

# STUDY PROTOCOL

## FIEBRE: Febrile illness evaluation in a broad range of endemicities

### Social science studies



### Zimbabwe Protocol

Version 1.1

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**ACRONYMS**

Antimicrobial resistance (AMR)

Antimicrobial use (AMU)

Low and middle income countries (LMICs)

Rapid diagnostic tests (RDTs)

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## 1 STUDY OVERVIEW AND PROTOCOL SUMMARY

Study design: Anthropologically-informed qualitative research involving participant-observation, interviews, and documentary and media analysis.

Study population: Health care workers (doctors, nurses, allied health professionals, clinical laboratory staff, community health promoters, traditional and/or religious healers); drug shop, market vendors, and members of pharmaceutical networks (pharmacists, sale representatives, other staff members in pharmaceutical companies); local residents (patients, family members, local leaders, shop owners); public health practitioners, policy-makers and scientist.

Site: Harare, Zimbabwe (involving comparison with sites in Malawi and Myanmar).

Study duration: 18 months of primary data collection at each site, plus documentary analysis and stakeholder engagement over 3 years.

Aim: To explore the roles of antimicrobials in fever case management in Zimbabwe with the application of a range of social science theories.

### Objectives:

1. To describe how fevers become classified in practice, how this relates to wider life and livelihoods as well as to guidelines or public health messages, and areas of certainty and uncertainty for different actors.
2. To establish how many and what kind of antimicrobials are being used in different ethnographically informed settings.
3. To shed light upon the roles of antimicrobials in homes, formal and informal health sectors, fever case management and algorithms, and how this relates to wider life and livelihoods.
4. To situate antimicrobial use, fever management and relevant discourses within public and global health priorities and scientific practices and institutions.

PhD studentship: The FIEBRE social science study will involve the training of a Zimbabwean student, Salome Manyau, to PhD level at LSHTM in the UK.

## **2 BACKGROUND AND RATIONALE**

### **2.1 Background**

Fever is the starting point for clinical management of many illness conditions. A key challenge for case management of fevers in malaria-endemic areas is to distinguish which require treatment with antimalarials, antibiotics, other medicines or no medicines (Amexo et al. 2004). Fever is also a classification with its own history, and we cannot take for granted that it carries a shared, translatable, static meaning. As a concept, it can be characterised by both its utility and its ambiguity for medical practitioners and for patients. For many years, a report of fever equated to provision of antimalarial medicines; now, with concerns of over-use of antimicrobials, eligibility criteria for antimalarials has tightened, moderated by the use of rapid diagnostic tests (Beisel et al. 2016). Two new categories of patients have emerged as targets for ongoing scientific study and intervention: those presenting with fever who are malaria test negative (Amexo et al. 2004; Hopkins et al. 2017), and those ‘self-medicating’ with antimicrobials at home or via retailers (Morgan et al. 2011; Ocan et al. 2015; Zellweger et al. 2017). In addition to these groups are those patients who do not mobilise the category of fever and who do not use antimicrobials. Understanding each of these groups is important for improving the scope of case management and in addressing the extent to which antimicrobial use (AMU) is a matter of access or excess.

### **2.2 Fever classification**

Fever is defined clinically as an abnormally high body temperature – a qualitative and relative measure of pathology which has its history in a particular philosophy of medicine (Canguillhem 1962). As a category, much like other biomedical categories, the power of fever is seen in the way that it transforms everyday experience into an ‘objective’, communicable form (Lock & Nguyen 2010; Beisel et al. 2016). It can be used for example to inform people about diseases and interventions; it can be used to allocate and access services; and provides a way of comparing and intervening upon bodies and diseases. Fever as a concept thus has utility in mobilising people and resources to deliver and direct care.

Biomedical categories, however, are not deployed in a vacuum; they interact with a multitude of other ways in which people classify, explain and act upon illness in their particular contexts. Historically, public health initiatives and health communication projects

in Africa have tended to assume a crude distinction between local 'beliefs' and biomedical 'knowledge' and been designed under the assumption that (a) belief is predictive of behaviour and (b) that a change in belief leads to change in behaviour (Becker 1974, 1988; Yoder 1999). Anthropologists have often been welcomed by public health planners because of their envisaged role as identifying prevailing beliefs and classifications and suggesting how they can be modified (Foster & Anderson 1978). However, and despite their popular image, anthropologists have long sought to challenge the ethnocentrism underlying biomedicine. A rich body of literature has sought to highlight the complexity and legitimacy of alternative classifications of illness and misfortune (Evans-Pritchard 1937, Feierman 1981; Nichter 1988; Good 1994), with studies in Zimbabwe focusing especially on the shifting role of traditional healers (Arkovitz & Manley 1990; Simmons 2012). Anthropologists have also shown that such classifications are enacted within plural, often inequitable health landscapes in ways that challenge the disproportional emphasis placed on 'belief' and its assumed linear association with behaviour (Yoder 1995, 1999).

An equally important contribution of anthropology to our understanding of the classification of sickness comes from how biomedical categories shift over time in response to wider social, political and economic processes (Singer & Clair 2003). The notion of 'syndemic' was introduced by anthropologists to capture how diseases interact synergistically as a result of noxious social conditions and relationships in ways that amplify suffering and mortality (Singer & Clair 2003; Baer et al. 1997; Janes & Corbett 2009). A syndemic approach suggests that we view illness not in terms of singular pathogeneses but as often multiple and overdetermined. Accordingly, biomedical concepts such as 'fever' and 'malaria' might be windows through which to view wider socio-medical realities in which people experience, categorise and act upon ill health. Given the recent public health urgency around the category of the (non-malarial) febrile patient, there is value in revisiting the 'fever' category afresh – for what it means to patients, and to health workers who themselves are situated in and responsive to the wider social context. The methods and concepts of anthropology are ideally suited to building upon aforementioned illness classification studies and investigations of local categories of fever; but in a way that is responsive to the syndemic nature of disease patterns and how this affects the way people make diagnoses, prescribe and use medicines. Furthermore, historical analysis and



anthropological studies of science (both research and education) and policy can assist in situating current ways of approaching fever (e.g. the classification of non-malarial fever in relation to malarial fever) and medical diagnoses, as well as elucidating their limitations, while pointing to alternative approaches.

### **2.3 Antimicrobial use**

Concerns over the ways in which antimicrobials are, and should be, used by prescribers and by patients to treat febrile illness have persisted since these medicines became mass produced (Podolsky 2015; Sosa et al. 2010). For decades, clinicians have described a challenging triad of diagnostic uncertainty; demanding patients and the fear of untreated serious febrile illness, often leading to the prescription of antimicrobials “just in case.” Remarkably similar reports of prescribing pressures have emerged from different contexts around the world (Cabral et al. 2015; Chandler et al. 2008; Paredes et al. 1996). Moreover, numerous accounts document high rates of antimicrobial self-medication across the world, made possible by the widespread availability of antimicrobials ‘over-the-counter’ in pharmacies and from other sources which do not require a prescription (Morgan et al. 2011; Ocan et al. 2015; Zellweger et al. 2017). A recent situational analysis in Zimbabwe reported widespread ‘misuse’ of antibiotics among a wide variety of actors, including medical professionals, private pharmacists, street vendors and lay publics (Zimbabwe AMR Core Group 2017). ‘Irrational’ AMU practices by both prescribers and health seekers have been identified as some of the main drivers of AMR, which have been described by the global health community as one of the greatest threats to modern medicine and indeed life as we know it (Podolsky 2015; Jasovsky et al. 2016; WHO 2014).

While fears of future AMR encourage prudent prescribing and use, on a case-by-case basis, distinguishing appropriate from inappropriate, and rational from irrational, AMU appears to be a major challenge. Anthropological and historical research have already gone some way to illustrating why this may be. People’s health-seeking practices and illness experiences often do not map seamlessly onto biomedical rationalities (Lock & Nguyen 2010), and moreover there are many diverse motives for medicine use (Whyte, Van der Geest & Hardon 2002), and AMU more specifically (Nichter 2001). To date, however, most analyses of AMU have focused on individual decision-making of the prescriber and/or patient. In line with this, efforts to change prescribing have taken approaches that focus on

individual behaviour, but have typically had little or no effect on AMU. A systematic review of nearly 500 prescribing interventions across LMICs, for instance, found even when such interventions had an impact, effect sizes were small (Rowe 2015). A synthesis of 9 studies evaluating the impact of malaria rapid diagnostic tests (RDTs) showed that while antimalarial prescribing decreased, antibiotic prescribing increased (Hopkins et al. 2017). Moreover, qualitative research alongside these studies raised questions about unintended consequences of restricting AMU – including relationships with patients versus the state/donors (Hutchinson, et al. 2015), shifting the status of health care providers (Hutchinson, et al. 2014) and shifting roles of gatekeepers, which can recast patients in terms of ‘deserving’ rather than ‘requiring’ medicines (Chandler, et al. 2017).

Taken together, we can observe similarities between public health practitioners’ approaches to fever classification and antimicrobial use: they assume the singularity of biomedical truths and rationality (in opposition to local beliefs), which not only fails to grasp the diverse motivations for prescribing and using antimicrobials, but also cannot easily be translated into people’s health seeking practices and ill health experiences, nor behavioural change. Here, the concepts and methods of anthropology, as well as history, can help to explore what wider roles antimicrobials have beyond their curative functions and how they have become entwined with our lives in ways that are now only becoming apparent as these medicines are deemed under threat. In addition, a closer look at the science (both research and education) and policy that informs much of health practices, nationally and globally, can assist with exploring how regional and historical differences in access to different technologies, medicines, knowledge and finance shape what is going on, as well as what is possible in particular contexts.

## **2.4 Rationale**

The Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE) project is undertaking clinical and laboratory research to improve fever case management, and this social research protocol proposes to explore how fever case management and AMU are entwined with social, economic and political life in Zimbabwe, as well as in Malawi and Myanmar (for which separate protocols have been submitted). Our research will expand the focus of case management to the realities of illness classification and action in Zimbabwe and other LMICs. By doing so, we will be able to offer insights that will be valuable to policy-

makers and public health practitioners at a crucial time in which national action plans on AMR are being designed and implemented. Such insights include: (a) elucidating the utility of the term *fever* for case management; (b) identifying the extent to which case management based on ‘fever’ adequately captures illness episodes that may culminate in antimicrobial use; (c) assessing feasibility of scaling back the use of antimicrobials; (d) understanding better the threat of the loss of antimicrobials, (e) anticipating better the potential unintended consequences of efforts such as shifting clinical guidelines or increasing reliance on diagnostic tests; (f) considering alternative means through which to accomplish the roles that antimicrobials currently play; and (g) understanding better the role of politics, culture, education and economics in policy development and scientific practices relevant to antimicrobial use and fever management. Such work is essential if we are to limit the impact of AMR on care, livelihoods and wider social and political life, as well as contribute to reductions in antimicrobial use.

The clinical and laboratory components of the FIEBRE study have been submitted as a separate protocol. In addition to Zimbabwe, Malawi and Myanmar (the locations of this social science component), the clinical and laboratory protocol also includes sites in Mozambique and Laos.

## **2.5 Theoretical Approaches**

The existing anthropological literature on illness and on medicines use has provided numerous conceptual devices for interpreting local idioms of distress as well as nuanced descriptions for the different motivations and reasons around AMU. However, much of this literature is absent in current discussions around case management and AMR. The current public health discourse on AMU and AMR tends to focus quite narrowly on individual decision-making, and has often framed the debate in terms of whether a given behaviour is ‘rational’ or ‘irrational’. Moving beyond this debate requires a re-framing of the question, which anthropological theory is well placed to do (Chandler, Hutchinson & Hutchison 2016). We propose to draw on both classic anthropological work on illness, disease and medicines, and on more recent re-framings that resist a biomedical reference point. Thus, rather than a given instance of prescribing/use being right or wrong (defined differently by clinical, public health or care-seeker perspectives), we adopt a perspective that centralises care.

The 'logic of care', Mol (2008) argues, works differently to the 'logic of choice', in that it is not the product of 'rational', 'informed' choices nor does it have a clear-cut beginning and end. Rather, care involves ongoing, obstacle-ridden processes of "tinkering" (Mol 2008:14) between multiple actors, including patients, their families, medical professionals, as well as microbes, medicines, technologies and procedures. Foregrounding the logic of care enables us to reframe the debate in much broader terms. Firstly, it decentres human actors and compels us to consider the diverse microbial-chemical-human relations involved in AMU (Mol 2008; Landecker 2015). This in turn allows us to follow the wider contexts which shape possibilities and probabilities for care in particular ways, with regard to the fabric that holds together life and livelihoods across local, national and international scales. In order to theorise care relations as they unfold in different contexts, we will draw upon a range of social science theories. Such theories will likely include: symbolism of medicines and biomedical care (Van der Geest & Whyte 1989); the social power of diagnoses (Parsons 1951); medicalisation and pharmaceuticalisation (Conrad 1992; Biehl 2007; Packard 2015); infrastructure (Bowker & Star 2000; Chandler, Hutchinson and Hutchison 2016); gender and intersectionality (Cornell 2012; Hankivsky 2012; Moore 1988); multispecies ethnography (Haraway 2008; Lowe 2010; Paxson 2012); and the anthropology of science (Helmreich 2009; Myers 2015; Yates-Doerr 2017). Ongoing comparative analysis within and between the study sites will allow for cross-fertilisation of conceptual inquiry as well as production of concepts that resonate across contexts.

### **3 AIMS AND OBJECTIVES**

Aim: To explore ethnographically the roles of antimicrobials in fever case management in Zimbabwe with the application of a range of social science theories.

Objectives:

1. To describe how fevers become classified in practice, how this relates to wider life and livelihoods as well as to guidelines or public health messages, and areas of certainty and uncertainty for different actors;
2. To establish how many and what kind of antimicrobials are being used in different ethnographically informed settings;

3. To shed light upon the roles of antimicrobials in homes, formal and informal health sectors, fever case management and algorithms, and how this relates to wider life and livelihoods;
4. To situate antimicrobial use, fever management and relevant discourses within public and global health priorities and scientific practices and institutions.

## **4 METHODOLOGY**

### **4.1 Study Design**

We will use ethnographically-informed qualitative methods, including participant-observation, stakeholder interviews and documentary and media analysis. The reason for using a qualitative methodology is that the aims and objectives are largely exploratory in nature, attempting to capture the ways in which fevers are classified in practice and how antimicrobials feature in people's everyday lives. These social phenomena are emergent and often unpredictable, making a hypothesis-driven, quantitative study design inappropriate for the purposes of this study. Qualitative methods, particularly ethnographic fieldwork (i.e. especially, participant observation combined with interviews), offer a rigorous inductive and iterative approach (Bernard 2011), making them ideal for capturing local fever classifications and the roles of antimicrobials across a variety of social spheres and levels of scale.

In line with the inductive approach we take in this study, our starting point for investigating febrile illness and AMU is further upstream than most previous approaches, which tend to assume a clear-cut category of 'fever' from which rational health-seeking and prescribing practices are envisaged to ensue. Taking lived experiences as our point of departure, we aim to capture the multiplicity of health-seeking trajectories in which febrile illness experiences and AMU are connected (or are not connected). Table 1 below offers a fever-AMU matrix, which represents a range of possibilities that will help guide us during fieldwork; and will likely be challenged by participants' divergence in conceptualisation of fever and antimicrobials.

**Table 1 Clinical fever – antimicrobial use matrix**

		Clinical Fever Classification	
		No Fever*	Fever*
Antimicrobial use	Antimicrobials	No Fever* Antimicrobials	Fever* Antimicrobials
	No antimicrobials	No Fever* No antimicrobials	Fever* No antimicrobials

\*May include non-clinically classified fever

Primary data collection will take place over a period of 18 months in Harare, Zimbabwe. In addition, documentary analysis and stakeholder engagement will be conducted over a period of 3 years. The groups of participants to be enrolled in this study are: health care workers (doctors, nurses, allied health professionals, clinical laboratory staff, traditional and/or religious healers, community health promoters); drug retailers, market vendors, and members of pharmaceutical networks (pharmacists, sales representatives, other staff members in pharmaceutical companies); local residents (patients, family members, local leaders, shop owners); public health practitioners, policy-makers and scientists. Selected patients and lay community members will include both adults and adolescents (for which appropriate ethical measures will be taken, see section 5.2). The total number of participants to be enrolled in the study is approximately 100-150; the number of participants from each group is proposed alongside specific methods (see 4.4 and 4.5). Participants will be identified using a combination of purposive and snowball sampling techniques, which will also be discussed alongside specific methods. These sampling techniques are appropriate given that the aim is not to produce a representative sample but rather to enrol particular stakeholders in fever case management and antimicrobial use (Bernard 2011). For a summary of the methods we will use and the corresponding research objectives, see table 2.

**Table 2. Summary of methods by research objectives**

Objective	Methods
1. To describe how fevers become classified in practice, how this relates to wider life and livelihoods as well as to guidelines or public health messages, and areas of certainty and uncertainty for different actors.	<ul style="list-style-type: none"> <li>- Participant observation in residential area and health care facilities</li> <li>- Key informant interviews with residents and health care providers</li> <li>- In-depth interviews with policy makers, public health practitioners and scientists</li> </ul>
2. To establish how many and what kind of antimicrobials are being used in different places	<ul style="list-style-type: none"> <li>- Review of dispensing logs and stocks at health care facilities</li> <li>- Medicine pile sorting exercises with residents</li> <li>- Key informant interviews with residents and health care providers</li> </ul>
3. To shed light upon the roles of antimicrobials in homes, formal and informal health sectors, fever case management and algorithms, and how this relates to wider life and livelihoods	<ul style="list-style-type: none"> <li>- Participant observation in residential areas and health care facilities</li> <li>- Key informant interviews with residents and health care providers</li> <li>- In-depth interviews with policy makers, public health practitioners and scientists</li> <li>- Documentary and media analysis</li> </ul>
4. To situate antimicrobial use and discourses within public and global health priorities and scientific practices	<ul style="list-style-type: none"> <li>- In-depth interviews with policy makers, public health practitioners and scientists</li> <li>- Documentary and media analysis</li> </ul>

#### 4.2 Site Selection

Primary data collection will be conducted in Harare, Zimbabwe in clinics, a hospital, and the high-density populations of Budiro and Mbare. Most of these sites were selected on the basis of the health facilities in which the FIEBRE clinical and laboratory work will be taking place, although the social research will be broader, including other clinics and the wider population. The health facilities in which we will collect data are: Harare Central Hospital, and two Harare City Health Clinics, Budiro clinic and Mbare clinic, including these clinics' smaller satellite clinics. Harare Central Hospital and Budiro clinic were selected because this is where data collection for the FIEBRE clinical and laboratory studies will be conducted. Mbare Clinic has also been selected because of its proximity to Harare Central Hospital as well as its expansive markets and informal health sector. Further healthcare facilities may be selected for the study, subject to study relevance and negotiations with local healthcare authorities. In addition, data collection will be conducted in other spaces in which fever case

management and antimicrobial use occurs within the study areas within the communities of Budiro and Mbare. This includes pharmacies, drug shops, markets, residential areas and individual households, as well as relevant social and cultural events.

### **4.3 Access and Permissions**

To gain access to study participants and ensure the legitimacy of the study, before commencing research activities we will approach the appropriate healthcare and social institutions. Permission to conduct the study in Harare City Health clinics and Harare Central Hospital will be sought through the ethics committees at Harare City Health Department and Harare Central Hospital. To obtain access to work with health care workers at Harare Central Hospital, approval to conduct the study at Harare Central Hospital will be sought from the Harare Central Hospital Ethics committee. After obtaining approval from the Harare Central Hospital ethics committee, permission to observe the flow of work and to interview health personnel will be obtained from the Matron and Sister in Charge at the outpatient and casualty department as well as the health personnel to be observed and interviewed.

Entry into populations in Budiro and Mbare will follow the structures of Harare City Health Department. Approval to conduct the study has already been obtained from the Harare City Health Department Director. Appropriate structures at the Harare City Health Department will be utilised to obtain entry into the Budiro and Mbare health facilities and communities. Approval of the District Medical Officers and District Nursing Officers for Mbare and Budiro will be obtained before visiting the Sisters in Charge at the local clinics. At the local clinics, the study will engage the Family Health Services department led by the Community Health Sister in Charge. The Community Health Sisters in Charge at the Family Health Services departments in Budiro and Mbare, as well as community health promoters, will act as the focal personnel to obtain entry into the Budiro and Mbare communities. The personnel at the Family Health Services department will provide information relating to the shopping centres, pharmacies, traditional doctors and apostolic sects in the community and will assist study personnel by introducing them to relevant community gatekeepers.

Subsequently, we will approach inhabitants to ask them to participate in our study and relevant ethical procedures followed; see section 5 for further details. In practical



terms, one of the first ways residents of the study area will become aware of the project will be upon invitation to participate in the medicines survey for which we will visit households (see 4.4.1). Below, we discuss the detail of the fieldwork methods to be undertaken with residents and then with health care providers (4.4 and 4.5). Some of these activities will be conducted in parallel.

#### **4.4 Ethnographic Fieldwork with Residents**

##### *4.4.1 Medicines Survey*

We will commence the data collection process by conducting a survey of the medicines that residents keep at home and what illnesses they are used to treat. Beforehand, between January and March 2018, we will assemble a 'library' of available medicines (specifically, antibiotics) by attending local markets, shops, pharmacies and health facilities. During the survey, we will firstly ask residents about, and ask them to show us, what medicines they keep at home, what illnesses they are used to treat, and compare them with our existing library (in turn enabling us to further build upon the library). We will then conduct an exercise called 'pile sorting' (Bernard 2011) using the medicines library. Pile sorting is an established anthropological method, and involves asking people to sort objects (in this case, medicines) into different piles based on similar attributes (Bernard 2011). We are specifically interested in discerning which antibiotics people recognise and use, and for what purposes, as well as which antibiotics they feel that they can and cannot access. The findings will help refine topics to pursue using the other research methods. We will take field notes during the survey, and will take photographs both of the medicines that people present to us in their homes, as well as photographs of the 'piles' from the pile sorting exercise (photography is discussed in more detail in section 4.5). Photographs will add a visual dimension to the research process and act as an additional record of the antimicrobial medicines that we encounter during the research, both for the antimicrobial log (section 4.5.1) and during the medicine survey in homes (4.4.1).

##### *4.4.2 Participant-Observation*

Participant-observation is an established anthropological method that involves the observation of and participation in people's routines and activities in order to produce data about what they *do* (as opposed to just say) and also to understand *why* in context (Geertz

1973; Hammersley 1992; Bernard 2011). Through the use of participant-observation, the study aims to produce a “thick description” (Geertz 1973) of fever classification and antimicrobial use in practice. The aim in doing so is to foster an appreciation of the everyday realities within which antimicrobial use is embedded, and to produce an account which illuminates and unsettles the ways in which antimicrobial use is currently framed, for instance practices described as ‘irrational’. Data from participant-observation will be collected in the form of field notes and will take place in a range of locations, including those mentioned in Section 4.2.

In residential areas, we propose to conduct participant-observation with members of 5-15 households per health facility catchment area to get a sense of daily life and priorities of peoples’ lives. The age, sex, socio-economic position and livelihood activity of household members are likely to shape how antimicrobial use is enacted and how fever is classified and treated. To capture this range of perspectives we will ensure we purposively sample men, women, girls and boys involved in a range of livelihood activities and ages. This is likely to include men and women working for day labour and interactions with animals.

To gain access to these households we will follow one or more of the following approaches:

- Identify interested households during the process of conducting the medicines survey in people’s homes.
- Some households may be selected on the basis of having a member enrolled in the FIEBRE clinical and lab studies.
- Households may be selected using snowball sampling from other identified points of entry, such as at community meetings, house visits in the study catchment area or during visits to health facilities and drug shops
- Other modes of entry, may include contacting controls from the FIEBRE clinical studies.

During the informed consent process, we will propose to potential participants the timeframes during which participant-observation might be performed, which will be subject to ongoing review during the research process (see section 5.2). During agreed-upon timeframes, ideally on a daily basis, we will spend time with participants to gain an

understanding of daily life, with particular attention to hygiene, work and interactions with others including animal and sexual relationships. We will explore gendered power dynamics within the household to understand division of labour, access to resources and how decisions around use of antimicrobials and treatment seeking are made. We will pay particular attention to illness episodes and follow people's treatment seeking activities when they occur, with the aim of understanding how illnesses become classified (Table 1), how antibiotics and other treatments are positioned within these scenarios and how power dynamics and social position within the household shape this.

We will also ask permission to follow 10-20 additional adults and emancipated minors ensuring we purposively sample adolescent girls, boys, men and women from a range of ages and livelihoods as they go about their daily work and social lives over several weeks, for example accompanying them to markets, visits to health care providers (both informal and formal) religious and cultural events. Data will be collected in the form of field notes taken by the participant-observer. We will also take photographs, for example, of medicines, houses, features of the urban and natural landscape, social and cultural events – which will act as valuable ways of aiding memory and stimulating conversation during key informant interviews, a technique known as 'photo elicitation' (Clark-Ibanez 2004; Harper 2002). Photographs will also be included with field notes as data that will help to convey the context and feel of fieldwork, as well as graphically convey themes that arise during fieldwork. When contextually appropriate and ethical consent is given, the faces of participants may be included in the photographs (see 5.3 for ethical considerations and further comments on use of photography).

#### *4.4.3 Key Informant Interviews*

Key informant interviews will be conducted with 15-30 adults and/or adolescents. We will ensure we purposively sample by age, sex and livelihood activity. Interviews allow for a greater degree of reflective discussion than is possible during participant-observation, and these will help us to understand what transpired during periods of observation, and also enable a deeper exploration of what residents assume to be 'common sense' knowledge in their daily lives (Bernard 2011; Bourgeault, Dingwall & de Vries 2010). Interviews may be repeated over time with the same participant wherever possible in order to increase the

likelihood of a good rapport and to establish changes in ideas and practices over time (Bernard 2011).

Interviews with residents (including patients) will be conducted at their homes, social spaces or, if this is contextually inappropriate (for instance if no private space is afforded), an alternative location will be selected. During interviews, participants will be asked about daily life and priorities, as well as about their experiences of illness, health seeking, and medicines use exploring how these decisions are made and enacted within households and whether they are different for different household members (see Appendix 1). Photographs taken during the participant-observation process will be used to guide interviews, and where contextually and ethically appropriate as data. If participants have not already participated in the antibiotic pile sorting exercise, we will also do this during the interview. Key informant interviews will typically last between 30-90 minutes, but may go on longer dependent on the flow of the interview and the availability of the informant (see section 5 for Ethics and consent).

#### **4.5 Ethnographic Fieldwork with Health Care Providers**

##### *4.5.1 Antimicrobial Log*

In the selected healthcare facilities, pharmacies and with informal drug vendors (and local healers if applicable), we will carry out an ongoing quantitative review of antimicrobial prescribing, dispensing and availability. This will take place alongside the participant-observation and key informant interviews. The purpose of this quantitative exercise is to give an understanding of the local availability and accessibility of antimicrobials, which affects the ways in which people prescribe and use them (Laxminarayan et al. 2016). The quantities of antimicrobials available will be counted through dispensing logs and stocks. The details of patients will not be recorded, as we are interested in the numbers and types of antimicrobials prescribed, rather than particular cases. However, if data on indication, diagnosis, or symptoms are listed in relation to dispensing of particular antimicrobials we may also collate this information in an anonymised format, to be presented in summary form.

#### 4.5.2 *Participant-observation*

We propose to conduct participant-observation in health centres, pharmacies, drug shops, markets and with local healers and pharmaceutical sales representatives. Informed consent will be obtained from selected participants prior to observation taking place, alongside consent for key informant interviews (see section 5.2). Time-frames will be arranged with participants such that routine service delivery is observed but not interrupted.

In the hospital and clinics, participant-observation will be conducted in numerous spaces, including waiting areas, consultation rooms, administrative spaces, clinical laboratories and tea rooms/staff rooms. Given our wide interest in antimicrobial use and the functioning of fever case management in the systems of facilities, our attention will be not only on staff but on the infrastructure, systems, spatial arrangements, materials and flows of the setting. In short, we are interested in what fever case management *is* in material practice (see e.g. Brown 2013; Street 2013). Although not all health facility staff will be directly observed, we will seek permission and consent from all of the staff in the areas where we are carrying out observations. Where any refuse, we will avoid timings of their shifts or the areas of facilities where they are working. We anticipate that in all this will involve observations with around 30 staff across the different facilities, including approximately 10 clinical professionals (medical doctors, nurses), 10 allied health workers (laboratory staff, cleaning and porter staff), 1-4 administrators, and up to 5 visiting researchers and donors. Importantly, the ‘participant’ in ‘participant-observation’ does not refer to the researcher’s participation in clinical practices. Rather, it refers to participation in the social dynamics of the setting: engaging in dialogue, asking questions, responding to questions – in short, not attempting to disengage from observed social phenomena unless contextually appropriate (Hammersley 1992; Bosk 2008; Bernard 2011).

Participant-observation will also be conducted with 2-3 pharmacists, 2-3 drug shop and market vendors, 1-3 pharmaceutical sales representatives, 1-4 community health promoters, and 1-2 local healers (approximately 7-15 participants in total). This will be conducted in the same manner as with health professionals in the hospital and clinics, that is, observing daily work routines and the material arrangements that enable them, particularly those practices relating to fever case management.

During the observations, we will also be noting power and gender dynamics within interactions with patients, exploring how men, women, girls or boys are treated and whether gender, age or social position shape this. In the wider observations we will seek to interpret these dynamics in the light of the history of social and economic structures.

#### *4.5.3 Key Informant Interviews*

Key informant interviews will be conducted with approximately 15-25 of the clinicians, allied health professionals, laboratory staff, administrators, pharmaceutical sales representatives, community health promoters, local healers and visiting researchers and donors at the healthcare facilities who are involved in our study. If possible, interviews will also be conducted with all pharmacists, market and drug shop vendors, and traditional healers involved in the study. We will aim to purposively sample both men and women to ensure we are capturing a range of perspectives. Most of these interviews will take place at the interviewees' place of work in a private space, at a convenient time that does not interfere with their work. Where interviews at their places of work are logistically challenging, interviews will be conducted at informants' homes or alternative appropriately designated locations. During interviews, informants will be asked about health seeking practices, routine care, fever case management, antimicrobial use and sales, and antimicrobial resistance. Key informant interviews will typically last between 30-90 minutes, but may go on longer dependent on the flow of the interview and the availability of the informant; see section 5 for discussion of ethics and consent.

#### **4.6 Stakeholder Interviews**

Approximately 20-30 in-depth interviews will be conducted outside the remit of the ethnographic fieldwork. These will last between 45 minutes to 2 hours, but may go on longer dependent on the flow of the interview and the availability of the informant. Consent will be obtained immediately before the interview takes place. As with key informant interviews, we will ask permission for interviews to be digitally recorded and transcribed. If participants do not feel comfortable with the use of a digital encrypted recorder, notes of the interview will be taken instead. Moreover, the identities of all participants will be protected in both transcriptions and in all subsequent references to interview proceedings including written accounts.

In-depth interviews will be conducted with key stakeholders who work on fever case management and antimicrobial use. We anticipate interviewing 5-15 policy makers, 5-15 public health practitioners and 5-15 scientists. These actors will be identified through a snowballing technique, through attending meetings and conferences on the topic of antimicrobial resistance and clinical care as well as through our research activity links such as teaching on relevant topics. We will ensure we purposively sample both male and female actors for these interviews. The interviews will be conducted in a private space such as their offices or a convenient location. The purpose of these in-depth interviews relates primarily to Objective 4 (see section 3). Thus, stakeholders will be asked about public and global health priorities as well as scientific practices, with the intention to situate the findings of ethnographic fieldwork within a broader field of activity surrounding antimicrobial use and fever management. If possible, we will follow up with subsequent interviews although we anticipate the opportunity to do so will be rare.

#### **4.7 Documentary and Media Analysis**

Documentary and media analysis will be conducted over a 3-year period. Archival material will be sought from a number of sources, including Ministry of Health archives, research institutes, university archives, libraries, non-governmental organizations and online repositories. Some of these sources will be located within Zimbabwe; others will be located in neighbouring countries as well as in other transnational research and NGO institutional archives. In the event that archival material is not publicly available, we will ask permission to access the material from the relevant authorising personnel and seek consent, where necessary, for its use as formal research data. In addition to documentary analysis, ongoing attention will be paid to media and popular discourse. Snippets from radio programmes, advertisements, documents in the public domain and other forms of media will be kept for analysis of discourses relating to febrile illness and antimicrobial use.

#### **4.8 Data Management**

Open Data Kit (ODK, [<https://opendatakit.org>]) and android devices will be used for the collection of all data during the study. ODK uses symmetrical encryption to ensure the security of all data and confidentiality of participants. ODK data will first be transferred locally to the researcher's computer, which will be secured and password protected. Data will then be securely backed up to LSHTM's secure cloud storage which is stored in London

and subject to the UK's Data Protection Act. Data to be uploaded to ODK will be collected using tablets, and will include interview recordings, field notes, quantitative data on antimicrobial stocks, and photographs. Data from each site will be accessible to the social science principal investigator (CC) responsible for that site throughout the study and the Zimbabwe social science team (SM and JD).

All raw data will be stored in password protected files/folders, and second-order summaries of fieldnotes and interview transcripts, photos and other field documents will be uploaded to the LSHTM institutional Research Data Repository (Compass) via LSHTM Research Data Management Support Service, where consent has been granted and anonymity can be maintained. Details of how to access the data will be published with each study publication, and access will be granted based on case-by-case request and approval. The LSHTM Data Compass repository will also enable access to repository contents through a searchable index.

## **4.9 Data Analysis**

### *4.9.1 Quantitative Data*

Quantitative data will be generated from both the medicines survey in people's homes (section 4.4.1) and the antimicrobial log with healthcare providers (4.5.1). Data from the medicines survey will be entered into a spreadsheet in Microsoft Excel for analysis and will be used to produce descriptive statistics, including ranking most common medicines used and illnesses disaggregated by gender, age etc.,. We will also aggregate the 'piles' from the pile-sorting exercise to discover which antibiotics in the medicines 'library' are most recognised and used among participants, and which antibiotics are most and least accessible. These outputs, including how participants' classified antimicrobials, will be compared to the WHO's Essential 'Access', 'Watch', and 'Reserve' Medicines Lists to see how they do or do not map on to relevant current global health policy.

Regarding the antimicrobial log, we will produce and periodically update spreadsheets documenting how many and what kinds of antimicrobial are being prescribed and dispensed in different settings, using data available from dispensing logs and stocks (e.g. drug, dose, and average monthly consumption). Explorations of the data will allow us to identify patterns in and between antimicrobial availability and use (e.g. how shortages or



stock-outs of certain antimicrobials might affect prescription practices). We will analyse and interpret the data and the patterns we identify in light of the qualitative data, as well as existing clinical guidelines and the Essential Medicines List (with particular attention paid to the categories of 'Access', 'Watch' and 'Reserve'). Running alongside the production of qualitative data, the antimicrobial log will form an iterative relationship with qualitative research methods, allowing us to identify and refine themes for key-informant interviews, stakeholder interviews and participant-observation.

#### *4.9.2 Qualitative Data*

Qualitative data in the form of field notes, interview transcripts and photographs will be entered into the qualitative data analysis software NVivo 11 for coding. The data will be analysed sequentially: we will begin by analysing data from the ethnographic fieldwork, followed by the stakeholder interviews, followed by all data across all field activities, including interpretations of the quantitative data. Codes will be generated on the basis of an ongoing, iterative process that spans the length of the analysis and dissemination phase of the project. Firstly, codes will be developed on the basis of patterns and themes that emerge from the data. As the coding process continues, codes of progressively higher orders of abstraction will be developed in order to explain and theorise the patterns and themes in the data. Social science theories and concepts – for instance, theories of pharmaceuticalisation, care, infrastructure, multi-species ethnography and gender (see section 2.5) – will be applied to the data in order to inform the coding process and further theorise the codes that emerge. Findings and interpretations, in the form of transcripts, fieldnote summaries and written interpretations, will be discussed and shared with the wider FIEBRE social science research team, so as to ensure consistencies in coding and depth of analysis.

#### *4.9.3 Documentary and Media Analysis*

Selected documents and media sources will be analysed to shed light upon the discourses underlying their production, using an approach derived from critical discourse theory. Critical discourse analysis theory acknowledges that discursive events are constituted of and by social context, social structures and the relations between them (Fairclough 2003). Selected documents and media will be read/listened to, with a number of considerations in mind, including patterns and commonalities in the use of language, the genre of the

documents/media, and the broader socio-cultural context and structures in which the discourse is situated and created. We will be especially concerned with identifying how antimicrobial use (in relation to febrile illness) is framed, for instance which actors/practices are brought into view (e.g. patients and prescribers), what structures and relations are obscured, and what interventions are thereby legitimised. We will then compare and aggregate these findings with other data sources.

#### *4.9.4 Cross-Country Analysis*

The data from the three countries (Zimbabwe, Malawi and Myanmar) will be analysed as separate project files in NVivo 11. However, to connect the separate country analyses we will use Nvivo Server, which will allow the country teams to view the other analyses. There will therefore be considerable cross-pollination of ideas during the coding process and, moreover, through comparison between the three analyses, we will aim to identify common themes and connections between countries as well as points of departure and difference. In addition, during the fieldwork process, we will have regular meetings and workshops involving all country teams, which will be fed back into the research process, ensuring an ongoing feedback loop between countries.

#### **4.10 Inputs into the FIEBRE Clinical and Laboratory Study**

The social science studies will be conducted alongside the FIEBRE clinical and laboratory study, which has been submitted as a separate protocol. The clinical and laboratory protocol has the following objectives:

1. To determine the treatable and/or preventable causes of fever in children and adults presenting as outpatients, and among those admitted to hospitals, in areas represented by the study sites;
2. To determine how fever aetiology varies according to patient age, geographical area, local malaria and HIV prevalence, and other risk factors;
3. To determine the prevalence and spectrum of antimicrobial resistance among bacterial pathogens identified in blood cultures from febrile patients

The social science studies are not directly dependent on the clinical and laboratory studies, with data to be collected separately. However, some participants in the FIEBRE clinical study may also be participants in this study (see section 4.4.2). In addition, the findings from the

clinical and laboratory study will be used to inform the analysis of our data, and the findings and conclusions from both studies will be used in conjunction to propose revisions to clinical guidelines for fever case management.

#### **4.11 Presentation of Results**

In publications and other outputs, the presentation of results will be grounded in “thick description” (Geertz 1973) of our interactions with participants in context from the ethnographic fieldwork, including both observational data and quotes from key informant interviews. Ethnographic data will be supported by other data – quotes from key informant interviews, document/media snippets and quantitative data on AMU – to illustrate key themes and concepts emerging from the qualitative analytical process.

#### **4.12 Dissemination of Results**

Results from this study will be disseminated to all participants and other stakeholders in this study (see the project timeline in section 7 for specific timeframes). During the data collection process, we will periodically have feedback discussions with participants, to seek their feedback on our ongoing interpretations. This is an established technique in anthropological research (Pool 2000). At the start of the study we will identify key stakeholders who will be interested in the findings, and towards the end of the data collection process, we will initiate dissemination dialogues with them and other participants with the use of dissemination materials. The dissemination materials will include an information leaflet summarizing the findings and key messages, as well as how the study’s findings can be used to improve fever case management and antimicrobial use. The dissemination dialogues will include stakeholder meetings in which we will both provide and ask for feedback, aiming to ensure a dialogical process, which may be used to inform outputs and further research. In order to reach an academic audience, we will publish the results in relevant high-impact social science and public health journals. Results will also be presented on the study website, which will link to publications and outputs, as well as being fed into the Antimicrobials in Society Portal (<http://www.antimicrobialsinsociety.org/>); a website that specialises in disseminating social science research to funders, scientists and policy-makers.

## 5 ETHICAL CONSIDERATIONS

### 5.1 Harms and Benefits

The social science studies will be observational and thus do not pose harm to participants beyond those they are likely to encounter in their daily lives. That said, the qualitative methods we employ will involve interactions with participants that may be both prolonged and affective (Bernard 2011). Thus, we take ethics as relational process, which means we will be open and sensitive to the diverse participants and circumstances we encounter during our research. While participant observation and interviews may raise and touch on potentially difficult or emotional topics, the extended nature of engagement of our research, means we will be able to develop an acute sensibility to these issues and contextually and culturally appropriate responses, including also rephrasing or dropping questions and disengagement where necessary. This echoes the centrality of care to both our research focus and the process of how we conduct the research itself.

In order to prevent any form of ‘undue inducement’ in to our study (Ballantyne 2008; Sachs 2011), we will not provide direct financial or material benefits to participants, nor coerce them into participating. Rather we will ensure participants understand the voluntary nature of their participation in the studies and no harm will occur to them if they choose not to respond to particular questions, refuse to participate or withdraw from the studies at any point. Where they travel for purposes of participation, reimbursements and refreshments or meals, will be provided where appropriate. More broadly, we will ensure that participants understand that this ethnographic study and the FIEBRE study aim to contribute to improved policy and guidelines for the management of febrile illness and antimicrobial use that will benefit people in Zimbabwe.

The approach we will take is in accordance with the ethical guideline for the Association for Social Anthropologists of the UK and the Commonwealth (2011). As researchers, we will follow the principles set out in this ethical guideline throughout the preparation for and during research, analysis and writing up processes. In addition, relevant local ethical codes will be followed. This protocol will be submitted for approval to relevant local research ethics committees upon attaining approval from the LSHTM (or LSTM) human subject research ethics committee. Specifically, the protocol will be submitted to both the

Biomedical Research and Training Institute (BRTI) Institutional Review Board and Medical Research Council Zimbabwe (MRCZ).

## **5.2 Informed Consent**

At the time of enrolment, written informed consent forms and information sheets on study participation will be provided for each adult participant (over the age of majority according to local regulations in Zimbabwe, that is, 18 years of age) and each emancipated minor participant (as defined according to local regulations in Zimbabwe) or parent/guardian (for adolescent participants). Assent forms and information sheets will be provided for adolescents (as locally defined in Zimbabwe, that is, 13-17 years of age) along with their parent/guardian. Where applicable, the consent forms will include consent for audio recordings, the use of direct quotes (see 5.3), and photography.

The consent process will be performed by a member of the study team with potential study participants and with parents/guardians. For the stakeholder interviews, the interview will take place with consenting participants immediately following the consent process. For the ethnographic fieldwork component of the study, the staff member performing the consent process will discuss with potential participants the timeframes during which participant-observation and interviews might be performed, which will be subject to ongoing dialogue during the research process. For residents, consent to perform the medicines survey (section 4.4.1) will be requested as part of the same consent process as for interviews and participant-observation.

We will ask permission for interviews to be tape recorded and transcribed. However, if participants do not feel comfortable with the use of a digital encrypted recorder, detailed notes of the interview will be taken instead, including verbatim quotes where possible. We will ensure that participants understand that the identities of all participants will be protected through the use of identification numbers or pseudonyms in both transcriptions and in all subsequent references to interview proceedings including written accounts.

Potential participants and/or their parents/guardians will have the opportunity to ask questions and discuss details of the study with study staff, and will be free to ask further questions at any time during or after completion of the study activities. It will be made clear

during the consent process that participants may withdraw or interrupt their participation in the study at any point and that data relating to them will not be used.

Informed consent will be conducted in the potential participant/parent/guardian's preferred language. Consent forms, approved by all relevant ethical review boards, will be available in English and in the local language. If an adult or parent/guardian consents to participation but is unable to write, oral consent or an impartial witness will attend the consent process and provide their signature and the participant's fingerprint will be substituted for a signature, as contextually appropriate. For participants under the age of adulthood, country-specific guidelines on the inclusion of minors in research (including guidelines related to consent from a parent or guardian, and/or emancipated minors) will be followed. In particular, in addition to parent/guardian consent, assent will be sought for participants under the adult age, according to local regulations and recommendations.

At enrolment, each participant's contact information (telephone number and place of residence) will be recorded. This information will be kept in locked and/or password protected files, separately from study data files, for the duration of the data collection period so that they can be contacted for participant-observation activities and/or follow-up interviews.

### **5.3 Privacy and Confidentiality**

As discussed in section 5.1 the intensive nature of qualitative methods, particularly participant-observation, may raise concerns about participants' right to privacy, and thus we will put detailed measures in place to ensure their privacy is respected and maintained. All interviews (both key informant interviews and in-depth interviews) will be conducted in a private space where conversations cannot be overheard. Where participant-observation takes place in public spaces, limitations will be made very clear to participants at the outset in order that they can make informed choices as and when to share information. Study researchers will ensure participants are aware that only the research team will have access to the raw data (including both raw data and data uploaded to ODK) and any data shared beyond the group will be subject to approval from the study team on a case-by-case basis. Because some of the medicines we photograph may have been obtained illicitly (see section 4.5), we will be careful to convey that photographs will made be anonymous by

removing any potential identifiers, so that they cannot be connected back to participants. Similar measures, will be taken for photos of buildings and other infrastructure. Where photos include people, they will be either done in a fashion to ensure they are not identifiable or they will be altered (e.g. faces blurred or blacked out). In the case that photos include people's faces, care will be taken to discuss and consider the contexts in which the photos will be used and published, to avoid any undue consequences. This process will be described to participants at the point of consent.

In all publications and other research outputs from this study, all participants, healthcare facilities and local area markets, shops, churches and pharmacies will be assigned pseudonyms. In the case of public health practitioners, policy makers and scientists – individuals with more unique and potentially identifiable roles – it will be made clear during the consent process that there may be limits to their anonymity in research outputs. We will also offer them the option for us not to use direct quotes from interviews. With this information, they can make an informed decision as to whether to participate and whether to allow us to use direct quotes from their interviews.

**6 PROJECT TIMELINE**

	2018				2019				2020				2021
	JFM	AMJ	JAS	OND	JFM	AMJ	JAS	OND	JFM	AMJ	JAS	OND	JFM
Phase 1: Fieldwork Preparation													
Pilot ethnographic fieldwork and access for fieldwork													
Stakeholder engagement													
Assemble Medicines (antibiotics) library													
Training research assistants													
Access and permissions													
Literature review													
Phase 2: Conducting Fieldwork													
Antibiotics survey in homes													
Prescriber logs													
Ethnographic fieldwork and key informant interviews													
Stakeholder interviews													
Feedback discussions with participants on all findings													
Phase 3: Analysis and Dissemination													
Analysis of antibiotic survey in homes													
PhD upgrading end of June in London													
Revisions to upgrading													
Analysis of prescriber logs													
Analysis of ethnographic FW													





## 7 POSSIBLE PROBLEMS AND SOLUTIONS

Potential problem	Proposed solution
Delayed start of study activities due to delays in ethics approvals and logistical impediments	<ol style="list-style-type: none"> <li>1) Work with relevant personnel/agencies, local and national authorities as needed to minimize impact on project timelines</li> <li>2) If necessary discuss with DFID re: adjustment of deliverables timeline</li> </ol>
High rates of consent refusal, resistance from particular groups of participants, or slower than expected enrolment	<ol style="list-style-type: none"> <li>1) Work with local community leaders, health facility staff and other relevant personnel to identify and address possible causes</li> <li>2) Increase number of health centre and community sites (within the same geographical area)</li> </ol>
Ethical issues emerging in the course of fieldwork, e.g. participants uncomfortable with questions or research aims	<ol style="list-style-type: none"> <li>1) Work with local community leaders, health facility staff and affected participants to identify and address possible causes</li> <li>2) Exclude participants who do not wish to continue and identify other potential participants.</li> </ol>
Protocol violations	<ol style="list-style-type: none"> <li>1) Report to appropriate ethical committee and EOC</li> <li>2) Prevention as appropriate through protocol amendment and/or personnel training</li> </ol>

## 8 POSSIBLE CONSTRAINTS

The strengths of qualitative methods are also their limitations. Qualitative methods and particularly when applied from an anthropological perspective prioritise depth of understanding over representativeness and generality. With our sample aiming to include individuals with a particular role in fever case management, our findings will be limited in the extent to which they are able to make statements that can be generalised over populations. With that said, the study has considerable breadth and depth, including three countries, allowing us to produce insights that will be a valuable complement to the findings of the FIEBRE clinical and laboratory protocols.

**9 SPONSOR**

London School of Hygiene & Tropical Medicine (LSHTM) will act as the main sponsor for this study. Delegated responsibilities will be assigned locally.

**10 FUNDING**

The UK Department for International Development (DFID) are funding this study through a grant to LSHTM. Activities at study sites and reference laboratories are funded through contracts established between LSHTM and collaborating institutions.

**11 AUDITS AND INSPECTIONS**

The study may be subject to audit by the London School of Hygiene & Tropical Medicine under their remit as sponsor, the Study Coordination Centre and other regulatory bodies to ensure adherence to relevant ethical guidelines.

## **12 APPENDIXES**

### **12.1 Appendix 1 - Interview Topic Guides**

Because of the iterative nature of ethnographic research, the interviews that we conduct with participants will be open-ended and iterative, limiting the extent to which the content and direction of interviews can be fully anticipated. However, the topic guides below indicate the broad topics that will be discussed with each group of participants, which will be refined in response to new themes and findings that emerge.

#### **Interviews with Community Members (Residents and Fever Patients)**

##### **(1) Life and Livelihoods**

- Occupation and income
- Household and neighbourhood demographics
- Kin networks
- Community and religion

##### **(2) Illnesses and Medicines**

- Common illnesses experienced (or currently experiencing)
- Fever classifications
- Commonly used remedies/medicines at home
- Medicines accessibility and costs

##### **(3) Healthcare seeking**

- Use of formal and informal providers
- Order in which providers are consulted
- Time taken before healthcare seeking
- Healthcare accessibility
- Costs associated with healthcare seeking

##### **(4) Drug Resistance**

- Which medicines work/don't work
- Perceptions and experiences of drug resistance

- Ideas about preserving medicines efficacy

### **Interviews with Providers (Clinic/hospital staff, pharmacists, healers, drug shop vendors)**

#### (1) Work life and routines

- Roles and responsibilities
- Daily routines
- Structure of organisation/group
- Relations with other providers

#### (2) Fever Management

- Fever classifications
- Diagnostics/causes of fever
- Provision of medicines and therapies for fever
- Onward referral

#### (3) Care Relationships

- Patient/client needs and expectations
- Meanings of 'care'
- Adherence
- Threats and limits to good care
- Resource constraints

#### (4) Antimicrobial use and resistance

- Antimicrobial use practices
- Resource constraints and medicines access
- Availability in formal and informal sectors
- Resistance patterns
- Causes of and solutions to resistance
- Excess vs. access

### **In-Depth Interviews (Public Health practitioners, policy makers, scientists)**

#### (1) Work life and routines

- Roles and responsibilities
- Daily routines
- Structure of their organisation/group
- Global networks and connections

(2) Health Priorities in Zimbabwe

- Epidemiological and socioeconomic situation
- Structure and resourcing of health system
- Skills and human resources
- Funding flows
- Key priorities and knowledge gaps

(3) Fever case management

- Differential diagnosis
- Current guidelines and recommendations
- Global and local priorities
- Antimicrobials used for fever

(4) Antimicrobial use and resistance

- Markets and regulation
- Availability in formal and informal sectors
- Causes of resistance
- Excess vs. access
- Global and local discourses of antimicrobial use/resistance
- Next steps for addressing resistance

**13 REFERENCES**

- Arkovitz, M.S. and M. Manley. (1990). Specialization and referral among the N'anga (traditional healers) of Zimbabwe. *Tropical Doctor* 20, 109-10.
- Amexo M, Tolhurst R, Barnish G, Bates I. (2004). Malaria misdiagnosis: effects on the poor and vulnerable. *Lancet*, 364, 1896-8.
- Association of Social Anthropologists of the UK and the Commonwealth (ASA). (2011). Ethical Guidelines for Good Research Practice. <https://www.theasa.org/ethics.shtml>
- Baer et al. 1997;
- [Ballantyne, Angela. \(2008\).](#) Benefits to research subjects in international trials: do they reduce exploitation or increase undue inducement? *Developing world bioethics*, 8(3), 178-191.
- Becker, Marshall H. (1974). The Health Belief Model and Personal Health Behavior. *Health Education Monographs*, 2, 324-508.
- Becker, Marshall H. (1988). AIDS and Behavior Change. *Public Health Reviews* 16, 1-11
- Beisel, U., Umlauf, R., Hutchinson, E., & Chandler, C. I. (2016). The complexities of simple technologies: re-imagining the role of rapid diagnostic tests in malaria control efforts. *Malar J*, 15(1), 64.
- Bernard, H.R., (2011). *Research Methods in Anthropology: Qualitative and Quantitative Approaches* Fifth., Lanham, Maryland: Altamira Press.
- Biehl, J. (2007). Pharmaceuticalization: AIDS Treatment and Global Health Politics. *Medical Anthropology Quarterly*, 80(4), 1083-1026.  
<http://joaobiehl.net/wp-content/uploads/2009/07/Biehl-Pharmaceuticalization.pdf>
- Bourgeault, I., R. Dingwall and Ray de Vries. (2010). *The Sage Handbook of Qualitative Methods in Health Research*. London: Sage.
- Bowker, G. C., & Star, S. L. (2000). *Sorting Things Out. Classification and Its Consequences*. Cambridge Massachusetts: MIT Press.

- Cabral, C., Lucas, P. J., Ingram, J., Hay, A. D., & Horwood, J. (2015). "It's safer to ..." parent consulting and clinician antibiotic prescribing decisions for children with respiratory tract infections: An analysis across four qualitative studies. *Social Science & Medicine*, 136–137, 156-164.
- Canguillhem, Georges. (1962). Monstrosity and the Monstrous. *Diogenes* 10, 27-42.
- Chandler, C., Eleanor Hutchinson, and Coll Hutchison (2016). Addressing Antimicrobials through Social Theory: An Anthropologically Oriented Report.  
<http://app.lshtm.ac.uk/files/2016/11/LSHTMAnthroAMR-2016.pdf>
- Chandler, C. I., et al. (2017). The impact of an intervention to introduce malaria rapid diagnostic tests on fever case management in a high transmission setting in Uganda: A mixed-methods cluster-randomized trial (PRIME). *PLoS One* 12(3), e0170998.
- Clark-Ibanez, Marisol. 2004. Framing the Social World with Photo Elicitation Interviews. *American Behavioural Scientist* 47(12).
- Connell, R. (2012). Gender, health and theory: conceptualizing the issue, in local and world perspective. *Social science & medicine*, 74(11), 1675-1683.
- Conrad, Peter. (1992). Medicalization and Social Control. *Annual Review of Sociology*. 18, 209-32
- Evans-Pritchard, E.E. (1937). *Witchcraft, Oracles and Magic among the Azandi*. Gloucestershire: Clarendon Press.
- Fairclough, N. (2003). *Analysing discourse: textual analysis for social research*. Abingdon, UK: Routledge.
- Feierman, Steven. (1981). Therapy as a System-In-Action in Northeastern Tanzania. *Social Policy and Administration*. 15b, 353-360
- Foster, George and Barbara Andersen. (1978). *Medical Anthropology*. New York: John Wiley and Son.
- Geertz, C., 1973. *The Interpretation of Cultures: Selected Essays*, New York: Basic Books Inc.



- Good, Byron J. (1994). *Medicine, Rationality, and Experience*. Cambridge: Cambridge University Press.
- Hankivsky, O. (2012). Women's health, men's health, and gender and health: Implications of intersectionality. *Social science & medicine*, 74(11), 1712-1720.
- Haraway, D. J. (2008). *When species meet* (Vol. 224): U of Minnesota Press.
- Harper, Douglas. (2002). Talking about pictures: A case for photo elicitation. *Visual Studies*, 17(1), 13-26.
- Helmreich, Stefan. (2009). *Alien ocean: Anthropological voyages in microbial seas*. California: University of California Press
- Hopkins, H., et al. (2017). Impact of introduction of rapid diagnostic tests for malaria on antibiotic prescribing: analysis of observational and randomised studies in public and private healthcare settings, *BMJ*, 356, j1054.
- Hutchinson, Eleanor, et al. (2014). 'It puts life in us and we feel big': shifts in the local health care system during the introduction of rapid diagnostic tests for malaria into drug shops in Uganda. *Critical Public Health*, 1-15.
- Hutchinson, Eleanor, et al. (2015). Bringing the state into the clinic? Incorporating the rapid diagnostic test for malaria into routine practice in Tanzanian primary healthcare facilities. *Global Public Health*:1-15.
- Janes, Craig and Kitty K. Corbett. 2009. Anthropology and Global Health. *Annual Review of Anthropology*, 38, 168-183
- Jasovsky, D., Littmann, J., Zorzet, A., & Cars, O. (2016). *Antimicrobial Resistance - A Threat to the World's Sustainable Development* Development Dialogue Paper no.16 Dag Hammarskjöld Foundation, Uppsala.
- Landecker, H. (2015). Antibiotic resistance and the biology of history. *Body & Society*, 1357034X14561341.

- Laxminarayan R, Matsoso P, Pant S et al. (2016). Access to effective antimicrobials: a worldwide challenge. *Lancet*, 387, 168–75.
- Lowe, C. (2010). Viral clouds: becoming H5N1 in Indonesia. *Cultural Anthropology*, 25(4), 625-649.
- Mol, A. (2008). *The Logic of Care. Health and the problem of patient choice*. London: Routledge.
- Moore, H. L. (1988). *Feminism and anthropology*. Minnesota: University of Minnesota Press.
- Morgan D.J., Okeke I.N., Laxminarayan R., Perencevich E.N., Weisenberg S. (2011). Non-prescription antimicrobial use worldwide: A systematic review. *Lancet Infect Dis.*, 11, 692–701.
- Nichter, Mark. (1988). From *aralu* to ORS: Singhalese Perceptions of Digestion, Diarrhea, and Dehydration. *Social Science and Medicine* 27, 39-52
- Nichter, Mark. (2001). Risk, Vulnerability, and Harm Reduction: Preventing STIs in Southeast Asia by Antibiotic Prophylaxis, a Misguided Practice. In Carla Makhlof Obermeyer (Ed.), *Cultural Perspectives on Reproductive Health*. Oxford: Oxford University Press.
- Ocan, Moses, Obuku, Ekwaro A. Bwanga, Freddie et al. (2015) Household antimicrobial self-medication: a systematic review and meta-analysis of the burden, risk factors and outcomes in developing countries. *BMC Public Health*, 15:742.
- Packard, R.M. (2016). *A history of global health: interventions into the lives of other peoples*, Baltimore: Johns Hopkins University Press.
- Paredes, Patricia, Manuela de la Peña, Enrique Flores-Guerra, Judith Diaz, and James Trostle. (1996). "Factors Influencing Physicians' Prescribing Behaviour in the Treatment of Childhood Diarrhoea: Knowledge May Not Be the Clue." *Social Science & Medicine*, 42(8), 1141–53.
- Parsons, T. (1951). *The Social System*. London: Routledge & Kegan Paul Ltd

- Paxson, H. (2012). *The life of cheese: Crafting food and value in America* (Vol. 41): Univ of California Press
- Podolsky, S. H. (2015). *The Antibiotic Era: Reform, Resistance, and the Pursuit of a Rational Therapeutics*. Baltimore: Johns Hopkins University Press.
- Poole, Robert. (2000). *Negotiating a Good Death: Euthanasia in the Netherlands*. Binghamton, NT: Haworth Press, Inc.
- Rowe, A. K. (2015). *Health Care Provider Performance Review In Presentation for the Institute of Medicine* Washington DC.
- Sachs, Benjamin. (2011). Going from principles to rules in research ethics. *Bioethics*, 25(1), 9-25.
- Simmons, David. (2012). *Modernizing Medicine in Zimbabwe: HIV/AIDS and Traditional Healers*. Nashville: Vanderbilt University Press.
- Singer M., Clair S. (2003). Syndemics and public health: reconceptualizing disease in bio-social context. *Medical Anthropology Quarterly*, 17, 423–41
- Sobo, E.J. (2009). *Culture and Meaning in Health Services Research*. Walnut Creek, CA: Left Coast Press.
- Sosa, Aníbal de J., Denis K. Byarugaba, Carlos F. Amábile-Cuevas, Po-Ren Hsueh, Samuel Kariuki, and Iruka N. Okeke, eds. (2010). *Antimicrobial Resistance in Developing Countries*. New York: Springer.
- Van der Geest, S., & Whyte, S. R. (1989). The Charm of Medicines: Metaphors and Metonyms. *Medical Anthropology Quarterly*, 3(4), 345-367.
- Whyte, S. R., Van der Geest, S., & Hardon, A. (2002). *Social Lives of Medicines*. Cambridge: Cambridge University Press
- World Health Organization. (2014). *Integrated Management of Childhood Illnesses (IMCI) chart booklet*. 2014. 978 92 4 150682 3.  
[http://www.who.int/maternal\\_child\\_adolescent/documents/IMCI\\_chartbooklet/en/](http://www.who.int/maternal_child_adolescent/documents/IMCI_chartbooklet/en/)

- World Health Organization. (2009). Integrated management of adolescent and adult illness (IMAI): interim guidelines for first-level facility health workers at health centre and district outpatient clinic: acute care. 2009. 978 92 4 159787 6.  
[http://www.who.int/hiv/pub/imai/primary\\_acute/en/](http://www.who.int/hiv/pub/imai/primary_acute/en/)
- World Health Organisation. (2014). Antimicrobial resistance: Global Report on Surveillance. *Bulletin of the World Health Organization*, 61(3), 383-394  
<http://www.ncbi.nlm.nih.gov/pubmed/22247201%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2536104&tool=pmcentrez&rendertype=abstract>
- Yates-Doerr, Emily. (2017). "Counting bodies? On future engagements with science studies in medical anthropology." *Anthropology & medicine* 24.2 (2017): 142-158.
- Yoder, P. Stanley. (1995). Ethnomedical Knowledge of Diarrheal Disorders in Lubumbashi Swahili. *Medical Anthropology* 16:211-247.
- Yoder, P. Stanley. (1999) Negotiating Relevance: Belief, Knowledge, and Practice in International Health Projects. *Medical Anthropology Quarterly* 11(2), 131-146.
- Zellweger, M. Carrique-mas, J. Limmathurotsakul, D. et al. (2017). A current perspective on antimicrobial resistance in Southeast Asia. *Journal of antimicrobial chemotherapy*, 72 (11), 2963–297.
- Zimbabwe Antimicrobial Resistance Core Group. (2017). Situational Analysis on Antimicrobial Resistance in Zimbabwe.