marianne van der Sande Date: 02/04/2022

Signed: 

Summary table

Name of the study	Optimization of antibiotic use and control of infections at the community level through a package of behavior-targeted interventions in Burkina Faso
Assumptions and objectives	Primary 1. Develop, implement, and evaluate the effect of a package of behavioral interventions targeting drug dispensers (including health centers, drug depots, community pharmacies, and informal vendors) and the general population on the use of antibiotics. "Watch" 2. Estimate and model the effect of the package of interventions on the transmission *of* resistant *Enterobacteriaceae* from *E. coli* and *Salmonella* carriage in stool at the community level. Secondary 3. Estimate the effect of the intervention package on - the quality of clinical management by healthcare workers - on the use of antibiotics without a prescription - sanitation, hygiene, and infection prevention practices at the community level. 4. Identify the pathways and motivations through which interventions improve the quality of care and treatment outcomes. 5. Analyze and compare the spatial, phylogenetic, and ecological characteristics of AMR *Enterobacteriaceae* populations and genetic clones identified in human carriers and those from routine hospital AMR surveillance, based on bacteremia 6. Quantify the transmission of AMR genes or AMR Enterobacteriaceae within households
Design	The behavioral intervention package will be evaluated by comparing clusters with interventions and clusters without interventions. A cluster is a village, several villages, or neighborhood(s) where there is at least one drug dispenser, e.g., health center, drug depot, community pharmacy, or informal vendor. The intervention package aims to change the behavior of medicine dispensers and the general population with regard to the use of antibiotics (without prescription), the use of healthcare and services (health literacy), and hygiene and sanitation practices. The package of interventions will be co-developed with health actors and members of the general population, following the "Intervention Mapping" framework. Changes in antibiotic use will be measured through surveys of patients purchasing medicines, the quality of care through visits by simulated patients ("mystery shoppers"), and hygiene and healthcare practices through community surveys, within the existing community demographic and health surveillance system. Based on repeated stool samples collected from household members across the population, followed by identification (culture) and characterization of strains, the prevalence of carriage and transmission of ESBL-producing *Enterobacteriaceae*, particularly *E. coli* and *Salmonella,* among household members will be estimated.

Study population Study	22 clusters will be included: 11 with intervention and 11 without (control arm). Patient survey: each patient who visited a drug dispenser, 100 per cluster before the intervention and one year after the start of the intervention. Simulated patient visits: 5 visits with well-defined clinical presentation scenarios to all dispensers in each cluster (at least one per cluster) before and one year after the start of the intervention. Community survey: each household participating in community surveillance (HDSS, all residents for >3 months included), integrated into HDSS rounds before and after the intervention Carriage and transmission of ESBL-producing *Enterobacteriaceae*: stool samples from all members of 264 selected households (sampling proportional to household size): 132 from the intervention clusters; 132 from the control clusters. Before the intervention, and 3, 6, and 12 months after.
Intervention	A package of interventions targeting (1) antibiotic use by community-level dispensers and (2) prevention of transmission of resistant pathogens within households will be developed during the first six months of the study in consultation with health actors and the general population. A decision will be made on the inclusion of individual interventions that have been shown to be effective in other studies and a systematic review. The package consists of three components: one focuses on the quality of care and the dispensing of antibiotics by community-level dispensers, the second focuses on the demand for and use of antibiotics within the population, and the third focuses on the prevention of transmission of resistant pathogens within households. The development of the intervention will follow the six-step Intervention Mapping framework (Fernandez 2019; Bartholomew 2006), of which three steps have been completed: (1) the conceptual framework of the problem to be addressed, (2) the conceptual framework of the solution, and (3) identifying intervention options. Step 4 will be to adapt the intervention package to the implementation context (program production). Step 5 will be to implement the package, involving community representatives (the entire population, staff/drug dispensers, local and regional authorities). Step 6 is to evaluate its implementation.

1. Introduction

1.1 Context

Antimicrobial resistance (AMR) is a global health emergency with a significant negative impact on health and socioeconomic development, particularly in low-income countries (LICs) (Antimicrobial Resistance Collaborators 2022). In high-income countries, the burden of AMR is largely attributed to healthcare facilities (Cassini 2018). In contrast, in LIUs, invasive infections caused by AMR pathogens mainly result from community-level transmission (MacFadden 2019). The emergence of AMR among *Enterobacteriaceae* such as *E. coli* and *Salmonella spp.* is of particular concern as these organisms are important causes of clinical infection in sub-Saharan Africa (Tack 2020; Marks 2017; Maltha 2014; Reddy 2010). Although reliable AMR surveillance data in LDCs are scarce, AMR prevalence rates >80% against commonly used antibiotics have been reported in sub-Saharan Africa (Klein 2019; GLASS 2018; Tadesse 2017). Lower but significant and increasing prevalence rates of resistance have been reported for fluoroquinolones and third-generation cephalosporins. These are critically important broad-spectrum antibiotics and often the only second-line treatment option available in low-income settings. Due to their importance and high potential for AMR, these antibiotics are classified in the WHO's "Watch" group of antibiotics, which means that their use should be limited to specific indications.

One of the main drivers of AMR emergence is antibiotic consumption at the community and individual levels (Low 2019). Due to difficult or delayed access to hospitals and health centers, the main sources of antibiotics in many communities in LICs are community pharmacies, private clinics, or informal drug vendors.

Staff at these various drug dispensers are often not medically qualified, and informal drug sales are common (Katengele 2021; Giles-Vernick 2016; Sudhinaraset 2013). Two recent systematic reviews estimated the pooled prevalence of self-reported self-medication with antibiotics in sub-Saharan Africa at 56% and in West Africa at 70% (Yeika 2021). Furthermore, in sub-Saharan Africa, it has been found that more than two-thirds of visits to community drug dispensers result in the dispensing of antibiotics without a prescription (Belachew 2021). Well-trained and committed pharmacy staff can be part of a successful antimicrobial resistance control program, particularly through their role in educating patients, promoting the appropriate use of dispensed antibiotics, and providing advice to health colleagues on the appropriate prescribing of antibiotics (Sakeena 2018). In the absence of clinical or microbiological diagnosis, pharmacies often dispense antibiotics without clear justification. It is important to note that these antibiotics are often Watch antibiotics (Ingelbeen 2000; Sharland 2018). Among the different types of providers listed, and even among those with a good understanding of AMR, there is a need to support appropriate antibiotic prescribing practices (Asante 2017). The complexity of interventions to reduce the over-the-counter sale of medicines, including antibiotics, lies in the fact that this over-the-counter sale provides significant economic benefits. In addition, pharmacy staff may face high demand from their communities for antibiotic treatments, which, in the absence of clinical assessment, can lead to unnecessary or inappropriate distribution and use of antibiotics (Kotwani 2011; Liu 2021). A recent study in six LDCs showed that context-appropriate intervention programs are essential to improve antibiotic use in the community (Do 2021). In any stewardship program targeting the unregulated distribution of antibiotics in the community, it is

therefore crucial to co-develop interventions targeting medicine dispensers while incorporating the identification of alternative (economic) motivations. These interventions must also target the community to simultaneously reduce both the demand for and dispensing of antibiotics.

Behavior is influenced by social norms, attitudes, and beliefs, among other factors (Charani 2011). Existing behavior change interventions have been classified as persuasive (e.g., peer feedback on dispensing), enabling (e.g., guidelines, training sessions), restrictive (e.g., expert approval before dispensing specific antibiotics), or structural (e.g., introduction of specific antibiotics, clinical algorithm). The effect of individual interventions targeting outpatient antibiotic dispensing in PHCs was heterogeneous; nevertheless, multifaceted interventions, integrating for example educational materials with audits and feedback or peer comparisons, were more effective in reducing inappropriate antibiotic use (Nair 2021). A randomized clinical trial in India evaluated a package of interventions targeting informal providers with an intensive nine-month multi-topic training program and found that it improved the correct management of clinical cases (Das 2016). However, this intervention, which targeted only healthcare providers, failed to demonstrate a direct effect on the frequency of antibiotic use. The intervention did not target the community's demand for antibiotics. The authors recommended involving formal and informal healthcare providers and local populations in the design and implementation of such interventions for a more effective and sustainable impact.

To develop locally acceptable, feasible, and relevant interventions, the COM-B model for behavior change has proven to be very appropriate (Essack 2018).

This model forms the center of the well-known behavior change wheel, which is widely used in intervention design and has been used by the National Institute for Health and Care Excellence (NICE) and the UK Department of Health (Michie 2011). COM-B identifies three essential conditions for behavior—ability, opportunity, and motivation—which thus offer opportunities for intervention for behavior change. Abilities include psychological (e.g., knowledge) and physical (e.g., skills) abilities. Opportunity includes social and physical opportunities (e.g., social influences and environmental context and resources). Motivation includes reflective and automatic motivation such as beliefs about abilities and consequences, goals, and ideas about professional role and identity (Cane 2012).

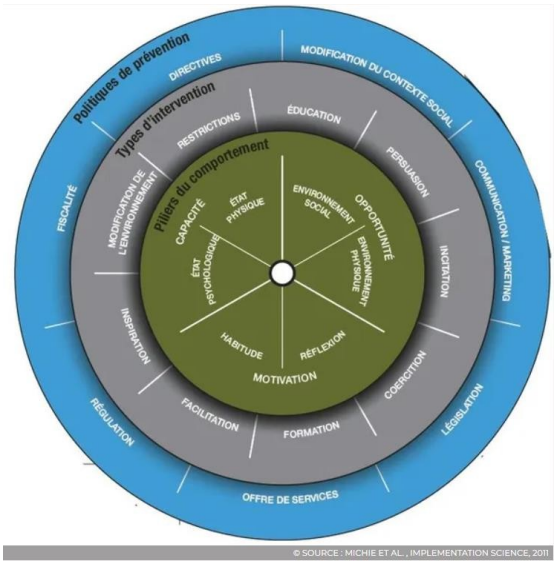


Figure 1. Behavior change wheel from the COM-B framework. Adapted from by Michie , and al, 2011.

We define optimizing antibiotic use as "improving access to antibiotics for communities when indicated, with choice, dose, and

appropriate duration, and in particular restricting the informal use of antibiotics without clinical indication and without prescription. Such optimized use should lead to reduced selection pressure that favors the emergence of resistant pathogens. While antibiotic resistance in high-resource countries focuses on reducing inappropriate antibiotic use, in low-resource countries, the lack of or delayed access to antibiotic treatment for those who needed it has been estimated to cause 445,000 deaths from community-acquired pneumonia in children under 5 years of age (Laxminarayan 2016). In addition, these difficulties in accessing formal health facilities and appropriate prescriptions are responsible for the high prevalence of self-medication with antibiotics in Central Africa (>50%) (Yeika 2021). At the same time, the continued transmission of newly emerging or existing (drug-resistant) bacteria and the exchange of antimicrobial resistance genes between bacteria hosted by humans, animals, and their environment are facilitated by substandard hygiene and sanitation practices (Collignon 2018). Mathematical modeling has demonstrated that household transmission of extended-spectrum beta-lactamase (*ESBL*)-producing *Enterobacteriaceae*, which cause significant AMR, in high-income countries (Musicha 2020; Haverkate 2017) and to quantify the relative importance of environmental transmission within healthcare facilities (Pham 2019; Wang 2017). However, the acquisition and spread of AMR in the community has rarely been studied, even in high-income countries, and there are major uncertainties regarding the relative importance of different transmission routes for AMR pathogens and the determinants of AMR, for which substantial geographical variation is to be expected (Mughini-Gras 2019; Dorado-Garcia 2018). ESBL-producing *Enterobacteriaceae* have also been identified in the domestic environment; for example, 31% of E. *coli* isolates identified in 115 water points in the Nanoro district, BF, were ESBL-producing (Post 2014). In addition, the extent to which the transmission of AMR bacteria could be amplified by antibiotic use is unknown. Models combining epidemiological data with high-resolution genetic data provide flexible frameworks that can help quantify the probability of different acquisition pathways, while taking into account genetic diversity within the host and unobserved colonization times (Wymant 2018; Klinkenberg 2017; Didelot 2017; Worby 2016).

1.2 Evidence

To date, evidence of effective interventions against AMR has largely come from high-income hospital settings (Wernli 2020). Formal evaluations of community-based or outpatient interventions are rare in low- and middle-income countries, particularly in sub-Saharan Africa. Furthermore, the outcome of any intervention is likely to differ depending on contextual factors or barriers to implementation (Wilkinson 2019; Nguyen 2019; Karen 2019).

The proposed study will evaluate the effect of a package of participatory behavior change interventions aimed at (1) facilitating infection prevention measures at the community level, and (2) in the event of illness, avoiding the regular use of inappropriate antibiotics, and (3) reducing the dispensing of Watch antibiotics by various drug dispensers at the community level. This strategy, targeting both demand (community) and supply (dispensers), will reduce the inappropriate use of antibiotics. (3) reduce the dispensing of Watch antibiotics by various drug dispensers at the community level. This strategy, targeting both demand (community) and supply (dispensers), will reduce the emergence and transmission of AMR. In addition to measuring the (direct) effect on antibiotic use, AMR transmission within households will be estimated in order to assess the (indirect) effect of the intervention on transmission. A similar study will be conducted in the Democratic Republic of Congo, with an additional component of environmental surveillance based on Enterobacteriaceae carriage in rodents.

2. Study objectives

Primary

1. Develop, implement, and evaluate the effect of a package of behavioral interventions targeting drug dispensers (health centers, drug depots, community pharmacies, and informal vendors) and the general population on the use of "Watch" antibiotics.
2. Estimate and model the effect of the package of interventions on the transmission of resistant Enterobacteriaceae from *E. coli* and *Salmonella* carriage in stool at the community level.

Secondary

3. Estimate the effect of the intervention package on
    - the quality of clinical management by healthcare professionals;
    - the use of antibiotics without a prescription;
    - sanitation, hygiene, and infection prevention practices at the community level community level;
4. Identify the pathways and motivations through which interventions improve the quality of care and treatment outcomes;
5. Analyze and compare the spatial, phylogenetic, and ecological characteristics of AMR Enterobacteriaceae populations and genetic clones identified in human carriers and those identified through hospital AMR surveillance based on bacteremia;
6. Quantify the transmission of AMR genes or AMR Enterobacteriaceae within households.

3. Study design

A package of behavioral interventions will be developed and evaluated in a **cluster-controlled study within the** Nanoro Health and Demographic **Surveillance** System (HDSS). A cluster is a village, several villages, or neighborhood(s) where there is at least one drug dispenser (see definition in section 4.1.1). An evaluation study of a package of behavioral interventions, developed independently and based on the specific context, will take place in Kimpese in the Democratic Republic of Congo. The present study protocol concerns only the study in Nanoro, Burkina Faso.

In order to optimize the use of antibiotics and reduce the risk of human-to-human or animal-to-human transmission, a package of interventions will aim to change the behavior of medicine dispensers at the community level and the general population with regard to the use of antibiotics (without prescription), the use of healthcare and services (health literacy), and hygiene and sanitation practices. The interventions will be developed, implemented, and evaluated with health actors, including medicine dispensers, health authorities, and members of the general population, following the Intervention Mapping framework (see 4.2.2 Interventions). The intervention package will be implemented in 11 intervention communities (clusters), and the results will be compared with 11 control communities where the intervention did not take place.

The direct effect of the intervention package will be evaluated through various surveys:

- The change in antibiotic use will be measured by **patient surveys** before and one year after the start of the intervention.
- Changes in the quality of care will be measured through **visits by simulated patients (mystery shoppers)** before and one year after the start of the intervention.
- Changes in hygiene practices and healthcare use will be assessed through **community surveys** conducted before and after the intervention, integrated into the community surveillance system (HDSS).
- The transmission of ESBL-producing *Enterobacteriaceae*, particularly *E. coli* and *Salmonella*, between household members will be estimated based on **repeated stool collections** before and 3, 6, and 12 months after the start of the intervention, followed by identification (stool culture), strain characterization, and antibiotic susceptibility testing.

The relationship between ESBL-producing *Enterobacteriaceae* identified in the stool samples of healthy carriers in the population and those identified in the surveillance of bacteremia at the Nanoro Medical Center with Surgical Unit (CMA) will be evaluated after characterization and sequencing of the strains. We will use maximum likelihood phylogeny reconstruction by species and sequence type, as well as dynamic transmission modeling to explore human-to-human transmission at the community level.

An evaluation of the implementation of the intervention package will aim to understand and analyze the relationship between interventions and context in order to explain how and why interventions work or fail (e.g., differences in context, populations, and delivery of the intervention package), the individual effect of each intervention/component of the intervention package, and whether they can be transferred to other contexts and populations (Grant 2013; Oakley, 2006).

4. Methods

4.1 Study environment, population, and recruitment strategy

4.1.1 Environment

This interventional study will be conducted in the rural HDSS and extension zone of the HDSS in Nanoro, Burkina Faso.

Drug dispensers include (1) health centers, (2) community pharmacies where drugs are dispensed by (semi-)qualified personnel, as well as (3) drug outlets owned by qualified health workers but where drugs are dispensed by unqualified personnel, and (4) informal drug sales in ordinary stores or markets. Public health centers and community pharmacies are the main healthcare providers in terms of frequency of healthcare use (Ingelbeen 2021; Guiraud 2017). Patients from public health centers may be referred to the district hospital.

AMR in this context is driven by various factors: limited and timely access to formal health facilities and appropriate diagnostic tools and services; suboptimal knowledge of the importance of correct diagnosis and quality of care; suboptimal antibiotic sales practices by medicine dispensers; and widespread incidence of infections linked to poor hygiene and sanitation.

We select as clusters villages or neighborhoods where there is at least one drug dispenser, as defined above, who covers the drug supply for the

population of that village or neighborhood (Appendix 11.6). The clusters will be divided between the intervention group and the control group in strata according to the type of dispenser: presence of a public health center and one or more private dispensers, or presence of only one or more private dispensers, in order to ensure the same number of public health centers in each group.

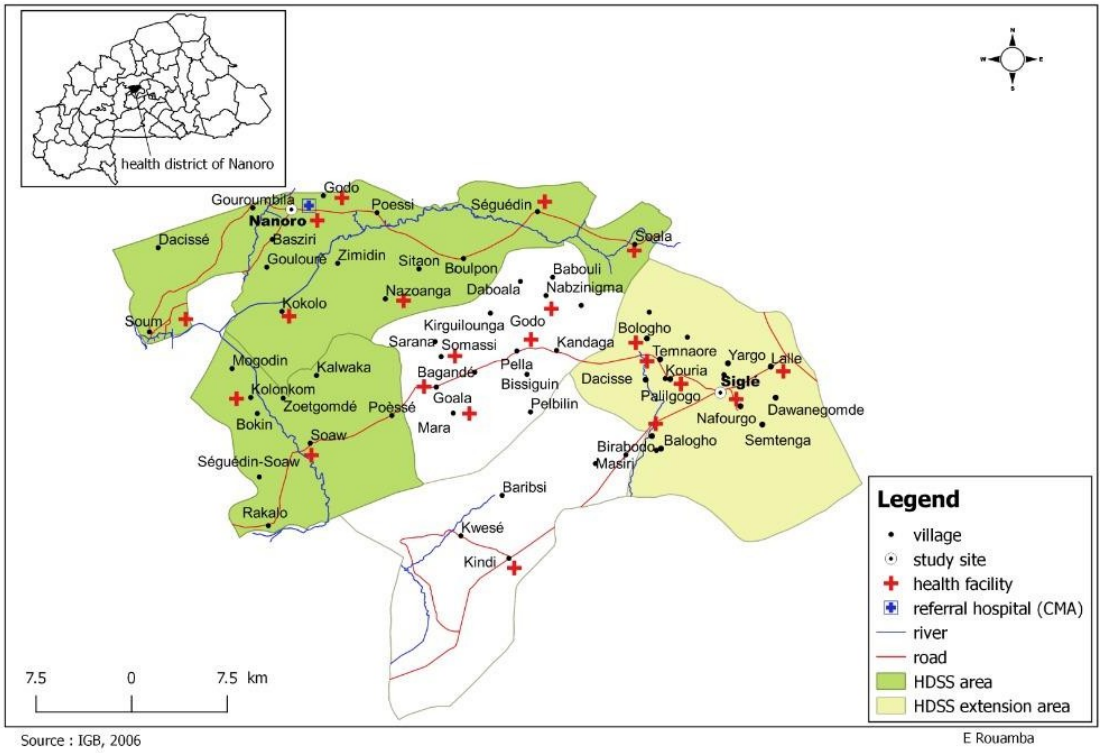


Figure 2. Map of the Nanoro health district showing the HDSS coverage area and its extension

4.1.2 Sample size and statistical power

a. Decrease in antibiotic use Watch in patient surveys

With 11 clusters per intervention arm (i.e., 22 clusters per site), at least n=100 patient discharge surveys per cluster, a Watch antibiotic use frequency of 24% in the DRC and 28% in BF (Valia 2021), and assuming an estimated intraclass correlation coefficient (ICC) of 0.01, a cluster-level correlation (rhoc) of 0 (a conservative assumption), a subject-level correlation (rhos) of 0 (different subjects at baseline and at 12 months), we have 80% and 85% power to observe a net difference of 40% (i.e., (I_post - I_baseline) - (C_post - C_base)) in antibiotic use in the DRC and BF, respectively. A clear difference (I_post - I_base) of >30% can be estimated with a power of >80% (https://github.com/esthervankleef/sample_size_jpiamr).

If several dispensers are present in a cluster, 100 surveys per dispenser will be recorded. The cluster-weighted prevalence of Watch antibiotic use will be determined by taking the sum of the prevalences of individual dispensers multiplied by the proportion of visits to these dispensers out of the total number of visits in the cluster (based on data on healthcare use from the community survey).

b. Carriage and transmission of ESBL-producing Enterobacteriaceae

In the 22 clusters, 132 households per intervention arm will be selected, with an expected average household size of 6 [IQR: 4-9]. A stool sample will be collected for each member of the selected households. Depending on logistical feasibility (collecting fresh stool samples and transporting them to the laboratory), some clusters may be excluded based on their distance from the laboratory, provided that the same distance criteria are applied in the other arm. We used a simulation-based approach to estimate the power of detection of reductions in transmission resulting from the intervention (https://github.com/esthervankleef/sample_size_jpiamr). We assumed a Markov model of transmission within households with parameters informed by a Dutch study (Haverkate 2017), i.e., the same rate of decolonization, a tenfold higher baseline transmission rate, and a person-to-person transmission rate within households before the intervention twice as high as the rate estimated in the Netherlands. The analysis was based on a generalized estimating equation approach (R gee package) taking into account the clustering of households with a Poisson family and an AR-1 correlation structure using robust z-scores applied to data simulated by the Markov model of households with 1,000 simulations for each assumed intervention effect size. Assuming that the intervention reduces the transmission rate by 40% and with a two-tailed Type I error of 5% (based on Lam et al 2021), the study was estimated to have 99% power to detect a reduction in transmission. For a 30% reduction in transmission, the power was estimated at 82%.

4.1.3 Inclusion and exclusion criteria

a. Preparatory study and implementation assessment

To be eligible, participants in this phase of the study must meet the following criteria:

Community members:

- Be a member of the community of a village or neighborhood within or outside the HDSS (also outside, as behavior may change as a result of the interviews);
- age 14 or older;
- have accepted the informed consent administered.

Dispensers:

- be healthcare personnel in a state or private healthcare facility OR be personnel in private pharmacies OR be informal dispensers or sellers of medicines OR be personnel in the health district;
- have accepted the administered informed consent.

b. Patient survey

At each of the identified drug dispensers, patients/visitors will be approached for medical visit surveys. Patients or visitors of all ages and for any reason visiting the dispenser will be included if they have given written consent to participate. If children or adolescents have completed the medical visit, their parents or guardians will be asked to respond on their behalf. For adolescents to be included in the study, they must give their consent (assent) for a parent or guardian to respond on their behalf. Recruitment will be consecutive, i.e., when one survey is completed, the next patient who finishes their visit will be approached.

To be eligible, participants in this phase of the study must meet the following criteria:

- be a patient or visitor of any age, seeking care for themselves or another person;
- have just finished a visit with the provider;
- have agreed to informed consent (for adolescents, assent will be requested + informed consent from one of the parents present. For children under the age of 14, the consent of a parent or guardian will be requested).

Providers will be included if they have given prior consent to participate in this component of the study.

c. *Simulated patient visits*

To be eligible, medication dispensers must meet the following criteria:

- prescribe or dispense medications in a community pharmacy, drug depot, or other private clinic or store within the HDSS village involved in the study or a village in the HDSS extension involved in the study;
- Have previously given consent to participate in the development and evaluation of the intervention package.

d. *Asymptomatic carriage and transmission of ESBL-producing Enterobacteriaceae*

To be eligible, participants must meet the following criteria:

- be a member of a household in the HDSS village or selected HDSS extension for this component of the study (resident for >/= 3 months);
- willingness or ability to provide written informed consent and agree to provide four stool samples during the study period (informed consent by a parent or guardian present for minors, and additional assent by minors aged 14 to 17);
- be in good physical health (no current infectious disease)

Potential participants who meet any of the following criteria will not be enrolled in the study:

- residents of HDSS villages who plan to move or be absent for an extended period in the coming year;

For individuals with an active infectious disease or undergoing treatment for an infectious disease, field workers will return to collect stool samples once the patient has recovered

e. *Community survey within the HDSS survey*

A one-time questionnaire concerning the entire household on hygiene practices, sanitation, access to water, and use of healthcare will be added to the routine HDSS questionnaire. The survey will be conducted with the heads of households or an adult member of the household delegated by the head of household. Each household in the clusters included in the HDSS will be asked to participate.

To be eligible to participate in this component of the study, the respondent must meet the following criteria:

- Be the head of household or representative of a household within the clusters selected for the study, and be part of the HDSS or HDSS extension population (resident for >/= 3 months);

- given their agreement (consent) to the use of data from the one-off survey on hygiene practices, sanitation, access to water, and antibiotic use.

4.2 Procedures

The procedures and results of the patient survey and community survey are the same as those of the pilot study, whose study protocol was approved: "Community-level antibiotic use in Burkina Faso, version 1.0, dated May 5, 2020 (reference of approval ITM IRB IRB/AB/ac/089; Health Research Ethics Committee 2020-8-171).

The procedures for *Enterobacteraceae* carriage will follow those of the approved study protocol "*Salmonella enterica* and Extended-Spectrum Beta Lactamases – Producing *Enterobacterales* asymptomatic faecal carriage in Nanoro and Nazoanga, Burkina Faso" (reference of approval ITM IRB IRB/AB/ac/013; Health Research Ethics Committee 2021-03-052).

4.2.1 Data collection

a) Preparatory study

To co-develop the actual intervention, we will explore starting with the activities described below. These activities will be carried out simultaneously, taking into account travel logistics, etc.

i) The **Photovoice methodology** (Hergenrather 2009) - a well-developed participatory approach that integrates the perspectives and priorities of local populations on a particular community issue - will be used with four groups to explore issues around health, MCH, and water, sanitation, and hygiene (WASH). In each country, there will be one group of men and one group of women (including older and younger people).

Training will be provided on the research process, camera use, the use of photography in research, ethics in research and photography, and the interpretation of visual images. With the help of experienced facilitators, participants will use cameras to explore issues such as the significance of antibiotics for them, sanitation problems, challenges, and solutions, common health problems, and AMR. The images and stories produced during several sessions will be analyzed collectively by participants, guided by facilitators, to identify and build consensus around problems and solutions. These activities will serve as a basis for deepening understanding of AMR and for co-developing concrete solutions and interventions to prevent AMR. Suggestions for intervention activities, including the use of photos in the stories, will be gathered from these discussions. The photos and stories from the photovoice exercise will be integrated into the intervention components in the form of materials, such as flashcards and plays for awareness-raising activities (see phase 2, components 2 and 3 below): of course, if a person is identifiable in a photo, their written consent will be required. This project is expected to take approximately four weeks.

ii) **Focus group discussions (FGDs)** with community members aim to further characterize the determinants of inappropriate antibiotic use and the drivers and barriers to change in antibiotic circulation. A recent systematic review indicated that theoretical saturation can be

achieved even with small sample sizes (4 to 8 focus groups) (Hennink 2022). However, while a small number of focus groups may be sufficient to identify themes (code saturation), a larger number of groups is needed to fully understand these themes (meaning saturation) (Hennink 2019). We therefore aim for 7 group discussions in each country with the following groups:

- Adult women, members of the community
- Adult men who are members of the community
- Young men (aged 14-17, with the consent of their parents/guardians)
- Young people ( ) Women ( ) Young men ( ) (14-17) ( ) with ( ) the ( ) consent ( ) of ( ) their parents/guardians
- Healthcare professionals
- Pharmacy staff
- Village authorities

We will conduct four focus groups per group with an estimated average participation of eight participants. Thus, we expect a total of 224 (7x4x8) participants in the focus groups per country. Using a discussion guide, the moderator will initiate a discussion with general questions before gradually moving on to more specific and targeted questions. The questions explored will include the diseases that affect them, the treatments used and the healthcare providers consulted, what antibiotics mean to them, the classification of a range of real-life medicines, including antibiotics and non-antibiotics, what AMR means to them, its severity and causes, and what the problems, challenges, and solutions are to sanitation and AMR issues.

iii) **Individual interviews and participant observations** will be conducted to supplement the FGDs in order to capture questions and concerns about antibiotic use that cannot be expressed in a group setting. Interviews will be conducted until theoretical saturation is reached. A recent systematic review indicated that theoretical saturation can be achieved even with small sample sizes (9 to 17 interviews). We are therefore aiming for a minimum of 20 interviews (Hennick and Kaiser, 2022).

Observations will also be used to assess the actual use of antibiotics in the population, for example by taking photos of family medicine kits as a starting point for discussion. The sample will include:

- Women, community members
- Men, community members
- Young men (aged 14-17, with the consent of their parents/guardians)
- Young women (aged 14-17, with the consent of their parents/guardians)
- Healthcare workers
- Pharmacy staff
- Village authorities

- Informal medicine sellers
- Traditional practitioners or other healers outside the formal system
- Religious leaders who prescribe antibiotics

iv) **Field journals** will also be used to record descriptive and reflective notes: notes taken on the spot (characteristics of individuals present, conversations with individuals) and detailed descriptions (description of places and events) as well as methodological reflections (conditions in the field, relationships with individuals, difficulties and challenges).

These three components of the preparatory study will be conducted simultaneously over a two-month period to allow sufficient time for logistics and travel. Once all data has been collected, it will be analyzed for one month using qualitative methods, and a technical report will be written to summarize the results of the analysis.

In order to use these results to generate intervention activities, the national team and social scientists from IMT and AU will meet and determine the conceptual angle and activities to be included in the intervention. The national team will then share these ideas with the community groups involved in the preparatory study to consult them on the penultimate list of activities and gather their feedback. The AU officials will then develop the intervention activities and the manual, with input, feedback, collaboration, and suggestions from the national team. A local artist will be hired to illustrate the manual and create illustrations for the activities, posters, etc. Theater groups/artists will then be hired and development workshops will be organized to develop the play that will be presented during the intervention.

At the end of this process, an intervention manual will have been produced detailing the activities and how to carry them out. A separate activity manual will be produced with all the necessary resources for the activities.

b) Patient survey

At the end of a healthcare visit, patients and parents of pediatric patients (whether or not they have received antibiotics) will be asked, using a structured questionnaire, about: symptoms, the quantity of antibiotics dispensed/purchased by antibiotic group, if applicable, the dose and duration of antibiotic treatment (including any increase/reduction), the method of administration, the number of antibiotics and antimalarials used concomitantly (including the reasons). Also information on the product purchased: unit price, brand name, declared manufacturer, expiry date. A photo of the antibiotic and its packaging (box, blister pack, sachet, or a combination thereof) will be taken using mobile data collection devices (stored in the data collection form). The initial survey will be followed by a follow-up of the clinical outcome of patients and treatment on the seventh day after the visit and initial survey (number of days before discontinuation of treatment). This follow-up will be done by telephone or the patient will be visited at home.

The questionnaires will be immediately entered into a tablet and uploaded daily to the study database. HDSS investigators will conduct the interviews.

This survey will be conducted before the intervention is offered and again one year later. Medication dispensers will be asked for their consent to participate in the survey and simulated patient visits, and informed consent will be sought from each patient participating in the survey.

A two-day training session on data collection will be organized for investigators before the first round, and a refresher course will be held before the second round. In a pilot study within the two HDSS, investigators were trained for this survey.

c) Simulated patient visits

Visits by simulated patients, i.e., actors who mimic a medical condition, are the gold standard for evaluating patient care and the appropriateness of antibiotic distribution by health workers or drug dispensers (Madden 1997).

Before and 12 months after the introduction of the intervention, five simulated patients will visit/consult each prescriber/dispenser of medication. Each will have a well-defined and standardized clinical presentation. The simulated patients will be trained to respond to the prescriber/dispenser's clinical or history questions in a standardized manner to mimic clearly recognizable medical conditions for which the indication for treatment or referral is not debatable (Xu 2012). The dispenser will be asked for their consent for this component at the beginning of the study and will be blinded, i.e., they will not be informed when these visits will take place and will not be notified by the simulated patients during the visit. The simulated patients will also be blinded, so they will not know whether the provider has received the intervention. Providers, and if possible those who train providers in clinical management, will not be informed of the clinical presentations that will be evaluated. The **five clinical presentations** will be:

1. Acute gastroenteritis (non-bloody/watery) after a night of frequent loose stools and vomiting (4 times during the night), which began during the night. No travel history, no other cases in the household, no fever. For this scenario, appropriate management will consist of at least (1) questions or examination of stool type or presence of blood in stool, (2) advice to stay hydrated (drink fluids, ORS), AND (3) no prescription or dispensing of antibiotics;
2. Acute nasopharyngitis in an adult patient: dry cough + cold + sore throat + low-grade fever (slight feeling of warmth), all of which have been present for 3 days but with improvement in fever on the day of the visit (history of fever). For this scenario, appropriate management will consist of at least (1) questions or examination for the presence of respiratory signs (type and frequency of cough, sputum, difficulty breathing) AND the presence of fever; AND (2) no prescription or dispensing of antibiotics;
3. Severe acute pneumonia in an adult patient: productive cough + mucous sputum + fever and headache, all of which have been present for five days. The cough, which was initially dry, became increasingly productive after the second day. This productive cough, accompanied by headache and fever, was subsequently complicated by difficulty breathing (high respiratory rate). A parent or guardian of the patient presented at the healthcare provider's office because the patient was too weak to travel. In this scenario, appropriate management would consist of at least (1) questions or examination for the presence of respiratory signs (type and frequency of

cough, sputum, difficulty breathing) AND (2) questions or examination for signs of systemic infection: fever, pulse, respiratory rate AND (3) (in the case of a drop-in clinic, informal vendor, or CSPS) referral to a CSPS or hospital OR (in the case of a CSPS) prescription of amoxicillin or phenoxymethylpenicillin.

4. Isolated acute fever: This is a young adult who presents to the healthcare provider with fever and no other additional symptoms. A rapid diagnostic test (RDT) for malaria will be negative. In this scenario, appropriate management will consist of at least (1) questions or examination for signs of respiratory disease; (2) a malaria test OR referral of such a patient to a health center, hospital, or other facility with malaria diagnostic capabilities; (3) if the malaria test result (negative) is available: a follow-up appointment in the next few days with or without a prescription for an antipyretic.
5. Acute urinary tract infection: This will be a young adult male presenting to the provider with fever + burning during urination + frequent urination in small amounts (more than 7 times during the day and/or more than once during the night). For this scenario, appropriate management will consist of at least a referral to a formal health center (CSPS or hospital) OR (1) questions about the duration and frequency of urinary complaints AND (2) antibiotic treatment from the Access group: nitrofurantoin every 6 hours (4 doses per day) for 5 days OR smx/tmp for 3 to 8 days (8 days based on the 2008 national guideline) OR tmp for 3 days OR amoxicillin/clavulanic acid for 3 to 5 days.

The conditions were selected based on an identification of the most common symptoms that prompt people to seek care involving the use of antibiotics at the community level, a review of the literature on syndromes used for simulated patient visits, and a selection of syndromes for which the indication for or against antibiotics is clearly defined in the Essential Medicines List Anti-biotic Book 2021" from the WHO (https://www.who.int/publications/m/item/the-who-essential-medicines-list-antibiotic-book-improving-antibiotic-awareness), and the feasibility of mimicking these presentations during a visit. The clinical presentations will be tested and piloted with known and informed healthcare professionals during the first few months, while the intervention package is being developed. Training and testing will be repeated before the second round of simulated patient visits.

After the visits, clinical care will be assessed using a checklist (Appendix), entered on a tablet, which allows the essential questions and examinations and the appropriate actions taken by the provider to be checked off. The practices (medical history questions, examinations) and treatment choices considered appropriate care, included in the checklist, are based on
(1) the 2021 WHO Antibiotic Book, which takes into account different contexts and medical conditions, (2) the 2015 WHO document on Integrated Management of Childhood Illness for children aged 0-4 years, and (3) the 2008 "Guide to Diagnosis and Treatment" (GDT) and its 2014 revision, which has not yet been formalized, for those aged 5 years and older. The actor/simulated patient will also measure the duration of the visit. Each question/examination/action has a weight that allows a score to be calculated from all three checklists per provider.

For visits at 0 and 12 months, the actors do not know whether the point of sale they visited has received training or not. Visits are unannounced to prevent providers from adopting more desirable behavior during these visits (Hawthorne effect).

d) Carriage and transmission of ESBL-producing Enterobacteriaceae

Stool samples will be collected from all eligible and consenting household members before the start of the intervention, and at months 3, 6, and 12 in both the intervention and control groups.

All individuals will be given a **questionnaire** and a **stool sample** will be collected for screening for ESBL-producing *Enterobacteriaceae*, *E. coli,* and *Salmonella*. URCN field workers will conduct the survey. The questionnaire will record (i) antibiotics stored at home, including the type of antibiotics, (ii) use of leftover antibiotics, (iii) use of antibiotics in the past month, (iv) use of healthcare in the past 3 months (visits to formal or informal healthcare providers), (v) hospital stays in the last 3 months, (vi) source of drinking water according to the WHO (well protected or unprotected from external contamination, borehole, surface water), (vii) use of toilets, (viii) Promiscuity with livestock, (ix) consumption of unwashed raw foods (lettuce, cabbage, etc.), (x) Hand washing with soap before meals. For each person surveyed, after obtaining individual informed consent (in writing) and authorization from the head of the household, a stool sample will be requested.

Participants will receive a labeled container for stool sample collection and will be asked to provide a fresh stool sample the following morning if they are unable to provide one during or after the questionnaire. The sample will be collected by the study field workers, and the date and time of sample collection will be recorded along with the participant's ID. The collected sample will be transported to the laboratory in a cooler within 8 hours of production in a manner that ensures the safety of the public and the transporter. The sample will be divided into two upon arrival at the laboratory, one for *Salmonella* testing and one for *E. coli* testing.

e) Community survey within the HDSS survey

During repeated household visits, before and after the introduction of the intervention, we will collect data on 1) factors and behaviors potentially associated with AMR transmission: hygiene, sanitation, and infection control practices; access to safe drinking water; and contact with animals; and on 2) health care seeking: episodes of illness and health care utilization (frequency and type of provider) for each household member (all ages) during the past month. To avoid seasonal bias in practices and behavior, there will be a one-year interval between the two community surveys. The questionnaire will be administered to the head of the household, who participated in the HDSS survey and will respond on behalf of all household members. Episodes of illness will be recorded without personal data on the household member, except for the household number.

The additional structured questionnaire will be added to the regular HDSS electronic questionnaire on a tablet. Each week, the data recorded on the mobile device will be synchronized between the HDSS teams' mobile devices and the HDSS database. Once the HDSS survey is complete, healthcare utilization data will be extracted from the HDSS database, without direct identifiers (pseudonyms) and without HDSS data not included in the healthcare utilization questionnaire, and recorded in a password-protected csv file on the study laptop.

f) Evaluation of intervention implementation

The implementation of the intervention, the response to the intervention, and the maintenance of its effect on health literacy or antibiotic dispensing practices will therefore be documented and analyzed through three repeated interviews with at least 20 trainers, healthcare providers, and participants (from villages involved in the intervention). The interviews will take place at the beginning, middle, and end of the intervention, allowing the results of these

process evaluations to adjust the intervention (capitalizing on successful elements and removing elements that are not useful).

4.2.2 Interventions

The intervention aims to combat AMR using three intervention components, each addressing one of the three conditions for behavior change in the COM-B model. The target behaviors of the intervention are based on considerations of potential impact, likelihood of change, potential spillover effects, and ease of measurement (Michie 2016). The COM-B model would therefore be ideally suited to guide interventions on antibiotic use involving highly complex behaviors, and will be used to design intervention packages to achieve simultaneous change in both antibiotic demand and supply.

The intervention package will be developed during the first six months of the study. In consultation with healthcare stakeholders and the general population, a decision will be made on the inclusion of individual interventions, whose effectiveness has been demonstrated in other studies, in three components of the intervention package. The package will consist of three components, one of which will target drug dispensers and two of which will target the general population. After these six months, the ethics committees will then be informed of the specific interventions selected for the package. Baseline surveys (of patients, simulated patients, carriers, and the community/HDSS) will be conducted in parallel, starting in the fourth month.

The development of the intervention will follow the six-step Intervention Mapping framework (Fernandez 2019; Bartholomew 2006), of which three steps have been completed: (1) the conceptual framework of the problem to be addressed, (2) the conceptual framework of the solution, and (3) identifying intervention options. Step 4 will be the adaptation of the intervention package to the implementation context (program production). Step 5 will be the implementation of the package, involving community representatives (general population, staff/medicine dispensers, local and regional authorities). Step 6 is the evaluation of its implementation.

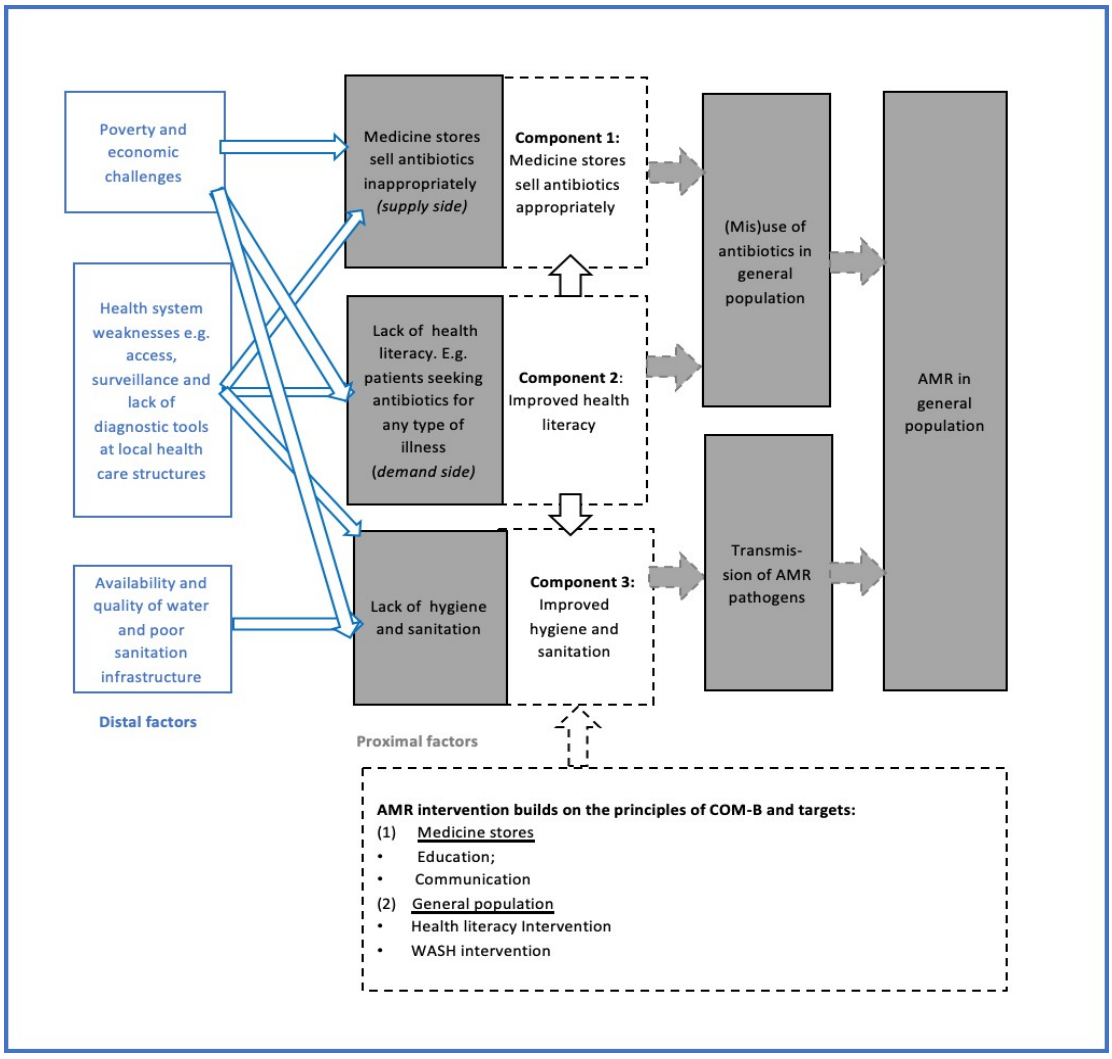


Figure 3. Distal and proximal factors influencing antibiotic use and AMR transmission, with components of the targeted behavioral intervention and examples of proposed activities for all interventions.

The first component of the intervention package **will target medicine dispensers**. Based on recent qualitative work on the motivations of medicine dispensing staff, this intervention will focus on education and structural change. This component may be sensitive as the intervention requires them to rethink a source of income. Examples of what this component could be, depending on the results of phase 1:

A. A series of individual and group sessions (between 5 and 10 depending on logistics) with formally trained community pharmacy staff and informal antibiotic dispensers focusing on education (when antibiotics should and should not be used, in general and Watch antibiotics in particular, and what alternatives exist, for example, the sale of soap or other alternatives instead of antibiotics in cases of mild and/or probable viral infection; antibiotics other than Watch antibiotics for the syndromic treatment of outpatients);

B. Individual and group sessions focused on communication skills with clients (how to refuse or modify a request for antibiotics when it is inappropriate);
C. Development, training, and introduction of a clinical algorithm;
D. Development of a peer feedback system on drug dispensing;
E. Development of a system requiring approval from healthcare professionals before dispensing specific antibiotics.

Table 1. Examples of behavioral aspects of pharmacy staff to reduce the sale of antibiotics (on duty)

COM-B components	What needs to happen for the target behavior to occur?	Is there a need for change? (hypotheses to be validated in phase 1)
Physical ability	Have the necessary skills to negotiate with customers	Change needed to give providers the skills to negotiate with clients
Psychological capacity	Knowing when to sell/prescribe antibiotics and when not to.	Change needed because dispensers do not know the appropriate use.
Physical ability	Restrict the supply of antibiotics	Change needed at the structural level : antibiotics are available to informal dispensers.
Social opportunity	See other drug store employees, including older people, who also sell appropriately.	This change is necessary because most dispensers currently sell inappropriately.
Thoughtful motivation	Believing that the sale excessive sale of antibiotics is harmful.	Change necessary because knowledge on the subject is limited
	Convince that the appropriate sale of antibiotics is a valuable skill	Change is needed because suppliers do not necessarily recognize the value of these skills.
Automatic motivation	Having established routines and habits for selling antibiotics	Change is needed to establish routine and habit formation

The second component of the intervention package **will target the entire population** and aims **to strengthen community health literacy** by improving knowledge about health, healthcare utilization, and communication with healthcare providers. Health literacy is a key concept in preventing antibiotic misuse, involving "the motivation, knowledge, and skills to access, understand, evaluate, and apply health information to make judgments and decisions about lifestyle, disease prevention, and healthcare use in daily life" (Sørensen 2012). The intervention will improve the population's knowledge about antibiotics and motivate and empower them to make choices appropriate to their health needs

. The activities used for these components are inspired by ideas around hygiene and disgust (Curtis 2011, 2018), activities from the World Bank's Handwashing Handbook (Curtis 2005), and successful WASH interventions such as SuperAmma (Biran 2014).

Table 2. Examples of behavioral aspects of the health culture of the general population, through the improvement of health-related knowledge, patient-provider communication, and medication-related knowledge.

COM-B components	What needs to happen for the target behavior to occur?	Is there a need for change? (hypotheses to be validated in phase 1)
Physical ability	Have the skills to discuss symptoms and appropriate medications with healthcare providers.	Change needed to build trust and discussion skills
Psychological capacity	Knowing the appropriate use of antibiotics	Change needed because the general public does not have sufficient knowledge of appropriate use.
Physical capability	Have a restricted to to antibiotics in the community Improve access to qualified personnel at drug outlets	Change is needed because antibiotics are available to the general public in pharmacies without a prescription. Access to healthcare is unequal, so change is needed
Social opportunity	Seeing other members of the community make similar decisions regarding the appropriate use of medicines.	A change is necessary because inappropriate use is widespread
Thoughtful motivation	Believing that excessive use of antibiotics is harmful.	Change necessary because knowledge on the subject is limited
Automatic motivation	Establishing routines and habits for accessing care.	Changes are needed to improve access to healthcare

The third component of the intervention package **will target the entire population**, focusing on improving the use of available **water and hygiene and sanitation practices to** prevent infectious diseases and the (perceived) need for antibiotics (Table 3).

Table 3. Examples of behavioral aspects affecting sanitation and hygiene practices in communities.

COM-B components	What needs to happen for the target behavior to occur?	Is there a need for change? (hypotheses to be validated in phase 1)
Physical ability	Ability to wash hands	No change needed; this is a simple skill that can be learned.

Psychological capacity Psychological	Knowing the impact of sanitation and hygiene practices of sanitation and hygiene practices	Change needed to raise awareness about the role of sanitation and hygiene in health
Physical possibility	Access to soap Access to water, and clean water	Soap is available but funding needs to be assessed. A structural change is needed for clean water; the availability of all water must be assessed
Social opportunity	Seeing other members of the community make similar decisions in terms of sanitation and hygiene.	Change needed to generalize the use of sanitation and hygiene practices.
Reflective motivation	Believing that, for example, it is important to wash your hands with soap.	Change needed because knowledge on the subject is assumed to be limited
Automatic motivation	Establishing routines and habits for purchasing soap and implementing practices	Change needed to establish appropriate routines.

Components two and three could use (a selection of) the following activities:

A. **Discussion sessions** with village, religious, and school authorities who play an important role in defining and enforcing norms and values. Intervention activities will be explained. If possible, with their consent, village and school authorities will be filmed washing their hands and expressing their support, to be used at future community events.
B. A co-created **Theater for Development (TFD) play** that will feature locally relevant stories, including those drawn from the Photovoice exercises (e.g., drinking water, washing water, soap use, taking antibiotics during menstruation), health pathways, and highlight the effects of antibiotic misuse and the accumulation of AMR through storytelling. The show should be humorous, incorporating disgust, for example, at handling food without washing hands. An abridged version would first be shown to children at school. Children are then offered handwashing activities to do throughout the week, including cards to take home to their families to invite them to the community theater event. Games centered on the idea of disgust can be played with schoolchildren, such as "poo tag." Certificates can be awarded at the end of a week of school activities around handwashing.
C. **Posters** are placed throughout the village to announce the community event: other activities may be suggested by students, teachers, and village authorities, such as a children's march through the village to announce the community event. During the community event, videos of teachers and village authorities can be shown, and the full-length version of the **development play can** be performed. Other activities, if deemed appropriate, can also be included, such as a commitment ceremony. The play is filmed for later broadcast. Questions will be asked of the audience before and

after the play to gauge their knowledge and understanding of AMR. This will be done in groups, with the actors asking questions and the audience raising their hands to take literacy levels into account. Discussions following the play will aim to ask audience members what challenges they face, such as the availability of soap, and what is available to overcome these challenges.

D. **Ad hoc sessions for groups of men and women,** focusing on knowledge, motivation, and skills, to enable more informed and safer choices regarding antibiotic use. Films can be shown on laptops to groups, with discussions facilitated afterwards. Volunteers from these sessions can be recruited for individual behavioral studies; participants receive soap and are asked to use it specifically for handwashing. A week later, they receive a home visit and are asked about their use of the soap, what they like and dislike about it.
E. A **social marketing campaign** to raise awareness of AMR, antibiotics, soap, and handwashing.
F. Community **outreach** on **the streets, e.g.,** photo exhibitions based on photovoice activities in markets, and home visits to discuss hygiene and sanitation, access to soap, especially in kitchens.

4.2.3 Laboratory procedures

Fresh stool samples collected from household members at baseline, months 3, 6, and 12 will be cultured on selective CHROMagar™ plates and species will be identified. If ESBL-producing *E. coli* and/or *Salmonella* isolates are detected, they will be typed and antibiotic susceptibility testing will be performed in accordance with CLSI guidelines for GLASS and ESBL pathogen-antibiotic indicators if the minimum inhibitory concentration (MIC) for ceftriaxone or ceftazidime is greater than 1 mg/L.

If a CHROMagar™ plate from a sample has 2 morphologically different colonies, both strains will be typed; with 3 different colonies, all 3 strains will be typed; and so on, up to a maximum of 5 morphologically different strains per sample.

All microbiology testing will be performed by the Nanoro clinical microbiology laboratory.

ESBL-producing Enterobacteriaceae strains will be sequenced and compared to strains identified in patients with confirmed bacteremia. Bacterial isolates will be cultured under standardized laboratory conditions, and DNA will be extracted and prepared for WGS using Illumina technology available at Cancer Research UK facilities.

WGS data will undergo bioinformatic quality assessment and will be analyzed to confirm the species and sequence type of each isolate. In addition, the genetic content of AMR genes (complete resistome) and the presence of plasmid replicons will be determined.

WGS expertise is currently being developed at the URCN, and as part of this project, additional training, support, and local capacity building in this expertise are planned.

4.2.4 Adverse effects

Potential adverse effects of the intervention will be assessed: a potential increase in antibiotic use (Watch) or a negligible effect on the patient's clinical progress. The clinical effect will be measured by calling patients who participated in the survey 7 days after the interview and comparing the clinical status between the intervention and control groups.

If prescribing errors, for example in the choice or dosage of treatment, are identified in the analysis of patient surveys, a physician from the study team will discuss the error with the prescriber in order to prevent such errors in the future.

4.3 Data analysis

4.3.1 Quantitative data analysis

a) Preparatory study and implementation evaluation

The evaluation of the implementation of the intervention package will be based on a comprehensive description of how and why the intervention was carried out. Predicted relationships, causality, or expected changes, such as which specific educational sessions will lead to behavioral change, will be examined. We will assess the feasibility and transferability of the intervention to other contexts, documenting the cost of the intervention, i.e., the working time of teachers, coordinators, and participants, as well as the financial cost of planning, logistics, and adoption of the intervention, while taking into account its application in different contexts.

b) Patient surveys and simulated patient visits

Based on **patient surveys,** we will estimate the proportion of visits resulting in the dispensing of antibiotics in general and Watch antibiotics in particular in the intervention group and control groups before and 12 months after the start of the intervention. We will adjust for (1) a cluster effect, (2) the number of dispensers per cluster (if more than one), and
(3) the population size per cluster (in case of differences in cluster population size between clusters, we will take into account patient sampling probabilities), using the R package "Survey." Antibiotics will be grouped into three categories: Access, Watch, and Reserve, in accordance with the WHO AWaRe classification (Sharland 2018). We will assess the antibiotic treatment dose for patients, the dosage, duration, mode of administration, and adherence to treatment in order to determine the defined daily doses (DDDs) that each treatment represents. For each treatment, we will assess whether the treatment is underdosed (including low dosage, shortened duration, interruption, poor compliance), based on the WHO 2019 list of essential medicines.

For each of the **simulated patient** visits, we will determine whether the care was generally correct (a few minimum conditions, as predefined by clinical presentation in section 4.2.1, binary outcome) and a care score will be determined from the checklist data by clinical presentation (Appendix 11.7), based on: (1) the presence or absence of questions, examinations, and actions during the visit, (2) the duration of the consultation/visit, (3) the number of drugs and antibiotics prescribed/dispensed, and (4) the use of injectable drugs. A higher score will be given for minimum conditions. This score also takes into account the dispensing of drugs, according to the indication for the clinical presentation. Patient care quality indicators will be compiled for all visits to providers in the intervention clusters and providers in the control clusters: the percentage of visits resulting in correct care, the median score of the five visits per provider (out of 100), the percentage of visits resulting in correct antibiotic treatment (or no treatment), and the percentage of visits with a correct medical history.

Changes in the frequency of antibiotic use, the percentage of visits with correct management, and the median management score before and after the intervention (months 0 and 12) in the intervention clusters will be compared with those in the control clusters over the same period (to avoid seasonal heterogeneity in use). We will determine the risk differences and risk ratios, which will be adjusted for socioeconomic indicators and other potential confounders. The effect assessment will use standard experimental methods and will employ multilevel statistical models (to account for clustering within villages and households), including time*intervention interactions. Sociodemographic data, socioeconomic status, healthcare utilization, and health behaviors of the population are regularly recorded during regular HDSS rounds, which will allow for secondary subgroup analyses of the intervention effect.

c) Carriage and transmission of ESBL-producing Enterobacteriaceae

To estimate AMR transmission within households, densely sampled household samples and multiple isolates per sample will undergo whole-genome sequencing. In addition to species, sequence type, resistome, and plasmid replicons, the number of single nucleotide polymorphisms (SNPs) will be extracted as a measure of genetic difference.

Confirmed cases of hospitalized bacteremia from the study area will be compared phenotypically and genomically to carriers to identify species with similar AMR profiles.

We will adapt the methodology we used previously (Musicha 2020, Worby 2016) and fit Markov models to longitudinal household data derived from repeated stool samples. This will allow us to estimate the rate of person-to-person transmission within households, the rate of loss of detectable carriage among individuals, and the association of these rates with the study intervention and baseline household covariates. We will perform this analysis at both the RAM gene level and, when typing data allow, at higher levels. Individuals will be classified as non-carriers and carriers of pathogens or AMR genes, and it is assumed that exposure to the intervention modifies the probabilities of transition between states. Based on the results of phylogenetic comparison of antimicrobial-resistant bacterial populations identified in human carriers, we will explore different hypotheses related to the relative importance of an environmental source of acquisition, considering different model structures allowing for the presence or absence of environmental acquisition. If sequencing indicates widespread dissemination of one or more well-defined lineages, we will consider using extensions of the Bayesian data augmentation approaches described above that allow for unobserved colonization times, false negatives, diversity within the host, and missing observations (Worby 2016). We will therefore quantify and compare household transmission and persistence of AMR pathogens from ESBL-producing and fluoroquinolone-resistant *E. coli* in the study cohorts with and without intervention. To incorporate the spread of pathogens or AMR genes from households to the community, we will explore metapopulation models that allow for transmission within and between households.

d) Community survey within the HDSS survey

Changes in reported indicators **of AMR transmission risk within households**, including hygiene practices, contact with domestic animals, and sanitation facilities, will be assessed using repeated HDSS surveys of the population (Annex 11.9). We plan to compare measures of central tendency (means, medians, proportions) between observations from intervention and non-intervention clusters.

4.3.2 Qualitative data analysis

Qualitative data will be analyzed using a program such as NVivo, applying grounded theory, which is an inductive technique for interpreting data to construct theories. Open coding identifies key concepts or ideas hidden in the data that are potentially related to the phenomenon of interest. The researcher examines each line of data to identify relevant events, incidents, ideas, actions, perceptions, and interactions, which are then coded as concepts: for example, images such as the good parent or the good pharmacist in relation to antibiotic use. Each concept is linked to specific parts of the text for later validation. Once a set of basic concepts is identified, these concepts are then used to code the rest of the data, while searching for new concepts and refining old ones. The concepts are then grouped into categories. Constructs from the existing literature can be used to name these categories.

The second phase involves axial coding, where categories and subcategories are assembled into causal relationships or hypotheses that can provisionally explain the phenomenon in question. The third phase of grounded theory is selective coding, which involves identifying a central category or central variable and linking that central category to other categories.

The aim is to understand the motivations, concepts, and ideas underlying the sale and prescription of antibiotics, as well as the role of hygiene, sanitation, and antibiotic use in the community. Knowledge of these concepts and their use will be vital in developing the conceptual angle of the intervention, as well as the imagery behind the intervention, for example, how do antibiotic sellers feel that this practice fits with their view of themselves and their profession?

5. Ethical issues

5.1 Review of the ethical component

This study will be submitted for formal review and approval to the Institutional Review Board of the IMT, the ethics committee of UZA (University Hospital of Antwerp), the University of Antwerp, and the National Ethics Committee for Health Research in Burkina Faso. The pilot studies on which this intervention study is based have been submitted to these same ethics committees. Copies with consent forms can be provided:

- "Community-level antibiotic use in Burkina Faso, version 1.0, dd 05/05/2020 (reference of approval ITM IRB IRB/AB/ac/089; Health Research Ethics Committee 2020-8-171).
- *"Salmonella enterica* and Extended-Spectrum Beta Lactamases – Producing *Enterobacterales* asymptomatic faecal carriage in Nanoro and Nazoanga, Burkina Faso" (reference of approval ITM IRB IRB/AB/ac/013; Health Research Ethics Committee 2021-03-052).

No participants will be enrolled and no participant-related activities will be performed until these committees have provided their written approval.

The study will be conducted in accordance with the principles set out in the Declaration of Helsinki, the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, and with the ethics of research in ethnography/anthropology.

5.2 Obtaining informed consent

Community participation

Verbal informed consent will first be sought from community leaders, following the methods established in each HDSS for informing and seeking community consent. Once obtained, individual consent will be sought and documented for a) drug dispensers, b) other focus group participants, c) patients participating in exit surveys, and d) household members invited to provide stool samples.

Participation of prescribers or dispensers in the intervention and its evaluation

Drug dispensers in the study area will be asked for written informed consent in advance, when the person is first approached in the context of the study or intervention (Appendix 11.1.1). EXCEPT if the dispenser is an informal drug seller, for whom identification or tracing (by the authorities) may pose an additional risk of participation, verbal consent will be requested and the researcher will sign a verbal consent statement (Appendix 11.1.2).

A single consent will be requested for participation in qualitative research to inform the development of the intervention package, that their patients will participate in surveys on antibiotic use, and that they will be visited by simulated patients, explaining that this is to assess the quality of care.

Participation of other individuals in the qualitative and exploratory component

Participants who only take part in qualitative interviews (individual interviews or FGDs), such as certain members of the population, patients, health authorities, and providers outside the HDSS area, verbal consent will be requested and the researcher will sign a verbal consent form, taking into account that the majority of providers approached will be engaged in informal activities and that identifying or tracing them would pose an additional risk. Verbal consent is justified, as required and accepted by the national ethics committee in previous studies conducted by CRUN in Nanoro. For example: “Community-level antibiotic use in Burkina Faso, version 1.0, dd 05/05/2020 (reference of approval ITM IRB IRB/AB/ac/089; Health Research Ethics Committee 2020-8-171).

EXCEPT for adolescent participants (between 14 and 18 years of age), written consent will be requested from a parent or legal guardian in addition to the adolescent participant's assent (Appendix 11.1.3). Adult participation will be kept to a minimum and will aim to understand aspects of healthcare research and specific antibiotic use among adolescents.

Participation of patients in exit surveys after a visit to a healthcare provider and household members invited to provide stool samples

Written consent will be requested at the time of the survey or at the first stool collection (Appendix 11.2 and 11.3). The entire procedure will be individual and will only concern participation in

this specific survey. All ages will be included (to avoid significant selection bias in estimating the prevalence of antibiotic use or the rate of transmission of AMR Enterobacteriaceae). For individuals under the age of 18, the parent or guardian will be asked to give written consent, while adolescents aged 14 and over will be asked for verbal assent (and their wish not to participate must be respected; Annex 11.2 and 11.3.2).

Additional questions in regular HDSS rounds

A written consent waiver is required for the use of community survey data, given that various conditions are simultaneously present: (a) the community survey questions are already part of the regular HDSS survey, and HDSS households have previously consented to periodic home visits for these surveys;
(b) the data will be pseudonymized and treated confidentially, so that any risks to privacy and confidentiality are recognized and minimized; (c) the study has potentially significant social value for the communities concerned. Researchers will inform participants that a few more questions than usual will be asked for use in the study, regarding healthcare use by the entire household and hygiene practices in the household; he/she will inform them of the purpose, subject matter, risks, and benefits of the (additional) survey questions, provide an information sheet, and, if they wish to participate, the interviewer will sign a verbal consent form (Appendix 11.4) that participants have verbally consented to these additional questions. Participants who give their verbal consent will receive a copy of the information sheet.

Authorization to take and use images (in the context of photovoice exercises)

In photovoice exercises, photos of people will initially be used for data collection and analytical purposes (by participants and facilitator-researchers). However, these photos are intended for internal and participatory use.

When taking a photo, participants should ask for permission to take and use the photo. A dedicated form (Appendix 11.5) must be shared with the person being photographed and signed by them beforehand.

If Photovoice participants decide to exhibit the photos and accompanying narratives as part of their participatory action research (this is an option but will depend on the participant's own decision), the selection of photos and narratives for the exhibition will be made collectively between the participants and the people whose photos were taken. If permission is refused or impossible to obtain (because the Photovoice project participants have been unable to locate the people photographed), we will blur the face of the person photographed so that they cannot be identified.

The informed consent procedure will describe the (legitimate) purpose of the study, the procedures to be followed, the risks and benefits of participating, etc. If a participant (or parent or guardian) cannot read or write, the signature of a witness to the informed consent discussion will be obtained. Study participants (or parents or guardians) will be informed that participation in the study is entirely voluntary and that a participant may withdraw from the study at any time without any negative consequences.

The consent forms are attached in Appendices 11.1 to 11.4. The assent forms (including verbal assent forms) documented and signed by the data collector or researcher must be kept in a secure location under the responsibility of the local PI. They will be in paper format, will be

read to the patient or be available for the patient to read. The information leaflets for prospective participants (also attached in the appendix) are tailored to each component of the study and will be available in French. A copy will be given to each participant for each component of the study. The informed consent interview will be conducted in French for participants who can read and write, or translated into the local language understood by participants who cannot read or write, in the presence of an impartial witness.

5.3 Insurance

For low-risk studies (insurance POS, classes 1 and 2), the study coordinator, namely the IMT, has taken out insurance (without fault attribution criteria) covering any injury, damage, or loss inflicted on study participants and caused directly or indirectly by their participation in the study. See Appendix 11.10.

5.4 Risks

Intervention development, patient surveys, and community surveys

There are no direct health risks. However, during the survey, interview, or group discussion, questions may be asked about personal experiences, which could bring back bad memories, or informal health care providers may feel stigmatized, or formal health care providers may fear that their opinions will be shared with their superiors/used to evaluate them. In addition, there are risks related to privacy and confidentiality, which are particularly important for informal healthcare providers. Finally, and most importantly, complete confidentiality can never be guaranteed in group discussions, as it also depends on the other participants, not just the researchers.

These risks will be minimized in various ways. First, by pseudonymizing quantitative data and protecting the confidentiality of qualitative data, as described in the section on data management; second, by choosing private locations for surveys and interviews (the questions and setting for these interviews will be prepared in such a way as to make the interviewee feel comfortable and safe, thereby minimizing this risk); thirdly, by explaining to focus group participants that they must commit to protecting each other's confidentiality, and by "separating" the focus group by participant category (e.g., no focus group will be held involving both informal caregivers and official health authorities at the same time); then, by discussing risks and confidentiality at the outset during the informed consent interview. How to deal with patients' bad personal experiences will be part of the investigators' skills and expertise, based on training prior to the start of the study and experience from the pilot study. When participants in focus groups or interviews have to travel, they will be offered transportation reimbursement.

Qualitative interviews may reveal poor medical practices or even legally questionable behavior. Qualitative researchers will be trained to identify major medical errors or poor medical practices. If such errors are identified, a feedback session with a physician involved in the study will be offered to advise the healthcare provider on good medical practices and educate them on correct, evidence-based treatment.

Patient surveys, conducted after a medical visit, could reveal individual medical errors, such as prescribing errors, e.g., contraindicated antibiotics such as the use of tetracyclines in children, or incorrect dosages. The survey teams will consist of a member of the medical staff and will be trained to detect serious and common treatment errors. If such errors are identified, they will be addressed/discussed as soon as possible after the survey with the patient and with the healthcare provider or practitioner, to enable the healthcare provider to learn about good medical practices and correct, evidence-based treatment.

If such errors are identified, they will be addressed/discussed as soon as possible after the survey with the patient and with the healthcare provider, to allow the provider to rectify the treatment. If it is not possible to resolve the error with the healthcare provider concerned, the patient will be referred to the Nanoro CMA. A clinician at the hospital will be informed when a patient is referred by one of the study team physicians and will follow up on these referred patients, while ensuring discretion regarding the healthcare provider from whom the patient was referred. CMA management will be informed of the possibility of such referrals from other healthcare facilities during the study.

Simulated patient visits

In order to evaluate changes in the quality of care, the use of simulated patients (mystery shoppers, actors who present with a well-defined clinical presentation but who are not actually ill and do not identify themselves as part of the study) is important to avoid bias: if providers know that the patient is a researcher, they will adapt their usual care and behavior. We will explain this component of the study with simulated patients and its rationale to participating providers in advance and ask for the provider's consent to participate in this component in order to avoid suspicion and tension. It is important that simulated patients are properly trained and prepared for this task. If potentially dangerous clinical practices are identified, the clinical case will be discussed between the healthcare providers or practitioners concerned and a physician involved in the study, including raising awareness of the correct clinical management. When the data are published, care will be taken to protect the confidentiality of all those involved and to avoid stigmatization. Therefore, no identifiers of the providers or individuals investigated will be revealed in study reports or subsequent publications.

Carriage and transmission of ESBL-producing Enterobacteriaceae in households

As in the pilot study in Burkina Faso, the collection of biological samples is limited to stool samples (from both adults and children). This poses no risk, nor is there any risk of incidental discovery, as fresh stool samples will be placed on selective plates for the culture of specific bacteria only, with the rest of the stool being discarded, as would have happened if it had not been collected and temporarily stored in a study container. For minors, the consent of a legal guardian will also be sought and documented.

The inclusion of minors, including stool collection, is crucial because a significant proportion of healthcare visits and antibiotic use are related to febrile illnesses in young children.

As in other studies, each participant in each household will receive systematic deworming after stool collection at 0, 6, and 12 months of the intervention (NB: There will be no deworming at 3 months of the intervention).

5.5 Obtaining personal data

After obtaining informed consent (see above), data will be collected on age, sex, and antibiotic use, in accordance with the data management plan.

HDSS data will be available on household demographics, healthcare-seeking behavior, and hygiene indicators. These data will be linked to study data by a unique identifier. All data will be pseudonymized and anonymized to the extent possible before being made available for analysis, in accordance with approved research procedures for all HDSS studies. Data will only be

transferred unless it is in accordance with the informed consent and laws of the country where the data is collected.

The Data Protection Officer (DPO) has been involved in reviewing and evaluating this research proposal. He will also be involved in assessing the impact on data protection. This is noted because data will be collected on the behavior of individuals in public places, different data sets will be linked, and vulnerable populations, including children, will be involved. Contact details for the IMT DPO: Jef Verellen, tel. +3232470743, email:informatieveiligheid@itg.be .

The data will be collected in full compliance with the laws of the country where it is collected. The IMT has a policy on the return of results (attached) which also covers incidental findings (although it is very unlikely that this will apply to this study).

6. Monitoring and quality control

During the collection of qualitative data for the development of the intervention, ongoing evaluation of the qualitative process will complement the comparative analysis of intermittent quantitative indicators in order to identify areas of focus that could not be anticipated at the study design and protocol development stage. This is an ongoing research process focused on detecting emerging issues and providing an immediate response in close interaction with stakeholders (i.e., healthcare providers, patients, health authorities).

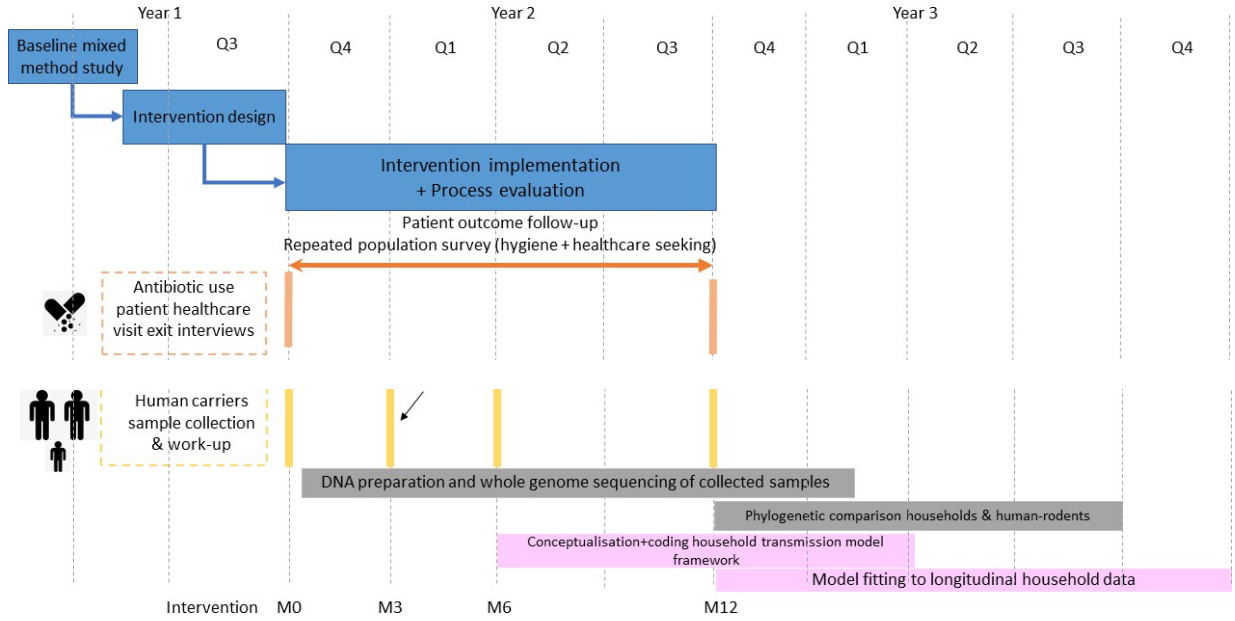
Community and household surveys are integrated into the routine HDSS cycles in Kimpese and Nanoro and will follow the procedures of these respective studies. Prior to data analysis, data completeness and accuracy will be verified (number of non-respondents, missing data, comparison of demographic data of the surveyed population with that of the source population, comparison of results from different survey teams). If the quality of the data for certain variables or observations cannot be guaranteed, the PIs, with the support of a statistician, may jointly decide to exclude certain observations and/or variables, justifying each exclusion (to be kept in the investigator's file and described and justified in the study report).

During patient surveys, the PI will be present on site and will produce a weekly descriptive report to assess data quality and inclusion progress. A potential error report will be generated (using an R script) to identify inconsistencies (including data entry errors, ranges, inconsistency checks related to antibiotics) in the data recorded that day. The report should allow for rectification the following day of the study when this is still possible. At the same time, a summary report will be generated on the progress of the interviews conducted, as well as the follow-up phone call.

For stool collection, electronic questionnaires will be completed during the collection visit, which allows the participant's HDSS code to be associated with a barcode on the container label. Thus, from receipt at the laboratory to entry of the result, the barcode can be scanned and later associated with the demographic data and the collection questionnaire.

7. Schedule

Please note that the intervention will be implemented gradually, so that post-antibiotic use interviews, rodent capture, and stool sample collection from human carriers will be spread over 3 months.



	Year 1				Year 2				Year 3			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
WP 1: Developing and implementing the behavioural intervention bundle												
Community engagement												
Study protocol development, ethical submission, approval												
Study tools development (SOPs, questionnaires, database, infrastructure) & training												
Mixed method study to inform the conceptual model for intervention design & implementation												
Baseline mixed method study data analysis & dissemination												
Intervention design												
Intervention programme production												
Stakeholder consultation and development of a medicine vendor accreditation system												
Intervention training of trainers and kick-off												
Intervention for medicine vendors roll-out												
Intervention for the general population roll-out												
Process evaluation (qual+quant) & dissemination												
WP 2: Evaluation of the intervention on Watch antibiotic use												
Study protocol development, ethical submission, approval												
Study tools development (SOPs, questionnaires, database, infrastructure) & training												
Cluster definition, randomization												
Antibiotic use patient healthcare visit exit survey												
Patient healthcare visit clinical outcome follow-up												
Simulated patient healthcare visits (incl. preparation and training)												
Repeated population survey (within regular HDSS rounds)												
Statistical analysis plan, data analysis & dissemination												
WP 3: Developing and implementing environmental AMR surveillance in rodents (Kimpese site only)												
Study protocol development, ethical submission, approval												
Community involvement												
Rodent collection & sample work-up (with visiting small mammal researchers UNIKIS)												
Statistical analysis plan for spatial and ecological comparison human population and rodents, data analysis & dissemination												
WP 4: AMR laboratory analysis												
Procurement and shipment for essential equipment and consumables												
Microbiology capacity extension and training												
Human population bacterial carriage collection, culture, identification and AST Kimpese site (linked to WP3, WP5, WP6)												
Human population bacterial carriage collection, culture, identification and AST Nanoro site (linked to WP3, WP5, WP6)												
Rodent bacterial carriage culture, identification and AST (linked to WP3 & WP5)												
Shipment of isolates for sequencing												
WP 5: Whole genome sequencing of E. coli and Salmonella isolates												
Isolate workup and DNA preparation												
Whole genome sequencing												
Bioinformatic analysis phylogenetic comparison of AMR bacterial populations/ genetic clones human population and rodents & dissemination (linked to WP3)												
WP 6: Modelling the community transmission-dynamics of multi-drug resistant gram-negative organisms												
Conceptualisation and coding of within-household and between-household transmission model framework												
Fitting model to longitudinal household data to estimate change in within-household transmission following the intervention and risk factors associated with transmission												
Generate simulation results for within- and between-household transmission model & dissemination												
WP 7: Coordination												
Establishment of the Executive Board												
Sample size simulation study (WP2, WP3, WP4, WP5, by WP6)												
Efficient managerial structures, roles and work-flows (monthly meetings)												
Procurement and shipment for essential equipment and consumables												

8. Data management and archiving

8.1 Data management

A comprehensive data management plan (DMP) will be developed for the project and approved by all partners, detailing all important aspects related to data management, protection, and open access. European researchers adhere to the European Code of Conduct for Research Integrity. These policies ensure data integrity, traceability, and confidentiality.

8.1.1. Data description and metadata

Quantitative data: sociodemographic data and socioeconomic status per household, frequency of healthcare use and health practices of each member of the population, individual survey data (antibiotic use, clinics), linear list of stool culture results, intervention implementation data.

Qualitative data: transcripts of group discussions as part of the Photovoice study
; transcripts of group discussions with lay people and medicine dispensers (including pharmacists); and transcripts of repeated interviews during the evaluation of the intervention package process.

Sequencing data from ESBL and Salmonella isolates grown on selective ESBL agar from human stool samples.

8.1.2. Security and confidentiality

Project data will be shared among consortium members on a need-to-know basis. As personal data is collected and processed, the project will comply with the EU General Data Protection Regulation (GDPR 2016/679), implementing in particular:

Appropriate transparency towards participants regarding data collection and processing and their rights, including appropriate informed consent procedures for the primary and secondary use of data and biospecimens. Community-level information and consent will be organized and documented according to existing HDSS protocols, in accordance with the requirements of the ethics committee.

Anonymization or at least pseudonymization will be performed as soon as possible. No data that could identify participants will be disclosed by the intervention sites/study partners, nor in the study databases, analyses, and reports. User roles and access controls for sensitive study data will be implemented. Access to confidential data will be granted on a need-to-know basis. Data will be stored on secure, centrally protected servers or clouds, with secure (encrypted) transfers of confidential study data as necessary.

Contractual confidentiality agreements will be put in place for all relevant study personnel. The duties and responsibilities for data processing between all partners will be clearly defined and documented, for example by the steering committee and by entering into a data processing agreement. The processing of HDSS data will be clearly defined in terms of purpose limitation, data minimization, and data proportionality.

Approvals from data protection authorities, ethics committees, and the performance of a data protection impact assessment will be sought where necessary.

8.2 Archiving

8.2.1. Data

The Principal Investigator is responsible for ensuring that the Investigator's file and any other study-related documentation present at the site are stored in a secure and appropriate location, and for ensuring that only competent personnel authorized to work on the study have access to the files.

After completion of the study, all study documentation must be retained in accordance with local legislation and must be kept for a period of at least 5 years following completion of the study. The IMT must be notified prior to the destruction of the files.

The Investigator's file must remain permanently available for audits and/or internal inspections by regulatory authorities, even after completion of the project.

8.2.2. Biospecimens/strains

When biospecimens need to be shipped from one partner to another, a material transfer agreement (MTA) will be established. If additional analyses other than those specified in the final approved study protocol need to be performed, an amendment to the protocol will be submitted for ethical approval. Specimens will be stored in local biobanks. The principles of the Taipei Declaration will be followed.

8.3 Open access to research data

The study protocol will be published in open access and registered on www.clinicialtrials.gov before the the start of the study.

Publications resulting from the study will, in principle, be published in full open access.

Access to project data (such as pathogen sequencing/resistome data, outcomes such as antibiotic use and quality of care) will be in accordance with FAIR principles. A distinction will be made between confidential/sensitive data (e.g., for privacy or stigma) and non-confidential data. Non-confidential data will be fully accessible (such as fully anonymized and aggregated data, pathogen sequencing data, intervention materials, recommendations, etc.). Confidential data (such as pseudonymized participant data, i.e., individual data without identifiers) may be made accessible through controlled access procedures (e.g., approval by local data access committees and/or the IMT data access committee). A data sharing agreement will always be put in place before confidential data is transferred.

When data is made (openly) accessible, this will be done as much as possible in open, unlicensed, and interoperable formats. We will also make available the metadata necessary for reinterpretation, reanalysis, or further use of the research results. We will strive to use open licenses such as CC-BY or CC-BY-NC as much as possible.

Participation information sheets will include the necessary information on the (future) scientific objectives and retention periods for their data. Pathogen isolates that no longer contain human biological material and are not linked to personal data may be stored for longer periods and distributed to other research institutions in accordance with the 2014 Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization.

9. Dissemination of results

Results will be disseminated to the HDSS study communities and relevant health actors on an ongoing basis, from the co-creation of interventions to implementation and evaluation. District health structures and authorities are and will be involved from the outset to avoid misunderstandings and interference between usual responsibilities. Both HDSS sites are well established in the communities and well connected to formal health structures.

National and local health authorities are and will be informed from the outset and invited to give their views on how the results could strengthen national efforts to promote the rational use of antibiotics. In collaboration with local and national health authorities, dissemination to formal and informal health actors and the general public will be agreed upon, for example through social media messages, leaflets, training, etc.

Scientific dissemination will be achieved through the submission of abstracts and presentations at national and international scientific conferences, as well as through the publication of peer-reviewed, open-access articles. The analysis code and transmission model will be freely available on a public repository (GitHub) under a standard open-access license.

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11. Appendices

11.1 Informed consent form for qualitative interviews, focus group discussions, and community consultations in the development of the intervention package and participation in the intervention (for drug dispensers)

11.1.1 Adult medication dispensers (excluding informal vendors)

INFORMATION FORM FOR FORMAL MEDICATION DISPENSERS

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit, the University of Antwerp, the Pasteur Institute, and the Institute of Tropical Medicine (ITM, Antwerp). The study and the intervention it will evaluate are described in this information sheet. If you have any questions about the study or the intervention, please do not hesitate to ask. In addition, you are of course free to discontinue your participation in the study or intervention at any time.

Purpose and description of the study

Increasing antibiotic resistance is rendering drugs currently used to treat bacterial infections ineffective. Before developing and introducing interventions that would enable better use of antibiotics in the community and prevent infections with resistant bacteria, we should first understand where, when, how, and why antibiotics are used and what conditions and hygiene and sanitation practices facilitate the spread of pathogens between people. That is why this study is being proposed.

Based on consultation with the actors involved, the goal is to develop a package of interventions (one for medicine dispensers and one for the general population) that addresses the risk factors for antibiotic resistance, with a view to improving the quality of care and responding to the perceived needs of health actors or the population.

The interventions and surveys will be implemented in 11 communities, and surveys will also be conducted in 11 other control communities—but without interventions. These surveys are:

- **A patient survey** will be conducted at the end of a visit to a medicine dispenser before and one year after the intervention to measure any change in antibiotic use.
- **Simulated patient visits** will take place before and one year after the intervention to assess any change in the quality of care: actors will present themselves as patients with five different clinical presentations, and care will be assessed using a checklist.

You will be asked to participate in consultations during the development of interventions, and - if you are a medication dispenser in the study area, you will be asked to agree to your patients participating in surveys on antibiotic use, and to receive visits from actors so that the quality of care can be assessed.

Time required for participation

You will be asked to set aside approximately one hour for an initial interview. A second one-hour session will be scheduled with some participants from the first session to provide feedback on the proposed interventions.

The intervention will take place over a period of one year and will be offered in the form of training sessions, feedback sessions, and clinical discussions between peers (i.e., between healthcare professionals) according to the needs identified.

Intervention evaluation surveys will not require dedicated time from healthcare providers.
health professionals.

Voluntary participation

Your participation in this study is entirely voluntary, and this choice is not documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand or to request explanations until you are satisfied. You are free to withdraw or stop participating at any time.

If you wish to participate, indicate your agreement to participate in the study by signing the consent form at the end of this document.

Confidentiality

All information collected about you during the study will remain strictly confidential. Your name will not be recorded, and all information you provide will remain confidential. Only two researchers from the research team will have access to the data and information collected. It is possible that an excerpt from the interview may be used in the dissemination of our results, but we will ensure that any information that could identify you is removed from the citation.

Your identity or contact details will not be shared with the authorities or health authorities under any circumstances. We guarantee that all information will be treated as strictly anonymous, and your name will be replaced by a code in all official study documents.

In the case of group discussions, we ask that you respect the other participants (their anonymity) and the confidential nature of the conversations that will take place. However, if you are uncomfortable participating in a group conversation/discussion, we can answer your questions to reassure you. Nevertheless, if you wish, you can cancel your participation.

Once your participation has been confirmed, we would like to record our conversation for research purposes only. You are free to refuse, but it will help our analysis and our work. All audio recordings will be destroyed after the study.

Benefits

Your agreement to participate in this study does not offer any direct personal benefits. However, the consultation gives you the opportunity to suggest interventions that may contribute to better public health in the community. Medication providers will be able to participate in educational or scientific support activities, such as training and treatment tools, in order to optimize the use of antibiotics and thus improve patient care. Those in the intervention communities will receive these for one year, while others will receive them after the one-year evaluation of the intervention package. There is no financial compensation

for participating in this study. If you have to travel, your transportation costs will be reimbursed (a lump sum).

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone: +226 70285553; Email: valiadaniel@yahoo.com

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CONSENT FORM FOR FORMAL MEDICATION DISPENSERS

Respondent's name (first name + last name): _____

Signature: _____

If the respondent cannot read or write, a witness who is independent of the research team, such as a member of the same household or a neighbor, must be present during the informed consent interview. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will provide a thumbprint in lieu of a signature.

WITNESS

Witness name (first name + last name): _____

Signature: _____

INTERVIEWER

- I confirm that the information sheet has been read and explained to the respondent in a language that the respondent understands well.
- I have ensured that the respondent understands that he/she is free to choose whether to participate in the study, that he/she does not have to answer any question he/she prefers not to answer, and that he/she may terminate the interview at any time.
- The respondent had the opportunity to ask questions about the study and its objectives. If the respondent had any questions, I or a colleague from the research team answered them correctly and clearly.
- The participant was told that their name would not be recorded except on the present form, which would be kept secure, used only if the participant chose to withdraw from the study, and destroyed one year after the end of the study. The information provided will be pseudonymized, meaning that direct identifiers such as names will be replaced by a code in all official study documents.
- The participant is 18 years of age or older.
- The respondent agreed (with signature or fingerprint) to participate in the study.

Researcher's name _____

Date (dd/mm/yy)__ /__ /_Researcher's signature _____

Participant number:

11.1.2 Adult informal vendor or adult participating only in the exploratory/qualitative study

INFORMATION FORM FOR INFORMAL VENDORS

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit, the University of Antwerp, the Pasteur Institute, and the Institute of Tropical Medicine (ITM, Antwerp). The study and the intervention it will evaluate are described in this information sheet. If you have any questions about the study or the intervention, please do not hesitate to ask. In addition, you are of course free to discontinue your participation in the study or intervention at any time.

Purpose and description of the study

Increasing antibiotic resistance is rendering drugs currently used to treat bacterial infections ineffective. Before developing and introducing interventions that would enable better use of antibiotics in the community and prevent infections with resistant bacteria, we should first understand where, when, how, and why antibiotics are used and what conditions and hygiene and sanitation practices facilitate the spread of pathogens between people. That is why this study is being proposed.

Based on consultation with the actors involved, the goal is to develop a package of interventions (one for medicine dispensers and one for the general population) that addresses the risk factors for antibiotic resistance, with a view to improving the quality of care and responding to the perceived needs of health actors or the population.

The interventions and surveys will be implemented in 11 communities, and surveys will also be conducted in 11 other control communities—but without interventions. These surveys are:

- **A patient survey** will be conducted at the end of a visit to a medicine dispenser before and one year after the intervention to measure any change in antibiotic use.
- **Simulated patient visits** will take place before and one year after the intervention to assess any change in the quality of care: actors will present themselves as patients with five different clinical presentations, and care will be assessed using a checklist.

You will be asked to participate in consultations during the development of interventions, and—if you are a medication dispenser in the study area—to give your consent for your patients to participate in surveys on antibiotic use, and to receive visits from actors so that the quality of care can be assessed.

Time required for participation

You will be asked to set aside approximately one hour for an initial interview. A second one-hour session will be scheduled with some participants from the first session to provide feedback on the proposed interventions.

Voluntary participation

Your participation in this study is entirely voluntary and this choice is not documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand or to request explanations until you are satisfied. You are free to withdraw or stop participating at any time.

If you wish to participate, indicate your agreement to participate in the study verbally, with a signature for this verbal consent by the researcher/investigator.

Confidentiality

All information collected about you during the study will remain strictly confidential. Your name will not be recorded and all information you provide will remain confidential. Only two researchers from the research team will have access to the data and information collected. It is possible that an excerpt from the interview may be used in the dissemination of our results, but we will ensure that any information identifying you is removed from the quote.

Your identity or contact details will not be shared with the authorities or health authorities under any circumstances. We guarantee that all information will be treated as strictly anonymous, and your name will be replaced by a code in all official study documents.

In the case of group discussions, we ask that you respect the other participants (their anonymity) and the confidential nature of the conversations that will take place. However, if you are uncomfortable participating in a group conversation/discussion, we can answer your questions to reassure you. Nevertheless, if you wish, you can cancel your participation.

Once your participation has been confirmed, we would like to record our conversation for research purposes only. You are free to refuse, but it will help our analysis and our work. All audio recordings will be destroyed after the study.

Benefits

Your agreement to participate in this study does not offer any direct personal benefits. However, the consultation gives you the opportunity to suggest interventions that may contribute to better public health in the community. Healthcare providers will be able to participate in educational or scientific support activities, such as training and treatment tools, in order to optimize the use of antibiotics and thus improve patient care. Those in the intervention communities will receive these for one year, while others will receive them after the one-year evaluation period for the intervention package. There is no financial compensation for participating in this study. If you had to travel, your transportation costs will be reimbursed (a lump sum).

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone: +226 70285553; Email: valiadaniel@yahoo.com

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VERBAL CONSENT FORM FOR INFORMAL SELLERS (TO BE COMPLETED BY THE RESEARCHER FOR EACH PARTICIPANT)

- I confirm that the information sheet has been read and explained to the respondent in a language that the respondent understands well.
- I have ensured that the respondent understands that he/she is free to choose whether to participate in the study, that he/she does not have to answer any question he/she prefers not to answer, and that he/she may terminate the interview at any time.
- The respondent had the opportunity to ask questions about the study and its objectives. If the respondent had any questions, I or a colleague from the research team answered them correctly and clearly.
- The participant was told that their name would not be recorded except on the present form, which would be kept secure, used only if the participant chose to withdraw from the study, and destroyed one year after the end of the study. The information provided will be pseudonymized, meaning that direct identifiers such as names will be replaced by a code in all official study documents.
- The participant is 18 years of age or older.
- The respondent has consented to participate in the study.

Name of the researcher _____

Date (dd/mm/yy)__ /__ /_Researcher's signature _____

Participant number:

11.1.3 Adolescents

INFORMATION FORM FOR ADOLESCENT PARTICIPANTS IN THE STUDY

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit, the University of Antwerp, the Pasteur Institute, and the Institute of Tropical Medicine (ITM, Antwerp). The study is described in this information sheet. If you have any questions about the study or the intervention, now or later, please do not hesitate to ask. In addition, you are of course free to discontinue your participation in the study or intervention at any time.

Purpose and description of the study

The purpose of this study is to understand the use of certain drugs to treat certain diseases in your community, particularly antibiotics. Increasingly, drugs (antibiotics) currently used to treat diseases are no longer effective. To try to solve this problem, we will develop and introduce a set of activities that will enable better use of antibiotics in your community while preventing certain infectious diseases. Therefore, we need to understand where, when, how, and why antibiotics are used and what facilitates the transmission of diseases from one person to another. That is why we are conducting interviews, discussions, and surveys with people who provide or receive care. The results of this study will help evaluate an information and training campaign for healthcare workers, which aims to improve the quality of care in the community and ensure that medications (antibiotics) that truly meet healthcare needs are now used properly to combat certain diseases that you encounter.

We will not collect any personal data that could identify you, such as your name or date of birth. Your name will only appear on this form and not in the study data.

We have contacted your family because we want to include young people, their thoughts, and their ideas in our research. We are asking young people aged 14 to 17 to participate in our research. We will also interview other people, such as healthcare professionals and community members, about antibiotics and maintaining health in the community. Once the intervention activities have been developed, we will implement them in 11 communities and see if there are any changes afterwards. We will look at antibiotic use and changes in hygiene practices. We will examine these before the intervention and one year after.

If you agree to participate in this study and at least one of your parents gives their permission, you will be asked to think about and talk about antibiotic use in your communities and families, as well as hygiene at home, at school, and in the community.

Time required for participation

You will be asked to set aside approximately one hour for the

interview/discussion. Voluntary participation

Your participation in this study is entirely voluntary, meaning that you have the right to refuse to participate, now or later (at the time of the home visits), without any consequences. The choice not to participate will not be documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand until you are satisfied. You are free to withdraw or stop participating at any time. You are also free to choose which questions you want to answer.

If you wish to participate, we will ask for your consent (the adolescent's) and for your parent/guardian to sign or affix their fingerprint as acceptance of participation in the study, and you will keep a copy of this "consent" document, signed by me and the parent/guardian.

Confidentiality

All information collected during the study will remain strictly confidential. Your name and your child's name will not be recorded, and all information you provide will remain confidential. Only the research team will have access to the data and information collected. The parent's contact information (phone number) will be kept until the follow-up call and will not be kept thereafter. We guarantee that all information will be treated as strictly confidential, and your name will be replaced by a code in all study documents.

Benefits

Although you will not receive any direct benefits from your participation, others may benefit from the knowledge gained through this study. There is no compensation for participating in this study. If you had to travel, transportation costs will be reimbursed (a lump sum).

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone: +226 70285553; Email: valiadaniel@yahoo.com

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CONSENT FORM FOR ADOLESCENT PARTICIPANTS IN THE STUDY

PARENT OR GUARDIAN of the adolescent participant

Parent/guardian name (first name + last name): _____

Date (dd/mm/yy): __/ __/ __Signature: _____

If the respondent cannot read or write, a witness who is independent of the research team, such as a member of the same household or a neighbor, must be present during the interview for informed consent. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will provide a thumbprint in lieu of a signature.

WITNESS

Witness name (first name + last name): _____

Date (dd/mm/yy): __/ __/ __Signature: _____

VERBAL CONSENT BY THE PARTICIPANT (to be completed by the researcher for each adolescent participant)

- I confirm that the information sheet has been read and explained to the adolescent patient and his/her parent/guardian named above and concerned in a language they understand well.
- I have ensured that the patient and his/her parent/guardian understand that they are free to choose whether to participate in the study, that he/she does not have to answer any questions he/she does not wish to answer, and that he/she may terminate the interview at any time.
- The adolescent patient and his/her parent/guardian have had the opportunity to ask questions about the study and its objectives. If there were any questions, I or a colleague from the research team answered them correctly and clearly.
- The adolescent patient and his/her parent/guardian were told that his/her name would not be recorded except on the present form, which would be kept secure, used only if the respondent wished to withdraw from the study, and destroyed one year after the end of the study. The information provided would remain pseudo-anonymous, meaning that direct identifiers such as names would be replaced by a code in all official study documents.
- The participant's age is between 14 and 17 years old.

Researcher's name _____

Date (dd/mm/yy)__ /__ /_Researcher's signature _____

Participant number:

11.2 Informed consent form for the survey on asymptomatic carriage and transmission of MR Enterobacteriaceae

INFORMATION FORM FOR PARTICIPATION IN THE SURVEY ON AND TRANSMISSION OF RESISTANT ENTEROBACTERIACEAE

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit (URCN), the Institute of Tropical Medicine in Antwerp, Belgium, the University of Cambridge, and the University of Oxford in the United Kingdom, by responding on behalf of yourself, your child, or the child for whom you are the legal guardian. At the end of the questionnaire, we will also ask you for a stool sample for laboratory analysis. The study is described in this information sheet. If you and/or your child have any questions, now or later, please do not hesitate to ask, including about the advantages and disadvantages of the study.

Purpose and description of the study

Increased antibiotic resistance is rendering the drugs currently used to treat these infections ineffective. This means that when you or a member of your family is ill with a disease caused by resistant bacteria, the antibiotics available on the market that were once effective will no longer be able to cure you. Your treatment may therefore require hospitalization and the use of rare and very expensive antibiotics. The stools of healthy people contain a number of bacteria called enterobacteria. These bacteria can be passed from one member of the community or household to another, all of whom are healthy, via the hands, food, water, or shared toilets or latrines, even without them realizing it or becoming ill. When the health of a child or adult deteriorates, these bacteria can become opportunistic and enter the bloodstream, which can lead to sepsis, a very serious illness that can be fatal. If these bacteria in the stool are resistant to antibiotics, infections in people who become ill from one of these bacteria can be difficult to treat with antibiotics.

The goal of our study is to understand the extent of these resistant bacteria in your community, how often these bacteria are passed from one household member to another, and what factors are associated with transmission. At the same time, we are implementing an awareness-raising intervention for the community and health workers, which will aim to reduce the spread of resistant bacteria and promote the use of better antibiotic treatments in cases of illness caused by such bacteria. We will assess the effect of this intervention on bacteria in stool samples.

We will ask each member of this household to collect a stool sample for testing for the bacteria we mentioned earlier, in a small container that we will collect tomorrow. At the same time, we will ask each of you a few questions about the possession and use of antibiotics at home, including the type of antibiotics and their use over the past month.

Please note that the presence of these bacteria does not mean that you or your child is sick. The aim is to isolate one or more bacteria from the sample and investigate their characteristics, such as their resistance and their relationship to other isolated bacteria. These bacterial isolates will no longer contain human bodily material and will not have any personal data on the label. The work of isolating and characterizing the bacteria will be done at Nanoro. It is possible

that some of the bacteria that are isolated may be stored, used in future studies, or shipped from one study partner to another. If you do not agree to the bacteria being stored, used in other studies, or sent, and will only be used to determine carriage and transmission, please indicate this (and let the investigator record it on the questionnaire).

Time required for study participation

Answering the questions should take a maximum of 5 minutes per household member. For the stool sample, the investigator will provide one collection jar per participating household member. We will return the day after consent is given to collect the stool samples.

Voluntary participation

Participation in this study by each household member is entirely voluntary,
meaning that you have the right to refuse to participate without any consequences.

Please feel free to ask if there is anything you do not understand or to ask for explanations until you are satisfied.

If you wish to participate, we will ask each household member and, for children, a parent or legal guardian, to confirm in writing that you agree to participate in the study, and you will keep a copy of this "consent" document, signed by both of us. For children over the age of 14, we will ask if they agree to participate after receiving approval from their parent or legal guardian.

Confidentiality

All information collected during the study will remain strictly confidential. Your names and your children's names will not be recorded, and a code will be used in all study documents.

Risks and benefits

There are no risks to your health or that of your child in participating in this study. At the same time, there is no direct individual benefit to participating in this study, and no financial compensation. However, at the community level, the intervention aims to reduce antibiotic resistance and the spread of disease. In addition, systematic deworming will be offered to each member of the household every six months.

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone:
+226 70285553; Email: valiadaniel@yahoo.com

CONSENT FORM FOR PARTICIPATION IN THE SURVEY ON CARRIER STATUS AND TRANSMISSION OF RESISTANT ENTEROBACTERIACEAE

The consent form will be completed by the participating household member

PARTICIPANT (if adult) or PARENT/GUARDIAN (if participant is <18 years old)

Respondent's name (first name + last name): _____

Date (dd/mm/yy): __/ __/ __Signature: _____

If the respondent cannot read or write, a witness who is independent of the research team, such as a member of the same household or a neighbor, must be present during the interview for informed consent. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will provide a thumbprint in lieu of a signature.

WITNESS

Witness name (first name + last name): _____

Date (dd/mm/yy): __/ __/ __Signature: _____

INVESTIGATOR

- I confirm that the information sheet has been read and explained to the respondent named above and (if the patient concerned is an adolescent) to the patient concerned in a language they understand well.
- I have ensured that the respondent and (if the patient concerned is an adolescent) the child have understood that they are free to choose whether or not to participate in the study, that the respondent does not have to answer any question they do not wish to answer, and that they may terminate the interview at any time.
- The respondent had the opportunity to ask questions about the study and its objectives. If the respondent had any questions, I or a colleague from the research team answered them correctly and clearly.
- The respondent was told that their name is not recorded except on this form, which will be kept secure, used only if the respondent chooses to withdraw from the study, and destroyed one year after the study ends. The information provided would remain pseudo-anonymous, meaning that direct identifiers such as names would be replaced by a code in all official study documents.

Name of the investigator: _____

Date (dd/mm/yy):__ /__ /__ Signature: _____

11.3 Informed consent form for the patient survey on antibiotic use

11.3.1 Adult

INFORMATION FORM FOR PARTICIPATION IN THE ANTIBIOTIC USE SURVEY

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit and the Institute of Tropical Medicine (ITM, Antwerp) by answering a few questions, mainly about the treatments used in your community. The study is described in this information sheet. If you have any questions, now or later, please do not hesitate to ask them,

including about the advantages and disadvantages of the study. In addition, you are of course free to discontinue your participation in the study at any time.

Purpose and description of the study

The purpose of this survey is to understand the use of certain medications to treat certain diseases in your community, particularly antibiotics. The results will help improve an awareness campaign for the community and healthcare workers, which will aim to reduce the spread of disease and improve the quality of care provided to the community.

We will ask you a few questions about the medications that have been prescribed, given, or purchased by you, such as the dosage and how often you take these medications. We will also ask you a few questions about why you sought these medications here, from this health worker or medication provider, and we will ask you to look at the medications you have just obtained. Finally, we also ask for your permission to call you in a week to follow up on your use of these medications.

We will not collect any personal data that could identify you, such as your name or date of birth. Your name will only appear on this form and not in the study data. Your phone number will only be used by the investigator to follow up on your use of these medications; the number will not be kept. Data without identifiers may be used in future studies on medication use.

Time required for participation

Answering the questions should take a maximum of 20 minutes. The follow-up phone call after one week should only take a few minutes.

Voluntary participation

Your participation in this study is entirely voluntary, meaning that you have the right to refuse to participate, now or later (at the time of the home visits), without any consequences. The choice not to participate will not be documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand until you are satisfied. You are free to withdraw or stop participating at any time. You are also free to choose which questions you want to answer.

If you wish to participate, we will ask you to confirm in writing that you agree to participate in the study, and you will keep a copy of this "consent" document, signed by both of us.

Confidentiality

All information collected during the study will remain strictly confidential. Your name will not be recorded, and all information you provide will remain confidential. Only the research team will have access to the data and information collected. Your contact information (phone number) will be kept until the follow-up call and will not be kept after that. We guarantee that all information will be treated as strictly confidential, and your name will be replaced by a code in all study documents.

Risks and benefits

There are no direct risks associated with this study. If any questions make you uncomfortable, please feel free at any time to not answer the question, take a break, or stop participating in this study. There is no direct individual benefit to participating in this study, and no financial compensation. However, at the community level, the intervention aims to reduce antibiotic resistance and the spread of disease, and to improve patient care. In addition, systematic deworming will be offered to each household member every six months.

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone:
+226 70285553; Email: valiadaniel@yahoo.com

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FORM	CONSENT THE SURVEY	CONSENT ON ANTIBIOTIC USE	FOR PARTICIPATION IN

PARTICIPANT (adult)

Respondent's name (first name + middle name (if available) + last name):

_____

Date (dd/mm/yy): __/ ___/ ___

Signature: _____

If the respondent cannot read or write, a witness who is independent of the research team, such as a member of the same household or a neighbor, must be present during the interview for informed consent. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will provide a thumbprint in lieu of a signature.

WITNESS

Witness's name (first name + middle name (if available) + last name):

_____

Date (dd/mm/yy): __/ ___/ ___

Signature: _____

RESEARCHER

I confirm that the information sheet has been read and explained to the participant named above in a language that the respondent understands well.

I have ensured that the participant understands that he/she is free to choose whether to participate in the study, that he/she does not have to answer any question he/she does not wish to answer, and that he/she may terminate the interview at any time.

The participant had the opportunity to ask questions about the study and its objectives. If the respondent had any questions, I or a colleague from the research team answered them correctly and clearly.

The participant was told that their name is not recorded except on this form, which will be kept secure, used only if the participant chooses to withdraw from the study, and destroyed one year after the study ends. The information provided would remain pseudo-anonymous, meaning that direct identifiers such as names would be replaced by a code in all official study documents.

Name of the investigator (first name + middle name (if available) + last name):

_____

Date (dd/mm/yy): __/ ___/ ___

Signature: _____

11.3.2 Teenager

INFORMATION FORM FOR PARTICIPATION IN THE COMMUNITY USE SURVEY OF ANTIBIOTICS (teenager with parent or guardian)

You are invited to voluntarily participate in a study on treatments used in your community, conducted by the Nanoro Clinical Research Unit (URCN) and the Institute of Tropical Medicine (ITM, Antwerp). The study is described in this information sheet. If you or your parent/guardian have any questions, now or later, please do not hesitate to ask. In addition, you are of course free to withdraw from the study at any time.

Purpose and description of the study

The purpose of this survey is to understand the use of certain medications to treat certain diseases in your community, particularly antibiotics. The results will help evaluate an information and training campaign for healthcare workers aimed at improving the quality of care while ensuring that medications are used properly to combat certain diseases encountered in your community.

We will ask you a few questions about the medicines that have been prescribed, given, or purchased by you, such as the quantity and how many times a day you will take these medicines. We will also ask you why you sought these medicines here, from this health worker or medicine supplier, and we will ask you to look at the medicines you have just obtained. Finally, we will also ask your permission to call you in a week to follow up on your use of these medicines.

We will not collect personal data that could identify you, such as your name or date of birth. Your name will only appear on this form and not in the study data. Your phone number will only be used by the researcher to follow up on your use of these medications; the number will not be kept. Data without identifiers may be used in future studies on medication use.

Time required for participation

Answering the questions should take a maximum of 20 minutes. The follow-up phone call after one week should only take a few minutes.

Voluntary participation

Your participation in this study is entirely voluntary, meaning that you have the right to refuse to participate, now or later (at the time of the home visits), without any consequences. The choice not to participate will not be documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand until you are satisfied. You are free to withdraw or stop participating at any time. You are also free to choose which questions you want to answer.

If you wish to participate, we will ask for your consent (the adolescent's) and for your parent/guardian to sign or affix their fingerprint as acceptance of participation in the study, and you will keep a copy of this "consent" document, signed by me and the parent/guardian.

Confidentiality

All information collected during the study will remain strictly confidential. Your name and your child's name will not be recorded, and all information you provide will remain confidential. Only the research team will have access to the data and information collected. The parent's contact information (phone number) will be kept until the follow-up call and will not be kept thereafter. We guarantee that all information will be treated as strictly confidential, and your name will be replaced by a code in all study documents.

Risks and benefits

There are no direct risks associated with this study. If any questions make you uncomfortable, please feel free to skip the question, take a break, or stop participating in this study at any time. There is no direct individual benefit to participating in this study, no financial compensation. However, at the community level, the intervention aims to improve the quality of care and reduce the spread of disease. In addition, systematic deworming will be offered to each household member every six months.

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone:
+226 70285553; Email: valiadaniel@yahoo.com

FORM	CONSENT	CONSENT	FOR PARTICIPATION	IN
	THE SURVEY	ON		
COMMUNITY USE OF ANTIBIOTICS (teenager with parent or guardian)				

ADULT PARENT/GUARDIAN OF THE PATIENT

Respondent's name (first name + last name): _____

Date (dd/mm/yy): __/ ___/ ___Signature: _____

If the respondent cannot read or write, a witness who is independent of the research team, such as a member of the same household or a neighbor, must be present during the interview for informed consent. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will provide a thumbprint in lieu of a signature.

WITNESS

Witness name (first name + last name): _____

Date (dd/mm/yy): __/ ___/ ___Signature: _____

INVESTIGATOR

- I confirm that the information sheet has been read and explained to the adolescent patient and his/her parent/guardian named above and concerned in a language they understand well.
- I have ensured that the patient and his/her parent/guardian understand that they are free to choose whether to participate in the study, that they do not have to answer any questions they do not wish to answer, and that they may terminate the interview at any time.
- The adolescent patient and their parent/guardian had the opportunity to ask questions about the study and its objectives. If there were any questions, I or a colleague from the research team answered them correctly and clearly.
- The adolescent patient and their parent/guardian were told that their name would not be recorded except on this form, which would be kept secure, used only if the respondent wished to withdraw from the study, and destroyed one year after the end of the study. The information provided would remain pseudo-anonymous, meaning that direct identifiers such as names would be replaced by a code in all official study documents.
- The patient's age is between 14 and 17 years old.

Name of investigator: _____

Date (dd/mm/yy): __/ ___/ ___Signature: _____

11.3.3 Child

INFORMATION FORM FOR PARTICIPATION IN THE COMMUNITY USE SURVEY ANTIBIOTICS (child with parent or guardian)

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit (URCN) and the Institute of Tropical Medicine (ITM, Antwerp) by answering a few questions on behalf of the child for whom you are a parent or guardian, mainly about the treatments used in your community. The study is described in this information sheet. If you, as a parent/guardian or as an adolescent patient, have any questions now or later, please do not hesitate to ask them, including questions about the advantages and disadvantages of the study. In addition, you are of course free to withdraw from the study at any time.

Purpose and description of the study

The purpose of this survey is to understand the use of certain medications to treat certain diseases in your community, particularly antibiotics. The results will help improve an awareness campaign for the community and healthcare workers, which will aim to reduce the spread of disease and improve the quality of care provided to the community.

We will ask you a few questions about the medications that have been prescribed, given, or purchased by you, such as the dosage and how often you take these medications. We will also ask you a few questions about why you sought these medications here, from this health worker or medication provider, and we will ask you to look at the medications you have just obtained. Finally, we also ask for your permission to call you in a week to follow up on your use of these medications.

We will not collect any personal data that could identify you, such as your name or date of birth. Your name will only appear on this form and not in the study data. Your phone number will only be used by the investigator to follow up on your use of these medications; the number will not be kept. Data without identifiers may be used in future studies on medication use.

Time required for participation

Answering the questions should take a maximum of 20 minutes. The follow-up phone call after one week should only take a few minutes.

Voluntary participation

Your participation in this study is entirely voluntary, meaning that you have the right to refuse to participate, now or later (at the time of the home visits), without any consequences. The choice not to participate will not be documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand until you are satisfied. You are free to withdraw or stop participating at any time. You are also free to choose which questions you want to answer.

If you wish to participate, we will ask you to confirm in writing that you agree to participate in the study, and you will keep a copy of this "consent" document, signed by both of us. If the sick child (the patient) is over 14 years of age, we will ask if he/she agrees to have his/her parent or guardian answer for him/her.

Confidentiality

All information collected during the study will remain strictly confidential. Your name and your child's name will not be recorded, and all information you provide will remain confidential. Only the research team will have access to the data and information collected. Your contact details (phone number) will be kept until the follow-up call and will not be retained thereafter. We guarantee that all information will be treated as strictly confidential, and your name will be replaced by a code in all study documents.

Risks and benefits

There are no direct risks associated with this study. If any questions make you uncomfortable, feel free at any time to not answer the question, take a break, or stop participating in the study.

participating in this study. There is no direct individual benefit to participating in this study, nor is there any financial compensation. However, at the community level, the intervention aims to reduce antibiotic resistance and the spread of disease, and to improve patient care. In addition, systematic deworming will be offered to each member of the household every six months.

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Phone:
+226 70285553; Email: valiadaniel@yahoo.com

FORM	CONSENT THE SURVEY	CONSENT USAGE	FOR PARTICIPATION	IN
ANTIBIOTIC COMMUNITY (child/teenager with parent or guardian)				

RESPONDENT (child's parent or guardian)

Respondent's name (first name + last name): _____

Date (dd/mm/yy): __/ ___/ ___Signature: _____

If the respondent cannot read or write, a witness who is independent of the research team, such as a member of the same household or a neighbor, must be present during the interview for informed consent. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will provide a thumbprint in lieu of a signature.

WITNESS

Witness name (first name + last name): _____

Date (dd/mm/yy): __/ ___/ ___Signature: _____

INVESTIGATOR

- I confirm that the information sheet has been read and explained to the respondent named above and (if the patient concerned is an adolescent) to the patient concerned in a language they understand well.
- I have ensured that the respondent and (if the patient concerned is an adolescent) the child have understood that they are free to choose whether or not to participate in the study, that the respondent does not have to answer any question they do not wish to answer, and that they may terminate the interview at any time.
- The respondent had the opportunity to ask questions about the study and its objectives. If the respondent had any questions, I or a colleague from the research team answered them correctly and clearly.
- The respondent was informed that their name is not recorded except on this form, which will be kept secure and only used if the respondent wishes to withdraw from

participation in the study, and destroyed one year after the end of the study. The information provided would remain pseudo-anonymized, meaning that direct identifiers such as names would be replaced by a code in all official study documents.

Name of the investigator: _____

Date (dd/mm/yy):___ /___ /___ Signature: _____

11.4 Verbal informed consent form for community surveys (additional, within HDSS surveys)

This consent will take place during the regular HDSS visit to the household, before the intervention has begun. The head of the household will be asked to answer questions on behalf of the entire household.

INFORMATION FORM FOR PARTICIPATION IN THE COMMUNITY SURVEY ON COMMUNITY USE OF ANTIBIOTICS AND TRANSMISSION OF ANTIBIOTIC-RESISTANT PATHOGENS

You are invited to voluntarily participate in a study conducted by the Nanoro Clinical Research Unit, the University of Antwerp, and the Institute of Tropical Medicine (ITM, Antwerp). The study and the intervention it will evaluate are described in this information sheet. If you have any questions about the study or the intervention, please do not hesitate to ask. In addition, you are of course free to discontinue your participation in the study or intervention at any time.

Purpose and description of the study

Increased antibiotic resistance is rendering drugs currently used to treat bacterial infections ineffective. This means that when you or a member of your family is infected with a disease caused by resistant bacteria, the antibiotics available on the market that were once effective will no longer be able to cure you. Resistant bacteria can be passed from one member of the community to another via hands, food, water, or shared toilets or latrines, even without them realizing it or becoming ill.

This can lead to increased resistance in infections in people who eventually become ill after contact with one of these pathogens. The stools of healthy people contain a number of bacteria, called enterobacteria, which are the leading cause of septicemia (very serious illnesses that can lead to death) in your community. Interventions will be implemented to address the risk of antibiotic resistance, improve the quality of care, and respond to the perceived needs of healthcare workers and the population. This package will target drug dispensers as well as the general population.

The aim of our study is to understand whether this intervention will lead to a change in hygiene practices and healthcare use within households participating in the Nanoro HDSS. At another point in time, repeated stool samples will be collected from households in the community to assess the carriage and transmission of resistant bacteria.

You will be asked to answer a few questions to assess hygiene practices and healthcare use that may have an impact on the risk of resistant bacterial infection.

Time required for participation

The additional questions will take five minutes of your time. Voluntary

participation

Your participation in this study is entirely voluntary and this choice is not documented or reported in the study documents.

Please feel free to ask if there is anything you do not understand until you are satisfied. You are free to withdraw or stop participating at any time.

Confidentiality

All information collected about you during the study will remain strictly confidential. Your name is not recorded, and all information you provide will remain confidential. Only two researchers from the research team will have access to the data and information collected.

Benefits

Your agreement to participate in this study does not offer any direct personal benefit. However, the intervention being evaluated may contribute to better public health in the community.

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after your participation, you can contact the study coordinator: VALIA Daniel; Telephone: +226 70285553; Email: valiadaniel@yahoo.com

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VERBAL CONSENT FORM FOR PARTICIPATION IN THE COMMUNITY SURVEY ON COMMUNITY USE OF ANTIBIOTICS AND TRANSMISSION OF ANTIBIOTIC-RESISTANT PATHOGENS

(to be completed by the researcher for each participating head of household)

- I confirm that the information sheet has been read and explained to the respondent in a language that the respondent understands well.
- I have ensured that the respondent understands that he/she is free to choose whether to participate in the study, that he/she does not have to answer any question he/she prefers not to answer, and that he/she may terminate the interview at any time.
- The respondent had the opportunity to ask questions about the study and its objectives. If the respondent had any questions, I or a colleague from the research team answered them correctly and clearly.
- The participant was informed that their name is not recorded except on this form, which will be kept secure, used only if the participant chooses to withdraw from the study, and destroyed one year after the study ends. The information provided

will remain pseudo-anonymous, meaning that direct identifiers such as the name will be replaced by a code in all official study documents.
- The respondent is 18 years of age or older.
- The respondent has consented to participate in the study

Name of the investigator: _____

Date (dd/mm/yy):__ /__ /__ Signature: _____

11.5 Image use authorization (adult)

Photos of individuals will be used internally and collaboratively for data collection and analytical purposes by participants and facilitator-researchers. When taking a photo, participants should ask for permission to take and use the photo from the person being photographed, who should receive a copy and sign the form below.

Purpose and description of the study

Increased antibiotic resistance means that diseases caused by bacteria can no longer be treated with existing drugs. The use of antibiotics exposes bacteria to antibiotics, allowing these pathogens to develop resistance. Sanitary conditions then allow these resistant pathogens to spread from one member of the community to another. In order to develop and introduce interventions that would enable better use of antibiotics in the community and prevent infections with resistant pathogens, we must first understand where, when, how, and why antibiotics are used and what hygiene and sanitation conditions and practices facilitate the transmission of pathogens between people. That is why this study is being proposed.

Ethics Committee

This study has been reviewed by the Institutional Review Board of the Institute of Tropical Medicine, the Ethics Committee of the University Hospital of Antwerp, Belgium, and the National Ethics Committee for Health Research in Burkina Faso, and has received a favorable recommendation.

If you have any questions or comments about the study, now, during, or after
If you would like to participate, please contact the study coordinator: VALIA Daniel; Phone: +226 70285553; Email: valiadaniel@yahoo.com

Authorization

- I, the undersigned, Ms./Mr. _____ *(Last name, First name)*, freely agree that, as part of this study on antibiotic use, photos may be taken in which I or my child appear.
- I fully understand the purpose of these photos.
- I authorize the team and its participants to take these photos and I agree to their use in the study.

- I understand that these photos and my image will not be used for commercial purposes or reproduced for activities outside of this project.

- As a result, I expressly waive any image rights and any action against _ that may arise from the use of my image in the aforementioned context.

Date (dd/mm/yy): __/ ___/ ___

Signature or fingerprint: _____

If the respondent is an independent witness to the research team (e.g., a member of the same household or a neighbor), they must be present during the interview for informed consent. If, at the end of the interview, the person agrees to participate, the witness will sign this consent form, and the participant will record their thumbprint in the box above.

WITNESS

Witness name (first name + middle name (if available) + last name):

_____

Date (dd/mm/yy): __/ ___/ ___

Signature or fingerprint: _____

One copy to be kept securely by the researchers; and one copy to be given to the participant/informant.

11.6 Clusters selected for the randomized study

No.		Village	Household	Working population	Market	CSPS
1	HDSS	NANORO	1425	7542	YES	YES
2		POESSI	308	2304	YES	NO
3		SITAON	187	1416	NO	NO
4		BOULPON	526	3658	YES	NO
5		NAZOANGA	765	5293	YES	YES
6		ZIMIDIN	294	1995	YES	NO

7		SEGUEDIN	563	3942	YES	NO
8		SOALA	329	2376	YES	YES
9		GODO	220	1520	NO	YES
10		BASZIRI	269	1891	NO	NO
11		GOULOURE	403	2840	NO	NO
12		KOKOLO	194	1440	NO	YES
13		DACISSE	227	1588	YES	NO
14		SOUM	746	5334	YES	YES
15		ZOETGOMDE	146	923	YES	YES
16		KALWAKA	307	2202	YES	NO
19		MOGDIN	163	1384	NO	NO
20		POESSE	543	4580	NO	YES
21		SEGUEDIN_SOAW	157	1215	NO	NO
22		RAKALO	245	2177	YES	NO
23		SOAW	903	7541	YES	YES
1	HDSS extension (acronym)	BOLOGHO	583	6953	YES	YES
2		TEMNAORE	452	5048	NO	YES
3		DACISSE _ SIGLE	146	1682	NO	NO
4		BALOGHO	107	1693	NO	NO
5		KOURIA	314	4215	YES	YES

6		PALLILGOGO	50	671	NO	NO
7		ACRONYM	308	2954	NO	YES
8		BOUKOU	245	1315	NO	NO
9		SEMTENGA	96	965	NO	NO
12		LALLE	276	2818	YES	YES
13		PELLA			YES	YES
14		DAWANEGOMDE	83	969	YES	NO

PHC = primary health care center

11.7 Checklist to be completed after each simulated patient visit

1. GASTROENTERITIS (adapted from Das et al, 2016, Science)	Yes(Y)/ No(N)
Medical history questions	
Type/consistency of stool (with question about whether it contains blood)	
Frequency of stools	
Amount of stool	
Questions about urination	
Is the child active/playing? General behavior of the child (lethargic?)	
Fever? History of fever?	
Abdominal pain?	
Vomiting?	
Health conditions? General condition?	

Source of drinking water? How is the water preserved?	
Meal preparation?	
The child's meals and food	
Does the child drink?	
Questions about the neighborhood or family situation	
Questions about the physical environment, hygiene conditions	
Actions	
Explain the need to stay well hydrated/drink fluids?	
Give one or more antibiotics	
Give an antibiotic watch	
Clearly explain why it is not necessary to treat acute diarrhea with an antibiotic	
Explain the importance of safe water and food and good hygiene and sanitation practices sanitation	
Advice on what to do if diarrhea persists	
Dispensing of medicines	numbe r
Number of medicines dispensed	
If applicable: number of medications prescribed	
Number of antibiotics dispensed	
If applicable: number of antibiotics prescribed	

Number of medications dispensed or received for injection	
Duration of visit (in seconds)	
2. RHINOPHARYNGITIS	Yes (Y)/ No (N)
Medical history questions	
Question about cough: type, duration, frequency	
Question about sputum (mucous? mucopurulent?)	
Question about difficulty breathing	
Question about fever	
History of respiratory disease	
Clinical examination	
Inspection of the throat	
Pulse	
Blood pressure	
Auscultation	
Actions	
Administer one or more antibiotics	
Give an antibiotic watch	
Clearly explain why it is not necessary to treat acute nasopharyngitis with antibiotics	
Dispensing of medications	number

	r
Number of medications dispensed	
If applicable: number of medications prescribed	
Number of antibiotics dispensed	
If applicable: number of antibiotics prescribed	
Number of medications dispensed or received for injection	
Duration of visit (in seconds)	
3. PNEUMONIA	Yes(Y)/ No(N)
Medical history questions	
Question about cough: type, duration, frequency	
Question about sputum (mucous? mucopurulent?)	
Question about difficulty breathing	
Question about fever	
History of respiratory disease	
Clinical examination	
Pulse	
Blood pressure	
Auscultation	
Actions	

Referral to a hospital or health center	
Explains the need to seek appropriate care	
Prescribes one or more antibiotics	
Prescribes an antibiotic watch	
Dispensing of medication	numbe r
Number of medications dispensed	
If applicable: number of medications prescribed	
Number of antibiotics dispensed	
If applicable: number of antibiotics prescribed	
Number of medications dispensed or received for injection	
Duration of visit (in seconds)	
4. ISOLATED ACUTE FEVER	
Medical history questions	
Duration of fever	
Question if other signs are present	
Actions	
Give one or more antibiotics	
Give an antibiotic watch	
Give an antimalarial drug?	

Refer for diagnostic testing?	
Dispensing of medication	numbe r
Number of medications dispensed	
If applicable: number of medications prescribed	
Number of antibiotics dispensed	
If applicable: number of antibiotics prescribed	
Number of medications dispensed or received for injection	
Duration of visit (in seconds)	
5. URINARY TRACT INFECTION	
Medical history questions	
Question about the duration of burning during urination	
Question about how often you pee during the day?	
Question about how often you urinate at night?	
Question about whether or not there is a fever?	
Actions	
Give one or more antibiotics	
Give an antibiotic watch	
Give an antimalarial drug?	
Refer to the health center or hospital?	

Dispensing of medication	number
Number of medications dispensed	
If applicable: number of medications prescribed	
Number of antibiotics dispensed	
If applicable: number of antibiotics prescribed	
Number of medications dispensed or received for administration by injection	
Duration of visit (in seconds)	

11.8 Questionnaire survey from patients to the end of a visit to a medication dispenser

Information to identify the cluster and healthcare provider
Cluster number (2 digits), village name, dispenser letter (1 letter)
Type of dispenser
Patient information
Person presenting is: 1) the patient themselves (adult) 2) the guardian (parent or other) of the patient under 14 years of age 3) the guardian (parent or other) of a patient aged 14-17
Patient age (months/years)
Patient's gender
Patient's place of residence (village, neighborhood)

Patient's level of education
Education level of the patient's caregiver if the patient is a minor (<18 years old)
Has the patient been discharged from hospital or observation?
If the patient is being discharged from observation or hospitalization, specify the date of admission to the health center or private clinic (drop-down calendar)
Clinical presentation
What was the illness or complaint that prompted your visit? (multiple options possible) ● Fever ● Cold ● Cough ● Sore throat ● Stomach ache ● Headache ● Body aches (pain throughout the body) ● Diarrhea ● Vomiting ● Constipation ● Fatigue ● Dizziness ● Burning sensation when urinating ● Other
Other (please specify)
Was a malaria diagnostic test performed?
If a malaria diagnostic test was performed, can you specify the result? (one option) ● Positive ● Negative ● Indeterminate ● Don't know
Have you had any other laboratory tests? Y/N/N/A. If yes, please specify:_____

Have you received a specific diagnosis for your condition? Y/N
If yes, please specify (multiple options possible): ● Malaria ● Cold/Rhinitis ● Pharyngitis/Nasopharyngitis ● Tonsillitis ● Ear infection ● Bronchitis ● Pneumonia ● Gastroenteritis ● Typhoid fever/Salmonellosis ● Dengue ● Urinary tract infection ● Sepsis/septicemia ● Other, specify:_____
Prescription
During this consultation/visit, did you receive a prescription (from a formal healthcare provider)?
If yes, take a photo of the prescription
During this consultation/visit, did you receive a prescription? ● No ● Yes, but not from a healthcare provider ● Yes, verbal or informal ● Yes, documented
Why did you choose to purchase your medication from this specific healthcare provider? (select one option, whichever applies most) ● The MEG depot is located in the CMA/CM/CSPS where I consulted ● The medications (all or some) are not available where I consulted ● Because it is closer to where I live

● Because the medications are of better quality ● Because the medicines are more effective ● Because the drugs are cheaper ● Because here I can buy just the amount I need ● Other, please specify _____
How much medicine did you buy/receive? (fill in the number)
For each medicine purchased/received, specify
a. Brand name
b. Generic name
c. Presentation ● tablet/capsule ● syrup/oral suspension ● injectable solution ● other, specify _____
d. Dosage (e.g., 500 mg, 5 ml/250 mg, 500 mg/5 ml, etc.)
e. Manufacturer indicated on the packaging
f. Expiration date
g. Price for the quantity received
h. Dosage (e.g., 2 tablets 3 times daily; 5 mL 3 times daily; 1 injection twice daily)
i. Route of administration (select one) ● PO ● IM ● IV ● IR ● Other, specify _____
j. Duration of treatment (in number of days)

k. Number of units received/purchased (e.g., number of tablets, bottles)
l. Photo of packaging/blister pack/product
If the medicines purchased were prescribed by formal healthcare professionals (doctors, nurses), do the purchases correspond to the prescription? Y/N
If not, why? (select one option) ● I did not have enough money to buy all the medicines ● The prescribed medicines were not available and the seller gave me equivalents ● The person who sold (gave) me the medicines told me that these medicines could solve my problem ● The prescribed medicines were too expensive for me and the seller offered me others at a better price ● I have more confidence in the effectiveness of the seller's medicines than those prescribed by the nurse, midwife, or doctor ● Other, please specify_____
For patients coming from hospitalization or observation, please list, for each medication received during hospitalization/observation
Photos to be taken
How much medication did you purchase/receive?
a. Generic name of the medication _____ Brand name _____
b. Presentation (● tablet/capsule ● syrup/oral suspension ● injectable solution ● other, specify _____
c. Dosage (in mg)
d. Route of administration (select one) ● PO ● IM ● IV

• IR • Other
Other Route of administration
e. Dosage
f. Duration of medication administration (in days)
Before this consultation/visit, did you consult or seek medication for the same illness or complaint? Y/N
If yes, which healthcare facility, provider, or point of sale did you consult/visit? • The same provider/dispenser • a public health center or facility • a private clinic • a pharmacy or community depot • another store • other, please specify _____
Why did you choose to visit the same healthcare provider or change providers? Select one option (the most relevant) • I was unable to purchase the medication and start treatment, so the same symptoms persisted • The same symptoms persisted and the illness worsened despite purchasing and taking the medication as indicated by the healthcare provider during the previous visit/consultation • I couldn't afford to pay for the prescription from the first healthcare provider. • I trust the latter more than the former • My illness could not be treated by the first healthcare provider • Other Specify _____
Before this consultation/visit, did you take any medication that you had at home for the same condition? Y/N
If you took any medication (previous consultation/visit, medication kept at home), can you tell us the names or point them out from among those we show you?
Photos to be taken

Number of medications presented

11.9 Community survey questionnaire on hygiene practices and health care seeking

General household information
Household number
Number of household members
Number of household members who sought care (or self-medicated) IN THE LAST 3 MONTHS
Main source of drinking water for the household (select one) • Regideso accessible to the dwelling, for household use only • Regideso shared with other households • Protected source/borehole/well • Unimproved or unprotected source/borehole/well • Other, please specify _____
If the main source of drinking water was 'Other', please specify
Is there drinking water stored in the dwelling? • No • Yes, in a closed tank • Yes, in an open container
Is hand washing soap available in the dwelling (as observed by the interviewer)? • No • Hand soap in use • Unused hand soap • Laundry detergent (powder or liquid)
Type of main latrine used by household members • Simple pit latrine • Improved ventilated pit latrine • Flush toilet (with or without siphon) • bucket latrines

• Open defecation
Is the main latrine shared with other households? • no • Yes, with another household • Yes, with 2 to 4 other households • Yes, with more than 4 other households
Hand washing after defecation by the oldest woman or girl in the household • always • sometimes • Never
Are there any pets present? • No • Yes, in the dwelling • Yes, on the property (but not inside the dwelling)
Check which pets are present • chicken • Duck or goose • Goat or sheep • cows or other cattle • dog or cat • pig • other poultry • other
If the pet was 'Other', please specify
If there has been any other contact with an animal outside the property during the past week, please specify (type of animal, type of contact, frequency of contact).
Are there any antibiotics stored in the house? Y/N
Specify the antibiotics stored in the home (generic name, method of administration, dose, quantity).
Type of house (according to construction material)

● Unconsolidated mud ● consolidated mud ● loose bricks ● consolidated bricks or multiple stories ● corrugated iron
Healthcare episodes DURING THE LAST MONTH: medical visit or other healthcare (if several visits to the same healthcare provider for the same episode of illness, answer for the first visit)
the code of the household member
age (in years) of this household member
Type of healthcare provider or care sought ● public health center or station ● clinic or dispensary or private first-aid provider ● private pharmacy ● other drug seller (not a pharmacist or doctor) ● hospital ● traditional healer or bokoko or nganga ● pastor or church or ntuadisi ● ta mfumu or ma ndona ● self-medication (with medicines stored at home, without the involvement of a health professional)
Which hospital department ● outpatient ● internal medicine ● gynecology ● pediatrics ● emergency ● surgery ● intensive care ● stomatology
If the answer was self-medication, specify the origin of the product (healthcare professional who prescribed, dispensed, or sold it)
Specify the reason for storing it, the initial prescription or purchase

Specify the generic name, dose, method of administration, dosage (frequency and quantity of units taken), and duration of self-medication.
Take a photo of the outer packaging and, if possible, the inner packaging if this self-medication treatment is still present in the home
What clinical signs prompted you to seek care (visit, purchase, or self-medication)? ● Fever or temperature or hot body for less than 3 consecutive days ● Fever or temperature or hot body for 3 days or more ● Vomiting ● Diarrhea ● Cough ● other respiratory symptoms ● skin rash or other skin redness ● stomach ache/abdominal pain ● wound ● muscle pain ● headache ● nausea ● convulsions ● dehydration ● dizziness/confusion/loss of consciousness ● blood pressure or heart problems ● blood loss or bleeding ● jaundice ● swelling or edema ● no symptoms ● other symptom(s)
If the answer was "other symptoms," please specify
If the answer was "no symptoms," check the reason for the visit to the healthcare provider ● pre- or postnatal visit, before or after childbirth, with no complaints prompting the visit ● vaccination (EPI, routine, or other) without complaints prompting this visit ● Regular visit for a chronic condition (hypertension, HIV, tuberculosis, diabetes) with no complaints prompting this visit ● other reason
If the answer was other reason, please specify

Date of medical visit, treatment, or start of self-medication
Duration between the onset of the first clinical signs and this visit (or self-medication) in days
If you visited this healthcare provider several times during the same episode of illness for the same household member, indicate how many times ● One visit ● Returned once ● Visited twice ● Returned more than twice
Specify the reason for multiple visits to the same healthcare provider for the same episode of illness

11.10 Proof of insurance for low-risk studies involving human participants

Insurance certificate

MS AMLIN Insurance SE, established in B – 1030 Brussels, Koning Albert II-laan 37, certifies that

Instituut voor Tropische Geneeskunde
Nationalestraat 155
2000 Antwerpen

has concluded a general Liability policy, the subject of which is to cover the Insured, within the limits stated below, against the financial consequences of his third party "no fault" liability as a sponsor of experiments mentioned below and according to the Belgian *law of 7th May 2004 regarding the experiments on humans.*

Policy number: 99.002.067

Effective date: 01/01/2022
Expiry on: 31/12/2022 (with tacit renewal)

Coverage is granted for the following experiments under risk classes 1 and 2.

Class 1 :

- Cohort studies – prospective or retrospective: simple clinical observation;
- Simple clinical research, without any therapeutic intervention, even if non-invasive;
- Studies on files;
- Non-invasive tests such as echography, electro-encephalogram;
- Standard radiography or CT-scan without contrast;
- Research on samples of urine, saliva, other externally extracted body secretions or excretions (non-invasive);
- Observational studies.

Class 2 :

- Experiments with peripherous blood sampling by single venipuncture or by finger prick;
- Experiments with external prostheses and ortheses;
- Effort test on a healthy participant;
- Research with NMR (Nuclear Magnetic Resonance);
- Research with peroral administration of contrasting agent;
- Research with sputum smears, vaginal and anal swabs.

Sum insured: 2.500.000 EUR per experiment

The company hereby declares that the above-mentioned insurance contract is not forfeited up to this date.
The present certificate is issued for information only, and does not alter the contents of the insurance contract, neither the rights and/or obligations of the parties.

Issued in Brussels, 22-12-20211

Luc Eeckhout – Specialist Underwriter Liability
Contact:
Phone: 0032(2) 894.71.35