

Antibiotic prescribing and resistance:

Views from low- and middle-income prescribing and dispensing professionals

Report to the World Health Organization,
researched and compiled by students and staff of
the Antimicrobial Resistance Centre at the London
School of Hygiene & Tropical Medicine



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Acknowledgements

This project was developed by the Antimicrobial Resistance Centre at the London School of Hygiene and Tropical Medicine (LSHTM) in 2017 and was funded by the World Health Organisation's Antimicrobial Resistance Secretariat. Additional funds for some student travel expenses were provided by LSHTM and the Royal Veterinary College (RVC).

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The authors, consisting of three LSHTM staff and nine students, are grateful to the following advisors and supporters of the project: the AMR Secretariat team in Geneva, particularly Liz Tayler, Karen Mah, Penelope Andrea and Marc Sprenger; project supervisors and administrative support based in London: Elizabeth Jackson, Jackie Cardwell and Nicola Lord; field based supervisors and local collaborators: Behzad Nadjm (Vietnam), Nasir Umar (Nigeria), Dr. Abhijit Chowdhury, Dr. Dipesh Das, Meenakshi Gautham, Sayak Manna, Dr. Partha Sarathi Mukherjee, Dr. Indranil Samanta (West Bengal), Nishi Ananth, Alakananda Bagchi, Dr. George, Ketevan Kandelaki, Subha Sundarmoorthy (Chennai), Ms. Barcelona, Ms. Sabijon, Ketevan Kandelaki, EMT team at WPRO (Philippines), Adamu Addissie, Tenaw Tadege, Gebremedhin Gebretekle (Ethiopia), Michael Callaghan, Dr. Imogen Clarke, Dr. Danny McLeron-Billows, Dr. Raj Rajarman, Kings Sierra Leone Partnership (Sierra Leone). We acknowledge with thanks all respondents in the studies for their time and engagement and for permitting their insights to be shared.

Citation: Maddy Pearson, Anne Doble, Rachel Glogowski, Stella Ibezim, Tom Lazenby, Ayda Haile-Redai, Nabila Shaikh, Ashley Treharne, Selin Yardakul, Rahel Yemanaberhan, Lucy Reynolds and Clare Chandler C.I.R. (2018) Antibiotic Prescribing and Resistance: Views from LMIC Prescribing and Dispensing Professionals. Report to World Health Organisation AMR Secretariat, available online at <http://www.who.int/antimicrobial-resistance/LSHTM-Antibiotic-Prescribing-LMIC-Prescribing-and-Dispensing-2017.pdf>

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Executive Summary

Antimicrobial resistance poses a threat to the future of human and animal health, compromising the treatment of basic infections and the capacity for routine medical procedures. Addressing prescribing and dispensing practice has been a focal point of strategies to decrease antimicrobial usage for many years, but implementers lack data on the current status of health care professionals' understanding and experience of antimicrobial resistance that could guide interventions.

This report draws together data from nine studies undertaken in April to August 2017 by Masters students at the London School of Hygiene & Tropical Medicine and the Royal Veterinary College. The students worked with 246 qualified health care professionals in six low and middle income country (LMIC) settings within India (3), Philippines (1), Vietnam (1), Sierra Leone (1), Nigeria (1), Ethiopia (2). The studies aimed to ascertain and situate awareness of AMR and knowledge of antibiotics within the lived experience of prescribing and dispensing across a range of LMIC settings. Qualitative methods were used including semi-structured interview and rapid ethnographic observation. Data analysis involved primary analysis by students who identified site-specific themes from the transcripts and their observations of the operational context, and secondary analysis of the 246 interview transcripts by researchers at the LSHTM to identify key themes emerging across field sites.

The following cross-site themes emerged:

- Health professionals had a higher level of knowledge surrounding antibiotics than expected.
- Health professionals had a greater awareness of AMR than expected, most often indicated through treatment failure rather than diagnostics.
- Health professionals' prescribing and dispensing practices responded to continued challenges of access to information on resistance patterns, access to next line antibiotics, access to diagnostics and access to patient medical records.
- Health professionals' prescribing and dispensing practices responded to concerns over the burden of infectious disease, attributed to poor infection control, sanitation, hygiene, nutrition and biosecurity.
- Health professionals reported prescribing in terms of the empirical weighing up of risks, on the one hand of not giving antibiotics, and on the other of *which* antibiotic to prescribe. Awareness of resistance, fake drugs and side effects of some types of drugs led to empirical tailoring of treatments.
- Health professionals' prescribing and dispensing practices responded in many cases to shortages of human resources coupled with high patient load.
- Health professionals across settings reported that medical or pharmaceutical representatives visited frequently and influenced their prescribing of antibiotics.
- Health professionals in the veterinary sector additionally reported problems with adhering to withdrawal periods in livestock.

Health professionals proposed their own solutions for addressing AMR, with a strong demand for more antibiotic medicines in order to respond to resistant infections; at the same time they asked for tighter regulations on the quality of those medicines and on the visits of representatives; there was a strong desire for a platform showing local patterns of resistance; and better infrastructure – in terms of medical records, human resources and basic hygiene inside and outside of health facilities.

These findings are limited to nine settings in six countries, most respondents were well qualified prescribers, dispensers and educators, and most study settings were urban or peri-urban. The period of time spent in each site was sufficient for a snap-shot assessment of the situation, but more in-depth understanding could be gleaned from longer term ethnographic work. A wider assessment of views and responses to AMR could be achieved through a questionnaire that builds on the findings in these studies, eliciting responses from across a larger number of health professionals and expanded range of settings. However, as a means through which to capture key aspects of the AMR awareness situation, this project demonstrates the value of rapid qualitative methods which could be implemented elsewhere.

The findings across these studies echo the calls from multilateral agencies for a holistic approach to addressing AMR. Contrary to the expectation of the need for more education to improve knowledge of AMR, this report finds that awareness of resistance amongst these health professionals – who were qualified prescribers and dispensers – was high. An important distinction can be made between *knowledge* of AMR and of prudent use of antibiotics, and *information* about, or needed to *address* AMR, which was lacking in terms of local patterns. Health professionals believed they could be more targeted about antibiotic treatment if they had access to this information. However, from our respondents' perspectives, the concerns over risks of non-treatment will remain while infrastructure to allow follow-up, to provide confidence in hygiene standards, and to ensure adequate time and investigation of each patient remains poor.

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Acronyms

ABR – Antibiotic resistance

AMR – Antimicrobial resistance

AMU – Antimicrobial usage

DGCA – Directorate General of Civil Aviation

FAO - Food and Agriculture Association

GAP – Global Action Plan

GLASS – Global Antimicrobial Surveillance System

HAI – Hospital acquired infection

INRUD – International Network on the Rational Use of Drugs

LMIC – Lower-middle income country

LSHTM – The London School of Hygiene and Tropical Medicine

MR – Medical representative

NAFDAC – National Agency for Food and Drug Administration and Control

NAP – National Action Plan

SAASP – South African Antimicrobial Stewardship Programme

SSI – Semi-structured interview

OIE – World Organization for Animal Health

OTC – Over the counter

UTI – Urinary Tract Infection

WHO - World Health Organization

Background

Antimicrobial resistance has been identified as one of the greatest threats to future human health ^{(1), (2)}, with an increasing number of resistant microbial strains reported each year across both human and animal populations in developed and developing countries ^{(3) (4)}. Policy makers, health organisations and research institutes have called for tighter control over their distribution and use in society ^{(5) (6)}, with an emphasis on front-line antibiotic prescribers and dispensers ⁽⁷⁾. While efforts have been sustained over many years to promote the ‘rational use of drugs’, for example through the WHO’s International Network on the Rational Use of Drugs programme (INRUD), the scale of antibiotic use appears to be escalating.

The joint effort of the WHO, OIE and FAO to define a Global Action Plan (GAP) led to five central objectives: the first was a priority on raising awareness about AMR, and the fourth was to optimise antimicrobial use in humans and animals. The WHO commissioned a survey of awareness amongst members of the public in 12 countries ⁽⁸⁾. Similar surveys amongst health care professionals in different countries are desired in order to provide a baseline assessment of awareness and to inform interventions that will address the GAP objectives of raising awareness and optimising use in different settings. The design of survey tools is challenging, especially if the key concepts to capture are difficult to define, and if the tools are to be adopted across different settings. Typically, survey design is improved through initial qualitative formative research. While there have been many qualitative studies that have explicated the rationales for antimicrobial use across different settings ^{(9), (10), (11)}, a focus on resistance and how understanding of resistance might be worked into prescribing decisions has not been at the fore of previous studies. Qualitative research that attempts to capture understandings of AMR and the context of prescribing is therefore relevant at this time, both to inform current discussions around awareness raising and optimal antibiotic use as well as to support the design of domains and questions for a survey tool.

Project Design

This report draws together data from nine student studies that aimed to ascertain and situate awareness of AMR and knowledge of antibiotics within the lived experience of prescribing and dispensing across different settings.

The project, developed by the Antimicrobial Resistance Centre at the London School of Hygiene and Tropical Medicine (LSHTM) with financial support from the World Health Organisation’s AMR Secretariat, included nine qualitative research studies across six LMICs covering India ⁽³⁾, Philippines ⁽¹⁾, Vietnam ⁽¹⁾, Sierra Leone ⁽¹⁾, Nigeria ⁽¹⁾, Ethiopia ⁽²⁾.

Objectives

While studies were individually tailored to accommodate variations in institutional setting and roles regarding antibiotic prescribing and dispensing, all studies shared the same overall objectives:

- To develop a qualitative understanding of how antibiotic resistance is understood in LMIC settings
- To explore the variety of roles antibiotics play for medical and veterinary prescribing and dispensing professionals

Participants

Informed by a one-health approach, the studies included interviews with a wide spectrum of antibiotic prescribers, dispensers and educators in human medicine, and in two settings also in veterinary medicine.

Purposive sampling was used to identify medical professionals for interview, with local contacts made prior to each study providing assistance in recruiting initial study subjects. Further interviewees were identified by students themselves through chain-referral or snowball sampling. Students aimed to interview a diverse cohort of participants regarding professional profile, work-setting, age and gender. Strict sample size was not set prior to data collection due to the iterative grounded theory approach taken. Sample size was thus determined when saturation point was reached.

Table 1. Samples across study sites

| Country | Region | Focus of Antibiotic use | Number of participants |
|----------------|---------------|--------------------------------|-------------------------------|
| Vietnam | Hanoi | Human | 24 |
| Nigeria | Abuja | Human and animal | 24 |
| India | West Bengal | Animal | 8 |
| | West Bengal | Human | 19 |
| | Chennai | Human | 30 |
| Philippines | Manila | Human | 61 |
| Ethiopia | Addis Ababa | Human | 33 |
| | Addis Ababa | Human | 36 |
| Sierra Leone | Freetown | Human | 11 |

Ethics

The LSHTM and relevant institutional ethics boards in each country study granted ethical approval and consent was obtained from all 246 informants represented in the report. With permission, interviews were recorded and transcribed and where interviewees declined to be recorded, with agreement the interviewer took written notes.

Methods

The primary method of data collection was interviews, with some students also carrying out observations. The West Bengal veterinary focused study made considerable use of observational methods, following vets in practice over several days. Interviews largely followed a pre-determined set of topics, as shown in Table 2. Students used pre-prepared questions guided by these topics (see Appendix 1) and follow-up probes to allow for a flexible participant-led approach to data collection. For this reason, not all informants were asked the same questions or gave indications of their knowledge on all topics. The included statistics are representative of those who contributed information in a way deemed to sufficiently fit the answer criteria. Across the sample the inclusion rate for each question ranges from 65% to 98% thus while results cannot be considered wholly representative, they give a strong initial indication of knowledge patterns and are sufficient for the purposes of this first project and report which uses these statistics as a springboard to stimulate discussion, rather than as conclusive statements.

While interviews worked to ascertain ‘what’ individuals knew in relation to antibiotics and AMR, they remained conversational and fluid, allowing narratives of knowledge to remain embedded within wider realms of social practice (5). Interviewers paid close attention to practitioner’s reflections, exploring the social and environmental factors that present challenges when grappling with responsibility for AMR in LMIC settings (10).

Table 2. Summary of *a priori* interview topics

| | |
|---|---|
| 1. Professional profile | <ul style="list-style-type: none">▪ Position, institution, role in prescribing/dispensing |
| 2. Teaching on antibiotics/AMR | <ul style="list-style-type: none">▪ Involvement in teaching▪ Curriculum for covering antibiotics/AMR |
| 3. Knowledge on antibiotics | <ul style="list-style-type: none">▪ Purpose of antibiotics▪ Biological mechanisms▪ Sources of knowledge/guidance |
| 4. Awareness of AMR | <ul style="list-style-type: none">▪ Understandings of AMR▪ Role of diagnostics/empirical evidence▪ Information on local resistance patterns▪ Causes/drivers of AMR |
| 5. Prescribing/dispensing practice | <ul style="list-style-type: none">▪ Position of antibiotics in diagnostic process▪ Differences between training and everyday practice |
| 6. Source, influences and regulation | <ul style="list-style-type: none">▪ Sourcing of antibiotics▪ Influences including medical representatives▪ Regulation including government bodies, awareness/efficacy of current laws |
| 7. Current initiatives, future suggestions | <ul style="list-style-type: none">▪ Awareness of current campaigns, antimicrobial stewardship programmes▪ Suggestions for future interventions, dissemination of information and resources |

Data management and analysis

Where necessary a translator aided both at interview and transcription stage. Interviews were transcribed verbatim, by the students themselves where in their own language, or with support from transcribers and translators. Data were kept securely on password protected computers and transcripts were anonymised.

Data analysis for this report involved primary analysis by students who organised and coded transcripts to identify emerging themes, drawing on their insights from field observations. Secondary analysis of all 246 transcripts was later undertaken by staff at LSHTM to identify themes emerging across the field sites. After the data was qualitatively analysed and coded it was imported into Microsoft Excel to produce retrospectively-coded percentages of respondents who had reported a particular view.

A central contribution of the report for future interventions is the importance of keeping quantitative findings embedded in their qualitative contexts when devising, constructing and implementing workable AMR strategies.

Limitations

In terms of potential limitations, all sites were urban or peri-urban thus findings are not representative of rural settings. A number of informants were practising in city based teaching hospitals therefore knowledge regarding antibiotics and AMR as well as access to diagnostics and resistance profiles may not be reflective of prescribers and dispensers in more peripheral areas or in less established institutions. The project does not explore the role of gender demographics in antibiotic prescribing and dispensing, something future projects may wish to consider. Informants have not been demarcated as public or private practitioners; during interview these categories showed themselves to be inherently porous⁽⁹⁾ with most individuals straddling this divide in highly informal, contextually specific ways.

Results

The results draw out key findings and themes that emerged across the nine studies and discusses their implications. Findings and themes are supported where possible and appropriate by figures of the number of respondents reporting a particular perspective, as well as quotes from field interviews to provide complimentary depth and context. Emphases are added in bold to highlight key points for readers. Table 3 summarises key findings that emerged across the field sites. Appendix 2 provides further illustrative quotes.

Table 3. Key themes and findings

| | |
|---|---|
| Knowledge and awareness is high | <ul style="list-style-type: none"> ▪ Understanding of antibiotics and awareness of AMR are higher than we assumed ▪ Knowledge of antibiotics biological mechanisms and awareness of AMR does not predetermine behaviour regarding best-practice prescribing and dispensing |
| Access remains a central issue | <ul style="list-style-type: none"> ▪ Access to information is limited and often unsuitable to local contexts ▪ Patient encounters are fleeting and variable ▪ Access to reliable, affordable diagnostic testing is limited ▪ Access to antibiotics is highly variable |
| Infection control, sanitation and hygiene influence practice | <ul style="list-style-type: none"> ▪ Poor infection control in communities, farms, and hospital environments encourages prescribing and dispensing of antibiotics ▪ Poor sanitation, hygiene, nutrition and biosecurity encourages prescribing and dispensing of antibiotics |
| Empirical risk management in prescribing and dispensing | <ul style="list-style-type: none"> ▪ Fear of adverse outcomes for patients, legal sanctions and physical violence encourages prescribing and dispensing of antibiotics ▪ Origin of antibiotics drives opinion on efficacy: Western European antibiotics are favoured among prescribers, dispensers and lay people ▪ Side effects influence the selection of antibiotics and patient compliance |
| Human resource pressures: staff shortages and medical representatives | <ul style="list-style-type: none"> ▪ Volume of patients is large compared to volume of medical professionals ▪ Volume of patients attended to per day limits time for counselling on antibiotics ▪ Medical representatives interact with prescribers and dispensers on a daily basis and influence decisions on prescribing and dispensing ▪ Regulation is lax or ineffective |
| Withdrawal periods challenge AMR stewardship | <ul style="list-style-type: none"> ▪ Withdrawal periods are difficult to enforce due to lack of supervision, lack of economic reimbursement for farmers and lack of infrastructure for adequate waste disposal |

1: Knowledge and Awareness is High

1.1: Understanding of antibiotics is better than assumed

Prescribing is often termed of ‘irrational’ or ‘injudicious’ when not following guidelines (12), (13). This often leads to the assumption that practitioners lack adequate education on antibiotics (14). The studies compiled in this report, with qualified health professionals, suggest that while prescribing might not follow guidelines, prescribers do have a good knowledge of antibiotics and how they should be used in theory.

When asked how antibiotics work in the body, quantified in this report as naming and describing at least one mechanism of antibiotic action (see appendix 2:1.1), 79% (118/149) of the informants could do so. In terms of understanding what kind of infection antibiotics can effectively be used to treat, 93% (154/166) either proactively stated that antibiotics should be used for bacterial and not viral infections, or when probed with questions answered in the negative.

‘If they get the diseases caused by virus, we never use antibiotic for them, if the pathogen is bacteria, we have to use antibiotic.’ NHTD_Huy – Vietnam

Int: ‘But when you say they are used to treat infections, what kind of infections are you talking about? What kind of infections?’

D002 Nigeria: ‘for antibiotics?’

Int: Yes

D002: You know definitely it's bacteria, it's bacteria ... you are targeting bacteria so if you mean the target as per classification organisms, so it's bacteria, you are targeting

Int: okay

D002: Not viral, not viruses

1.2: Awareness of AMR

All but three participants 99% (238 of 241) for whom responses on this topic were available either proactively mentioned antimicrobial resistance or antibiotic resistance or recognised resistance as an issue when asked directly if they had heard of it. When further probed and asked how or what indicated this as an issue, AMR was overwhelmingly identified with or ‘seen’ as a manifestation of treatment failure. 92% (173 of 188 discussing this topic) reported incidents of failure, of seeing little or no relief of symptoms or witnessing recurring illness episodes despite recent courses of antibiotics and described this as indicative of resistance.

Int: What shows you there is a problem with AMR?

PR002 Chennai: ‘Usually we see patients not responding to medication, sometimes they even encounter death.’

‘During the treatment we will come to know, for example lower generation antibiotic we are giving and still infection is not clearing, symptoms are still not suppressed then we will know that it may be resistance.’ ED006 – Chennai

Int: have you seen much evidence of resistant infections, or?

28-3 Philippines: Yes

Int: can you give us an example?

28-3 Philippines: Well there's the use of ciprofloxacin. Sometimes it doesn't work with the recurrent UTI anymore.

'Usually what happens is when you are about to write him the same drug the patient has previously been on, he might say that he had taken that before and is not feeling better and prefers you to prescribe for him something else. So that is indicative of resistance.' D001 – Ethiopia (2)

'I saw a patient far back, in a community pharmacy I was superintending as a pharmacist, that told me she was feeling a scratch and whenever she takes doxycycline the scratch in her vagina will go off, but now even if she takes all the doxycycline that is available, the scratch persists. So, I said, "Well maybe if that is what you've been doing then it is probably that the doxycycline is no longer working in your system." So, I took her off. Even those (cases that) are not evidence based, but from history and discussion I think those are just drug resistant cases.' P001 – Sierra Leone

When asked what could be driving AMR 98% (214/219) could mention at least one facilitating factor. Drivers commonly mentioned included antibiotic usage for colds, coughs and fever, inadequate dosage, duration and frequency. Contextually specific issues were also raised as causing resistance, including inadequate hospital acquired infection (HAI) control, tendency to overuse broad-spectrum antibiotics, failure to de-escalate from broad to narrow-spectrum antibiotics after sensitivity testing (where available), over the counter (OTC) prescribing, counterfeits, poor biosecurity in farms and antibiotic enriched animal feed.

'These are the factors that cause resistance, not only indiscriminate prescription, inadequate dosing required to eliminate the bacteria encourages resistance as well.' D003 – Nigeria

'In terms of risk factors for AMR, I think if we use antibiotics with an inappropriate dose or inadequate duration.' Ba Vi_02 – Vietnam

'Drugs which are over the counter and those which come through in the form of contraband with poor quality create a problem. They expose you to toxicity, they contribute highly to the emergence of resistance.' D004 – Ethiopia (2)

'They (patients) take unnecessary antibiotics, for example for viral infections.' PR012 - Chennai

Although AMR was commonly identified through or as treatment failure, this was itself problematic in many of the field settings where concerns over counterfeits were high and patient follow up was lacking. In these situations informants could not be sure whether treatment failure was due to AMR, lack of patient compliance or counterfeit antibiotics. This lack of certainty influenced subsequent prescribing and dispensing practice. Where compliance was ruled out (by questioning the patient to be sure duration and frequency had been followed) and AMR was suspected, the antibiotic was usually changed for a higher-

generation antibiotic, or culture and sensitivity would be carried out, however lack of availability and affordability often made this a last resort. If treatment failure was attributed to a counterfeit antibiotic, a different brand of the same antibiotic was often used. In most cases it was this process of conversation, trial and error that established the cause of treatment failure, a process which could itself contribute to AMR.

Int: Have you seen anything...are there any examples where you suspect there could be resistance?

C8 – Sierra Leone: ‘Yes, that actually happens a lot, but I don’t want to clearly say it’s because of resistance. You know, in Africa, and in Sierra Leone in general, the efficacy of some of these drugs I cannot validate, so it’s possible I might be prescribing the right antibiotic, but the drug is not proper, it’s like a fake drug, so that will definitely affect the management of the patient. Most likely it might be there is resistance, but if the drug is not good it might not be resistance.’

‘So many patients are coming with not healing wounds, not healing the infection in the wound. So I am thinking that it is a case of resistance. So I think of another antibiotic.’ D012 – West Bengal

‘There are lots of times you don’t know which one is happening is it resistance? Is it counterfeit drugs? D003 – Nigeria

‘If there is treatment failure, resistance is one factor. Among those it’s one reason, but treatment failure could also be due to adherence issues. It may have failed because the patient didn’t adhere. If he adhered properly but treatment failed, we could come to say its resistance. But still the inadequate tests we have make that issue worse. So that means, for example if we are saying there is resistance without there being any, we are exposing another drug. We are using additional drugs and giving chance for the other drug to develop resistance. E001 – Ethiopia (1)

‘When you have a patient you prescribed (antibiotics) two three times and don’t respond and you may wonder (has) the patient developed resistance, if the patient had taken the medication appropriately?’ D003 – Ethiopia (2)

Taken together these insights suggests that where diagnostics are not routinely used, prescribers and dispensers ‘see’ or become ‘aware’ of AMR as a problem in the empirical sense of treatment failure, which can be complicated by contextual issues of counterfeits and lack of follow up, making it hard to ascertain the true cause of failure and leading to antibiotic practice that might exacerbate the problem of resistance.

1.3: Knowledge and awareness does not predetermine behaviour

While respondents were vocal about the appropriate use of antibiotics and knowledgeable about the drivers of resistance, the in-depth questioning method used revealed a notable discrepancy between knowledge and behaviour. While 93% (154/166) showed awareness either proactively or through probing, that treating viral infections with antibiotics would be ineffective (many claiming that prescribing for viral infections facilitate ABR) a number of

the same informants reported prescribing antibiotics for viral conditions in day-to-day practice:

'Even the patient (that) shows that he has viral pneumonia, we do prefer empirical antibiotic cover to prevent a bacterial pneumonia because once we are admitting patients we are exposing him to an array of cross-contaminating pathogens which are present in the ward due to previous ABR and presence of other infectious patients. Just to prevent a complication from growing into the patient and further complication we would provide them empirical antibiotic cover.' D021 – West Bengal

'I would rather over treat and risk the resistance because there is indoor cooking the environment is not good there is malnutrition they are source of the factors so I would rather give antibiotics knowing that respiratory tract infection which is viral because I have no other way to treat.' D008 – Ethiopia (2)

These insights echo previous observations that a simplistic relationship between knowledge and behaviour cannot be assumed, particularly in environments where extraneous variables such as hygiene, sanitation and restricted potential for follow up remain central to considerations in prescribing and dispensing antibiotics (15).

2: Access Remains a Central Issue

2.1: Access to information is limited and often unsuitable to local contexts

Informants existing knowledge and awareness of antibiotics and AMR fed directly into a desire for more relevant and timely information that would reflect local disease contexts and profiles. 87% (123/141) felt they did not have access to adequate data on local resistance patterns and many found guidelines both on antibiotic best practice or HAI control to be insufficient, unhelpful, difficult to implement in practice or outdated.

'I have downloaded the policy, I have the protocol in bound manner and distributed to all the doctors in my facility and I personally visit there to supervise whether the doctors are following that, but (it is) not possible for them to follow continuously, they are trying. You just go and see the situation of my ward.' D014 - West Bengal

'We don't get such information (on local resistance patterns). We ourselves follow our patients if they don't respond...I know this is very irregular, unorganized way of working but that is how it is.' D011 – Ethiopia (2)

'Some people still feel that this collaboration ... this One Health thing is more of a theoretical ... there are no practical implementation or guidelines on how to implement those things.' PM02 – Nigeria

While respondents said that diagnosis, prescribing and dispensing was made difficult because of the lack of available information and inadequate guidelines, 66% (88/134) of informants explicitly reported using internet based resources to mitigate such challenges

with Google, PubMed, Medscape and Facebook being mentioned as sources of information. A further 19% (25/134) reported using journals but did not specify whether these journals were accessed online or in print. This demonstrates a conscious commitment to good care despite constraints and points to the role the internet is already playing in the AMR strategy landscape (7) (16).

'Thank god for my android and these latest phones... the internet is the best way of sourcing for information.' P003 – Nigeria

'One doctor in Hue University had 4 video clips sharing his experience in antibiotic use on clinical cases which are very interesting. I love those lectures a lot.' Ba Trieu_01 – Vietnam

'On outpatient basis you don't really get much guidance on what you prescribe, or why you prescribe it. That's why, as I said, I use a lot of internet and Netscape stuff.' C3 – Sierra Leone

'To update we mostly look up Medscape because after diagnosis it gives at least (a) choice of antibiotics and quick to access.' D008 – Ethiopia (2)

2.2: Patient encounters are fleeting and variable

Access to information on antibiotic best practice and local resistance patterns has already been identified as a crucial part of the AMR strategy landscape (2); however, the issue of access to patients beyond the fleeting moment of a consultation has been less discussed. Informants across the study sites expressed difficulty in prescribing and dispensing due to transient encounters with patients both physically and administratively. There was a strong recognition that the moment of consultation with a prescriber or dispenser was only a part of a care-seeking path: patients or farmers may have sought care elsewhere before, including for OTC antibiotics (17), and may go elsewhere after. Follow-up was uncommon and medical records were lacking. The absence of information surrounding a patient's case and knowledge that follow-up (if any) would likely be with a different practitioner, affected the decision to prescribe or withhold antibiotics, as well as which type of antibiotic to select.

'You don't get the monopoly of handling a patient from beginning to end, so it gets to affect what you do, so that's why often times, you just take a broad-spectrum.' EDD01 – Nigeria

'Based on experience in the community, maybe because of the hygiene... ahem and maybe because of the compliance with ah.. medication, ah I tend to give antibiotics. Especially if I see that the mother doesn't have... the caregiver won't follow up with me.' AH28-1 – Philippines

'It's not like in London where you can even see where the patient has gone, here when they change doctors they disappear.' PR002 – Chennai

'Compliance is a big deal, a lot of patients are lost to follow-up because they come from remote areas to get government treatment at subsidized rate or free rates. So that is also there. There we know like on seeing patients you know like there would be patients who

would not be able to come for follow-ups. So for them you would try to do something definitive and then you will let them go after prescribing what you feel is the best option for them over a long time. So that part is there basically. It is a very you know kind of case to case basis it varies.' D022 – West Bengal

'The issue is the people are coming and presenting to us after starting antibiotics. **After taking antibiotics that they are getting from the medical shops. Only then are they coming to us.**' ED011 – Chennai

2.3: Access to reliable, affordable diagnostic testing is limited

While informants felt medical practice in urban areas was more advanced than rural areas in terms of both practitioner knowledge and provision for diagnosis and treatment, the utilisation of diagnostic testing across the study sites was dependent on multiple factors including affordability, accessibility, reliability and human resource availability. These variables contributed to minimal usage of diagnostics in day-to-day practice making the identification of bacterial infection and resistant bacterial strains more difficult and affecting prescribing and dispensing practice, often leading practitioners to opt for broad-spectrum antibiotics.

'Culture and sensitivity testing is quite a cost intensive idea for place like Bengal.' D022 – West Bengal

'In Vietnam the lab is not really strong. We're lucky that X hospital is in good condition. In the district hospitals the facility is not available. They have to base on CBC or CRP.' EN-NHTD – Vietnam

'One of the problems we are facing in Nigeria, we use the broad-spectrum antibiotics, and so ... it's not supposed to be like that, it's preferable, there's one article I read ... WHO standard, that you are supposed to use a narrow-spectrum antibiotics... go for a specific antibiotics that will target that agent, but **we go for broad-spectrum because these labs are not available.**' V007 – Nigeria

'Even if it is a private (institute), to have a microbiology lab is a very expensive thing. Mostly they don't have it. In the private set up as well as in the governmental set up microbiology is an issue. In terms of resources, you need a microbiologist, incubators, blood agar, a good analysis etc. it is usually big laboratories which have these things. In this institute for example there is no setup for that.' D001 – Ethiopia (2)

2.4: Access to antibiotics is highly variable

The project findings support recent works that problematise antibiotic practice not as a use-abuse dyad (18) but as an access-excess relationship (6),(19), (20), (21). Across all field sites, the unavailability and unaffordability of particular antibiotics (particularly 3rd and 4th generation) was juxtaposed to the cheap OTC availability of other antibiotics (amoxicillin was mentioned frequently). The bioavailability of antibiotics, counterfeits and the circulation of expired drugs or those rendered less effective through inadequate storage conditions concerned informants across the studies.

'Nowadays we encounter drug insufficiency frequently. We can't get some of the drugs at all... There is a delay in order because of currency and because of the long queue.' D004 – Ethiopia (1)

'You want to prescribe ceftriaxone, but there is no ceftriaxone in the hospital.' C6 – Sierra Leone

*'I think the system is corrupted a lot, **the system supply based on demand is weak.** This can be also contributing factor for drug resistance because not providing the right drug at the right disease condition is a problem.'* P008 – Ethiopia (1)

*'They are getting from the pharmacies, here they can get **directly if they go and ask the pharmacist for a throat infection, they will give amoxicillin.**'* ED011 – Chennai

'Now you have very expensive drugs and patients can't take those drugs, but those are the drugs that really the patient needs, but they prescribe an alternative which actually might not be very active for the condition and the organism becomes resistant.' P1 – Sierra Leone

'Sometimes expired drugs might be available in the market. Our system is prone to such availability of ineffective drugs in the market. Certain drugs are not imported by the government and legal importers...It is very difficult to assure the effectiveness of such drugs obtained from black market. Since the storage condition in case of black market is not according to the standard, the quality of the drug might be deteriorated.' E001 – Ethiopia (2)

'This is a problem all over India. For example we do welcome generic drugs because the cost is becoming less but at the same time generic drugs, there is a problem of consistent quality.... The problem with the generic drugs is that they need to pass the DGCA authorities, they have to document 80% bioavailability, not 100%.' ED009 – Chennai

3: Infection Control, Sanitation and Hygiene are Central to Prescribing, Dispensing and Usage

Across all field sites, the decision to prescribe, dispense and use antibiotics was inextricably linked to concerns over infection control, sanitation and hygiene across professional healthcare settings, communal living arrangements and livestock rearing. Many felt not enough resources were directed towards prevention and that the focus on treatment ignored the underlying structural, social and environmental causes of vulnerability to infection (22). Doctors and vets in particular highlighted the difficulties posed by poor HAI and sanitation for managing bacterial infection and the spread of ABR (23).

'I will not blame the doctors or the nurses that prescribe antibiotics, because the way... the type of life we live in Nigeria is different from the type of... the people in Europe live, like for example, filthiness is still part of our culture.' N002 – Nigeria

'How can you practice sterile techniques and good hygiene practices when you have patients lying on the floor?' AH30-01 – Philippines

'So what happens (is) that these bronchoscopes and these endoscopes they are not allowed sufficient time for disinfection, so there is high chance of cross transmission from one patient to another because bronchoscopy is often done for TB patients and non-TB patients as well.'
D016 – West Bengal

*'There is overcrowding which leads to cross contamination and cross infection. Emergency hospitals, many patients are stuck together; many attendants are in the same room so there is an overwhelming overcrowding of patients and attendants. **There is no proper isolation of infectious diseases**; for example you have to isolate a certain disease...like TB, pertussis, measles. **There are no proper isolation rooms with ventilation and air.**'* P009 – Ethiopia (1)

'When I entered the farm, the problem they had was fowl typhoid, and I anticipated this fowl typhoid a week up to before the arrival of the fowl typhoid, why? Because I saw a lot of rats in the house, and these rodents are reservoirs of this organism.' V003 – Nigeria

'We don't have facilities for the coordinated disposal of drugs in the country so... antibiotics are dumped in refuse dumps... rain water wash it down into the soil.' EDP01 – Nigeria

4: Empirical Risk Management in Prescribing and Dispensing

Health professionals reported prescribing in terms of the empirical weighing up of risks, on the one hand of not giving antibiotics, and on the other of *which* antibiotic to prescribe. Awareness of resistance, fake drugs and side effects of some types of drugs led to empirical tailoring of treatments.

4.1 Risks of neglecting to prescribe an antibiotic

In line with study findings across Europe, America and LMIC's (11) decisions to prescribe and dispense were often part of a risk management strategy in which it was seen as 'less risky' or 'safer to' (9) prescribe antibiotics than not. Prescribers described this most acutely in the case of paediatric patients as has been described elsewhere (24), especially from low socioeconomic backgrounds. Providing antibiotics was part of a wider rationale to mitigate risk and to defend oneself against accusations of neglect. Across the Indian study sites in particular, doctors reported cases of physical violence against clinicians perceived by families to have undertreated patients. Veterinarians also reported prescribing or dispensing antibiotics to reduce the chance of conflict or economic compensation expected by clients if livestock were lost. This situational context led informants to refer to antibiotic prescribing and dispensing as a form of 'defensive medicine'.

'Antibiotic prescription for paediatric populations is with empiric management because you don't want to wait for lab results for children because (they) are highly viable and we may lose the child.' ED003 – Ethiopia (1)

'If you cause the client to lose this animal, the client like, can take up a case against you and if you are so found guilty, you will be asked to pay off any damages.' V008 – Nigeria

'They're afraid of surgical site infections, and then if they don't give, they're afraid they'll get sued... so they get defensive... it becomes defensive medicine.' AH30-1 – Philippines

4.2 Risks of poor drug quality

In addition to the risks of neglecting to prescribe, health professionals described having to navigate risks of *which* antibiotic to prescribe. In the absence of information on patterns of resistance, quality of medicines and side effects, these characteristics had to be inferred. Like all commodities, antibiotics have cultural biographies (25) and social lives (26). Their perceived efficacy is an inseparable part of their identity and across the study sites the perception of an antibiotic's strength and potency was often linked to its country of origin (3). Many prescribers and dispensers associated European and Japanese antibiotics with strong quality control standards and regulation and favoured these over their Indian and Chinese counterparts, which were believed to be dubious in quality and poorly regulated. There was also a divide amongst practitioners over whether branded and innovator drugs were more effective than generics. While some informants were adamant that this was the case, others believed this to be a false perception based on MR promotion and media advertising. This finding poses interesting questions for antibiotic prescribing and dispensing, particular in LMIC settings where most prescriptions constitute out-of-pocket payments and where European branded or innovator drugs are notably more expensive than generics.

'I've prefer to use drugs from ... from Holland, from Europe, from Europe and some few instances, I use drugs from China but if I'm using them, I'm using them sceptically.' V008 – Nigeria

'We are not sure about the efficacy of generic brands because the brand names come from reputed companies like Cipla, Ranbaxy, but the generic drugs they come from obscure companies that we haven't heard the names of before.' D021 – West Bengal

'People feel that the cheaper the medicine probably the lesser its efficacy is.' D022 – West Bengal

'Sometimes we look at even country, there are some countries or ... that you know that there is high level of corruption and fakeness in that country, so you also look at ... if you know this drug is coming from this country that you know that lots of fake ones have been coming from there, you need to scrutinize the drugs.' P003 – Nigeria

'Most of it could be perception, it could well be perception. But the problem is this issue of quality, if no authority takes responsibility for this and gives me a 100% confirmed information in this country all I can do is try and prescribe a better brand, international brand or innovator drug if possible.' D011 – Ethiopia (2)

4.3 Risks of side effects

When weighing up risks of treatment options, respondents across the field studies voiced concerns about patient compliance in relation to side effects. Practitioners stated patients were likely to discontinue antibiotic courses if side effects were unpleasant or if they

interrupted daily work routines, with nausea and diarrhoea being the most commonly cited side effects affecting compliance. Aware that such discontinuation could lead to resistance, prescribers and dispensers often tried to mitigate this risk by selecting a different molecule with less harsh side effects or choosing the branded version of the same antibiotic (generics were often said to produce worse side effects than branded or innovator antibiotics). Other undesirable side effects such as teeth discolouration both prevented lay use of certain antibiotics and prevented some prescribers selecting these antibiotics for treatment.

'Take for example he will take ampiclox and nothing will happen, he will take it ingest it and he will be okay, but you, you will take ampiclox, and you will be fainting...it's not everybody that can take all drug, natures are different.' N002 – Nigeria

*'Some of the antibiotics are gastro irritant, nausea, vomiting, even when the patient is having fever, he is a bit nauseating. So if you give an antibiotic which has potential side effect of nausea and vomiting, then **it is better to avoid that antibiotic.**'* D011 – West Bengal

*'Tetracycline, nowadays, we don't prescribe it that often. You may find at the community health centres but I have not prescribed it neither in my work in the government hospital nor here at the private institute. **Because it has a lot of side effects, for example it results in teeth discoloration in children.**'* D002 – Ethiopia (2)

'It's always better for you to consider, oral route okay? it is safer in case of toxicity and side effects.' P003 – Nigeria

'If you keep giving and giving the patient will acquire side effects from the medication, not only resistance.' C4 – Sierra Leone

5: Human resource pressures: staff shortages and medical representatives

Across the study sites, human resource shortages combined with high volumes of patients were common. This affected the amount of time spent with patients; increased the likelihood of an antibiotic prescription and decreased the likelihood of counselling on optimum usage and potential for ABR⁽¹¹⁾. Human resource shortages also had an impact on HAI, especially where the families of patients filled gaps in hospital care, a common practice observed in the Vietnam study. Shortages of personnel put strain on prescribers and limited the time devoted to antimicrobial stewardship.

*'We don't have enough human resources, we can't do, even if we have all the correct procedure to care the patients, **we have not enough human resources, we can't comply all the steps in each procedure.**'* PHU-EN - Vietnam

*'It's overflowing with patients. **People lie on the floor actually, we call them floor admissions. It is actually a term, 'floor admission'*** D021 – West Bengal

'We have more or less 700 to 800 patients per day in OPD and only one doctor is there for them.' D014 – West Bengal

Medical representatives (MRs) were reported to play a significant role in prescribing and dispensing behaviour across study sites and were viewed in both a positive and negative light, a theme also documented in recent studies among other LMICs (27). The ethical sensitivity of this topic made some informants hesitant to report direct interaction with, or knowledge of representatives, however of those who answered, 95% (98/103) felt representatives influenced prescribing and dispensing. Legal restrictions on MR advertising and interaction was described as lax with daily encounters reported by doctors in West Bengal. Practitioners expressed anxiety in navigating relationships with MRs acknowledging that while they might provide information on new antibiotic developments, they were ultimately selling a product and often used bribery and financial incentives to encourage prescribers and dispensers to select particular antibiotics. This could have implications for resistance especially where later generation antibiotics were encouraged as a first option treatment.

'They try to come through relationships for example they may say "Let me take you out for lunch or dinner". There are seminars, medical seminars you go to. They may sponsor those and if you want to attend it's fine. So yeah, it's like that.' D011 – Ethiopia (2)

'Representatives motivate doctors to prescribe more antibiotics and more expensive ones, higher generation too. Before doctors just used to give first generation, amoxicillin but now nobody prescribes basic antibiotics.' PH002 - Chennai

'Then this corruption creeps in, like I am a medical company, I am giving you 10% profit, another company is giving you 8% profit, so you will always try to push my drug because you are getting more profit.' D011 – West Bengal

'If promoter comes and promotes one drug today it's something that we see that for certain number of days it's only that drug that gets prescribed.' P004 – Ethiopia (2)

'Over-zealous pharmaceutical marketing practices sometimes means ah.... putting the physician in a situation where he owes the pharmaceutical company a favour.' AH29-4 – Philippines

6: Withdrawal Periods Challenge AMR Stewardship

Despite studies that link antibiotic use in livestock to residues in consumer food products (4), (23) and evidence that AMU in animal husbandry and aquaculture far outweighs human usage (28) (29), its role in global drug resistant infections resistance remains understudied, including from a social science perspective (15). This study contained two sites with a focus on antibiotic use in animals, and explored the practical decision-making that goes into

prescribing and dispensing antibiotics for livestock; the importance, but difficulty of observing withdrawal periods, the potential impact of financial losses incurred by farmers and the necessary, but often lacking, provision of sanitary waste disposal for animal products deemed unfit for sale and consumption. Veterinarians across the two settings felt pressured to protect the efficacy of antibiotics and to reduce the potential for antibiotic residues in human consumables while simultaneously ensuring the economic survival of farmers and their families. The Nigerian respondents observed that these commitments were often contradictory and led to hard decisions in which behaviour often diverged from knowledge of best practice.

'You tell a farmer, destroy all the eggs because it is not fit for human consumption because of the trace of antibiotic residues, now if you tell such a farmer are you going to compensate the farmer? So those are some of the challenges we face and the farmers also face.' V008 – Nigeria

*'The farmer cannot afford to lose money, some of these drugs you cannot use without the farmer losing money, because if I administer a drug and it says that withdrawal period one week, **what will the farmer do with one week supply of eggs? Is he supposed to destroy them? Or is he supposed to do what? Give them away?** is there a way that he can use them without having to ... there is no way that he can use them, **if he decides to sell them, he is endangering public safety, but he has to find a way of disposing them, unfortunately we are not at that level of industrialization.**'* V001 – Nigeria

7: Suggestions from Health Professionals

Suggestions for improving AMR strategy and reducing ABR were made by educators prescribers and dispensers across the study sites. Their ideas demonstrate the importance of utilising multiple strategies in tandem as none of the suggestions stand in silo; they remain inextricably linked to each other and to the wider social, economic and environmental landscape. Table 4 lists the key suggestions that emerged across the field sites.

Table 4. Health professionals' suggestions for addressing AMR

| |
|---|
| 1. Improve access to essential antibiotics and strengthen OTC restrictions |
| 2. Tighten regulation of antibiotics and medical representatives |
| 3. Provide a platform dedicated to resistance patterns and engagement |
| 4. Computerise medical records and prescriptions |
| 5. Invest in human resources, infrastructure, nutrition, sanitation and biosecurity |
| 6. Make alternatives available: vaccines and probiotics |

7.1 Improve access to ‘essential’ antibiotics and strengthen OTC restrictions

Practitioners (particularly doctors and educators) stressed the importance of making essential antibiotics more accessible in terms of location, stock and price. Desired essential antibiotics included next line (better, stronger) drugs which would work when first line drugs were found to be ineffective. Ensuring consistent stock would positively affect affordability as during shortages the price of antibiotics was reported to rise significantly. Increasing the physical and financial availability of essential antibiotics across a wider range of healthcare settings was also proposed to reduce OTC purchasing of antibiotics. Procuring antibiotics OTC has been described as an understandably attractive option for many patients, not just for those in rural locations who lack the time and financial resources to travel to formal healthcare settings for medical care but increasingly for urban dwellers (particularly migrants) with precarious work contracts and no medical insurance (30). Informants in this study stressed that any efforts to restrict OTC prescribing and dispensing would have to address such issues in tandem since legally enforcing bans on OTC sales without addressing access could have detrimental effects on the health of vulnerable populations in both rural and urban locations, as noted elsewhere (6).

‘Even NAFDAC they come around once in a while, they are trying but they are not doing ... they need to do more about it, most especially at the importation level, that’s where the problem is, not here, because if the drugs are not coming in, the fake ones hmmm ... so err ... they are doing it but they need to do more, honestly, they need to do more, it’s not, it’s like maybe once in a year or twice that you’ll see them, they need to make it more frequent and they are ... a lot need to be done because a lot of non-pharmacists are opening premises.’
P003 – Nigeria

‘I recommend title regulations but before that you have to revisit the system again. I mean the whole system. That means the drug supply management system.’ D012 – Ethiopia (1)

7.2 Tighten regulation of antibiotics and medical representatives

Across the Indian and African studies, informants felt regulation of antibiotics to screen for counterfeits and to guarantee effectiveness (‘bioavailability’) was inadequate. Despite government initiatives such as the NAFDAC text message scheme in Nigeria and the red line strip on antibiotic packaging across India, informants felt that in reality these schemes were ineffective. Informants suggested more stringent regulations from the government; more frequent testing of antibiotics for bioavailability and wider dissemination of information on the findings as well as stronger border checks and harsher penalties for those involved in manufacturing and transporting counterfeits.

‘NAFDAC doesn’t have a good follow up system... to make sure that these companies are being ... producing the standard that it’s required. So mostly new drugs, they do it for a while, the drugs have good quality, after a while they just reduce the quality or they reduce the quantity of the active ingredient.’ P003 – Nigeria

'I will suggest, maybe recommend strongly that there has to be a strict regulation with respect to use of antibiotics in our poultries, in our livestock.' P002 – Nigeria

*'The Pharmacy Board is in charge of regulating all of those things. But again, **the border is so porous it's hard to control**. Like, people go everywhere. You can cross everywhere, and I'm told that if you pay a small fee anything passes. At the port it also happens...this is actually one of the major problems with antibiotic resistance in Sierra Leone. In this country...counterfeit drugs.'* C5 – Sierra Leone

Across all study sites, informants felt MRs needed to be better regulated or banned from interacting with front-line prescribers and dispensers. Those who used MRs as a main source of knowledge on new antibiotics stated that if they were to continue disseminating information to practitioners directly, a centralised medical body should first validate all material. In the Philippines and Ethiopia practitioners stated that existing laws forbidding MRs from directly promoting their products were not fully effective and needed to be both strengthened and enforced to curb persisting bribery.

'Currently it's being...ahem....being regulated, but not really followed...The ah...Mexico Law ...prohibits the, you know, sponsorship of pharmaceuticals for certain activities for the doctors, yeah... So it's being followed here, but not...you know....fully practised.' AH29-2 – Philippines

*'It is very controversial. **They may not advertise but** they usually do promotion. **Promotion is not forbidden**. Promotion has got a lot of branches. You could go and visit the factory, they give you samples, they lobby you. Sometimes, after the pharma representative leaves, you may tend to prescribe that particular antibiotic he was promoting.'* D001 – Ethiopia (2)

7.3 Provide a platform dedicated to resistance patterns and engagement

The internet is playing an increasing role in global health strategy and comprises a relatively cheap means for disseminating information (7). Informants across the studies suggested that local resistance patterns should be made available and delivered in an easily accessible format that practitioners could not just read but interact with, posting their own experiences, discoveries and questions. Many felt an internet forum with a repository of information on resistance patterns would be most useful and practical. Some suggested that short educational videos on social media platforms such as Facebook could be used to raise awareness of AMR among the public.

'We would like to get updated knowledge on antibiotic resistance. Secondly, we would like to have more training courses or experience sharing about antibiotic use.' Ba Trieu 01 – Vietnam

7.4 Computerise medical records and prescriptions

Several Informants suggested the computerising of medical records and prescriptions to prevent human error, in the Indian studies dispensers commented on the difficulties illegible handwritten doctor's prescriptions caused for dispensing practice. Informants

across the studies said any form of concrete medical record would make it easier to decide which antibiotic to prescribe and would facilitate more accurate and timely practice. A few informants said a more robust system was needed to track when prescriptions had been dispensed, preventing patients using the same paper prescription repeatedly.

'If the whole system was automated, and if all necessary information is fed to the computer, I think that might decrease the misuse of antibiotics.' D012 – Ethiopia (1)

7.5 Invest in human resources, infrastructure, nutrition, sanitation and biosecurity

All informants conveyed the critical need for investment in human resources, infrastructure, sanitation and general aspects of wellbeing such as nutrition. This would reduce the initial prevalence and burden of bacterial infection in both human and animal populations but would also allow for quicker response to infection and higher chance of recovery. It would also reduce the chance for cross-contamination within and across hospital, communal and farm settings – reducing the potential spread of resistant bacterial strains.

'Top priority should be to change the socioeconomic condition or the hygiene, like in India still the rural people go to the field for defecation, so there is so much high chances of contamination, so much high chances of infection.' D002 – West Bengal

'Good infection control, it needs a lot. The first is the infrastructure of the hospital, and the structure of the department. The second is the staff, we need to have enough staff, human resources, to care the patients.' Phu_EN – Vietnam

'The government sometimes invest too much on treatment but too little on infection control.' EN-NHTD 0X – Vietnam

7.6 Make alternatives available: vaccines and probiotics

Vaccination programmes could reduce the chance of contracting particular bacterial infections and thus can be utilised as a preventive strategy to reduce ABR (7), (13), (31). Veterinarians across the study sites suggested the use of vaccinations and probiotics as safer preventive measures to prophylactic antibiotic use. Veterinarians explained that vaccines and probiotics would not only reduce the potential for ABR but would be a workable strategy since they would not compromise the income of prescribers and dispensers, a crucial factor that stewardship interventions must consider.

'Part of the reason why people use antibiotics is no vaccine for chronic respiratory disease in poultry available in Nigeria, and it's a very important disease, if vaccines were available in the first place people wouldn't use antibiotics.' PM02 – Nigeria

'Most bacterial infection in poultry stems from GI system so if you can occupy those areas with beneficial bacteria then there is no need for antibiotics even as a preventive measure. This is what I see as the future of the practice.' PM02 – Nigeria

'There are other things I can sell that will make more margin than selling antibiotics, there are biosecurity products, like disinfectants that you can sell for the prevention of contamination of the environment you understand? You can sell vaccinations, there are alternatives.' PM02 – Nigeria

'I was not using... prescribing antibiotics, I was rather doing prophylaxis using probiotics.'
V001 - Nigeria

The ideas of vaccination or probiotics as alternatives to antibiotics were not raised by any of the human health professionals, although in West Bengal and Chennai health professionals did suggest vitamins and antihistamines as alternatives to antibiotics.

Discussion

These findings echo the calls from multilateral agencies for a holistic approach to addressing AMR. A key challenge facing countries committed to deliver National Action Plans on AMR is the content and delivery of awareness campaigns, as well as methods through which to optimise medicines use. The analysis presented here, representing nine study sites in six countries, suggests that information is essential but insufficient for prescribing practices to change. This report finds that awareness of resistance amongst participating health professionals – who were qualified prescribers and dispensers – was high. A range of other factors were described and observed to shape prescribing, with health professionals navigating a set of risks and uncertainties around treatment and non-treatment in challenging circumstances. Empirical case management included tailoring treatment according to previous experience and operational circumstances. Health professionals were acutely aware of high infection risk in and outside of health care facilities, the inadequacy of their capacity to diagnose each patient and to predict the most effective treatment with the least side effects. Ideas of treatment failure due to resistance mixed with experience of fake drugs, led to the inference of quality and efficacy through branding, drug origin, advice from medical representatives and personal experience. Respondents were able to identify numerous ways forward to improve prescribing – including information in conjunction with infrastructure to allow follow-up, good hygiene standards, and to ensure adequate time and investigation of each patient.

When considering approaches for behaviour change interventions, an important distinction may be made between attempting to increase *knowledge* of AMR and of prudent use of antibiotics, and increasing access to *information* needed to address AMR, in terms of local patterns of resistance, patient histories, quality and side effects of different medicines and so on. Health professionals believed they could be more targeted about antibiotic treatment if they had access to this information. However, practitioner's narratives also highlight other aspects that affect practice, illustrating the contingent nature of the knowledge–behaviour nexus ⁽¹⁵⁾ and emphasising that this relationship is not linear and predictable ⁽³²⁾. This is

amplified for antibiotic prescribing in resource constrained environments with high infection rates. In this study, awareness of treatment failure due to AMR was related to use of stronger doses and stronger – next line – antibiotics.

These findings are limited to nine settings in six countries, most respondents were well qualified prescribers, dispensers and educators, and most study settings were urban or peri-urban. The period of time spent in each site was sufficient for a snap-shot assessment of the situation, but more in-depth understanding could be gleaned from longer term ethnographic work. A wider assessment of views and responses to AMR could be achieved through a questionnaire that builds on the findings in these studies, eliciting responses from across a larger number of health professionals and expanded range of settings. However, as a means through which to capture key aspects of the AMR awareness situation, this project demonstrates the value of rapid qualitative methods which could be implemented elsewhere.

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Appendices

Appendix 1. Topic guides with selection of questions used in interview that produced important insights

Questions marked with an asterisk were considered particularly useful and are recommended for development in future questionnaires.

1. Profile

What is your professional background and current role?

Do you work in the public or private sector?

What is your role regarding antibiotic prescribing and dispensing?

2. Teaching

Do you cover the use of antibiotics/safe prescribing of antibiotics in your teaching? If so how much time is dedicated to this topic?

Are you involved in choosing and designing what you teach the students, or are you advised/following a curriculum? If so where does the curriculum come from and how often is it updated?

Is AMR on the syllabus? How much time is dedicated to AMR?

Do you think teaching on AMR and antibiotic prescribing is adequate? Why/why not?

3. Knowledge of antibiotics

How would you explain the purpose of antibiotics?

Where did you acquire your understanding of how antibiotics work and how to use them?

If you found yourself unsure what to do in relation to an antibiotic, who or what would you refer to?

*Do you follow guidelines? How do you access guidelines? Who has produced these guidelines and are they relevant to your day to day practice? Where can I find them? Are they free to access?

Do all antibiotics work in the same way?

Can you describe the basic mechanisms of antibiotics?

What kind of infections can antibiotics be used for?

What are the effects of antibiotics? When you give antibiotics, what are the consequences?
What are the outcomes you are expecting?

*What affects your choice of antibiotic?

*What conditions do people in this community take antibiotics for?

*For most of the patients that you see, would you say you just see them once, or do you see them often? Do they come back?

Is it common for pharmacists and clinicians (doctors/veterinarians) to discuss any issues with prescriptions between themselves?

How do you keep up to date with new developments in your field?

Do you ever refer to journals? Which ones?

Is there any opportunity for continuing medical education? Is this something you would be interested in?

4. Awareness of AMR

*Are you aware of any proof/evidence to support the existence of antibiotic resistance in people, animals, hospitals or communities?

How does antibiotic resistance develop?

When resistance exists in one species of bacteria, can it spread to different types of bacteria?

*What shows you that there is a problem with antibiotic resistance?

Do you think the issues of AMR you raised are a problem only in certain places or is it happening everywhere?

*Are there any particular diseases or antibiotics that you are worried about as far as antimicrobial resistance goes?

Are there some departments which are better at understanding the risks of AMR than other departments?

Is this (resistance) something you know about because of your line of work or is it something that is common knowledge?

*Do you have access to sufficient information on common resistant bacteria around the community where you practice?

Do you have access to local or regional, and national data on laboratory antibiotic resistance?

*Do you think your education gave you enough information on how resistance works and spreads?

*Do you think resistant infections are originating in the community or in the hospital?

*In your daily conversation with your colleagues, do you use those terminologies (superbug/abbreviations such as AMR/ABR/MDR) or do you just use antibiotic resistance?

5. Prescribing/Dispensing practice

Could you talk me through the process of diagnosis?

At what point do you prescribe/dispense antibiotics?

During your day to day practice, how do you and your colleagues decide what antibiotic to prescribe/dispense?

How do you decide the route to administer antibiotics and how do you make decisions about the dose?

*Which antibiotics do you commonly prescribe/dispense? Do you prefer any particular antibiotics over others – why?

*When do you prescribe broad spectrum and when do you prescribe narrow spectrum?

What do you tell your patients about when to terminate their course of antibiotic treatment?

What happens if treatment is stopped too early or too late?

What happens if there are interruptions in treatment?

*What do you do if a patient comes back and their symptoms have worsened?

What measures are prescribers/dispensers taking locally to limit antibiotic abuse?

Do you prescribe/dispense antibiotics for preventive or prophylactic reasons?

*Do you have lab facilities for culture and sensitivity and testing?

*How common is it to have culture and sensitivity test done? Or is it only in the case of repeated infection?

Are there any constraints with lab capabilities? Are you usually able to get those tests that you want?

Are there any differences between the way you were trained to use antibiotics and the way it is in actual practice? What do you think have caused these differences?

*Have you had any cases in which the drugs you wanted to prescribe were not available in your clinic? What did you do?

Have you ever altered your prescription for any reason?

Is there anything that is done within this institution to support clinicians without many years of experience of prescribing?

Is there any difference in practice between public and private medicine/hospitals/pharmacies/veterinary practice?

We have spoken to some people about something they call de-escalation or stepping down, so they go from broad spectrum to more specific antibiotics where they might go like a stronger antibiotic and after two or three days they go to a less strong one. Is this something which is done here?

6. Sources, influences and regulation

Where do you get your antibiotics from/the antibiotics you prescribe where are they sourced from?

What are fake drugs?/What are counterfeit drugs?/Have you had any experience with fake/counterfeit drugs?

Is there any governing body in your country that tests for drug quality?

When you prescribe for your patients, where do you ask them to go and get the prescription?

If the drugs are not available, what do you tell the patients?

Do pharmaceutical company representatives come to promote products amongst health professionals like you?

Information coming from pharmaceutical companies and their sales representatives, how useful is that for appropriate use of antibiotics? Or do they have an influence to the contrary?

Do you know what the law around such types of promotion is?

7. Current initiatives, future suggestions

Are you aware of any AMR awareness campaigns in your country?

Are you involved or is this institution involved in anything locally in terms of AMR awareness campaign?

*Is there any more information that you would like regarding local resistance patterns? Is there any documentation that you receive currently about local resistance patterns?

What sort of information would be most useful to you?

*How would you suggest that we make resources on AMR available ...commonly available for researchers, clinicians and other professionals?

How would you suggest the AMR problem be tackled?

Do you have any other questions or suggestions for us?

*In terms of reducing transmission like say in a hospital setting, in an ICU setting, what recommendations do you have? What do you think are the biggest reasons for these hospital transmissions?

Appendix 2. Additional quotes corresponding to sections of the report.

1.1

Int: Could you tell me briefly the mechanisms of action, for example for cephalosporins?

ED002 Chennai: Broadly we classify them as those acting on the cell wall of bacteria and those inhibiting the protein synthesis. Those working on the cell wall are the b-lactam antibiotics which include penicillin, cephalosporins and glycopeptide antibiotics like vancomycin. And those inhibiting protein synthesis are the aminoglycosides.

Int: Do you think that all kinds of antibiotics work with the same mechanisms? The way they affect the pathogens, is it the same?

HDC-02 Vietnam: No antibiotics are different. Some types are bacteriocidal and some are bacteriostatic. Their effects are different, not all are the same.'

2.1

'So you can see an antibiotic that is very good in BNF and then you prescribe and then it's not available in the country.' EDPO2 – Nigeria

'American Academy of Paediatrics says that the initial choice of antibiotics for UTI is a cephalosporin to start with. But we are not having much of oral antibiotic choices if we are going to treat well. Usual organism is E. coli, most of the E. coli we see is ESBL, not much oral antibiotic choices are there, that means if we need to start treatment empirically, not much choices are there.' PR007 - Chennai

2.2

'So.... By the time they consult with the doctor they have tried various antibiotics already.' AH28-3 – Philippines

'For example, when they come to us, we only have amoxicillin but they've already used the stronger drugs then our drugs do not provide any effectiveness, we need to prescribe other drugs.' EN-Ha Dong_03 – Vietnam

'Outpatient antibiotic prescription is rather haywire. Maybe not only here because you order a urine culture for an outpatient, they come from far away, maybe 30km, they may not come back. So what I do is for a first episode of lower urinary tract infection, I routinely don't do culture. I give them five days of empirical antibiotics.' ED009 – Chennai

'I am not sure whether the patient has had antibiotics for other ailments and especially in India what the common trend is that people start using antibiotics for something like as a common cold or a flu. So when I consider the resistance to antibiotics I don't know if whether the patient has generated antibiotic resistance due to previous dental infection or some other disease, it's very hard to quantify that basically.' D022 – West Bengal

'We ask questions, we have to ask questions from this patient and we ask her, which drug did you take? what's the make? what's the brand? when did you take it? how did you take it? where did you buy it? is the drug this, the drug that? we ask questions, that's where ... that's what will take us to know what happened.' N002 - Nigeria

2.3

'The number of lab tests available is so limited, and we have to spend some time waiting for the results.... So, I mostly base on the clinical symptoms.' EN-Ba Trieu 01 – Vietnam

'You don't have cultures to guide you... It's all negative but he's so very sick so you... you just keep on giving those... many antibiotics.' SL14-1 – Philippines

'Everything comes to the patient, the hospital doesn't pay anything for it, each and everything comes down to the patient's will. So even in a setup like this, patients really don't have that much money, we cannot really send cultures.' D017 – West Bengal

'The problem here is we don't have culture to culture every sample so you usually prescribe broad spectrum antibiotics.' D012 – Ethiopia (2)

'The only constraint is sometimes the labs are very expensive, so you send a patient to a lab and they tell the patient, "Your test costs 250,000 Le," the patient prefers to just go and get the drugs. Whether that is the condition or not, the patient still prefers the drug to the test. So, because of the cost, and sometimes delay. Some labs do delay with test results.' P1 – Sierra Leone

2.4

'After doing cultures, you can't even find the relevant drug... even if you can get the drugs, the clients have affordability problem.' P008 – Ethiopia (1)

'We go with what is available rather than what is the best drug to treat that infection.' D002 – Ethiopia (2)

'Some ABs in this international guideline are not available in Vietnam, we cannot use like that and we maybe use another.' Ngan_EN – Vietnam

'In Ethiopia especially, I don't think there is much availability. We may not be able to find what we want when we want it, especially on government facilities. And from private, it's so expensive to afford.' D003 – Ethiopia (1)

'For the common cold or cough there is no need to take antibiotics, but here people will take the antibiotics. That's the problem. Actually immediately people will take amoxicillin.' PH003 – Chennai

'So if I prescribe Augmentin for them, I think I'm not fair to that individual, bearing in mind that there are a lot of adulterated, fake Augmentin in circulation so I looked around, what are the best ones that doesn't (have) a lot of adulterated drugs and probably cheaper? I will look for the other one that's a bit cheaper and usually it is not being adulterated... usually pharmaceutical doesn't fake Seprin, so I will rather start with that Seprin.' D002 – Nigeria

'For central bidding, sometimes we do not have the drugs that we need, even if we have the money. Morbidity patterns and AMR patterns change every year, so even when we want to use appropriate antibiotics, we still don't have such. We have to use what we have.' FGD_SP – Vietnam

*'So the prescriptions that we write have 2 sections: **first I write the drug that would actually cure the problem of the animal, which would be slightly more expensive. I then insert an 'OR' and write the cheaper alternative to the drug.** As doctors, we put the recovery of the animal as our first priority, but since our clients can't use those drugs, we have to write a cheaper alternative as well.'* A007IDI – West Bengal (2)

'As this is a rural area and the patients that come to us are not financially backed well, we always try to prescribe the cheapest treatment.' A008IDI – West Bengal (2)

'It might be half strength, not full strength drugs, because there is no policy guiding the importation of drugs, medicines into the country, anybody who has money can go and import whether he is a professional or not.' D006 – Nigeria

'They sell them on the street, antibiotics. Amoxicillin, Tetracycline.' C5 – Sierra Leone

3.

The drug resistance transmission in the hospitals has many mechanisms. Over-crowdedness, many patients have to stay in one bed, too many patients in one room. So disinfection is very important, especially in ICU. The surgical ward is overloaded, no time for disinfection. EN-NHTD-0Y – Vietnam

'My department does not have the ventilation system. It means that we do not have enough space to isolate patients who have hospital acquired infections. Secondly when we can isolate these patients, we would have to equip many things like separated shoes and clothes. It is totally due to economic conditions so the implementation is still very difficult.' EN-SP-2 – Vietnam

4.2

'There is one company that produces Ciproxin, it's in England, Medrick, their drugs are very nice, once you use it, the sickness is gone.' N002 – Nigeria

'When you give the patient this drug and the patient is not responding, it's either the drug is fake or the patient has developed resistance, do you understand? but if it's a generic drug, okay definitely what will come to your mind is that it's because the active ingredient is not up to the actual dose.' P004 – Nigeria

'I like products from Japan and Germany. They are mostly effective.' D005 – Ethiopia (2)

4.3

'If you drag treatment for too long, you are unnecessarily exposing the patient to toxic substances, that you can do without, because they have their own side effects, so the longer you use the more likely you can see manifestation of side effects.' EDV01 – Nigeria

5.

'One promoter may enter the physicians room and he will tell him about a certain kind of antibiotics and the next patient definitely may get medications that were just promoted.' ED003 – Ethiopia (1)

'The major reason I assume juniors prescribers dare to prescribe last resort drugs is because of promoters influence on them.' ED001 – Ethiopia (2)

'Even us experienced doctors have been fooled (laughs) Because the way they present themselves they are very persuasive. After their visits, we sometimes go out and we talk amongst ourselves and say this particular drug is much better than the others. But you need to understand this is for business. The pharma companies are very tactical. When they produce one new drug, they get one famous scientist to do a clinical trial, produce a paper and present all over the world. They have this type of mechanism. And I think one should be aware.' D001 – Ethiopia (2)

'Promoters are assigned to different areas and they will go to their respective doctors and remind them as need be every 10-15 days' P015 – Ethiopia (2)

'Medical representatives are not for updating the doctors, they are there for their brand promotions.' D011 – West Bengal

'Before 2005, they (pharmaceutical company) worked directly with doctors. But now... Especially in my department, I did not allow. It means...if they want to present something, they will present with all department staff, we will all discuss together about the benefit of the medicine. If it is good, we will use it, if not, we will never use it. In my department, I don't know about in the other departments, but it is not allowed in my department. But when I went to other province or some Clinics, I still saw this. This is the management issue...' NHTD_Huy – Vietnam

'It is very controversial. They may not advertise but they usually do promotion. Promotion is not forbidden. Promotion has got a lot of branches. You could go and visit the factory, they give you samples, they lobby you. Sometimes, after the pharma representative leaves, you may tend to prescribe that particular antibiotic he was promoting. To a certain extent, it is useful because they give you up to date information and latest discoveries. In this country, continuing medical education is not really common.' D001 – Ethiopia (1)

6

'If you are using antibiotics growth promoters in the feed, there's no withdrawal period, because they'll eat that feed till you sell them, so it's the consumers that will be facing that problem.' V003 – Nigeria

'I have a client that I prescribe a drug for and he said doctor, the withdrawal period is 3 days in the egg, I was silent for over an hour, I cut the phone and was thinking, because it's a he's asking what to do, the withdrawal period is 3 days that means for 3 days, he shouldn't sell eggs, and that guy is producing over 100 crates of eggs per day.' V003 – Nigeria

'Withdrawal period is something that is bigger than an individual practitioner... it's something that err ... really, really is a public health (issue).' PM02 – Nigeria

7.1

'Somebody will just sit in a chemist somewhere, it's just one room and he is selling drugs, and no control, nobody does anything, and I am happy you are collaborating with the Kaduna State government, maybe they should do something about that'. D001 – Nigeria

7.2

'You can see a drug, written 500 mg amoxicillin, but what is in that drug is not up to 500 mg, honestly that is a common ... its' a tradition right now, okay? The regulatory body they are not doing much to dampen such problem.' P003 – Nigeria

'Sometimes because of our porous border, some drugs leak into the country. Those drugs don't go through the pharmacy board for proper regulation like testing for efficacy. Yeah, I'm worried about that.' P2 – Sierra Leone

7.4

'it has been able to close the communication gap, it has been able to bring me very much closer to the prescriber and the lab scientist and I myself as a pharmacist, even though we are working at different units.' P002 – Nigeria

7.6

'I don't want my client's birds to come down with Salmonella, with e-coli... now I will prefer him to use water sanitizer in his water, water acidifier, that make the environment unconducive with eh... for the bacteria to thrive, rather than telling him to use antibiotics to prevent.' V008 – Nigeria

'For us in the livestock, in the food industry, probiotics do very well, they are cheaper, okay? they don't create huge companies like Pfizer or Welcome but they can work, they can serve people, they are convenient to less developed countries and I assure you that it is safer for humanity not the drugs, so I think that we are not doing enough we are shying away from the alternatives to antimicrobial agents, if the same amount of money that is put into research of new antibiotics, is put into research of alternatives to antibiotics.' EDV01 - Nigeria

'How do you promote alternatives to antimicrobial agents? because again, I don't share the same philosophy that "okay, let's use these antimicrobials rationally, the problem will go away, okay? the problem will not go away, because like I said, it's a natural process, but I prefer to subscribe to the philosophy which says, can we device better ways of co -existing with microorganisms rather than increasing divisive ways? because I can see two sides to this debate, pharmaceutical companies are saying" okay let's make better drugs, then the problem will go away, make alternative drugs, but again on the other hand, is why don't we emphasize less on the drugs and more on the alternatives?' EDV01 - Nigeria