OPTIMISING ANTIBIOTIC USE: SOCIAL AND CONTEXTUAL ISSUES

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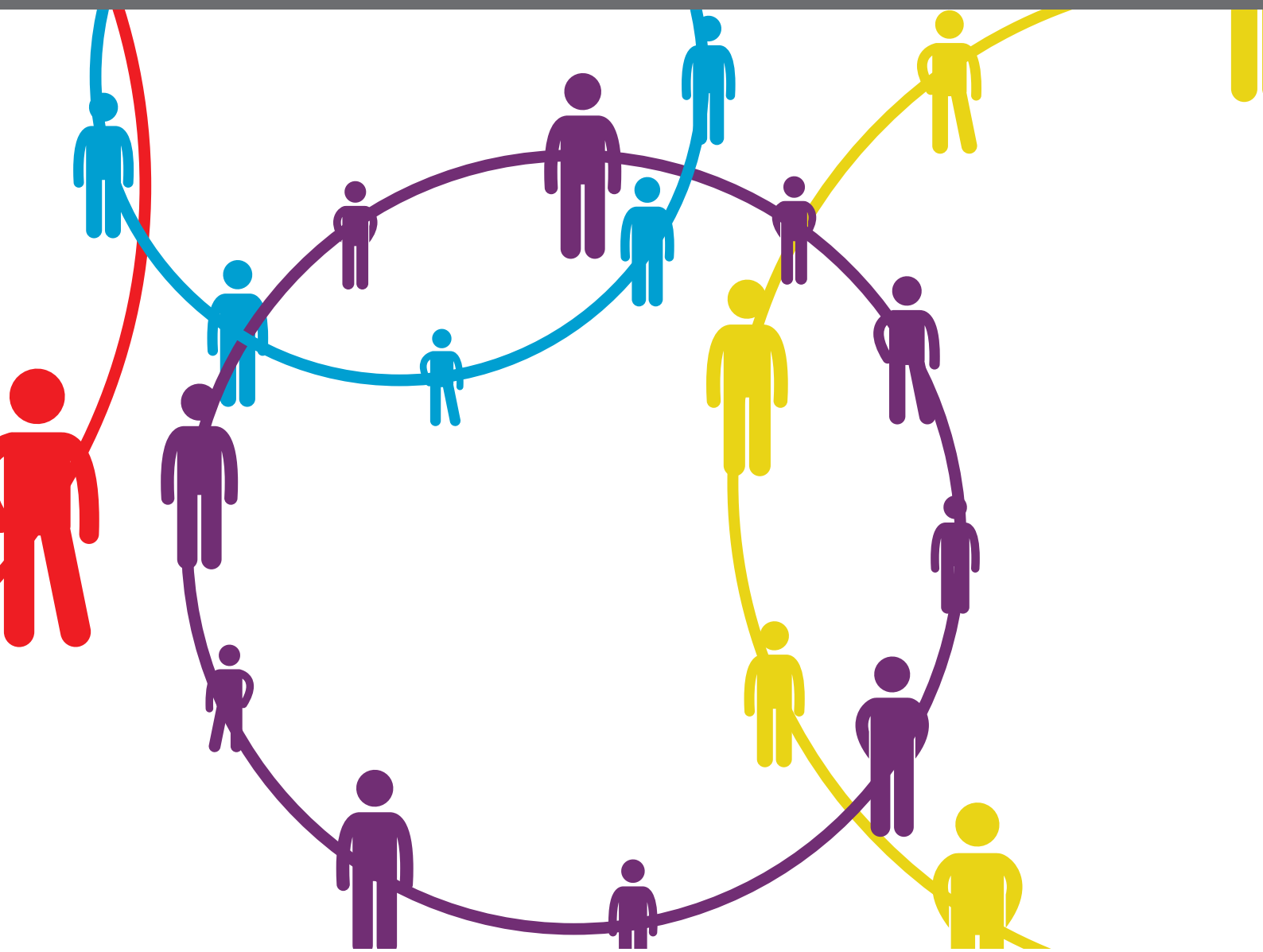

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OPTIMISING ANTIBIOTIC USE: SOCIAL AND CONTEXTUAL ISSUES

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EDITORIAL
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Editorial: Optimising Antibiotic Use: Social and Contextual Issues

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Editorial on the Research Topic

Optimising Antibiotic Use: Social and Contextual Issues

Modern medicine is founded on the availability of effective antimicrobials, but antibiotic resistance is an inevitable consequence of widespread use of antibiotics. The rise in multidrug resistant organisms, and the increasing numbers of pan-resistant infections being identified, mean that antimicrobial resistance (AMR) is now a pressing global concern (Jee et al., 2018).

The factors contributing to the growth and spread of AMR are multiple and intertwined, including antibiotic use in human and animal health and agriculture, hygiene and sanitation, and international travel. Overuse of antibiotics in healthcare is a contributing factor, with evidence suggesting that around 30% of antibiotics in hospitals are prescribed or taken inappropriately (Fridkin et al., 2014). The global COVID-19 pandemic has led to increased antibiotic prescribing and made it more difficult to maintain efforts to optimize antibiotic use (Getahun et al., 2020).

Given the global nature of the threat of AMR, efforts are underway to tackle the problem using approaches such as policy, regulation, and international coordination. Alongside these macro-level approaches, an extensive body of research and interventions focuses on understanding and changing the behaviors of individuals—health professionals and patients—to reduce antibiotic use (Charani et al., 2011). In contrast, meso-level issues, including the social and organizational context in which antibiotic use takes place, have received less attention. Prescribing behavior is socially and contextually embedded—influenced by identities, attitudes, social norms, hierarchy, local culture and systems (Charani et al., 2013; Broom et al., 2016). Antibiotic use involves a range of stakeholders and institutions (Broom et al., 2019). The articles in this Research Topic provide insights into the complex and embedded nature of antibiotic use.

Five of the articles in this Research Topic consider antibiotic prescribing and antimicrobial stewardship (programmes to optimize antibiotic use) in healthcare. The first article in the collection, by Rzewuska et al., sets the scene by reviewing the literature on antimicrobial stewardship interventions in hospitals in high income countries. The authors identify that efforts to change physician prescribing behavior are frustrated by contextual factors—inadequate information systems and unavailability of key personnel and funding—as well as facing competition from other initiatives seen as having a higher priority.

Rynkiewich's article goes further by challenging a common assumption of antibiotic stewardship approaches—that the problem lies in individual physician behaviors and habits. Based on vivid ethnographic case studies in two American hospitals, the author argues that decision-making about antibiotics is instead a collective practice, which happens between institutions, physicians, pharmacists, nurses, and other staff. The implications are that, rather than targeting "bad" physician practice, stewardship efforts should recognize the collective nature of antibiotic use.

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Tarrant et al. look in detail at the notion of "inappropriate" antibiotic prescribing in their interview study, involving hospital prescribers in the UK, South Africa and Sri Lanka. They identify that prescriber definitions of inappropriate antibiotic use are not purely objective. Inappropriate antibiotic use can't be pinned down by precise technical definitions. Instead, prescribers' judgements about the appropriateness of prescribing decisions reflect their moral position and the context in which they work.

Shifting the focus to China, Chen et al.'s qualitative study provides another example of the complexities of antibiotic decision-making, this time in rural primary care. They find that physicians work to balance their understanding of rational use of antibiotics against the need to maintain good relationships and protect the safety of their patients. The idea of "suzhi" (human quality)—respecting and protecting their patients—is drawn on by prescribers to explain their liberal prescribing of antibiotics.

How patients and professionals perceive suspected infection is consequential for antibiotic use. Saukko and Rousham's article focuses on patients' and health professionals' affective experiences related to diagnosis and management of urinary tract infections. Using the conceptual framing of illness narratives, they describe narratives of chaos and control, and point to the need for stewardship programmes to consider the affective dimension of decision-making about antibiotic use.

The majority of efforts to tackle AMR to date have focused on the preservation of existing antibiotics through stewardship, and investment in development of new antibiotics. The final article in this Topic, by Jamie and Sharples, offers a refreshingly different perspective. The authors describe how natural materials such as clay may offer alternatives to antibiotic treatment. They provide some theoretical lenses through which sociologists could study how their materiality (i.e., what they are made from, what they look like, how they are produced) might influence the use of these materials in healthcare.

Taken together, the articles illuminate the ways in which the use of antibiotics (and materials with antibacterial properties) are shaped by social and organizational infrastructures, individual meaning-making, as well as the materiality of the substances themselves. Addressing AMR will require us to think differently about the nature of the problem and about our possible futures (Chandler, 2019). This Research Topic offers some new perspectives to stimulate further research.

AUTHOR CONTRIBUTIONS

The authors confirm being the only contributors of this work and approved it for publication. All authors contributed to the article and approved the submitted version.

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ORIGINAL RESEARCH
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Finding "What's Wrong With Us": Antibiotic Prescribing Practice Among Physicians in the United States

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Antibiotic stewardship—or the responsible use of antibiotics—has been touted as a solution to the problem of antibiotic resistance. Antibiotic stewardship in medical institutions attempts to change the antibiotic prescribing "behaviors" and "habits" of physicians. Interventions abound targeting "problem prescribers," or those physicians whose practice is out of line with physician peers. Thus, the locus of decision-making in antibiotic prescribing is thought to be the found with the individual physician. Based on 18 months of participant observation and in-depth interviewing of antibiotic-prescribing physicians at two medical institutions in the United States, this paper will question notions of antibiotic stewardship that center on individual "behaviors" and "habits." Many physicians have taken to heart a reductionist approach in studies of antibiotic prescribing, including several physicians I encountered during research who enthusiastically located the benefit of my research in the ability to identify "what's wrong with us." In this paper, I use two representative ethnographic case studies to argue that antibiotic stewardship interventions aimed at identifying and correcting "bad" physician practice limit the possibilities of understanding the social dynamics of the institution. Through an analysis of everyday encounters in the hospital setting, I show how decision-making in antibiotic prescribing can more productively be located between and among institutions, physicians, patient charts, and other hospital-based staff members (e.g., pharmacists, nurses). By demonstrating that *antibiotic prescribing is a collective practice* occurring through engagement with social and material surroundings, I argue that we can better account for the weighted ways in which social action and relations unfold over time.

Keywords: antibiotic stewardship, antibiotic prescribing, social theory, antimicrobial resistance, social determinants, physician behavior change

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INTRODUCTION

> *"Antibiotic stewardship is very complex. Half of it is psychology. How do you make people do what they don't want to do? This is not medicine, it's not evidence-based medicine which is the thrust of what we were trained to do. I feel sometimes like a salesperson figuring out how people think. I don't understand this. This is a completely different field." -Infectious disease practitioner*

Antibiotic resistance is a global threat to our health and well-being. Though resistance to antibiotics is not a new phenomenon, only recently have countries like the United States begun

to take on antibiotic oversight as one of the defining issues of our time. In recent approaches to combating antibiotic resistance in the United States, there has been a central focus on the policy of antimicrobial or antibiotic stewardship—the responsible use of antibiotics. Antibiotics are overused and misused on a regular basis, and thus antibiotic stewardship endeavors to bring errant use of antibiotics into line with appropriate practice.

In attempts to correct inappropriate practice, antibiotic stewardship teams[1] in medical institutions use interventions to target the antibiotic prescribing "behaviors" and "habits" of physicians. For example, if a physician overuses ceftriaxone by prescribing every patient to take 10 days of the antibiotic, the antibiotic stewardship team might utilize careful messaging to get the physician to switch how they prescribe ceftriaxone. Sometimes, antibiotic stewardship can intervene in simple ways that reduce overall antibiotic use. However, as this paper illustrates, there are shortcomings with this approach to antibiotic optimization. Primarily, antibiotic stewardship that identifies the crux of the problem with antibiotic prescribing as originating in the individual physician (i.e., their thoughts and behaviors) leans on a fallacy: though a single physician may sign a prescription order for antibiotics, they are likely not the only person considering, discussing, and ultimately deciding on antibiotic therapy for the patient.

Through the use of ethnographic data collected during fieldwork at two medical institutions in an urban midwestern setting in the United States, I will demonstrate how individual physicians operate within a complex web of relationships and institutional protocols that emphasize the distributed, collective nature of antibiotic prescribing. I will use two representative ethnographic case studies to show that *antibiotic prescribing is a collective practice* occurring through engagement with social and material surroundings.

Social science research has established that there is a myriad of factors, such as professional influence (Livorsi et al., 2015; Papoutsi et al., 2017) and communication styles (Linkin et al., 2007; Skodvin et al., 2017), that go into antibiotic decision making in medical settings. Drawing on this research and the data presented in this article, I propose that antibiotic stewardship interventions could be improved through greater acknowledgment and integration of the social dynamics of the institution. Thus, I argue that antibiotic stewardship interventions aimed at identifying and correcting "bad" physician practice limit the possibilities of understanding the ways in which physicians are interconnected and interdependent in their practices of antibiotic prescription.

THE FOUNDATIONS OF ANTIBIOTIC STEWARDSHIP

Antibiotic agents have been in circulation since the advent of sulfonamide drugs in the early twentieth century (Barrett and Armelagos, 2013; Podolsky, 2015). Antibiotics have minimized the threat of infectious diseases while they simultaneously encourage antibiotic resistance. Overuse and misuse of antibiotics has led to what is commonly referred to as a "crisis" of antibiotic resistance (Neu, 1992; Ventola, 2015; Mendelson et al., 2017). Physicians and researchers have long cited the dangers of antibiotic use (Hardin, 1968; see Barrett et al., 1998). However, little oversight of antibiotic use has been achieved globally. In fact, there are only two major antibiotic oversight programs worth mentioning: antibiotic control programs and antibiotic stewardship.

Antibiotic control programs in the United States began in the 1970's (Haley et al., 1985; Podolsky, 2015) and involved measuring institutional use of antibiotics. The control programs largely aimed to alter institutional use of antibiotics by regulating access and purchasing. Control programs in the United States were critiqued for their inability to enforce change at the institutional level due to the powerful resistance of the pharmaceutical industry (cf. Podolsky, 2015). Eventually, antibiotic control programs were integrated into infectious disease divisions with specialized pharmacy staff. Antibiotic stewardship, introduced in the mid-1990's, was intended as an expansion of influence over antibiotic use for specialists such as infectious disease physicians and pharmacists.

Antibiotic stewardship first appeared in the medical literature in McGowan and Gerding (1996), where it was described as "the limitation of use of inappropriate agents, but also the proper use, dosing, and duration of antimicrobial agents to achieve optimal efficacy in treating and preventing infections" (p. 371). Early definitions of antibiotic stewardship highlighted the potentially global impact of reducing antibiotic use. The association between the use of antibiotics and the emergence of antibiotic resistance has since catapulted antibiotic stewardship into a standard in medical practice. In the past 20 years, antibiotic stewardship has been heavily endorsed by international organizations and governments (Mendelson et al., 2017).

In the United States, a government-issued report detailing plans to combat antibiotic resistance was published in 2015. The Centers for Disease Control and Prevention (CDC) has published several guidelines for antibiotic stewardship in medical institutions including hospitals (Centers for Disease Control Prevention, 2014), nursing homes (Centers for Disease Control Prevention, 2015), and outpatient settings (Centers for Disease Control Prevention, 2016b). Additionally, the CDC has created an online education program for antibiotic stewardship (Centers for Disease Control Prevention, 2016a). There is now a medical management standard for the policy meaning that institutions accredited by The Joint Commission must maintain an antibiotic stewardship team that follows established guidelines as set by the accreditation agency.

What Is Antibiotic Stewardship?

Antibiotic stewardship is a set of interventions put in place with the goal of reducing overall antibiotic use thereby combating antibiotic resistance. Antibiotic stewardship appears similar to environmental stewardship (Welchman, 1999) since a forward-oriented goal is kept in mind. However, antibiotic stewardship in the United States has primarily been focused on changing

[1]The Centers for Disease Control and Prevention now recommend that every medical institution have an antibiotic stewardship team comprised of individuals specially trained to monitor and advise on antibiotic use.

the use of antibiotics in institutions (i.e., inpatient antibiotic stewardship) and therefore has a more specific target than environmental stewardship (cf. Welchman, 1999). Practically, antibiotic stewardship requires additional microbiological testing and monitoring of the patient condition in order to assess whether antibiotics are needed, and if so, then what dose for what duration. For a physician conducting antibiotic stewardship, antibiotics are only appropriate if a patient's infection is confirmed via the microbiological testing and susceptibility testing that would confirm the efficacy of a selected antibiotic. Recognizing that antibiotic use is not always targeted to an infection, the activities of antibiotic stewardship also suggest that reducing overall antibiotic use would have a positive impact while not sacrificing a patient's health. Common activities in antibiotic stewardship programs include optimizing selection, dose, route of administration, and duration of antibiotics (Pakyz et al., 2014; Dyar et al., 2017). Typically, infectious disease physicians or specialized pharmacy staff will make calls to physicians giving recommendations designed to support good antibiotic stewardship policy.

Though antibiotic stewardship is a popular policy endorsed by the United States government and key infectious disease agencies, there are limits to the reach of antibiotic stewardship. At the level of the institution, antibiotic stewardship is just one of many interventions coming from various departments and divisions within the institution. Antibiotic stewardship programs vie for funding and support, building up an array of "champions" and "problem physicians" on either side of the cause. "Champions" are tasked with influencing the decisions (read: mindsets) of their colleagues in the direction of becoming stewards of antibiotics, meaning that they utilize antibiotics responsibly. "Problem physicians," on the other hand, resist the advances of "champions" and continue prescribing antibiotics according to their own logics. While "problem physicians" are not seen as problematic by the institution as a whole, they are considered barriers to the implementation of antibiotic stewardship.

The heart of the social dynamics of antibiotic stewardship in the United States is the idea that "good behavior," which here means responsible antibiotic use, can be achieved through careful, targeted attempts at changing the prescribing habits of other physicians. The focus is on bringing outlier physicians more in line with the prescribing habits of a department or division of the medical institution. For example, in the surgery department an individual is overprescribing cefazolin, giving two times the amount of antibiotic compared with their peers. This individual becomes a "problem physician" to the antibiotic stewardship program that is succeeding with the other physicians in the department but is not seeing change in this prescriber. According to the principles of behavioral economics and behavioral psychology, this individual can be brought into line with their peers through the utilization of "nudges" (Thaler and Sunstein, 2008) or small changes in the individual practices making up the institution.

What Are Some of the Disciplinary Foundations of Antibiotic Stewardship?

Behind the structure of antibiotic stewardship lie tenets of behavioral psychology and behavioral economics best described in Thaler and Sunstein's *Nudge: Improving Decisions about Health, Wealth, and Happiness* (Thaler and Sunstein, 2008). Recently, behavioral economics has exploded on the scene as the intervention style of choice for nations and large institutions. Even before the popularity of behavioral economics, the underlying theories of behavioral psychology had a heavy influence on medical research (Pedwell, 2017: 14) leading to a focus on attitudes, perception, thoughts and behaviors. These epistemologies link up with the birth of behavioral economics, as Thaler describes in a recent Freakonomics appearance (Dubner, 2018) and as Scott Podolsky describes in relation to antibiotics in *The Antibiotic Era: Reform, Resistance, and the Pursuit of a Rational Therapeutics* (Podolsky, 2015). Thus, the antibiotic stewardship that we see promoted nationally appears to be continuing in the tradition of leaning heavily on the individualism that is prominent in both psychology and economics.

The disciplinary foundations of antibiotic stewardship have a heavy influence on the day to day practices of antibiotic stewards. The relationship between behavioral theories and antibiotic stewardship policy is exemplified in the tangible efforts at changing individuals, and thereby expecting to change overall trends in behavior. Thaler and Sunstein (2008) introduce Carolyn as an example. Carolyn learns that if she prominently displays healthier food in her school cafeteria, students tend to go for the healthier options. This example is a good representation of the logics behind behavioral economics which have become palpable among antibiotic stewardship researchers. Nudging students toward healthier lunch options is said to "...make ameliorative contributions to much bigger issues, from childhood obesity to adult heart health" (Pedwell, 2017).

Similarly, nudging prescribers toward better antibiotic choices can contribute to the much bigger issue of antibiotic resistance. Nudging promises low-cost, high-impact solutions. However, as Pedwell argues, citing Carolyn's cafeteria solution, "...such techniques do nothing to acknowledge the interrelated psychic, social, and economic factors that may play into cafeteria behavior and eating habits...from poverty, to academic pressure, to abuse and trauma, to sexism" (2017: 17). Importantly, these interrelated factors do not simply constitute context but influence understandings and behaviors of the individuals involved. In the following section, I introduce my fieldsite and describe the understandings of antibiotic stewardship leaders and antibiotic prescribing physicians at this site. By illuminating the social dynamics of antibiotic practice, I will show how antibiotic stewardship targeted at individual behavior is a reductionist approach that does not do justice to the real contexts of antibiotic use, leaving corresponding antibiotic stewardship interventions prone to failure.

METHODS

The research for this paper was conducted over an 18 months period at two adjacent medical institutions in the United States with outside support from the Wenner-Gren Foundation for Anthropological Research. The objective of the research was to understand antibiotic prescribing among hospital-based physicians. This objective was achieved by conducting

participant observation and semi-structured interviews with specialists in infectious diseases (infectious disease practitioners and antibiotic stewards) and antibiotic prescribing non-specialists (intensive care unit practitioners). Ethnographic methods were chosen to illuminate the social milieu of the hospital through close observation and careful attention to cultural norms. Over 520 h of participant observation and over 39 h of semi-structured interviews were completed between July 2017, and December 2018.

Setting

Two adjacent medical institutions in an urban midwestern city in the United States were chosen for this research. The first is a public teaching hospital with an over 20 years history of antibiotic control and antibiotic stewardship programs. The public teaching hospital shared an infectious disease fellowship program with the second institution, a private academic medical center with a more recent entrée into the world of antibiotic stewardship. The private academic medical center is a nationally-recognized center for orthopedic and geriatric care. Together, these institutions comprise a center for antibiotic stewardship as designated by the Centers for Disease Control and Prevention. This study is based at a single site for the purposes of analyzing specific iterations of antibiotic stewardship at a well-known duo of institutions, thus limiting the breadth of the study while allowing for a more in-depth look at local practice.

Data Collection

As the researcher leading this study, I contacted infectious disease practitioners directly according to patient rounding schedules for the infectious disease consult service in the months of July 2017—January 2018. Once practitioners provided verbal consent, I joined individual infectious disease consult teams for their 2 weeks patient service. In total eight services were observed. Following the initial period of participant observation, I interviewed 25 infectious disease practitioners (attending physicians, fellows, and pharmacists). Though some interviewed participants were also observed in the first part of the study, select additional participants were added based on their research interests and involvement in antibiotic stewardship.

For the intensive care unit practitioners, similar methods were utilized. I contacted surgical intensive care unit practitioners directly according to patient rounding schedules for 1 week services in the months of April 2018—June 2018. Once practitioners provided verbal consent, I joined individual surgical intensive care unit consult teams for their 1 week patient services. In total 10 services were observed. At the end of each 1 week service I arranged to conduct a semi-structured interview with the attending practitioner (surgeon or anesthesiologist) and their physician fellow. The schedules for physician fellows follow a 1 month rotation, therefore fewer physician fellows were included in the study compared with attending practitioners.

Data Analysis

For all periods of data collection, fieldnotes were taken during participant observation. At the end of every day, fieldnotes were typed into a document held within a qualitative analysis software (MAXQDA). Semi-structured interviews were recorded and transcribed at a later date. Thematic coding (Gibbs, 2007) of typed fieldnotes and semi-structured interviews was assisted by MAXQDA. First, a review was conducted through open coding of the typed data. Key themes that arose during open coding were solidified as overarching concept-driven codes that were then applied to the data. This allowed me to analyze the data inductively and perform a check on the initial open coding analysis. The data analysis was conducted onsite and as such I had contact with participants throughout the data analysis period (cf. Liberati et al., 2019). Participant feedback was solicited regarding the key themes and codes that were formed during data analysis. In order to protect participant anonymity, all data has been deidentified and pseudonyms are used throughout my written publications. The presentation of data in this article follows a thematic narrative approach (Emerson et al., 2011) aimed at ethnographic storytelling that leads to a culmination of central ideas in the text. As such, in the following you will find two ethnographic case studies followed by a discussion and analysis. The selected ethnographic case studies are representative in that they demonstrate key themes identified during the data analysis phase of research. Additionally, though the ethnographic case studies describe scenes from different medical institutions[2] they are indicative of broader social dynamics and underlying beliefs found in many medical institutions (e.g., Charani et al., 2019).

Ethical Issues

Ethical approval for the study was received prior to the start of data collection. All participants were informed about the research. All participants including the practitioners quoted in this paper provided verbal consent prior to involvement in the study and were informed that by giving their consent they may be included in a future publication of the study results. Furthermore, all participants were informed that they were free to leave the study at any point including during a scheduled interview. Participants mentioned in this article have been given pseudonyms used throughout the text as a safeguard to protect anonymity. The names of the medical institutions involved in this study are not disclosed to further protect the anonymity of participants.

LIMITATIONS

This ethnographic research focused on two medical institutions in the same urban area of the United States. Therefore, suburban or rural medical institutions were not included in the data collection. Additionally, antibiotic use varies regionally and this research was conducted in a single region of the United States. Though this study did not aim to include these variables in the

[2]The first ethnographic case study took place at the public teaching hospital while the second ethnographic case study is a composite case based on participant observation in the surgical intensive care unit at the private academic medical center. Though the institutions varied in their organizational structure and resources, several key practitioners were employed at both institutions and the antibiotic stewardship teams had a close working relationship. The foundational principles of antibiotic stewardship at both institutions were more similar than they were different.

data collection, future research is needed to address how social dynamics are altered based on geographic region and type of medical institution.

ETHNOGRAPHIC CASE STUDY: ENCOUNTERING LOCAL ANTIBIOTIC STEWARDS

The following ethnographic case study shows that antibiotic stewardship is predicated on the notion that improving antibiotic use necessitates altering the mindsets, thoughts, and behaviors of individual antibiotic prescribers. The former Chair of the Division of Infectious Diseases had increased the visibility of antibiotic control programs, and later antibiotic stewardship, in the institution. An early committee on the subject had made a simple antibiotic switch that saved the hospital system millions. Successes such as these gave antibiotic stewardship notoriety amongst hospital system heads. The current chair, Dr. Martin, had been at his post for the past 5 years, and was attempting to increase the efficacy of antibiotic stewardship by fostering collaborative relationships with "champions" in diverse specialties. I met regularly with Dr. Martin in the early days of my ethnographic fieldwork. He explained, "For your champions, they have to be willing to say "This is not right." They get to influence their colleagues, their patients, all the people they work with. They get to really champion that (good antibiotic use)." For example, the infectious disease pharmacist who often made calls for antibiotic stewardship purposes was improving the chain of communication to floor pharmacists who managed certain areas of the hospital (e.g., the medical intensive care unit pharmacist). Infectious diseases fellows were also involved in antibiotic stewardship, doing daily reviews of not only their own patient lists but antibiotic stewardship-specific lists. One such list involved all new cases of bacteremia (the presence of bacteria in the bloodstream) in the institution, which infectious disease fellows reviewed for antibiotic appropriateness and the potential need for an infectious disease consultation request. These additional pharmacists and fellows, through their involvement in antibiotic oversight, were recognized as antibiotic stewardship "champions."

The general approach to antibiotic stewardship on a practical level was to find errors in the data (i.e., evidence of overuse or misuse in patient charts) and correct the error by speaking personally or through a formal channel such as consultation with the individual who had committed the error. I found it was a search and change mission that focused its efforts at ground level or the individual behaviors and habits of physicians. Throughout the course of my fieldwork, when trends became obvious to those on the antibiotic stewardship team, some additional steps might be taken such as giving a morning lecture to the targeted specialty or having a one-on-one conversation with the head of the targeted specialty. Additional methods of correction involve monitoring and restricting which antibiotics are available for use in the institution. By controlling the menu of antibiotic options for physicians, the stage is already set for a decision concordant with antibiotic stewardship policy. In other words, the behind-the-scenes work done by antibiotic stewards like Dr. Martin impacted the menu of options for physicians attempting to prescribe antibiotics.

When antibiotic stewardship approaches still fails to create change among other physicians, the individual physician mindsets and thought processes are thought to be at fault. An antibiotic steward described the limits to her involvement in a patient case:

> "In the outpatient setting, you come in with a cold, you come in with a runny nose and a sore throat and a cough and you want antibiotics? There's no benefit. No! I'm not doing it. But in the inpatient setting it's not that cut and dried. It's not a "Yes" or "No." There's so much gray. I've heard physicians say, "But is there a possibility that they would do better on the antibiotic? Because if there's even the slightest possibility then we'll give it." It frustrates me because we don't live in a world of zero risk, you know, everything has a possible benefit and a possible risk. So we as individuals need to determine how comfortable we are with those possibilities."

Here, again, the individual physician is seen as the deciding factor for antibiotic use. Antibiotic stewards in my research emphasize good decision making among individual prescribing physicians as an ultimate goal of their practice. For example, Dr. Martin invited me to observe a talk he gave to the obstetrics and gynecology group of the institution in late July. Here, he talked about having the capability of deciding for oneself when to switch antibiotics. "You have to decide, because it is your practice"[3] he told them. Dr. Martin was walking the line between pushing for more appropriate use of antibiotics, a bread and butter antibiotic stewardship standard, and cornering the department into taking more responsibility for their antibiotic decisions without intervention from the antibiotic stewardship team. The combination of wanting physicians to choose antibiotics well and wanting to control the choices of physicians left Dr. Martin, and others involved in antibiotic stewardship, frustrated. During my observations this frustration often came to a head when discussing next steps for the antibiotic stewardship program.

In fact, Dr. Martin often approached conversations about antibiotic stewardship from the perspective displayed above. "What's wrong with us?" Dr. Martin asked me 1 day before an antibiotic stewardship meeting as he gestured toward the other individuals in the room. He continued in this vein. "We want to learn about how we can improve our (antibiotic stewardship) program…because I do think it is all in here (he points at his head)." It was not uncommon at my fieldsite for physicians to question their own behavior, though certainly it was more common to question the behavior of others they interact with. However, what Dr. Martin identifies as the error in this case is the behavior or himself and others as individuals. He assumes that the error is behavior affected by the mind in a negative way.

[3]This approach is reminiscent of Former United States President Ronald Reagan's War on Drugs slogan: "Just say No." The generally neoliberal assumption is that people are free to make choices and thus just need a slight push to make the right decision. Behavioral economics draws on some of these principles (McMahon, 2015).

The something wrong, here, is guiding individuals in the wrong direction, away from appropriate antibiotic use. According to this framework, altering the mindsets of individuals would thereby create change at the level of antibiotic prescribing. "What I want to do," Dr. Martin says, "Is find out what it is that makes a physician behave the way they do. Mindsets, concepts, whatever it is so that we (the antibiotic stewardship team) can intervene and improve (antibiotic) stewardship." The day Dr. Martin lectured to obstetricians and gynecologists in late July, he was intervening where he saw the error occurring, which was at the individual level. In the next section, I will show how the focus on individuals and individual behavior eschews understandings of antibiotic prescribing practice as a collective practice occurring within weighted institutional contexts.

ETHNOGRAPHIC CASE STUDY: BUCKING ASSUMPTIONS IN THE SURGICAL INTENSIVE CARE UNIT

This ethnographic case study demonstrates how antibiotic decision-making in the surgical intensive care unit is carried out across multiple individuals and teams, thereby illuminating the limitations of a framing of antibiotic stewardship that focuses on individual behaviors. Surgeons at my fieldsite, as they are in much of the world, were known for their stubborn nature. Throughout my fieldwork, each medical institution had particular surgeons known to all rotating physicians. Certain names kept coming up in my notes. One recurring figure was Dr. Kline. The physician I was observing 1 week said, "Dr. Kline keeps *whipples* (patients who have undergone a Whipple procedure) 7 days so let's make sure we do that." Another day in the unit, a different physician commented, "Dr. Kline is particular about pain control—ask him what he wants." My notes continually referred to Dr. Kline as a surgeon with peculiar preferences for his patients, a "problem physician" who ensures their preferences are enacted.

One morning I was part of the group of resident physicians rounding with Dr. Tuttle on the surgical intensive care unit. These patients had undergone surgery and were not yet stable enough to begin recovery on the hospital floors or at home. Dr. Tuttle's team oversees the care of these patients and collaborates with the operating surgeons to decide trajectories for each patient's care. As we walk the floors that morning, I notice the following interaction unfold: Dr. Tuttle is engaged in conversation with the resident physicians as they discuss Mrs. Rodriguez, the current patient. Dr. Tuttle asks about fluids, chastising the resident physicians for not being more vigilant. "Fluids are like a vital in the intensive care unit, you need to trend those." The new bacterial cultures were in, the resident physician copies down the results from the computer-on-wheels and conveys the message to Dr. Tuttle. The cultures showed growth, and the patient had a fever and hypotension. Now, vancomycin, cefepime, metronidazole,[4] and micafungin could be peeled back to a streamlined course of antibiotics targeted to the culture results. The team discussed options, and Dr. Tuttle noted, "Dr. Kline always does 7 days." The resident physician took note but nothing was decided at that moment.

We continued rounding on patients for another hour and a half. Later in the morning, as rounds died down, Sarah the team pharmacist checked in with the resident physicians. She clarified the dose and duration of antibiotics for several patients, including Mrs. Rodriguez. For Mrs. Rodriguez, Sarah left two options. If Dr. Kline does want to change the antibiotics, it'll be to this combination and this duration (Sarah put a paper down in front of the resident). If Dr. Kline doesn't want to change the antibiotics, go ahead and get rid of the micafungin. Either way, she instructed the resident physician, "Check in with me before you enter the changes."

Dr. Tuttle and Sarah broke off to go to meetings while the resident physicians headed back to the work room to write their notes. I would often stay and write notes alongside the residents. After an hour of working independently, the resident physician in charge of Mrs. Rodriguez's case, Steve, picked up the work room phone and called one of Dr. Kline's resident physicians. Steve brought up the new bacterial culture results, Dr. Kline's resident physician confirmed that they've seen them. But there was a holdup. Unfortunately, Dr. Kline was in surgery at that moment. The choice was to try to reach Dr. Kline or move forward without his input. Dr. Kline's resident physician didn't ask to wait until Dr. Kline was out of surgery. Instead, with the bacterial culture results at hand Dr. Kline's resident physician decided that getting rid of micafungin was a good plan. There was no discussion of duration. Steve nodded, then confirmed the other antibiotics: vancomycin, cefepime, and metronidazole. Already, Dr. Tuttle's team was not solely responsible for the prescription of antibiotics for Mrs. Rodriguez. Steve, through his conversation with Dr. Kline's resident, had ensured that additional teams were involved.

The resident physicians continued working for another hour, then we broke for lunch. I returned to the work room at 1 p.m. to a new update in Mrs. Rodriguez's case. The infectious diseases consulting team on her case had put their notes in the medical record. This team commented on bacterial cultures, antibiotic selection, and antibiotic duration, among other specialty-related topics. The infectious diseases recommendations suggested that removing micafungin is indeed the first step for Mrs. Rodriguez. However, the infectious diseases consult team also recommended removing metronidazole on the basis that the bacterial culture results did not show evidence of microbes that would be targeted with metronidazole, thus rendering it useless in Mrs. Rodriguez's case. Finally, the infectious disease consult team suggested only two additional days of antibiotic, arguing that the patient had already received 3 days and a total of 5 days was all that was necessary per the institution recommendations. Now, even more input had been solicited for Mrs. Rodriguez's case. The expanding number of individuals involved in the decision-making had reached well-beyond the original prescribing physician.

At this point, Steve had gathered information from various teams regarding Mrs. Rodriguez's antibiotics. He wrote up his note in a hurry, he was being called in to another patient's room. The note was entered into the medical record, though the recommendations in his note were not put into action. Further

[4]This antibiotic was referred to as Flagyl© at my fieldsite but I am keeping the references uniform as with the other antibiotics I have used generic names.

action was required. Dr. Tuttle settled the case by signing the patient note and recommendations at just after 5 p.m. It was one of the last notes that she signed for the day. The completed recommendation? Dr. Tuttle commented that she agreed with Steve's characterization of the case and updates for the day. The antibiotics that will continue into tomorrow include vancomycin and cefepime, but not metronidazole or micafungin. Steve had written that the duration of antibiotics would total 7 days, or four additional days from the current date. Dr. Tuttle signed off on this duration. In the beginning, we have one team, even one physician, suggesting the course of action for a patient. Often, initial reactions like the one from Dr. Tuttle are taken as the most significant behavior in antibiotic decision-making. However, as I demonstrate here, this initial reaction was not the final say. In fact, the number of individuals involved expanded to include multiple teams. Later, the number of individuals shrunk again until the final action in the case was made: Dr. Tuttle signed the antibiotic recommendations.

DISCUSSION

In "Encountering Local Antibiotic Stewards," Dr. Martin searches for the reasons behind individual physician "behaviors" and "habits." With his research agenda, Dr. Martin is determined to identify and ultimately change individual prescribers to come more in line with antibiotic stewardship recommendations. With the obstetrics and gynecology group, Dr. Martin attempts to reinforce the physicians' power and responsibility to prescribe appropriately, telling them "…it's your practice." He walks through case studies of obstetrics and gynecology patients where antibiotics were prescribed and poses questions to the practice group about what antibiotic they would choose. By retraining the physicians, Dr. Martin is addressing what he sees to be the underlying concern with antibiotic overuse and misuse: there is something wrong with us.

Dr. Martin is ultimately interested in improving antibiotic stewardship at the medical institution where he works. Both segments of the literature (ex. Meeker et al., 2014) and his own personal instincts tell him that it is individuals that need to be changed. Thus, in my conversations with Dr. Martin, the focus continually returns to the individual physician and more specifically, their thought processes. The antibiotic stewardship goals that Dr. Martin creates while I am at my fieldsite follow the precipitated notions regarding who is at fault with antibiotic overuse and misuse (i.e., "bad" prescribers) and how they can be changed into good prescribers (i.e., "champions").

Antibiotic stewardship based on Dr. Martin's question "What's wrong with us?" involves targeting individuals from every facet of the institution. It can be considered a holistic approach in one sense, that individuals from every specialty and hospital floor are targeted. However, it is ultimately a reductionist approach since it rarely addresses the collaborations and interactions shaping antibiotic use in medical institutions. Though many antibiotic stewardship programs operate as though the social and institutional dynamics at play simply constitute context, in fact these interrelated factors contour the processes of how antibiotics are prescribed on a daily basis.

In "Bucking Assumptions in the Surgical Intensive Care Unit," we find a scene in which multiple physicians at various points in time and at different locations within the medical institution are involved in making antibiotic decisions for the surgery patient Mrs. Rodriguez. There are three key elements demonstrating the collective nature of antibiotic decision making in Mrs. Rodriguez's case. First, Dr. Kline isn't really involved in making antibiotic decisions. We see that he is unavailable during the call between teams asking about antibiotic preferences. Further, we do not see any later intervention on Dr. Kline's behalf to change what others have prescribed to the patient. Thus, Dr. Kline has effectively delegated responsibility to the resident physician. The resident physician from Dr. Kline's team, though he could have waited to confirm with Dr. Kline which antibiotic and what duration of antibiotic were needed, took the initiative to make recommendations himself. This scenario can be compared to Charani et al. (2019), where antibiotic decisions for surgical patients are similarly delegated to junior physicians.

Second, other physicians and pharmacists are involved in making decisions regarding Mrs. Rodriguez's antibiotics. Though Dr. Kline does not have an active role, Steve, Dr. Tuttle, and Sarah all have significant influence over the decision to give Mrs. Rodriguez vancomycin and cefepime for a total of 7 days. In the morning during patient rounds, these individuals were communicating and making suggestions for how to reach a decision on the antibiotic course. Steve took notes on what was being said by Dr. Tuttle and the pharmacist Sarah. Later in the day Steve had written out his note including the antibiotic orders. Dr. Tuttle then signed off on this note and it became a signed order in the electronic medical record, meaning that the antibiotic was scheduled to be given as ordered[5]. The engagement of multiple individuals in the case demonstrates the collective nature of antibiotic decision making. These social determinants are important considerations that do not fit easily into current formulations of antibiotic stewardship.

A third key element in "Bucking Assumptions in the Surgical Intensive Care Unit" is how time pressures and the structure of medical practice impact the antibiotic decision. Importantly, had any of these individuals been called away or with another service that day (ex. Sarah often rotates which intensive care unit team she works with), the outcome could have been different. Additionally, had the team had several days to ruminate over the antibiotic choices, the outcome could have been different. During my research, I was constantly aware of the time pressures that physicians were placed under. Since notes in the medical record must be signed within the time limit set by insurance companies, notes end up getting signed by end of day (or night). Thus, the requirements of the structure of medical practice also shape the manner in which antibiotic decisions are made.

[5]Though an antibiotic order is placed in the electronic medical record, there are many steps that have to be taken for it to actually be administered by the nursing staff. How and when antibiotics are actually administered is not within the purview of this article as I have focused on how and when antibiotics are prescribed.

In the context of the tendency of antibiotic stewards to locate the power of decision making within individual physicians, and in light of evidence to the contrary, a deeper analysis of the data reveals complex social dynamics and institutional structures of practice that are otherwise invisible. There has been emphasis placed on the "behaviors" and "habits" of antibiotic prescribers that hinder antibiotic stewardship such as "defensive prescribing" (Mol et al., 2006) and "stealth dosing" (La Rosa et al., 2007). Furthermore, and for a variety of reasons including the social dynamics of medical practice, some physicians actively avoid following antibiotic stewardship recommendations, performing "workarounds" (Szymczak et al., 2019). Antibiotic stewardship interventions to address misuse and overuse of antibiotics by physicians have largely targeted these "bad" individual physicians.

CONCLUSION

The principles of behavioral economics suggest that by altering the conditions of the environment surrounding an individual one can influence that individual in the direction of a more favorable decision (Thaler and Sunstein, 2008). Meanwhile, social psychology encourages a more inward look at the rationales for behaviors and habits that individuals have (see Pedwell, 2017). Both of these approaches are inadequate to account for what really happens. Yet, antibiotic stewardship has a history of targeting individual physicians based on the underlying theoretical assumption that antibiotic decision making is an isolated act made in the mind of a physician. This study shows the fallacy of assuming antibiotic prescribing is an action completed by individuals by contrasting the common view represented by Dr. Martin with the ethnographic case study of the team working on Mrs. Rodriguez's antibiotic prescription.

Dr. Martin's perspective presented in this article is not unique among antibiotic stewards. In fact, it was the common view at my field site. In conclusion, I argue that while antibiotic stewardship programs often target individual physician prescribers, *antibiotic prescribing is a collective practice* influenced by social and material surroundings. Rather than just focus on the "behavior" and "habits" of physicians, the complex social dynamics present in the medical institution are actually more representative of where decisions regarding antibiotic use are made and signed off on. The ethnographic data illuminate (1) how entrenched the idea of individual prescribers is at my field site, and (2) how difficult it is to give credit to a single prescriber given the other individuals and institutional surroundings that direct decision making. Thus, while the antibiotic steward's understanding of the way to change physician prescribing behavior follows the tenets of behavioral economics and social psychology suggesting that problems are the result of individuals making bad choices, I have argued here using iterative and inductive research (cf. Karen O'Reilly, 2005) that deeper social dynamics in physician practice operate as agents shaping the conditions and determinants surrounding antibiotic use.

To optimize antibiotic use, antibiotic stewardship programs must appreciate the historic lack of input from the social sciences (particularly the qualitative social sciences, see Smith, 2015) that contributes to an underappreciation of the collective nature of antibiotic use (Chandler, 2019). Some antibiotic stewards have recognized that a one-size-fits-all program does not meet the needs of each culture and context (Jeffs et al., 2015; see "bespoke stewardship" Charani et al., 2019). I would like to suggest that beyond valuing context, antibiotic use can be optimized by reassessing where we consider to be the locus of antibiotic decision making (i.e., with the individual or the collective). We can begin to think of antibiotic prescribing as an activity occurring between persons amidst an institution harboring specific practices, physical spaces, and time pressures. For the antibiotic steward, this might mean changing the targets of antibiotic stewardship interventions. Furthermore, antibiotic stewardship programs could be pressed to reexamine existing notions of antibiotic prescribing processes by conducting observational and comparative research in their own local settings. Going forward, moving from the perception of antibiotic prescribing as something that is decided in our minds to something that unfolds and arises in context is critical.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Institutional Review Board of John H. Stroger Jr. Hospital of Cook County. Written informed consent for participation was not required for this study in accordance with institutional requirements.

AUTHOR CONTRIBUTIONS

KR conducted the research for and wrote this article in its entirety.

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Moral and Contextual Dimensions of "Inappropriate" Antibiotic Prescribing in Secondary Care: A Three-Country Interview Study

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Overuse of broad-spectrum antibiotics in secondary care is a key contributor to the emergence and spread of antimicrobial resistance (AMR); efforts are focused on minimizing antibiotic overuse as a crucial step toward containing the global threat of AMR. The concept of overtreatment has, however, been difficult to define. Efforts to address the overuse of medicine need to be informed by an understanding of how prescribers themselves understand the problem. We report findings from a qualitative interview study of 46 acute care hospital prescribers differing in seniority from three countries: United Kingdom, Sri Lanka and South Africa. Prescribers were asked about their understanding of inappropriate use of antibiotics. Prescriber definitions of inappropriate use included relatively clear-cut and unambiguous cases of antibiotics being used "incorrectly" (e.g., in the case of viral infections). In many cases, however, antibiotic prescribing decisions were seen as involving uncertainty, with prescribers having to make decisions about the threshold for appropriate use. Decisions about thresholds were commonly framed in moral terms. Some prescribers drew on arguments about their duty to protect public health through having a high threshold for prescribing, while others made strong arguments for prioritizing risk avoidance for the patients in front of them, even at a cost of increased resistance. Notions of whether prescribing was inappropriate were also contextually dependent: high levels of antibiotic prescribing could be seen as a rational response when prescribers were working in challenging contexts, and could be justified in relation to financial and social considerations. Inappropriate antibiotic use is framed by prescribers not just in clinical, but also in moral and contextual terms; this has implications for the design and implementation of antibiotic stewardship interventions aiming to reduce inappropriate use of antibiotics globally.

Keywords: antibiotic prescribing, antimicrobial resistance, hospital, qualitative investigation, international

INTRODUCTION

Antimicrobial resistance (AMR) is a health threat with potentially devastating global consequences (O'Neill, 2016). A key contributor to resistance is the overuse of antibiotics in healthcare; there are a range of drivers including unregulated access to antibiotics in the community in some lower-income settings, and unnecessary and excessive prescribing in community and hospital settings. Previous research indicates that more than one third of antibiotic prescriptions for hospital patients globally may be inappropriate (Zarb et al., 2010).

Appropriate prescribing choices are typically defined as the right drug, administered at the right time, using the right dose, for the right duration (Dryden et al., 2011). Antimicrobial stewardship interventions in hospitals focus on reducing the excessive use of antibiotics, and avoiding the use of inappropriate types of antibiotic, broad-spectrum antibiotics in particular (Hood et al., 2019). Broad-spectrum antibiotics are effective against a wider range of pathogens than narrow-spectrum antibiotics. While they are typically necessary in situations where information is lacking about the cause of an infection, broad-spectrum antibiotics come at the cost of being stronger drivers of AMR (Karam et al., 2016), and ideally their use should be limited to emergency cases (e.g., severe sepsis of unknown origin). Stewardship programmes have been implemented in hospitals worldwide, although with more difficulty in some contexts (Cox et al., 2017; Charani et al., 2019), resulting in positive but variable impact (Hulscher and Prins, 2017; Nathwani et al., 2019).

One challenge for stewardship is that it may be difficult to pinpoint what inappropriate or excessive antibiotic use means in practice, although efforts have been undertaken to try to develop consensus definitions and quality indicators for antibiotic prescribing (Spivak et al., 2016). Defining and measuring inappropriate or suboptimal use is complicated by the tensions that exist between the aim of reducing antibiotic prescribing in order to tackle the growing systemic problem of AMR, and the risks of failing to administer medication to individual patients when there is a potential risk of mortality and morbidity (Fitzpatrick et al., 2019). While prescribing antibiotics in the absence of bacterial infection is clearly inappropriate, clinicians have to base the majority of initial prescribing decisions on clinical judgement–prescribing empirically based on indicative signs and symptoms as opposed to a definitive diagnosis. This is particularly the case for acute medical patients presenting with a spectrum of symptoms that could possibly be indicative of infection. This initial decision could be supported by guidelines and anti-biograms (Liang et al., 2016) where available, and subsequently be refined based on microbiological results or review as part of a hospital's stewardship programme. For individual physicians, however, making these initial treatment decisions under conditions of uncertainty often involves balancing risks; their views about what constitutes the "correct" or most appropriate course of action may differ.

One of the underlying challenges to antimicrobial stewardship is a lack of agreement amongst physicians on what constitutes a "right" choice when making decisions about whether or not to prescribe an antibiotic, and whether to use a broad-spectrum antibiotic as the primary treatment. This variety of conflicting opinions may be grounded in different contextual influences of their medical training, past clinical experiences and current work situation, as well as their orientation toward the uncertainties and risks involved in managing patients with potentially serious conditions.

Drawing on qualitative interview data involving prescribers from a range of different international hospital contexts, this article aims to provide insights into the opinions held by prescribers about what counts as inappropriate prescribing, and the factors that mediate their judgements.

METHODS

Design

This study used a qualitative interview design, involving interviews with prescribers in secondary care in Sri Lanka, South Africa and the United Kingdom. Semi-structured interviews were conducted between 2016 and 2017. Interviews were conducted in each country by local researchers. We used a detailed shared topic guide (see **Appendix A**), containing 17 questions about antibiotic use. The guide included questions exploring a range of aspects of antibiotic use, with several questions focusing specifically on identifying the participant's understanding of inappropriate prescribing and asking for examples. In developing the guide we drew on previous research into the determinants of prescribing in hospitals (Krockow et al., 2019), as well as theoretical literature on social dilemmas as this was our overarching theoretical perspective for the study (Tarrant et al., 2019). We piloted and revised the topic guide based on interviews with two junior doctors. We conducted in-depth training and practice interviews for researchers, and held regular telephone meetings to discuss emerging findings through the course of data collection. The interviews were audio recorded and ranged in length between 20 and 80 min. Written consent was obtained from participants for recording of interviews and use of anonymised quotes in reports and publications. All data were anonymised prior to analysis, and participating institutions were offered debriefs about the research findings. Ethical approval was obtained separately in Sri Lanka, South Africa and the United Kingdom.

Participants

Our study participants included prescribers from three different countries (Sri Lanka, South Africa and the United Kingdom), recruited from a total of seven different hospitals across the three countries. These countries and participating hospitals were selected based on existing collaborations between the research team, and included high and lower resource settings, with diverse challenges in terms of resourcing and patient population.

In Sri Lanka and South Africa a significant proportion of medical care happens in the private sector (in Sri Lanka around 50% of outpatient and 10% of inpatient care is in the private sector (The Economist, 2014), and doctors commonly work across both sectors; around 20% of the South African population are seen in the private sector; Meyer et al., 2017) In both these countries we included public and private hospital settings to

explore how these different contexts shaped prescribing. Public health care makes up the majority of care the United Kingdom (Klein, 2005) (and is often used combination with public healthcare) hence both hospitals chosen for the study were public (National Health Service) hospitals. In Sri Lanka we included one private hospital and one public hospital located in a major city, and a publicly funded hospital located in a rural area. In South Africa we included two different hospitals located in a major city. One hospital was publicly funded while the other belonged to a chain of private hospitals. The two hospitals in the UK included a large city teaching hospital and a smaller hospital in an urban area.

Recruitment of participants was conducted using a snowball sampling approach: researchers were introduced to potential participants via email or personal introduction by the local contact in each hospital, or by previous interviewees. We aimed to purposively sample participants to include prescribers with different roles and levels of seniority. We aimed for a minimum sample size of 12 participants per country (total of 36 participants) as our previous experience indicted that this would be a reasonable number to enable us to fully explore the issues. We continued to recruit participants to interviews in each country until the team agreed we had reached a point of data saturation (Aldiabat and Le Navenec, 2018).

Data Analysis

All interview recordings were transcribed verbatim and anonymised data were analyzed by the United Kingdom-based research team using the constant comparative method (Charmaz, 2014). Starting with open, descriptive coding of a selection of transcripts, an initial coding framework was created using NVivo Software. This was followed by an iterative process of coding and evolution of the coding framework, with reference to existing literature and theoretical concepts (Tarrant et al., 2019). Drawing on this coded data, we focused on codes specifically pertaining to participants' understanding of inappropriate antibiotic prescribing. We generated data summaries for key themes. Visual methods were used to display data extracts and clusters of codes, and to map themes.

RESULTS

Participants

We interviewed a total of 46 participants: 18 participants in Sri Lanka, 13 participants in South Africa, and 15 participants in the United Kingdom. The majority of participants were doctors and ranged in seniority from junior doctors to consultants. In the United Kingdom, two advanced nurse prescribers were also included in the sample.

Findings: Definitions of Inappropriate Antibiotic Use

Our findings highlighted diverse definitions of inappropriate use. There was consensus that some cases of antibiotic use could be seen to be objectively "incorrect" based on the patient's condition or symptoms, but participants' accounts demonstrated that there was often significant ambiguity and lack of consensus about what they judged to be a "correct" decision. Excessive antibiotic use, and high levels of reliance on broad spectrum antibiotics could be justified based on arguments about the duties of a doctor/healthcare professional to their individual patients, and as being appropriate given the local context.

"Incorrect" Use of Antibiotics

Prescriber definitions of inappropriate use included examples of relatively clear-cut and unambiguous cases of antibiotics being used "incorrectly." These definitions included situations where antibiotics were prescribed but where infection was unlikely to be the cause of symptoms, for example, in cases in which symptoms or patient presentation indicated a different root cause such as a viral infection. Indeed, the vast majority of study participants across all countries and hospitals discussed detailed examples of patients being treated with antibiotics for viral illnesses such as the flu. This was seen as problem for patients in primary care settings, but also in hospitals, particularly in ambulatory emergency care.

> *I think the most common scenario, too common personally in my experience, where […] antibiotics in general are prescribed inappropriately, are viral illnesses. […] especially in, in the ambulatory [emergency] care setting. (UK 001) Some patients clearly having viral infections but they are on antibiotics. (SL 013)*

A related type of inappropriate prescribing described by participants was the use of antibiotics in the absence of any symptoms pointing to a bacterial infection. For example, participants reported cases where the mere acuity of a patient triggered a prescription of antibiotics despite the absence of any infection-specific symptoms.

> *They just come into the emergency unit, and [they are…] getting antibiotics, even though they have a multitude of other reasons for their admission. (SA 012)*
> *So the inappropriate use will be you don't have any evidence that the patient's having bacterial infection. The patient might be unwell due to other reasons, for example they might have asthma exacerbation with very little evidence of infection. (UK 007)*

Participants also pointed to situations in which the diagnosis was unambiguous, where clear guidelines about antibiotic choice, dose, and duration existed, but the prescriber failed to prescribe in accordance with these guidelines without justification–resulting in the patient receiving an inappropriate antibiotic or the incorrect dose or duration of treatment.

> *If there's a clear clinical scenario of infection that we know this is hospital-acquired pneumonia, and you know what kind of antibiotic is that, and you start prescribing a very broad spectrum, then you are not following guidelines, then you are just harming the patient. (SA 009)*

Overall, participants from all hospitals and countries shared similar opinions about what constituted an unambiguously clinically "incorrect" decision about antibiotic prescribing, or suboptimal antibiotic use. These types of incorrect or suboptimal

uses of antibiotics were commonly seen as reflecting unjustified individual preferences and habits, a lack of appropriate knowledge, or, for more junior doctors a lack of experience or senior supervision. Organizational systems and processes were also seen as playing into this, for example, a lack of access to guidelines, workload and demand on practitioners, or inefficient systems for monitoring and regulating antibiotic use. Participants shared the view that these types of incorrect uses could and should be tackled to reduce antibiotic overuse.

Ambiguities of Inappropriate Use: Uncertainty and Moral Framing of Antibiotic Prescribing Decisions

Beyond these shared definitions of incorrect antibiotic use, participants described gray areas of inappropriate use, where the appropriateness of prescribing decisions was less objectively clear. Participants recognized that many antibiotic prescribing decisions involved decision-making under uncertainty, where clinicians were using their clinical judgement to assess the likelihood of infection, the likely source of infection and infective agent, and therefore the best course of action. Prescribers had to make decisions about the threshold at which they would prescribe antibiotic treatment, and their certainty over whether they could use a targeted narrow-spectrum antibiotic as opposed to a broad spectrum antibiotic. This threshold might vary from patient to patient, depending on their vulnerability and level of risk (e.g., young children, frail older people), but also individual prescribers were seen to vary in their approach.

> *[There] are generally two camps that you get with dealing with uncertainty. So you get the one which is very prone to jump in and do something, and that might be prescribing antibiotics [. . .], which may or may not be appropriate. And then you get the other, which is more likely to just, to try to investigate and work out what's happening before giving an antibiotic. (UK 004)*

Under conditions of uncertainty, where judgements had to be made about where to set a threshold for prescribing, antibiotic use was less easy to classify as appropriate or inappropriate in objective terms. Participants recognized that setting a low threshold–i.e., erring on the side of caution and prescribing antibiotics to acutely ill patients "when in doubt," was an easy and low risk approach to avoiding the risks of deterioration and death for their patients. They also recognized, however, that overuse of antibiotics had negative consequences for society by contributing to the problem of AMR. The tension between the interests of different stakeholders was well-understood by most. Where prescribers were prepared to set the threshold was seen as reflecting, to some extent, their experience and confidence in assessing risk and tolerating uncertainty.

> *When I started working in this setting, I would be very over-careful of missing something. I think, as I got more confident, I start the conversation with "I don't like prescribing antibiotics. If I feel your child needs an antibiotic, I will give it. But I would prefer to rather wait and see" (SA 007)*

In considering how they judged whether their own, and others', levels of prescribing were inappropriately high or low, participants on drew on moral arguments in relation to balancing the interests of the different stakeholders. These arguments reflected participants' underpinning beliefs about what it meant, for them, to be a good doctor or good healthcare professional, and resulted in nuanced, and sometimes contradictory, accounts, of what was inappropriate and why.

Some participants made moral arguments about the importance of considering their duty to broader society (and protecting public health) when making decisions about antibiotic use under uncertainty. For some, appropriate antibiotic use was seen as being grounded in a consideration of the risks to society of excessive antibiotic use, balanced against their duty to their individual patients.

> *It's kind of a public health like obligation, isn't it, to make sure that you're giving decent antibiotics correctly, to reduce resistant strains. (UK 009)*
> *So we have to balance that risk constantly. And I would say obviously people can argue that your individual patient takes priority, but then other considerations would be society as a whole, or the broader community has to be taken as the priority. [. . .] You have to be cognizant of the fact that these treatment decisions you make on this patient has an impact on the next one and society as a whole. (SA 010)*

They made critical judgements about other clinicians who were quick to prescribe antibiotics or relied too heavily on broad spectrum antibiotics.

> *For the vast majority of cases, the use of broad-spectrum antibiotics is [. . .] a consequence of lackadaisical or poorly worked up clinical decision-making. [. . .] You've got a better chance of getting [the patient] better quicker, because you're covering all possible ills. But it's not good medicine. (UK 002)*

While this reasoning sits in line with broader goals of antibiotic stewardship, conversely, other participants made counterarguments to this position, also grounded in moral terms. Although recognizing the tensions in balancing the interests of individuals and society, some participants framed their duty, and correspondingly their understanding, of what it meant to be a good doctor or healthcare professional, in terms of prioritizing the wellbeing of the individual patients in front of them. Although they recognized the clinical importance of treating patients appropriately, they minimized the risk of AMR and their responsibility for the problem, in comparison with the risks and their responsibilities for sick patients in front of them.

> *I think I try to do what is good for the patient and that is the only thing [. . .] The only agenda I have is that. (SL 007)*
> *As a doctor, the most important is the patient's interests, you know, so you try and do the right thing for that specific patient, and then, the other interests are probably less important. (SA 006)*
> *I have that sense at a societal level [of the problem of AMR], but my job as a doctor is to treat the person in front of me. [. . .] so I don't balance. . . [. . . I'm] just doing what I can to make the patient better. (UK 012)*

These participants drew on such arguments as justification for using antibiotics, and particularly broad spectrum antibiotics, when in doubt, even if this was at a cost of increased resistance.

> *As a doctor we need to save patients, [. . .] even if we think that this is broad-spectrum antibiotics, and [we should be concerned about] resistance with the [hospital] trust, but at that time I think the most important thing is to treat your patient well. (UK 005)*

As such, judgements about the appropriateness of antibiotic prescribing decisions could not always be pinned down in objective clinical terms. Instead, how participants justified their approach to antibiotic prescribing under conditions of uncertainty reflected their orientation to risk, and their position about what it meant to be a good doctor in terms of moral responsibilities. Participants took different standpoints in relation to where their duties as a doctor or healthcare professional lay, and therefore, what was and was not appropriate practice.

Ambiguities of Inappropriate Use: Inappropriate Prescribing as Contextually Dependent

Notions of whether levels of antibiotic prescribing were considered to be inappropriate were also contextually dependent: what could potentially be seen as over-use of antibiotics, or excessive reliance on broad-spectrum antibiotics, was re-framed in some cases by participants as a rational and appropriate response to the conditions in which they worked. Although they recognized such antibiotic use as excessive, they did not always see it as inappropriate in the context of the demands they faced and the resources available to them. This was a particularly common response from participants in low resource settings.

Such challenging circumstances in low resource settings included conditions of high patient throughput–including high numbers of patients presenting at a late stage when they were acutely ill. Problems also arose when patients who had already taken (often unspecified) antibiotics in the community prior to coming into hospital–including antibiotics that had been prescribed without any microbiological testing, or had been purchased. This constrained the choices about how these patients could be treated once they arrived in hospital. It also meant that that waiting for microbiological tests prior to prescribing was commonly seen as futile, and this futility was exacerbated in some contexts by the lack of rapid and high quality testing services.

> *When the patients come very late [i.e., present at hospital with infections at an advanced stage] by that time they will have at least more than one system affected. [. . .] so we will again be using the broad spectrum even without [waiting] for the cultures and things like that (SL 003)*
> *Unfortunately, because our diagnostic tests are not that great, and turnaround times are poor, and sensitivities etc. are not that good, you might have to go [with] broad [spectrum antibiotics] (SA 012)*

Unsanitary and overcrowded environments were seen as vastly increasing the risk of hospital-associated infections, increasing the need to rely on antibiotics.

> *We are seeing a lot of [. . .] infections in our wards because we [don't] have the facilities, I mean like the beds are very close and they are not in separate parts, cubicles. (SL 015)*

In these cases, it was not the antibiotic use that was seen as wrong or inappropriate, but the precipitating conditions. Participants felt they were able to respond to these conditions only in the best way that they could. While these problems–access to hospitals and use of antibiotics in the community, and insanitary hospital environments–remained as they were, participants were able to justify high levels of antibiotic use and saw little opportunity for reducing their use.

Other contextual factors that shaped views about whether antibiotic prescribing was the "right" thing to do, even at a cost of increased resistance, related to financial and social considerations. Although some participants flagged the problem of costs of excessive use of antibiotics for their organizations, others argued that financial and social considerations for patients could make antibiotic use the appropriate choice. In private hospitals, some argued that using broad-spectrum antibiotics could help reduce costs for patients arising from length of stay. In lower income settings, participants recognized that a hospital stay could be financially devastating for wage earners in families and had an impact on the economy: treating patients aggressively to get them well and out of hospital quickly was seen in some cases as a priority.

> *Most people with private medical insurance, they have to [. . .] get out of the hospital as soon as possible. They work for themselves, a lot of the people, they cannot afford to stay long in the hospital. So if you give [. . .] a good broad-spectrum antibiotic to start off with [. . .] it's a win-win situation all the way. (SA 004)*
> *Broad-spectrum benefit was, [. . .] start medications, there will be improvement, so these people are working, I mean, going back to working. (SL 005)*

DISCUSSION AND CONCLUSIONS

The interview findings from doctors and nurse prescribers across three countries and different hospital sites suggest ambiguities in opinions about what counts as inappropriate antibiotic prescribing and antibiotic over-use in hospital settings. Our focus in this paper was on how prescribers made judgements about the appropriateness of antibiotic use, and how they justified their own and others' use of antibiotics. In terms of prescribers' own understanding of appropriateness, there was consensus that antibiotic use under certain circumstances could be judged to be clinically "incorrect" (e.g., "incorrect" the use of antibiotics for viral illnesses). Not all decisions about antibiotic use could, however be judged as objectively appropriate/inappropriate in clinical terms. There was significant ambiguity about judgements of appropriateness of antibiotic use in case of diagnostic uncertainty. Such judgements were mediated by personal perceptions of working within the frames of risk and uncertainty, and participants' comfort in tolerating risk. As identified in previous research, this could vary dependent on individual training, experience, and seniority, but also on

the extent of concern about the impact of negative patient outcomes, and the risk of personal and reputational damage (Krockow et al., 2019).

Judgements about the appropriateness of antibiotic use also drew on moral reasoning about what it meant to be a good doctor or healthcare professional. This reflects what has been referred to as *relational ethical reasoning*: reasoning aimed at working out "what is the right thing to do" based on an individual's role, and relationship with and responsibility for others (Austin et al., 2003; Pollard, 2015). In the context of medicine, relational ethical reasoning is directed at answering such questions as: What makes a good doctor or health professional? Am I a good doctor or healthcare professional (Lindseth, 1992)? This reasoning reflects not only individual skills and experience, but also how an individual sees themselves as positioned, and where their responsibilities lie, in relation to their patients and other stakeholders (Sørlie et al., 2001). Prescribers see themselves as "acting wisely in the face of inevitable uncertainty" (Tanenbaum, 1993), but make different interpretations of what it means to do so. Individual participants varied in their views of their responsibilities in relation to public health and for considering wider society in their decision making; some felt the individual patient was their only concern. This finding builds on other research demonstrating that individual prescriber decisions about antibiotic use are underpinned by different perceptions: the extent to which they are oriented toward AMR and infectious diseases (Björkman et al., 2010) as opposed to having a dominating focus on the care of the patient. This tension between attending to the needs of individual patients vs. tending to the needs of the population as a whole has been recognized as a central ethical problem in diverse areas of medicine, particularly preventative medicine (Rosenberg, 1998; Griffiths et al., 2006). Our study highlights how this tension underpinned moral judgements about antibiotic use: what one prescriber judged to be excessive antibiotic use, based on their perceptions of duty to consider public health, could be seen by another as an appropriate response based on their sense of responsibility to minimize risk to the individual patient in front of them. These findings raise questions about what good practice can mean within existing health care systems: with attendant regulatory and structural drivers that prioritize immediate patient outcomes; and formalized ethical principles for professional practice (General Medical Council, 2019; Sri Lanka Medical Association, 2019)[1] that define being a "good doctor" in terms of making the care of the individual patient their primary concern, and protecting the life of their patients.

Judgements about the appropriateness also reflected the context within which prescribers were working: high levels of antibiotic use could be seen as a rational and morally justifiable response to challenging conditions such as patient acuity and poor environments in hospitals for hygiene and infection control. The importance of cultural and contextual factors in shaping antibiotic use is well-recognized (Hulscher et al., 2010,?; Pearson et al., 2018; Wilkinson et al., 2019): our study shows how these factors also played into prescribers' reasoning about appropriateness of antibiotic use. "Excessive" antibiotic use could be recognized as such by prescribers but nonetheless be seen as representing a reasonable response to local conditions. In this sense, although levels of prescribing were seen as excessive, they were not seen as inappropriate. As such, judgements about the appropriateness of antibiotic use did not solely reflect a fixed individual moral position, but were situated in context of the local systems and structures of care, and the temporality of the patient's presentation. It is apparent that the way doctors and other prescribers make judgements about appropriateness are grounded in individual moral reasoning, and are highly contextualized: they cannot be reduced to purely technical criteria.

Our study has limitations. We included participants from three countries, including high and lower resource settings, hence the generalizability of our findings to other international settings is necessarily limited. We conducted interviews with a small number of participants in each hospital, although we included prescribers with different roles and different levels of seniority and experience. Our study design did not allow us to explore how practitioners actually behaved in practice in relation to decision-making about antibiotic use. Also, our analysis focused specifically on antibiotic prescribing decisions; we did not explore other dimensions of antibiotic use such as medication review, stopping or switching antibiotics. Reviewing antibiotic prescribing is an important focus for stewardship, providing a way of updating or correcting initial prescribing decisions particularly in the light of new information that can provide more certainty about the best clinical course of action. Activities around reviewing, stopping and switching antibiotics present a range of different challenges (Schouten et al., 2007) which were not the focus of our study.

A strength of our study is the inclusion of a range of different organizations across three international contexts, including high and lower-income settings, and public and private hospitals. We did not include a private hospital in the United Kingdom, because the majority of acute healthcare provision is through publicly-funded NHS providers. A further strength is the conduct of the interviews in each locality by local researchers, who were familiar with local health systems and could build rapport effectively with participants. Although contextual factors, patient characteristics, and stewardship activities varied significantly between countries and hospitals, it is notable that we found strong concordance across the settings in terms of definitions of "incorrect" use, and of uncertainty and moral aspects of decision-making. Findings relating to contextual influences mainly came from the interviews in lower-income settings, although NHS staff in the United Kingdom did reflect on some of these considerations including cost to the healthcare system.

Our findings have implications for antimicrobial stewardship. As highlighted earlier in this paper, lack of consensus among prescribers about what constitutes inappropriate use presents a challenge for stewardship efforts. Our findings suggest that this lack of consensus is unlikely to have a technical solution–for example, through drawing up more specific definitions–because

[1] Africa HPCoS. Ethical guidelines for good practice in the health care professions [Available from: https://www.hpcsa.co.za/Uploads/Professional_Practice/Ethics_Booklet.pdf].

judgements about appropriateness are morally and contextually framed. Stewardship interventions that directly target behavior change using techniques such as education, restrictions and controls on prescribing, and audit and feedback (Davey et al., 2017) may have value where there is consensus that prescribing is wrong or suboptimal. These types of interventions may, however, be less effective at addressing the underpinnings of moral reasoning about antibiotic use, or the structural and contextual factors, that from the point of view of prescribers can make antibiotic overuse a rational and justifiable action. Aiming to tackle inappropriate prescribing may be problematic where consensus is lacking about what in fact constitutes "inappropriate" prescribing: where this phenomenon is morally contestable and contextually-embedded. The terminology of "inappropriate" or "suboptimal" prescribing itself may be unhelpful, given the implicit assumption that this can always be judged objectively based on the facts of the matter.

One implication of our findings is that, rather than assuming that inappropriate prescribing can be objectively specified and therefore reduced through simple interventions, there may be a need to look at how to provide more support for prescribers in managing uncertainty. Stewardship approaches that aim to support empirical decision making, improve documentation of rationale for antibiotic use, and focus on reviews of antibiotic prescriptions (based on updated information providing more certainty, such as microbiology results) are clearly important. There is also a need, however, to address the moral aspects of prescribing decisions. This might involve including vignette-based debates in stewardship training, and providing opportunities for collective input to difficult decisions. We may also need more explicit societal debate, and the establishment of collective agreements around, the duty of prescribers to consider the interests of society in making antibiotic prescribing decisions (Tarrant et al., 2019). Consensus guidelines and decision-support tools have been identified as approaches to managing moral dilemmas in antibiotic prescribing (Leibovici et al., 2012). Another implication is the need to recognize that efforts to reduce inappropriate antibiotic use by targeting prescribing behavior (for example, through education, or auditing) may be futile if they fail to conceptualize antibiotic overuse as a rational response to local cultural and contextual conditions. Even antibiotic use that can be objectively defined as "clinically incorrect" could reflect the accepted practice of using antibiotics as a "quick fix" to complex problems such as poorly integrated health systems (Denyer Willis and Chandler, 2019), particularly in resource limited settings. This points to the need for a more holistic approach (McLeod et al., 2019) that considers the broader drivers of antibiotic use in secondary care settings globally, including issues such as sanitation, community healthcare, and the financial implications for patients of hospitalization.

Our study suggests that inappropriate antibiotic use is framed by prescribers not just in clinical, but also in moral and contextual terms; this has implications for the design and implementation of antibiotic stewardship interventions aiming to reduce inappropriate use of antibiotics globally.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Leicester Research Ethics Committee, Sri Lanka Medical Association Ethics Review Committee, and University of Stellenbosch Health Research Ethics Committee 1. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

CT, AC, EC-B, DJ, NP, SM, and EK planned and designed the study. EK, CT, WN, and MB conducted interviews. CT and EK conducted the data analysis and drafted the first manuscript version. All authors helped to review and refine the final version.

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APPENDIX A: TOPIC GUIDE FOR INTERVIEWS

Questions About Their Role

Can you tell me briefly about your job role? What is your involvement in the antibiotic prescribing for acute medical patients?

What education or training have you had specifically on antibiotic prescribing?

Prescribing Decisions

I'd like you to consider antibiotic prescribing for an acute medical patient with a suspected infection, that is, when it is not confirmed that the patient has an infection, or what the infective organism might be (also known as empirical prescribing).

1. How do you go about making the decision whether or not to prescribe an antibiotic?
   - *Are there any 'rules of thumb' that you use? What influences this decision?*
2. Can you tell me about how you decide which antibiotic to use, for an acute medical patient with a suspected infection?
   - *Local or national guidelines on antibiotic prescribing?*
   - *Any limitations/restrictions on the antibiotics you can use?*
   - *Do you ever get advice on your prescribing decisions? Who from & why?*
3. How important do you feel it is to collect microbiology specimens, in making antibiotic prescribing decisions? Why?

I would be interested to hear your thoughts on choosing between a broad vs. a narrow spectrum antibiotic. Broad spectrum antibiotics being an antibiotic with activity against a wide range of pathogens. A narrow spectrum antibiotic is one that is targeted at a specific organism.

4. How easy do you find this decision? What do you see as the uncertainties and how do you deal with them? *What sort of influences are there on your decision?*
5. What would you see as the benefits of prescribing a broad spectrum antibiotic (BSA), as opposed to a narrow spectrum antibiotic?
6. What would you see as the risks of prescribing a BSA, as opposed to a narrow spectrum antibiotic?
7. Do different stakeholders have different interests? [patient / doctor / hospital / society] To what extent do you consider these in your day to day prescribing, and how do you balance these interests?
8. If you prescribe a BSA, how likely is it that the patient would be switched to a narrow spectrum antibiotic at a later point? *Why? What are the barriers to this? What helps make it easier?*
9. How do you know whether you are making good decisions about antibiotic prescribing? Do you get any feedback about your antibiotic prescribing approach?
10. Do you ever feel patients are prescribed BSAs inappropriately? Could you start by saying what you see as inappropriate use? Are there common situations where this happens? Why do you think this happens?
11. What steps could be taken to stimulate appropriate use of BSAs?
    - *Main barriers to improving the way BSAs are used in this hospital? e.g.: local culture / lack of lab facilities / organizational policies / external incentives or pressure*

    I'd like to focus now on antibiotic resistance, that is, the ability of a bacteria to stop an antibiotic from working against it, meaning that some antibiotic treatments become ineffective, infections persist and can spread to others. This can mean having reduced or no antibiotic treatment options. Do you worry about the problem of antimicrobial resistance in your day to day practice? Why?
12. Do you ever see examples of resistance? How often does this happen in your experience?
13. How much does the problem of antibiotic resistance influence your decision-making about prescribing antibiotics?
14. Do you get information about overall levels of antibiotic resistance in this hospital?
15. Do you think that reducing the use of BSAs in hospitals would make an important difference to addressing the overall AMR problem? Why yes or no?

ENDING

Is there anything else you'd like to add about the use of BSAs, or the problem of AMR? Thanks for participating!

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The Social and Material Life of Antimicrobial Clay: Exploring Antimicrobial Resistance, Medicines' Materiality, and Medicines Optimization

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While sociologists have made significant theoretical contributions to the antimicrobial resistance (AMR) debate, little attention has been given to the antimicrobial products themselves. Here we advocate a significant new direction which centers on the social and material life of antimicrobials, specifically on what they are made from and how this affects their use. This focus is timely because, in the context of declining efficacy of biomedical antibiotics, diverse materials are increasingly taking center stage in research and drug discovery as potential agents for new antimicrobial treatments. Of particular significance are natural antimicrobials, such as plants, honey and clay, whose antimicrobial potential is well-documented and which are increasingly moving into mainstream antimicrobial research. Alongside this biomedical focus, we suggest that the *social and material lives* of these antimicrobial materials require attention to (i) highlight the ways they have been, and continue to be, used in diverse cultures globally, (ii) explore ways we might theorize these materials within wider AMR debates, and (iii) examine the impact of antimicrobials' materiality on their use by patients. This article takes the example of clay, whose antimicrobial properties are well-established and which has been used to treat wounds and gastrointestinal problems for millennia. We first locate clay as an exemplar of a wider shift toward natural products drug discovery in pharmaceutical science and antimicrobial research. We then offer a number of theoretical "ways in" for sociologists to begin making sense of clay as it comes under the western biomedical gaze. We map these conceptual lenses on to clay's physical and symbolic mobility from its use in the global south into western biomedical research and commercialization. We particularly concentrate on post-colonial theory as a means to understand clay's movement from global south to north; laboratory studies to examine its symbolic transformation to a black-boxed antimicrobial artifact; and valuation practices as a lens to capture its movement from the margins to the mainstream. We finish by reflecting on the importance of materiality in addressing optimal use of medicines and by advocating an interdisciplinary approach to AMR which positions sociology as a key contributor to AMR solutions.

Keywords: clay, materiality, optimization, social life, geophagy, value, laboratory life, post-colonial theory

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INTRODUCTION

This paper argues for a significant new direction in sociological approaches to antimicrobial resistance (AMR) which focuses on the materiality of antimicrobial artifacts. While social scientists have made significant theoretical contributions to understanding AMR, as well as its framing and responses to it [see Macintyre (2014), Wood (2016), and Will (2018) for overviews], limited attention has been given to antimicrobial products *themselves* and how their materiality (i.e., what they are made from, what they look like, how they are produced) may influence their use. This is despite a recent "materiality turn" in the social sciences (see Pinch and Swedberg, 2008) and the well-established tradition, particularly in science and technology studies (STS), of centralizing non-human artifacts; Bruno Latour, after all, reminds us to "follow the actors" (Latour, 2005, p. 237).

Such a focus on antimicrobials' materiality is important because, in the context of the declining efficacy of existing antimicrobial medicines, diverse materials are beginning to take center stage in research and drug discovery as potential agents for new treatments (Newman, 2019). Of particular significance are natural products such as honey, plants, and clay whose antimicrobial potential is well-known and are therefore prime candidates for new antimicrobial drug discovery programmes (see McLoone et al., 2016 for a review of honey). The application of computational biological approaches and modern high throughput screening techniques to uncover nature's "treasure trove" Davies (2011, p. 5) opens up the potential for a fresh generation of antimicrobials derived from natural products (Thomford et al., 2018). Alongside this biomedical focus on diverse materials, we suggest that sociologists are best placed to make sense of the *social and material lives* of these natural antimicrobials, particularly to locate their materiality within discussions of optimizing their use.

In this article we take the example of clay, whose antimicrobial properties are well-documented and which has been used for centuries to treat wound infections and gastrointestinal problems (e.g., Williams and Haydel, 2010; Williams, 2019). As an exemplar of the accession of natural products into western antimicrobial research, we suggest that clay provides a fruitful lens to explore the shifting material life of antimicrobials. We offer a number of theoretical "ways in" to this exploration, which we map onto the physical and symbolic mobility of clay from its use in the global south into western biomedical research. These "ways in" are not intended to be comprehensive; we offer only brief overviews of each theoretical approach and pose questions and suggestions, rather than answers, as to how they may be useful in understanding natural product drug discovery approaches to antimicrobials. We also deliberately avoid over-synthesizing these "ways in" as we do not wish to present an instructional schema for researchers approaching clay sociologically. The intention, then, is to set an agenda for a novel approach to AMR which centers on antimicrobial products and to demonstrate its theoretical feasibility.

First, we offer an overview of the shift toward natural antimicrobials before we hone in on clay and examine the ways that social scientists have previously made sense of medicinal applications of clay, primarily through its ingestion. We then suggest a number of theoretical "ways in" for sociologists to begin thinking specifically about the place of clay in the antimicrobial landscape, but more widely about the materiality of diverse antimicrobial products and what this might mean for their use by practitioners and patients. We then consider what insights can be learned for optimizing antibiotic use through this focus on materiality. Finally, we argue for an interdisciplinary approach to AMR in which sociologists collaborate not just with our closest disciplinary neighbors, but across the natural and physical sciences boundaries in order to position sociology as an important contributor to AMR policy and practice solutions (see Will, 2018).

ANTIMICORBIAL RESISTANCE AND THE SHIFT TOWARD NATURAL PRODUCTS DRUG DISCOVERY

Antimicrobial Resistance

AMR refers to changes in pathogenic (that is disease-causing) microorganisms (viruses, bacteria, fungi, or protozoa) that allow them to acquire resistance to existing medication or treatment regimes. Promoted by inappropriate and excessive use of antimicrobials in human and veterinary medicine, AMR poses a significant global public health problem as common infections become increasingly challenging to treat and previously routine surgical procedures become potentially hazardous (World Health Organization, 2014). Coupled with this, few new antimicrobial drugs have been discovered or developed in recent years while history has demonstrated that further evolution of resistance is inevitable (Rodríguez-Rojas et al., 2013). This has created an "antimicrobial perfect storm" (Broom et al., 2014, p. 81) which the United Nations (2019, p. 1) suggests will have a "disastrous impact within a generation." In the UK, a recent government report predicted that AMR is likely to overtake cancer as the leading cause of death over the next 30 years (O'Neill, 2016), while the World Health Organization (2014, p. 19) estimated that the current $21–34 billion/year cost of AMR to the US health system will escalate as drug resistance increases. de Sosa et al. (2010) note that the impact of AMR is likely to be more extreme in developing countries where a higher infectious disease burden and precarious financial circumstances prevent the rapid development and deployment of new treatment agents.

Natural Products Drug Discovery

In the context of the declining efficacy of existing antimicrobials, biomedical researchers are turning to increasingly innovative methods, approaches and materials to identify new agents. A key aspect of this is "natural products drug discovery" where researchers look to natural materials for their therapeutic potential; in other words, science "revert[s] to 'nature' for answers" (Thomford et al., 2018, p. 1). While this movement toward natural products represents a shift in contemporary drug discovery practice, the natural world is not uncharted territory for pharmaceutical research and drug discovery

(Mandal et al., 2018). Rather, a significant number of well-established biomedical therapies are derived from natural products, including quinine (antimalarial from the bark of the Cinchona tree), codeine (painkiller from poppies), and Taxol (cancer therapy from the Pacific yew tree). Indeed, natural products drug discovery as an approach within the pharmaceutical industry had a "golden age" in the 1950s and 1960s during which time the US Department of Agriculture undertook a specific programme of plant extract collection and screening (Cragg and Newman, 2015) and a significant number of naturally-derived pharmaceutical products were brought to market (Shen, 2015, p. 1297). This heyday of natural product drug discovery was tied up with what has been called the "golden age of antibiotics" during the middle decades of the twentieth century when the discovery of new antibiotics coincided, in the UK, with improvements in social housing and the introduction of the National Health Service. In this new healthcare and public health milieu, antibiotics were positioned as wonder-drugs heralding the end of infectious disease (see Burnett, 1953). It should be noted that the majority of antibiotics discovered during this period, and subsequently, originated as natural products (Newman, 2019).

In the latter half of the twentieth century, however, many pharmaceutical companies scaled back their focus on natural products as high throughput screening and novel synthesis methods enabled the creation of large libraries of synthetic chemicals (Shen, 2015). Moreover, accessing, harvesting, and growing natural products involves navigating diverse, and often competing, political, environmental and financial interests, potentially making naturally-derived products practically and financially unviable [see Goodman and Walsh's (2001) overview of the political landscape surrounding Taxol]. As such, natural products drug discovery largely fell out of fashion as pharmaceutical companies favored the use of synthetic compounds in drug manufacturing. Antibiotic development is also faced with significant difficulties associated with passing drug trial hurdles and the perceived and genuine lack of profitability inherent in short-term treatments.

More recently, however, in the context of the AMR crisis, natural products have begun to (re)take center stage as companies explore new avenues for potential antimicrobial drug candidates (Cragg and Newman, 2013). In this context, the natural world has been described as an "endless frontier" (Li and Vederas, 2009) and an "inexhaustible" (Davies, 2011, p. 5) source of potential candidates for new antimicrobial therapies (see Brown and Wright, 2016). Coupled with advances in microbial genomics, bioinformatics, and synthetic biology (see Thomford et al., 2018), it has been suggested that drug discovery is undergoing a "renaissance…inspired by natural products" (Harvey, 2007, p. 480) where "we are surely entering a new golden age of natural products drug discovery" (Shen, 2015, p. 1297).

The therapeutic use of natural products is, of course, not limited to pharmaceutical medicines. Natural healing products on general sale such as Aloe Vera, Manuka honey and Echinacea have been used as antimicrobial treatments for centuries and are growing in popularity in the west. Sociologists have theorized this increased use of natural products (mostly subsumed under the umbrella of "complementary and alternative medicines") as a result of their commercialization (Collyer, 2004), increased skepticism toward biomedicine, dissatisfaction with traditional doctor/patient relationships and a proliferation of discourses of holism in health [see Gale (2014) for an overview]. For Carter et al. (2016), the increased use of these natural products and, in many cases, their adoption as potential antimicrobial drug candidates by pharmaceutical companies, repositions them from alternative, marginal therapies into the mainstream.

The Case of Clay

One such example is clay (or more specifically minerals found naturally in clay), whose antimicrobial properties are well-documented (e.g., Williams, 2019) and which has been used in various therapeutic forms since the earliest human civilizations (Hosseinkhani et al., 2017). While therapeutic clay use has a long history, the contemporary biomedical story of antimicrobial clay minerals begins in 2002 when French humanitarian worker Line Brunet de Courssou approached the World Health Organization with a series of case studies in which she had used clay, specifically French green clay, to treat Buruli ulcer (a necrotising soft tissue disease caused by *Mycobacterium ulcerans* and where treatment involves combined antibiotic therapy and often surgery, including amputation) in Côte d'Ivoire (Williams and Haydel, 2010). In her report, Brunet de Courssou suggested that clay may provide an effective way to treat bacterial skin infections commonly found in Africa and requested financial support to further research the area. Her application for funding was unsuccessful but nonetheless prompted scientists in North America to pursue the antimicrobial potential of clay and its mode of action. Williams and Haydel (2010, p. 746), for example, state that Brunet de Courssou's findings "were the stimuli for our research into the healing mechanism of clays" and, in the same paper, thank Brunt de Courssou for bringing antibacterial clays to their attention.

In the years following Brunet de Courssou's report, western researchers began to analyse the mineralogical properties of the clays used in her work and to ask, more generally, "what makes… clay antibacterial?" (Williams et al., 2011). In other words, while the healing properties of clay have been known around the world for thousands of years, researchers began to investigate the biochemical and mineralogical basis for their therapeutic benefits. In more recent years, as AMR has loomed larger as a global health threat, the antimicrobial potential of clay minerals has been centralized as part of the so-called "new golden age of natural products drug discovery" (Shen, 2015, p. 1,297) and the antimicrobial properties of clay are beginning to gain traction in drug discovery science (e.g., Morrison et al., 2016). Within this, clay-based topical therapies have been shown to be effective in treating skin conditions, including necrotising fasciitis, as noted above (Williams et al., 2004), open wounds (Sirousazar et al., 2011), and acne (Toombs, 2005). Detailed analysis of clays and their impact on bacterial survival has

led to the suggestion that the aluminum and iron content of clays is the toxic component (i.e., what kills bacteria), probably as a result of localized release of reactive oxygen species at the bacterial surface (Morrison et al., 2016; Wang et al., 2017; Zarate-Reyes et al., 2018). The antibacterial action of clays has been further evidenced in other studies. Considerable work has been undertaken to characterize the chemical and physical properties of clays responsible for antibacterial activity (Williams, 2017, 2019). The efficacy of clay against pathogenic bacterial biofilms has also been confirmed (Caflisch et al., 2018) and antibacterial clays have been found to reduce drug-resistant *Staphylococcus aureus* infection and inflammation in wound infections in mice (Otto et al., 2016). As such, there is a clear, and continually emerging, body of scientific evidence that clay is an effective antimicrobial, and Williams (2019, p. 7) suggests that in the context of a growing antimicrobial crisis "mimicking the antibacterial mechanisms exhibited by natural clays could be advantageous in the development of new antimicrobial agents."

While the story of clay, and other natural antimicrobials, in contemporary drug discovery is interesting in itself, in this article we are concerned with how sociologists might make sense of this shift in drug discovery science and theoretically locate natural antimicrobials within the wider AMR landscape. To begin to address this, for the remainder of this paper we highlight clay as an example of the (re)entrance of natural materials into AMR research and drug discovery. Through this example, we show that the reinvigoration of natural products drug discovery requires a collaborative, interdisciplinary approach which locates the social and material life of natural antimicrobial products alongside their biochemical and antimicrobial potential. Such an interdisciplinary approach not only makes visible the uses of these products across cultural contexts but also, by centralizing the materiality of natural antimicrobials, has potential impacts for optimizing antimicrobial use.

To do this, we suggest theoretical "ways in" through which sociologists might explore the material life of clay and map these onto its mobility. Here we mean both the physical movement of clay (from the global south to the global north, from poor countries to rich ones, from black to white bodies, and from natural contexts to research laboratories) and its symbolic mobility from the margins of western medicine into the mainstream. We do not intend to provide a comprehensive or instructional account of how to explore medicinal clay and other antimicrobials. There are undoubtedly other theoretical framings left unexplored here which could be effectively mobilized to theorize the use of clay, and other natural products, in antimicrobial research. Rather, the "ways in" we propose are intended as heuristic devices to stimulate a novel sociological discussion of, and focus upon, the materiality of antimicrobial artifacts. While we focus on the case of clay specifically, the approaches we outline below are applicable to other materials emerging from natural products antimicrobial discovery and, throughout, we provide examples of this wider applicability.

SOCIOLOGICAL "WAYS IN" TO ANTIMICROBIAL CLAY

Existing Social Science Research on Clay: Geophagy

Unsurprisingly, clay has not been prominent on the radar of medical sociologists. That is not to say, however, that clay has wholly escaped the attention of social scientists; anthropologists and geographers have had a sustained interest in clay's medicinal uses, particularly the practice of geophagy, which is the deliberate eating of soil, earth, or clay. Ingestion of clay has a number of proposed benefits, notably through its mineral content serving as a nutritional supplement and its absorptive properties in detoxification and lining the gut to settle gastrointestinal infections (potentially also as an antimicrobial), and is common across the global south and east (Henry and Cring, 2013, p. 181). The practice of geophagy, broadly speaking, has been conceptualized in one of two ways (see Henry and Matthews Kwong, 2003). It is either (i) pathologized as a form of "pica," that is "compulsive eating of non-food substances" (Walker et al., 1997, p. 280), or (ii) understood as a routine part of everyday nutritional life and foodways (Loveland et al., 1989). While medicine (particularly psychiatry and public health) has focused on the neurological causes of geophagy, its negative health consequences and possible treatments, social scientists have foregrounded geophagy's cultural-locatedness and ordinariness in many cultures and communities globally.

Central to this tension, following Douglas (1966), is the distinction between "food" and "non-food" (Gonzalez Turmo, 2009) and the positioning of soil within it. In the contemporary west, soil is understood as "a polluting non-food" which is "too natural to be acceptable" (Henry and Matthews Kwong, 2003, p. 361–2). Consuming soil in this context is, therefore, highly stigmatized (Forsyth and Benoit, 1989) and associated with groups already viewed with a degree of "otherness" such as women (Allport, 2002), children (Young, 2011) and poor, rural, black populations of the Southern US states (Frate, 1984).

Conversely, social science approaches to geophagy have highlighted clay's legitimacy as a foodstuff and a routine part of health and nutritional practices in, among other places, Nigeria (Vermeer, 1966), Ghana (Vermeer, 1971; Hunter, 1973), Kenya (Geissler et al., 1997), and the Southern USA (Hertz, 1947; Frate, 1984; Forsyth and Benoit, 1989). For Henry and Cring (2013, p. 181), geophagy's embeddedness within the ebbs and flows of everyday life brings with it knowledges and practices, particularly around selecting and preparing clay, which "bring it into culture." In other words, skilled knowledge of choosing which clays are edible and how to prepare them correctly for consumption brings geophagy out from hidden sub-cultural corners and into the mainstream. In his colonial explorations of South America, Von Humboldt (1872, p. 495) noted that people do not "eat every kind of clay indifferently" but, rather, select specific types of clay for eating based on smell, taste and texture (Geissler et al., 1997) or location (Hertz, 1947). In the Southern USA, Frate (1984, p. 35) compared the selection of edible soil to the selection of wine,

with both gaining "a reputation over the years" and becoming known for their provenance (also Forsyth and Benoit, 1989, p. 66).

Across both medical and social science approaches to geophagy, pregnant women occupy a particularly prominent position as wider pica behaviors are associated with pregnancy cravings. Reported rates of geophagy among pregnant women vary considerably from 0.2% in Denmark (Mikkelsen et al., 2006) to 92.5% in Nigeria (Izugbara, 2003). Medical approaches to geophagy in pregnancy focus on the risks of helminth infection, lead poisoning, dental injury, and gastrointestinal complications (Ezzeddin et al., 2015). Thus, the predominant medical discourse has constructed geophagy and pica in pregnancy as a "dangerous form of self-injurious behavior" (Williams and McAdam, 2012, p. 2050) and focused on prevention, particularly through educational programmes for women in the global south.

Conversely, social scientists have pointed out that geophagy in pregnancy in non-western settings is tied up with wider cultural practices, beliefs, and "symbolic links between people, fertility, good health, and ancestral blessings" (Njiru et al., 2011, p. 455). Geissler et al. (1998) and Izugbara (2003) also highlight the sacredness of pregnancy-related geophagy and its associations with fertility deities and the perceived life-giving forces of the earth. As such, as a highly gendered practice where history, place, culture, family, gods, and female bodies meet, the medical approach of simply educating pregnant women against geophagy becomes complex (Corbett et al., 2003). Researchers have demonstrated that treating indigenous people, places, and cultures as *tabula rasa* onto which western biomedical messages can be inscribed ignores existing cultural practices, and can lead to significant, and potentially harmful, distortions of public health messages (e.g., Williams-Blangero et al., 1998).

Clay has, then, enjoyed some prominence in social science literature albeit amalgamated with other types of soil and earth and examined almost wholly through the lens of geophagy by anthropologists and geographers. There is limited research on what clay-based practices are currently occurring globally as wider medicinal uses of clay only occasionally appear in geophagy research (e.g., Izugbara, 2003, p. 194) and anthropological research on geophagy has slowed considerably since a flurry of activity in the 1970s. While geophagy research provides a useful context and establishes the widespread use of clay as a medicinal antimicrobial artifact, this article advocates a broader sociological investigation into clay as it moves into mainstream biomedical research as part of a focus on natural products antimicrobial drug discovery. As clay and other natural antimicrobials increasingly take center stage in antimicrobial drug research, credible theoretical lenses to their social, and material lives will be vital for ensuring sociologists are included in the policy, practice, and research conversation. We now turn to propose three theoretical "ways in" to understanding clay as an antimicrobial agent which we map onto the physical and symbolic mobility of clay into, within, and out of western biomedical laboratories.

Way in 1: Clay in Context: Post-colonial Approaches

A post-colonial lens is perhaps the most logical entry point into a sociological analysis of medicinal clay as it provides a way to theorize clay, and its use, in its de-westernized context prior to its movement and adoption into western biomedicine.

In short, post-colonialism, as a set of intersecting theoretical approaches, is concerned with the legacies of colonial ideologies and power and the ways in which contemporary global economics, politics and culture are rooted in colonial projects. Said's (1978) seminal text *Orientalism* is pertinent here. In it, he outlines the ways that western powers, through centuries of colonial rule, came to define indigenous people and practices in the global south and east [what Hall (1996) calls the "non-west"] as oriental "other," engaging in and driven by "savage," strange and "primitive" beliefs and practices.

Post-colonial theories have usefully been applied to understand the history of medicine (see Anderson, 1998) and science (see Seth, 2009) where researchers have, among other foci, drawn attention to colonialism's consistent devaluing of traditional practices and knowledge in favor of a model where western medicine and science were understood as "gifts" to colonies (Seth, 2009, p. 373). Philosopher Lévy-Bruhl's work on "the primitive" is a striking example of the naturalization of European medical and scientific superiority which post-colonial scholars seek to untangle. In it, Lévy-Bruhl consistently utilizes anecdotes of behavior from diverse contexts to reproduce a distinction between "primitives" and the "civilized" world, confirming the superiority of Europe and entrenching the notion that colonized nations "are simply different from us" [see Bernasconi (2005), p. 231–22 for an overview].

Similar devaluing of indigenous cultures is echoed elsewhere in relation to medical practice specifically. In her overview of British colonial perceptions of Indian and Burmese medicine, Edwards (2010, p. 28) notes that in the late nineteenth century, traditional Indian medicine was dismissed as "despicable quackery" despite some "western" practices, such as inoculation against smallpox, having been practiced for centuries before the British arrived. In Zimbabwe, this valorization of traditional medicine went further where, under the Witchcraft Suppression Act (1899), the majority of traditional medical healers, practices, materials, medicines and objects were criminalized for being non-scientific and dangerous (Mawere, 2014).

By centralizing and problematizing this process of devaluing traditional medical practices, post-colonial approaches offer a useful lens for understanding the ways medicinal clay is positioned within modern, western medical practice. This can clearly be seen in the case of geophagy where colonial gazes "are still active today" in framing this practice as a form of pica (Henry and Cring, 2013, p. 186). Beyond this, however, post-colonialism can help us question some of the fundamental constructs underpinning the story of medicinal clay's emergence into western biomedicine, most notably claims about its newness and the infrastructure through which it physically moves to the west.

First, as we have mentioned above, the use of clay for antimicrobial purposes is not novel; clay has had a sustained prominence throughout medical history. While most contemporary biomedical papers on clay outline this longer history as context for a biomedical framing, this in itself is part of the problem—medicinal clay use is constructed, through this narrative, as an historical artifact, and a set of knowledges circulating around the great ancient civilizations, rather than a practice which is *still* continuing in formerly colonized spaces. Williams' (2019) recent overview of clay's historic and continued use globally, for example, opens with accounts of clay use by the earliest humans and its importance in ancient Greek and Roman medicine while devoting almost no space to the *current* use of clay in the global south.

This kind of positioning of natural antimicrobials invisibilizes medical knowledge and practice from contexts where natural products form the basis of much traditional and contemporary medical practice. In the case of plants, the World Health Organization (2005) suggests that 80% of the world's population uses traditional, plant-derived medicine as primary health care. Moreover, in a report on the *State of the World's Plants,* Willis (2017, p. 22) notes that at least 28,187 species are recorded as being of medicinal use, mostly in rural areas of the global south where traditional medicine is accessible and affordable, and often trusted more than western pharmaceuticals.

Despite this, the contemporary relevance of medicinal clay is located almost wholly within the frame of contemporary, western medicine. The "story" of clay's emergence into medicine (much as we have told it above) starts at the point of its mobility into the western biomedical gaze through Brunet de Courssou's work and constructs a future which is entangled with western biomedical agendas (AMR, safety concerns), technologies (screening, analytics), and practices (patenting, commercializing). Taking a post-colonial approach helps to elaborate on the de-westernized story of medicinal clay, locating it within non-western knowledge assemblages, markets and traditions.

Post-colonial approaches can also help us attend to the implications of clay's physical mobility as it moves from its natural (potentially sacred) contexts in the global south into western biomedical research spaces. Here, the notion of "bioprospecting" becomes useful. For Hayden (2003, p. 1) this refers to "corporate drug development based on medicinal plants, traditional knowledge and microbes culled from the 'biodiversity-rich' regions of the globe." Schiebinger (2004) has related the modern practice of bioprospecting to the actions of early European colonialists who exploited plant sources in the global south in the name of botany and medical science. While contemporary bioprospecting legislation requires corporations to remunerate indigenous populations for the exploitation of their land and resources, this model nonetheless naturalizes the trade of goods from south to north, poor to rich, and prioritizes western scientific and corporate development. Most of the existing work on bioprospecting looks specifically at the case of plants but, as clay begins to gain traction as a biomedical substance, this scope could be broadened to interrogate where the clay in western biomedical laboratories has come from, and through what means it arrived.

Way in 2: Movement Around and Out of Science: Revisiting Laboratory Life

Once clay has, then, moved from the global south into the western biomedical gaze, it is subject to scientific work where the evidence of its antimicrobial potential is established. Given this, our next "way in" to understanding antimicrobials derived from natural products is slightly different in proposing both a theoretical *and* methodological approach. In particular, we suggest a return to "laboratory life" to capture the ways that "the daily activities of working scientists lead to the construction of scientific facts" (Latour and Woolgar, 1979, p. 40). We use the phrase "return to" deliberately because, as Doing (2008) points out, following a flurry of publications during the 1970s and 1980s, few laboratory studies have actually emerged out of STS scholarship, despite their foundational impact on the field. Given this, Doing (2008, p. 281) goes further and calls for "a reengagement between ethnographic work in laboratories and the now established field of STS." We suggest that the (re)emerging field of natural product drug discovery would provide an excellent site for such a reengagement and would illuminate the ways in which the antimicrobial potential of clay is brought into being.

Briefly, classical laboratory studies were concerned with how scientific facts are produced interactionally, through everyday scientific experimentation, discussion, technologies and negotiation. As Knorr Cetina (1995, p. 141) argues, the mission of these studies was to show the "process of knowledge production as 'constructive' rather than descriptive." Such a focus represented a shift from demarcationist philosophy such as that of Karl Popper who argued that a distinct demarcation between science and non-science could exist. In contrast, laboratory studies were, and still are, concerned with the production of scientific knowledge *in situ* and uncovering the messiness of scientific practice which is invisibilized in publications where scientific facts and methods are presented as fixed and logical (Knorr Cetina, 1981). More recently, in his research on pharmaceutical company chemical laboratories, Barry (2005) shows that molecules are not "discovered" but, rather, "invented" as "informed materials" through laboratory work wherein the material structure becomes richer and better-known through the compilation of information and data. This is echoed by Hardon and Sanabria (2017, p. 118) who suggest that "there is no pure (pharmaceutical) object that precedes its socialization and interpretation." Laboratory studies are, then, concerned with uncovering the processes of this socialization and interpretation.

While research in this tradition primarily focused on the microsocial action of everyday work within specific laboratories, Fujimura (1987) usefully demonstrated the constraints and influences on scientific work from "outside" of individual laboratories, such as from regulators, sponsors and industries. In this sense, the construction of scientific facts is not just contingent upon everyday work in the laboratory but an alignment of local (the necessary

laboratory tasks are doable), institutional (these tasks are feasible within a given laboratory space), and wider field (the research is viewed as worthwhile by the broader scientific community) concerns and constraints (Fujimura, 1987).

Given we are advocating a directional shift toward the materiality of natural antimicrobials, the laboratories in which this materiality is produced is a logical research site for sociologists. Such a focus would illuminate the ways in which clay materials are inscribed with antimicrobial potential and how this potential is represented to the wider scientific community through publications (see Latour and Woolgar, 1979). In the case of clay, scientists use microbiological and biochemical techniques to probe the susceptibility of microorganisms (e.g., minimum inhibitory concentrations, viability assays) and define the mechanism of action (e.g., structural and elemental analysis of the clays themselves coupled with molecular effects on microbial constituents, such as lipids, proteins and nucleic acids) (see Williams, 2019). These methodologies and technologies act as an "inscription device" to "transform [the] material substance into a figure or diagram" (Latour and Woolgar, 1979, p. 51), which is then used to tell the story of the antimicrobial action of a particular clay. A sociological investigation into the inner workings of this process would be valuable but so too would an analysis of the entanglements of actors, both human (e.g., scientists, marketers, funding panels) and non-human (e.g., technologies, images, research agendas). For example, Goodman and Walsh (2001) highlight the case of Taxol obtained from the Pacific yew tree, whereby disharmony in natural antimicrobial science was not limited to members of a particular scientific group but extended to politicians, funders, associated industrial stakeholders (lumber or mining companies) and indigenous populations. This final point, of course, circles back to post-colonial approaches.

A focus on the laboratory life of natural antimicrobials would also usefully go beyond the physical limits of the laboratory to follow clay on its physical and symbolic journey to its scientific facthood in other spaces. In other words, we might usefully ask how is the "fact" of clay's antimicrobial potential constructed, and what happens to this "fact" once it is black-boxed and leaves the laboratory through scientific papers as "evidence." This focus particularly calls to mind other STS work around the role of hope, promises and expectations. Much of this work is centered on the future-oriented discourses to emerge from the Human Genome Project and its resultant technologies (e.g., Hedgecoe and Martin, 2003). This approach recognizes the social and political life of scientific expectations, acknowledging that these promises shape research agendas and can hold significant power in mobilizing resources at micro, meso and macro levels of science work (Borup et al., 2006). In the case of natural antimicrobials, scientific papers are awash with expectations of their revolutionary potential. In some cases, these promissory discourses have also crossed the rubicon into media reporting which is predictably filled with sensationalized accounts of natural antimicrobials' potential. For example, the Daily Mail (Andrews, 2018) reports the antimicrobial action of Atlantic sponges as "revolutionary," while *Independent* journalist Rodgers (2007) asks whether clay might be the "new Penicillin." Research is needed to understand what purpose these promises serve. In particular because as the (re)emergence of natural antimicrobial drug discovery is in its infancy and global attention is increasingly turned toward innovative approaches to AMR, the political potential of these promises is worth unpacking.

Way in 3: Moving From the Margins to the Mainstream: Developing Clay's Value

As clay physically moves from the global south into western biomedical research spaces and out again as a black-boxed antimicrobial fact, it also shifts symbolically from inert "non-stuff" into an artifact with potential value.

Here we are not talking only about commercial worth but rather value as an entanglement of social, cultural, scientific, medical, and economic value. What we are specifically referring to is clay's movement from the margins of biomedicine (associated with "alternative" medical practices of the non-west) into the mainstream (as a credible biomedical antimicrobial) and the concomitant social legitimization and economic valuation of clay as an artifact or material. In other words, using Saks (1995) power model, as clay moves toward the power structures of science, medicine and healthcare, it attains value and legitimacy and its placement within the category "alternative" becomes ambiguous.

This movement of clay from the margins to the mainstream is partly driven by the changing evidence base around its antimicrobial potential. As clay moves into the western biomedical gaze, evidence about its antimicrobial functionality is increasingly obtained from standardized research practices which are understood as more legitimate than "anecdotal" observations or case studies from the past or from the global south (see Timmermans and Berg, 2003). A sociological exploration of clay would do well to interrogate this evidential shift to analyse the ways that clay's antimicrobial "facthood" comes into being and becomes reified.

Here too the notion of valuation practices can help create a more holistic approach which incorporates, by moving beyond, economics, and evidence. Dussauge et al.'s (2015) recently developed notion of "valuographies" may be helpfully employed to understand the potential antimicrobial value attributed to clay as it moves into the western biomedical gaze. In the concluding chapter of their anthology on value practices, Dussauge et al. (2015, p. 266) call for more research exploring "values in-the-making" in medicine and the life sciences to "examine how certain things come to be considered valuable and desirable" and what the implications are of increased desirability. In one of the anthology's chapters, Löwy (2015), for example, highlights how the increased valuation of prenatal screening for Down Syndrome (by both clinicians and parents) repositioned the test from a niche procedure in high risk cases to a mainstream tool enmeshed in discourses of eugenics. In other words, as the non-essential desirability of prenatal screening increased, it shifted out of specialist obstetric practice and into mainstream pregnancy

care carrying with it financial implications for service providers, and increased surveillance of pregnant bodies.

Central to Dussauge et al.'s (2015, p. 7) work is an ambition is to move away from a construction of value *wholly* "revolving around capital and labor" to one in which multiple value forms are commensurable and are dynamically created and recreated in practice. A complementary reading of Garcia-Parpet's (2007) work on the construction of "perfect" markets is useful here to shed light on the social construction of new economic markets. Through a focus on a strawberry auction in Fontaines-de-Sologne, Garcia-Parpet demonstrates that the development of "perfect" markets (see pages 25–26 for an overview) is not solely reliant on financial equilibrium massaged by "invisible hands" of self-interest but is in a constant state of (re)creation through the development of networks, vigilance, and the social identities of the actors involved. In other words, Garcia-Parpet (2007, p. 20) shows that "social factors… [intervene] all across the practical processes of making up this, the purest of 'economic' markets."

Such entanglements of actors, technologies, products and finances (as captured by the valuographies model) are important for understanding the ways in which natural antimicrobials attain both social and economic value; in other words, how they come to be both desirable (i.e., legitimized) and profitable (i.e., have markets created around them). We might, for example, ask how clay is positioned within a scientific research landscape where fundamental research is increasingly eclipsed by research guided by industrial agendas, which are necessarily profit-driven (Quaglione et al., 2014). How, as clay gains mainstream biomedical value, do research questions change from fundamental explorations of how clay works (e.g., Williams et al., 2011) to questions of application, commercialization and increased efficiency of clay-based medical products and practices? Furthermore, how might a "perfect market" as exemplified in Garcia-Parpet's work, develop around clay?

However, clay's increased social and economic value does not just lie in its potential scientific and medical applications, but also in its marketability as a beauty and cosmetic artifact. In recent years, clay has made a rather startling appearance onto the western beauty scene with promises to do things like "clean," "detoxify" and "renew" in a "natural" and environmentally-conscious way. This entrance of clay into the western beauty landscape has yet to be theorized but the increased value of clay in this space chimes with several existing social science research concerns such as the movement toward ecologically-sound capitalism, the increased appetite for "natural" lifestyles (Edmonds, 2008), and the desire to engage in non-western practices which are seen as "authentic" (Campbell, 2008).

This increased presence of clay in beauty and cosmetic products raises questions about the discourses of "detoxification" and "cleansing" which underpin clay-based beauty products, particularly with respect to what they accomplish and to whom they are addressed. Theoretically, one might put Douglas (1966) to work here to understand the construction of bodily pollutants and read this alongside feminist work which highlights the inscription of gender norms (in this case to be clean, pure, and detoxified) onto female bodies (e.g., Wolf, 1991). This would help us to appreciate, again employing Dussauge et al. (2015) work, how a commercial market (this one focused on beauty and cosmetics) around clay is developing.

EXPLORING THE RELEVANCE OF MATERIALITY FOR ANTIBIOTIC ADHERENCE AND OPTIMIZATION

While research through any, and all, of these "ways in" would be intellectually meaningful, this novel focus on materiality goes beyond theoretical talking points and has implications for optimizing antimicrobial use. Most adherence research to date has been preoccupied with identifying patterns of medicines use based on demographic factors such as age, sex, socio-economic status and ethnicity. These models, however, fail to address how, within complex social worlds, medicines-use decisions are actually formulated, and the nuanced reasons why patients may utilize medicines sub-optimally (Rathbone et al., 2017).

Within social sciences, progress has been made on remedying this rather one-dimensional approach by placing patients' beliefs and wider lifeworlds at the core of analysis, positioning medicines as "socially embedded phenomena" where decisions about use are made within a complex web of relationships, spaces, roles and identities (Cohen et al., 2001). Conrad (1985) calls this "medication practice" and highlights the ways suboptimal medicines use can be a form of control for patients. Others highlight the importance of place and space in patient relationships with medicines (Hodgetts et al., 2011; Dew et al., 2014) and the mobility of clinical categories between spaces Webster, Douglas and Lewis (2009).

Anthropologists have made the most significant leaps in mapping the "social lives of medicines," highlighting that medicines are more than just chemical *things* and, instead, take on social, economic, and political meanings which can affect the ways they are used (Whyte et al., 2002). In their comprehensive review of recent work in the anthropology of pharmaceuticals, Hardon and Sanabria (2017, p. 118) convincingly outline the ways that "drugs are rendered efficacious in laboratories, therapeutic settings, drug outlets, and everyday lives across regulatory settings." Refreshing, and relevant here, is that their paper aims to "examine what lies beneath the pharmaceutical object's surface, unpacking the thing" (ibid). Through an overview of the construction of medicines at five key sites in their lifecycle (trials, regulatory frameworks, marketing, care practices, and in individual bodies), they demonstrate that the use of medicines is relational and intertwined with their diverse inscriptions, and part of an on-going, constantly evolving interaction between the identities of patients and medicines themselves (Rathbone et al., 2017).

Despite this, their review falls somewhat short of its promise to burrow beneath the surface of medicines and open up the "thing" (Appadurai, 1986). Inasmuch, they commence their narrative with randomized controlled trials (RCTs), overlooking the underpinning scientific studies during which the material life of the medicinal thing is of central importance. Hardon and Sanabria's (2017) paper is an exemplar of a wider approach wherein medicines themselves (particularly their active

ingredients) are essentialised and positioned as black-boxed objects around which practices, values, beliefs, behaviors and identities circulate. In other words, while the focus on social and cultural lives of medicines is important, there is limited attention given to what medicines themselves actually *are*—what is the *thing* that patients are not adhering to or taking optimally?

While anthropologists have credibly highlighted that medicines are not just chemical objects, their "chemical lives" should nonetheless feature in a holistic analysis of medicines themselves as they are often implicated in how they are used and adhered to. Formulation science has repeatedly demonstrated that the physical properties of medicines (their size, shape, taste, smell, mode of delivery) are important for how medicines are perceived and used by patients. In their review of formulation challenges for pediatric practice, for example, Nunn and Williams (2005) note the importance of masking the naturally bitter taste of medicines to encourage adherence in children. Similarly, through experimental research, Wan et al. (2015) reveal how the shape and color of tablets significantly affects patients' perceptions of their ease of use and effectiveness, which in turn impacts adherence.

Beyond this, others have highlighted that medicines' ingredients are vital for patients' decisions about their use. This is perhaps most obvious in the case of dietary preferences, and religious and cultural beliefs. In their research on the impact of religious beliefs in medicines use, Eriksson et al. (2013) found that Muslims, Hindus, and Sikhs refused medicinal devices containing porcine and/or bovine derivatives in all but emergency circumstances. While Enoch et al. (2005) suggest that healthcare practitioners should inform patients about medicinal ingredients, they also found that none of the practitioners surveyed knew the correct ingredients of the medicines prescribed, potentially leading patients to their own research and harmful "tinkering" with their prescribed regimes (to quote Mol, 2008). Sattar et al. (2004) outline four case studies in which patients, upon discovering their medicines contained products prohibited by their religion, immediately stopped treatment, leading to relapses in condition.

In the context of the (re)emergence of natural products drug discovery, the active ingredients in new antibiotics may well be products which have historically sat outside of conventional biomedical models (notably here, clay). Opening up the black box of medicines and their chemical and material lives will enable us to grasp how diverse active ingredients are perceived and influence use. For example, will patients accept clay-based poultices as a legitimate medicine for treating wound infections? How will their perceptions affect their use of poultices? How can prescribers best counsel patients to ensure optimal use of innovative novel medicines? These are important questions for scientific researchers, practitioners and policy-makers in AMR, and ones which sociology is well-placed to answer.

DISCUSSION

In this paper, we have suggested a new direction for sociological research on AMR that examines the social and material life of antimicrobials themselves. Such a focus is pertinent at a time when diverse materials, particularly natural products, are being explored for their potential as new antimicrobial drug candidates. We selected clay as an appropriate example since its antimicrobial potential is well-documented (Williams, 2019) and it has a thriving research community to which sociology has much to offer but has not yet engaged with. For instance, sociology is conspicuously absent from Henry and Matthews Kwong's (2003, p. 354–355) observations on the diversity of disciplinary perspectives on geophagy: "research is conducted by a striking variety of specialists in the fields of primatology, biology, chemistry, mineralogy, parasitology, medicine, nutrition, anthropology, geography and public health." Henry and Cring (2013) similarly note that interdisciplinarity is vital for deeper research into the social life of clay. More broadly, sociologists have advocated the need to include our research, approaches, theories and methodologies in AMR research. For Lorencatto et al. (2018), sociologists have a key role to play in supporting prescribing behavior change interventions while Will (2018) argues that more nuanced theorizing around AMR will support sociology to become part of the policy and practice solution.

Taking the illustration of antibacterial clay, we have suggested a number of approaches for sociologists to begin exploring the social and material life of natural antimicrobials. We have mapped these theoretical lenses onto the physical and symbolic mobility of clay into, within, and out of western biomedical laboratories. This is not an exhaustive list of theoretical "ways in" to explore the (re)emergence of natural products in antimicrobial research; there are certainly additional lenses which would be valuable to employ in tandem that we have not touched upon here. Our goal was not to compile a comprehensive account, but to present what we see as fruitful "ways in" as heuristic devices to stimulate discussion within our discipline, and beyond, as to how we might credibly tackle this new direction in AMR research. Moreover, the "ways in" that we have proposed here also have currency for exploring other natural product-based medicines more broadly (i.e., not limited to antimicrobials). The "ways in" we have presented are deliberately disparate to both draw out the diversity of issues enmeshed in questions of natural antimicrobials, and to demonstrate that sociology has the broad theoretical arsenal to approach these. We are not suggesting that any given future research on natural antimicrobials should attempt to synthesize and incorporate *all* of these theoretical frameworks but, rather, bring specific frameworks in and out of prominence in addressing particular aspects of natural antimicrobial materiality. We are, then, suggesting these frameworks as "ways in" for sociologists to begin thinking about a materiality approach to antimicrobial products, rather than providing an instructional schema.

Nonetheless, there are several thematic coalescences and points of confluence in the disparate concepts and frameworks outlined above. Most notably, taken together in much the same way we have presented them here, these frameworks and foci provide a holistic theoretical reading of the "story" of natural antimicrobials' movement into and around western biomedicine. In other words, a single aspect of clay's (and other natural antimicrobials') entrance into the western biomedical gaze should not be fully understood in isolation but, rather,

should give space to the tangential issues. For example, an examination primarily focused on the development of new markets around clay products (both medical and cosmetic, from a valuographies perspective) ought to nod to the development of evidence underpinning this market (from an STS perspective) which is, in turn, informed by clay's longer history as a therapy (from a post-colonial perspective).

These diverse theoretical frameworks are all, at various times and to varying degrees, underpinned by notions of space, legitimacy, and practice, where the legitimacy of clay shifts (from "alternative" to mainstream) as it moves into diverse spaces (from global south to north) and is practiced upon in diverse ways (through scientific experimentation). For example, post-colonial approaches can help us to illuminate the ways "traditional" uses of clay in the global south are positioned as illegitimate through "colonial gazes" (Henry and Cring, 2013: 186) and STS frameworks can show us how legitimacy of clay is achieved through scientific experimentation. Outside of the laboratory, legitimacy of a medicine or a drug regime is central to its use by patients (Cohen et al., 2001).

This new route in AMR research requires a considerable degree of interdisciplinarity. While we have argued here in favor of a sociological focus on the social and material lives of natural antimicrobials, we are not advocating a partisan approach where sociologists focus exclusively on the analytical frameworks offered by others in our discipline. Indeed, as we have shown, discipline-hopping frameworks such as STS and post-colonial studies need to be at the heart of this new direction. We contend, moreover, that sociologists should not just collaborate with our close disciplinary neighbors (namely anthropology, geography, and psychology). Rather, we ought to develop networks spanning social, biological, physical, and earth sciences to promote a holistic approach to social and material life. Many of the questions at the center of natural antimicrobials (e.g., the nature of the *stuff* itself, its movement into biomedicine and its commercial value) are shared across disciplines and best addressed through collaborative approaches. Working in pre-existing disciplinary silos constrains the degree to which the material life of natural antimicrobials can be fully understood and their practical and clinical utility fully realized. While laboratory scientists are keenly focused on identifying the physical, mineralogical, and chemical nature underpinning clay's antimicrobial action, its usefulness as a western biomedicine is an inherently social and cultural question. These questions concern, among other issues, whether prescribers are convinced by medicines with clay as an active ingredient and whether patients will adhere to clay-based medicines regimes. Similarly, while sociologists can identify an interesting story in clay's mobility, to convincingly take a materiality approach such as we have advocated above requires a degree of engagement with the production of physical and chemical materiality through diverse scientific techniques.

AUTHOR CONTRIBUTIONS

KJ led on the preparation of the manuscript with significant conceptual and design input and contribution from GS.

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frontiers in Sociology

SYSTEMATIC REVIEW
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Barriers and Facilitators to Implementation of Antibiotic Stewardship Programmes in Hospitals in Developed Countries: Insights From Transnational Studies

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Objectives: To identify perceived influences on implementation of antibiotic stewardship programmes (ASPs) in hospitals, across healthcare systems, and to exemplify the use of a behavioral framework to conceptualize those influences.

Methods: EMBASE and MEDLINE databases were searched from 01/2001 to 07/2017 and reference lists were screened for transnational studies that reported barriers and/or facilitators to implementing actual or hypothetical ASPs or ASP-supporting strategies. Extracted data were synthesized using content analysis with the Theoretical Domains Framework as an organizing framework. Commonly reported influences were quantified.

Results: From 3,196 abstracts 75 full-text articles were screened for inclusion. Eight studies met the eligibility criteria. The number of countries involved in each study ranged from 2 to 36. These studies included a total of 1849 participants. North America, Europe and Australasia had the strongest representation. Participants were members of special interest groups, designated hospital representatives or clinical experts. Ten of the 14 theoretical domains in the framework were present in the results reported in the included studies. The most commonly reported (≥4 out of 8 studies) influences on ASP implementation were coded in the domain "environmental context and resources" (e.g., problems with data and information systems; lack of key personnel; inadequate financial resources) and "goals" (other higher priorities).

Conclusions: Despite an extensive transnational research effort, there is evidence from international studies of substantial barriers to implementing ASPs in hospitals, even in developed countries. Large-scale efforts to implement hospital antibiotic stewardship in those countries will need to overcome issues around inadequacy of information

systems, unavailability of key personnel and funding, and the competition from other priority initiatives. We have enhanced the evidence base to inform guidance by taking a behavioral approach to identify influences on ASP uptake.

Systematic review registration: PROSPERO registration number CRD42017076425.

Keywords: antimicrobial stewardship, systematic review, barriers and facilitators, theoretical domains framework, hospitals, behavior change

INTRODUCTION

Overuse or inappropriate use of antibiotics is a key driver of the worldwide escalation of antibiotic resistance (Carlet et al., 2011), which is a major threat to global public health and patient safety. Antibiotic resistance is associated with excess mortality and morbidity, prolonged hospital stay and increased health care costs (De Kraker et al., 2011). Antibiotic resistance has predominantly been a clinical problem in hospital settings (Llor and Bjerrum, 2014), which are particularly susceptible to harboring multidrug-resistant organisms (Chemaly et al., 2014).

Transnational response to this global crisis have been co-ordinated by a World Health Organization Global Action Plan (World Health Organization, 2015) and through a strategic research agenda on antibiotic resistance, which currently unites 28 partners globally (JPIAMR, 2017). The global action plan sets out five strategic objectives (World Health Organization, 2015): (1) improve awareness and understanding of antibiotic resistance; (2) strengthen knowledge through surveillance and research; (3) reduce the incidence of infection; (4) optimize the use of antibiotic agents; and (5) ensure sustainable investment in countering antibiotic resistance. A key approach to optimizing the use of antibiotics is the deployment of antibiotic stewardship programmes (ASP) in hospitals. An ASP involves a team that implements a coherent set of actions that promotes the responsible use of antibiotic agents (Dyar et al., 2017).

Effectiveness of ASPs implemented by hospitals is likely to differ depending on both ASP elements and contextual factors. In practice, ASP initiatives are a heterogeneous group of system- and organization-based strategies and actions (Dyar et al., 2017), and countries and organizations may vary greatly in their capacity to deploy the necessary resources to implement those interventions (Tiong et al., 2016). For example, there is substantial transnational and even national variability in appropriate prescribing and compliance with antibiotic guidelines (Sandora et al., 2016; Turnidge et al., 2016; Dentan et al., 2017; Mousavi et al., 2017). The international research community faces the challenge of optimizing implementation initiatives, such as ASPs, by producing generalisable evidence that incorporates relevant theory and an understanding of the contextual influences (Ivers and Grimshaw, 2016).

Amongst the key research gaps identified in the WHO action plan is the need to understand the behaviors required to support effective ASPs (World Health Organization, 2015). The difference between recommendations for appropriate antibiotic use (the "what") and behavioral change interventions (the "how") is key (Hulscher and Prins, 2017). ASPs require clinicians to change their behaviors. There is a wealth of theoretical and empirical evidence from the behavioral sciences about how to change behavior, yet this is currently underutilized in antibiotic stewardship studies (Charani et al., 2011; Rawson et al., 2017). Hence there are opportunities to enhance the effects of ASPs using behavioral approaches (Davey et al., 2017). Methods and tools from the behavioral sciences should be used to select the most promising interventions to change behavior, based on a careful assessment of barriers and facilitators to practice change (Davey et al., 2017; Hulscher and Prins, 2017). To date, one systematic review has explored the evidence on barriers and facilitators of antibiotic prescribing behavior in acute care (Charani et al., 2011); however, an evidence synthesis using behavior change theory to identify influences on implementation of ASPs is lacking.

Aims and Objectives

The aim of this study was to inform the development of large-scale contextually optimized quality improvement hospital ASPs, by improving the understanding of contextual influences on ASP implementation, through the framework of identifying "barriers and facilitators." The objectives were:

1. To conduct a systematic review of transnational research to identify commonly perceived barriers and facilitators to implementation of actual or hypothetical ASPs in hospitals.
2. To provide an exemplar of the use of a behavioral framework analysis to conceptualize identified barriers and facilitators to ASPs in hospitals.

METHODS

This systematic review was conducted in accordance with the Center for Reviews and Dissemination's guidance for undertaking reviews in healthcare (Centre for Reviews Dissemination, 2009) and reported adhering to the PRISMA guidelines (Liberati et al., 2009).

Search Strategy

A search strategy was developed by an Information Specialist in collaboration with the review authors, who generated a list of possible relevant keywords related to antibiotic stewardship, hospital settings and national or international study scope. The search strategy was not intended to be restrictive to a specific study design, but excluded studies on animals, and editorials and

abstracts. The review team screened a random sample of 100 identified abstracts to verify if relevant studies were identified. Based on the results of this verification and a study protocol, the search string was amended so that the search became more sensitive to data on barriers and facilitators and infection control and antibiotic policies research. A new search was performed and achieved satisfactory comprehensiveness such that no further amendments were applied. The final search strategy can be found in the protocol.

Data Sources

An initial scoping search for published literature was performed using the Medline and EMBASE electronic bibliographic databases. There was no start date limit; the EMBASE and Medline databases were searched from 1980 and 1946 respectively to 18th July 2017. We observed a sudden increase in numbers of identified studies published after 2000. The first global strategy to lead the response of 193 United Nation states to antibiotic resistance was developed by the WHO in 2001 (World Health Organization, 2001). The first guideline for designing an ASP was published by the Society for Healthcare Epidemiology of America (SHEA) and Infectious Diseases Society of America (ISDA) in 2007 (Dellit et al., 2007). Consequently, we included only the papers published between 2001 and 18th July 2017. References of retrieved articles, systematic reviews and personal files were searched for relevant studies.

Study Selection

A random sample of 100 titles and abstracts was double screened by two reviewers (EMD and MR) to assess consistency, and revisions were made to the definitions and criteria to enhance clarity. In the next, single screening phase, the same two reviewers independently screened the remaining titles and abstracts using an Excel spreadsheet. For record keeping purposes, we documented details of excluded abstracts, including topic, scope (country-level or international), setting, participants and design. Five randomly selected full-text articles were double screened for inclusion by two reviewers (MR, CRR) to assess reliability. Disagreements were resolved by discussion and the remaining selected full-text articles were assessed by one reviewer (MR), with any uncertainties related to eligibility of a specific article resolved by discussion with a second reviewer (CRR or EMD).

Inclusion Criteria

Studies were included in the systematic review if they met the following eligibility criteria:

- Transnational studies, i.e., in which participants were from more than one country, were included.
- Studies on ASPs or specific antibiotic stewardship strategies used to support ASPs, such as selective reporting of antibiotic susceptibility test (AST) results (a laboratory-based ASP intervention which consists of reporting to prescribers only few antibiotics or not reporting at all when colonization is likely) (Barlam et al., 2016).
- Reported primary data published in full-text articles, from structured (e.g., questionnaires with specific response formats) and semi-structured (open-ended questions) methods of inquiry.
- Settings included hospital inpatient care settings or mixed hospital inpatient and outpatient settings.
- Reported barriers and/or facilitators to implementing an ASP. Studies which did not use the terms "barriers" and "facilitators" explicitly were included when they used associated terms such as "issues," "difficulties," "problems with," "(in)adequacy of support for an ASP," "obstacles," "enablers," "solutions."
- There were no restrictions for languages.

Exclusion Criteria

We excluded review articles, guidelines, studies focused on antimicrobials other than antibacterials (i.e., antituberculous, antifungal, antiparasitic, antiviral drugs), and studies of patients from ambulatory care or long-term healthcare settings.

Data Extraction

For each included study, one reviewer (MR) completed data extraction using a data extraction spreadsheet to include the following information: methods (author, study design, study response rate), population (country, type of hospital setting and participants, sample size), description of an ASP; barriers and facilitators to implementation (a method of assessment, response rate to a question, results verbatim including type and quantification (e.g., rates or ranks). A second reviewer (EMD) double-checked the extracted information. In one case a study author was contacted via e-mail to obtain additional information that was not reported in the published article.

Appraisal of Methodological Quality of Included Studies

We used relevant parts of the Mixed Methods Appraisal Tool (MMAT) (Pluye et al., 2011) to conduct quality appraisal. Specifically, if the research question was judged to be clear and the data collection methods were judged to be appropriate, further methodological appraisal was undertaken. For quantitative studies, four criteria (sampling strategy, representativeness, appropriateness of measurement and response rate) were applied. Two reviewers (EMD and MR) independently assessed the methodological quality of each included study by scoring each study against each MMAT item with the following nominal scale: yes (clearly met), no (clearly not met) and unclear (not clear if met) resolving disagreements by discussion.

Data Synthesis and Presentation

Qualitative analysis was conducted using theory-based content analysis, which involves a directed approach to content analysis (a systematic method of making specific inferences from differential levels of text) (Hsieh and Shannon, 2005). Levels of text can be broadly divided into primary content (i.e., themes and main ideas of the text) and latent content (i.e., context information) (Vaismoradi et al., 2013). We applied the Theoretical Domains Framework (TDF), a theoretical framework, developed by synthesizing behavioral theories through a systematic consensus process, as a framework for

investigating the barriers and facilitators to behavior (Cane et al., 2012). TDF is a synthesis of 33 theories of behavior and behavior change clustered into 14 (originally 12) domains (Cane et al., 2012). It has been applied across a range of healthcare systems and healthcare behaviors (Atkins et al., 2017). Two reviewers (EMD and MR) jointly coded the barriers and facilitators reported within the studies into domains of the TDF (the coding manual, including detailed descriptions of 14 domains and their underlying constructs, is included in the **Supplementary Materials**). Two codes were applied to the same extract if applicable. All codified extracts were then reviewed and discussed with a third reviewer with expertise in the TDF (JJF). In the next step of analysis the same reviewers (MR, EMD, JJF) used an inductive approach to identify subthemes (specific barriers and facilitators), within the coded domains of the TDF.

For the quantitative summary, the numbers of studies in which subthemes of barriers or facilitators were nominated or endorsed by participants were totalled. This do not reflect how many respondents cited the specific barriers/facilitator within studies. Subthemes that were reported in the majority ($\geq$50%) of identified studies are referred to as 'most commonly reported' influences on ASP use.

RESULTS

Search Results

The flow chart of the search and screening results is presented in **Figure 1**. Briefly, from 3,196 abstracts within the specified date limits, 75 full-text articles were screened for inclusion, of which 67 were excluded. Reasons for exclusion were: no full-text ($n = 1$), no original data ($n = 11$), not transnational ($n = 15$), study setting ($n = 3$), type of participants ($n = 4$), not an ASP (Charani et al., 2011), barriers or facilitators unreported ($n = 18$). Eight studies met the criteria and were included in this review (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Bryant, 2015; Fleming et al., 2015; Livorsi et al., 2016; Wolf et al., 2016; Pulcini et al., 2017).

Participants

All eight included studies were cross-sectional surveys. These studies included a total of 1849 participants, with sample sizes ranging from 14 (Bryant, 2015) to 660 (Howard et al., 2015). Two studies involving 704 participants reported individual participant level data (Itokazu et al., 2006; Johannsson et al., 2011). Five studies involving 1,057 institutions reported institutional level data (Howard et al., 2015; Bryant, 2015; Fleming et al., 2015; Livorsi et al., 2016; Wolf et al., 2016). One study reported country-level data and included national representatives of 36 countries (Pulcini et al., 2017). Two studies did not report numbers of respondents per country (Itokazu et al., 2006; Bryant, 2015) and one study provided incomplete information on a geographic location of participating institutions (Livorsi et al., 2016). The number of countries involved in each study ranged from 2 to 36, but overall participants from the North America, Europe and Australasia had the stronger representation in the identified studies. Participants were members or associates of established special interest groups or designated hospital representatives or ASP experts in charge at their hospitals. The characteristics of included studies and participants are presented in **Table 1**.

Characteristics of Antibiotic Stewardship Programmes

Six studies explored barriers or facilitators to specific ASPs (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Bryant, 2015; Wolf et al., 2016). Between 58% and 99% of respondents were from an institution with an ongoing ASP. Two studies referred to specific antibiotic stewardship strategies: audit and feedback (Livorsi et al., 2016), and selective reporting of antibiotic susceptibility test (AST) results (Pulcini et al., 2017). Respondents in the study on audit and feedback had to be engaged in this strategy to be eligible for participation (Livorsi et al., 2016). One study was restricted to ASP in pediatric oncology and bone marrow transplant (Wolf et al., 2016). Moreover, in one study (Bryant, 2015) pediatric hospitals accounted for half of included hospitals.

Measures of Barriers and Facilitators

Seven studies examined barriers to antibiotic stewardship programmes or strategies (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Bryant, 2015; Livorsi et al., 2016; Wolf et al., 2016; Pulcini et al., 2017) and one study reported possible facilitators (Fleming et al., 2015). One study asked participants to report solutions they employed to address experienced barriers, but findings related to this question were not reported (Pulcini et al., 2017). None of the studies explored the impact of health system factors (e.g., public vs. private healthcare systems). Three studies considered the impact of country context on reported barriers and facilitators (Howard et al., 2015; Fleming et al., 2015; Wolf et al., 2016). Five studies used closed-ended questions (i.e., a multiple-selection list of options) on barriers with prelisted response options (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Bryant, 2015; Wolf et al., 2016). Three studies used open-ended questions to identify barriers and/or facilitators, one reported identified themes only (Livorsi et al., 2016) and two reported both themes and exemplary quotations (a qualitative component) (Howard et al., 2015; Fleming et al., 2015). Amongst studies that used closed-ended questions on barriers, two did not detail methods of questionnaire design (Itokazu et al., 2006; Johannsson et al., 2011), one used an amended questionnaire from a previously conducted survey based on literature search and expert opinion (Bryant, 2015), two searched literature, of which one also used expert advice (Howard et al., 2015) and one a focus group (Wolf et al., 2016). Only one of the three studies that used open-ended questions on barriers reported the method of data analysis (Pulcini et al., 2017), namely the framework method proposed by Flottorp et al. (2013). Overall, comprehensiveness and precision of the methods of how studies identified barriers and facilitators used was limited.

Methodological Quality of Included Studies

Details of the Mixed Methods Appraisal Tool (MMAT) (Pluye et al., 2011) quantitative descriptive subsection scoring are

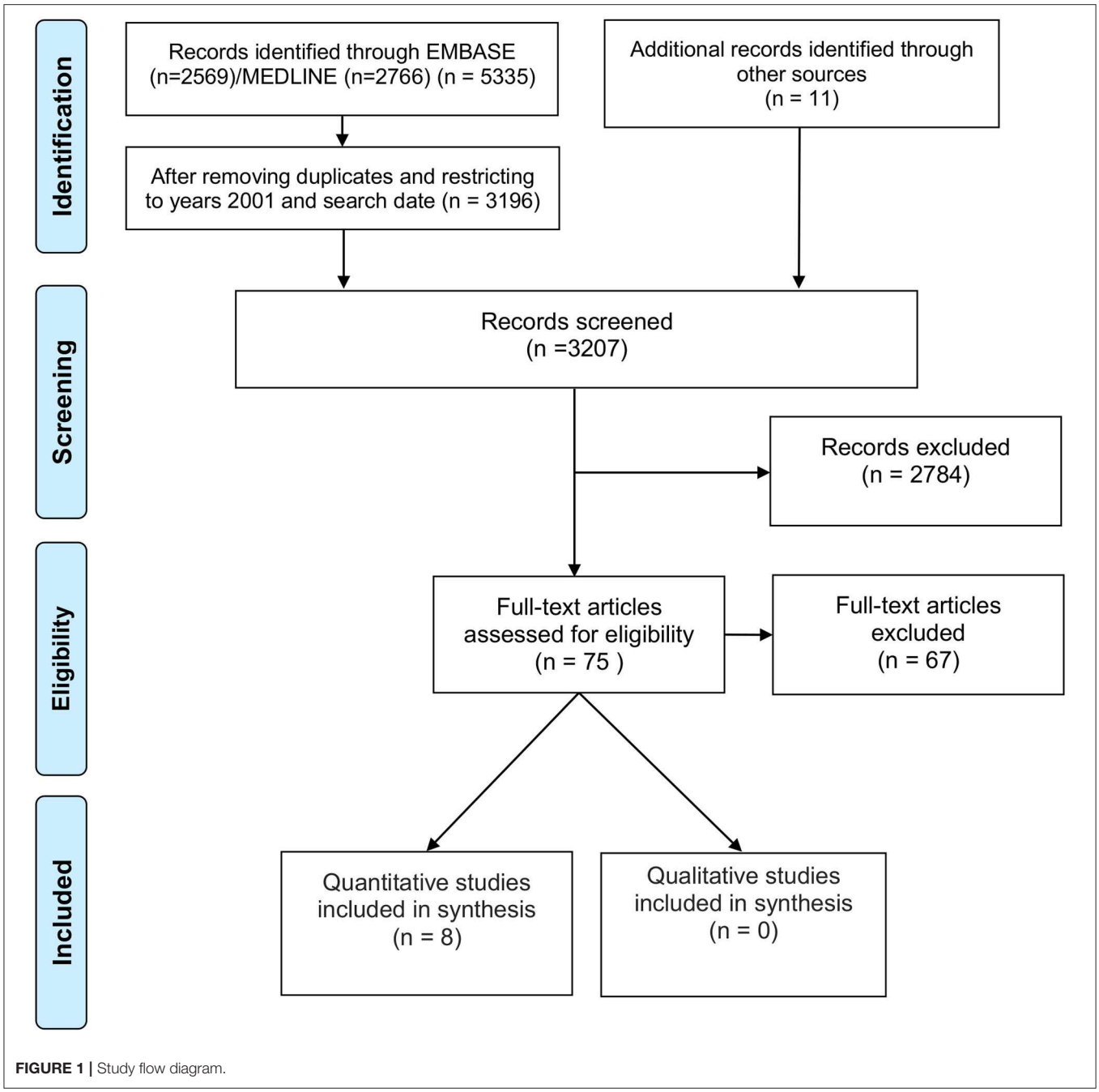

FIGURE 1 | Study flow diagram.

presented for each study in **Table S1**. All included studies fulfilled the two screening criteria in the MMAT, suggesting that further methodological appraisal was feasible. All eight studies used an appropriate sampling strategy. The main methodological limitation was appropriateness (i.e., clear origin or known validity or standard measurement) of methods of assessing barriers and facilitators, with six studies not meeting this criterion (details in **Table S1** footnote). Six studies scored negative or unclear on adequate response rate and four on representativeness, raising concerns of possible selection bias.

Qualitative Synthesis

All barriers and facilitators were coded from the eight included studies into theoretical domains of the TDF. A summary of identified themes and subthemes of influences is presented in **Table 1**. Results of this coding can be found in **Table S2**. Data extracts coded into subthemes of TDF domains can be found in **Table S3**. Ten of the 14 domains of the TDF were present in the results reported in the eight studies (as presented in **Table 2**—"*Optimism*," "*emotion*," "*memory, attention and decision processes*" and "*beliefs about capabilities*" were not present in any of the results reported). Subthemes within each domain are

TABLE 1 | Description of the included studies.

References	Continent (country)	Response rate	Sample size	Design (origin)	Setting (number of institutions)	Participants (*n*)	Unit of analysis	Ongoing ASP	Reported ASP strategies (% actual)
Itokazu et al., 2006	North America (USA and Canada)	88.5% (further 27.8% were excluded)	Total: 233 USA: NC Canada: NC	Electronic and postal survey (NC)	Teaching acute care hospital (NC)	Infectious disease pharmacists SIDP members (233)	Participants	99%	Education (88), prospective chart review (82), retrospective chart review (71), closed formulary (76), prior written or verbal approval (69), clinical practice guidelines (67), formal infectious diseases consultation (62), antibiotic switch (50), automatic stop order (47), antibiotic order form (30)
Johannsson et al., 2011	North America (USA and Canada)	50% (further 9.8% were excluded)	Total: 471 USA: 464 Canada: 7	Electronic survey (NC)	Community, teaching, city or county, veteran's affair hospitals caring for inpatients (NC)	Infectious disease physicians SHEA member (471)	Participants	61%	Formulation restriction pre-authorization and audit and feedback, education, guidelines and clinical pathways, conversion protocol, dose optimization, streamlining or automatic dose adjustment, time-sensitive stop orders, antimicrobial order forms, and antimicrobial cycling; (NC)
Bryant, 2015	Oceania (Australia; North and South Islands of New Zealand)	NC	Total: 14 Australia: NC North and South Islands of New Zealand: NC	Online survey (amended national survey, authors' ample ASP expertise)	Children's hospitals (*n* = 7), or hospitals with a large majority of adults (6) and one hospital with a majority of children plus a maternity unit (1)	Paediatric infectious disease physician (12), paediatrician (1), antimicrobial stewardship pharmacist (1)	Institution	64.3%	Treatment guidelines, education, selective susceptibility reporting, and point of-care interventions, approval for restricted antimicrobials, audit of antimicrobial use, monitoring of antimicrobial resistance; (NC)
Fleming et al., 2015	Europe (UK and Republic of Ireland)	Total: 36.4% Ireland: 73% UK: 32.7%	Total: 277 Ireland: 51 UK: 226	Postal survey (literature based, clinicians validated, piloted)	Ireland: private (15) and public (36) hospitals; UK: public hospitals (226)	Specialist antimicrobial pharmacists (NC), hospital pharmacists in charge (NC)	Institution	96.4%	Three most common strategies: empirical treatment of common infections, surgical prophylaxis and gentamicin protocol (NC)
Howard et al., 2015	Europe (26 countries), Oceania (2), Africa (10), Asia (14), North America (5), South and Central America (12)	? (9.8% were further excluded)	Total: 660 Europe: 361 Oceania: 30 Africa: 44 Asia: 25 N. America: 49 South and Central America: 44	Online survey (literature based, opinion leaders validated, piloted)	Tertiary teaching (319), district or general (161), community or private hospitals (56)	Hospital designated representatives (660)	Institution	58%	Treatment guidelines, surgical prophylaxis guidelines, closed formulary, reserve antibiotics needing authorization by indication, infectious diseases or microbiology advice by telephone or on ward rounds, dose optimization on request, intravenous-to-oral switch guidance, review of intravenous therapy at Day 3, systematic advice for bacteraemia by infectious diseases or microbiology, care bundles, automatic stop or review policy, pre-authorized pharmacy-driven dose optimization, separate antimicrobial chart or section, inflammatory markers to prevent initiation of antibiotics or to stop antibiotics early, restrictions on access by pharmaceutical representatives, antibiotic cycling; (NC)

(Continued)

TABLE 1 | Continued

References	Continent (country)	Response rate	Sample size	Design (origin)	Setting (number of institutions)	Participants (*n*)	Unit of analysis	Ongoing ASP	Reported ASP strategies (% actual)
Livorsi et al., 2016	USA and elsewhere	28.4%	Total: 61 USA: 52 Not reported a geographic location or institutional affiliation: 9	Online survey (NC)	Acute-care inpatient hospitals that participated in the SRN (61)	Physician (48), pharmacist (10), physician or pharmacist (3), SRN members engaged in prospective audit and feedback	Institution	NA	Prospective audit and feedback (100)
Wolf et al., 2016	North America (USA, Mexico, Canada); Oceania (Australia and NZ)	37.4% (4.9% were further excluded)	Total: 97 Australasia: 18 N. America: 72 Not reported a geographic location or institutional affiliation: 7	Online survey (literature search, a focus group)	Institutions that care for paediatric haematology, oncology and bone marrow transplant population (45)	ID physicians (55), fellows (13), clinical pharmacists (29), PIDS conference attendees or other relevant	Institution	91.1%	Clinical guideline development (80), dose optimization (78), resistance monitoring (76), prospective audit with feedback (71), monitoring of cultures (67), clinician education (64), encouraging oral switch (62), audit with delayed feedback (29), antibiotic cycling (9)
Pulcini et al., 2017	Europe (35 countries)[¥] and Asia (Israel)	94.7%	Total: 36 Europe: 35 Israel	Online survey (literature search, ASP specialists validated)	Inpatient and outpatient care institutions-mainly tertiary university hospitals (NC)	EUCI (11) or EUCAST (13) members and appointed national representatives (12)	Country	NA	Selective reporting of antibiotic susceptibility test results (NC)

EUCIC, European Committee on Infection Control; EUCAST, European Committee on Antimicrobial Susceptibility Testing; NC, not clear, SHEA, the Society of Healthcare Epidemiology of America; SRN, the Healthcare Epidemiology of America Research Network; PIDS, the Paediatric Infectious Diseases Society; SIDP, Society of Infectious Diseases Pharmacists.
[¥] Austria, Azerbaijan, Belgium, Bosnia, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kosovo, Latvia, Macedonia, The Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, UK, Ukraine.

described below, commencing with the domain with the largest number of subthemes.

Environmental Context and Resources

There was a perceived paucity of funding (Johannsson et al., 2011; Howard et al., 2015; Pulcini et al., 2017) and accordingly securing financial resources to develop and implement ASPs was mentioned as a facilitator (Fleming et al., 2015).

Insufficient pharmacist and clinician time allocated to ASP activities was also reported to hinder ASP efforts (Itokazu et al., 2006; Livorsi et al., 2016; Wolf et al., 2016). Conceptually related to this issue was a reported shortage of key personnel (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Bryant, 2015; Livorsi et al., 2016; Pulcini et al., 2017), such as dedicated infectious disease clinicians, pharmacists or pharmacy staff, and microbiologists.

A range of barriers related to data and information systems availability and support were identified (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Livorsi et al., 2016; Wolf et al., 2016) that resulted in poor access to patient information (Johannsson et al., 2011; Howard et al., 2015; Pulcini et al., 2017). Participants cited problems of inadequate quality of clinical data on the current use of antimicrobials (Livorsi et al., 2016) and insufficient data analysis resources (Wolf et al., 2016). Given the absence of dedicated information technology staff to support the selective reporting of AST results, additional technical support to manage the data was required. Lack of such support was seen to increase the workload for information technology staff (Pulcini et al., 2017).

Setting- and context-specific barriers included a lack of a reliable supply of laboratory provisions (i.e., shortage of laboratory materials) for selective reporting of antibiotic

TABLE 2 | A summary of barriers (B) and facilitators (F) to implementing an antibiotic stewardship programme (ASP) or an ASP-supporting strategy.

Theoretical domains framework–domains	Subthemes (Table S3) within each domain derived from coded data (Table S2)	No. of studies
Environmental context and resources	(B) Lack of key personnel (e.g., infectious disease clinicians, pharmacy staff, microbiologist)	6
	(B) Problems with data and information systems (e.g., inadequate information technology, lack of dedicated IT assistant, lack of good quality data, and resources to utilize it)	6
	(B, F) The influence of adequacy of financial resources	4
	(B) Lack of time	3
	(B) Inadequate supply of laboratory provisions	1
	(B) Problem of limited antibiotic options available in settings with prevalent multi drug resistant bacteria	1
Goals	(B) Other higher priority initiatives hindering the ASP's use	4
Social influences	(B) Resistance from medical staff	3
	(B, F) The influence of clinical leadership (e.g., pharmacists, infectious diseases physicians, senior clinicians)	3
	(B) Lack of leadership from hospital administration	3
	(B) Poor communication, including interpersonal, within teams (e.g., inconsistency or conflict) and between private and public sectors	3
	(B) Perceived unhelpful attitudes of oncology clinicians	1
Behavioural regulation	(B, F) The influence of local guidelines and clinical practice protocols	2
	(F) Electronic prescribing as a mean to effectively change prescribing patterns by providing easier and quicker feedback	1
	(B) Lack of national and/or international standards required for a specific antibiotic stewardship strategy	1
	(B) Lack of standards for measuring performance of a specific antibiotic stewardship intervention	1
Knowledge	(B) Lack of knowledge of patient test or results	3
	(B) Lack of knowledge about ASPs (e.g., due to poor education or inevitable loss of knowledge due to high staff turnover)	2
	(B) Lack of knowledge of current use of antibiotics	1
Beliefs about consequences	(B) Lack of certainty about usefulness of an ASP or a specific antimicrobial stewardship strategy	2
	(B) ASP clinicians' belief in competing consequences of managing infections in different patient groups acting as a barrier	1
	(F) Focussing ASPs efforts on serious infectious disease as a mean to improving effectiveness of ASPs	1
Social/professional role and identity	(B) ASP derived jurisdiction gives antimicrobial stewardship clinicians limited power or authority	1
	(B) Uncertainties around overlapping responsibilities between multiple infectious diseases groups within a hospital	1
Intentions	(B) Lack of willingness to change	1
Reinforcement	(B) A specific antimicrobial stewardship strategy not being covered by a reimbursement system	1
Skills	(B) Medical professionals lacking relevant skills for a specific antimicrobial stewardship strategy (e.g., training in clinical microbiology)	1

susceptibility testing (Pulcini et al., 2017), and the challenge of limited availability of antibiotic options faced by ASPs in hospital settings where multi-drug resistant bacteria are prevalent (Pulcini et al., 2017).

Social Influences

Interpersonal processes among healthcare professionals (including communication, cooperation and leadership) influenced ASP implementation. Poor communication was reported (Livorsi et al., 2016; Wolf et al., 2016; Pulcini et al., 2017), including within infectious disease and ASP teams (Wolf et al., 2016), between staff (e.g., antibiotic stewardship and pediatric oncology clinicians) (Wolf et al., 2016) and between public and private hospital systems (Pulcini et al., 2017). Studies also reported a lack of cooperation and even resistance from medical staff (Itokazu et al., 2006; Johannsson et al., 2011; Howard et al., 2015; Livorsi et al., 2016). An unsatisfactory relationship between antibiotic stewardship clinicians working in pediatric oncology settings and pediatric oncology clinicians was characterized by role conflict and lack of trust or shared beliefs (Wolf et al., 2016). Finally, a lack of leadership from hospital administrators (Itokazu et al., 2006; Howard et al., 2015; Bryant, 2015) and a lack of clinical leadership from pharmacists and infectious diseases clinicians were perceived to be barriers (Itokazu et al., 2006; Bryant, 2015). Participants suggested that the latter could be overcome by introducing a microbiologist team leader to facilitate the establishment of an antibiotic stewardship team (Fleming et al., 2015).

Behavioral Regulation

Availability of adequate guidance documents or recommendations at all levels (strategy-specific national and international, local, and setting-specific) influenced implementation of ASPs. A lack of national or international clinical practice guidelines to set professional standards for applying the selective reporting of AST results acted

as a barrier (Pulcini et al., 2017). The selective reporting of AST results was reported to be particularly difficult in complicated cases (e.g., polymicrobial infections, severe infections, pharmacodynamics or pharmacokinetics factors) (Pulcini et al., 2017). As susceptibility testing occurs *in vitro,* this difficulty might be related to a need for specific guidance with accounting for many *in vivo* factors (e.g., pharmacokinetics factors) that can influence treatment success. Depending on the stage of ASP implementation, finalizing local guidelines on existing ASP efforts and developing implementation strategies was reported to be potentially helpful with implementing ASPs (Fleming et al., 2015). In pediatric oncology settings, insufficient input of antibiotic stewardship clinicians into clinical practice guidelines, and oncology clinicians following externally derived treatment pathways, were reported to be barriers to stewardship (Wolf et al., 2016).

Influences on behavioral regulation related to audit and feedback were also identified. A lack of performance metrics needed for audit and feedback was reported (Livorsi et al., 2016). Developing processes for the implementation of audit and feedback was cited to be potentially beneficial for implementation of ASPs (Fleming et al., 2015). To optimize feedback needed for adjusting prescribing patterns and to improve patient monitoring, the introduction of an electronic prescribing system was felt to be possibly useful (Fleming et al., 2015).

Knowledge

Studies indicated that limited access to relevant education (Bryant, 2015; Pulcini et al., 2017) and high level of turnover of junior staff was felt to be associated with an inevitable leakage and loss of ASP knowledge (Bryant, 2015). Insufficient knowledge about antibiotic resistance or clinical microbiology are examples of gaps in scientific background reported by participants (Pulcini et al., 2017). Lack of knowledge about patient clinical data (e.g., insufficiency of patient clinical data in a laboratory and delays in obtaining results) (Johannsson et al., 2011; Howard et al., 2015; Pulcini et al., 2017) and the current use of antimicrobials (Livorsi et al., 2016) were also identified.

Beliefs About Consequences

A lack of awareness among hospital administrators about the current value of ASPs was reported to hinder the delivery of functional and effective stewardship (Johannsson et al., 2011). Similarly, some unawareness of the value of the selective reporting of AST results and conflicting evidence on its usefulness, effectiveness or applicability were felt to impede its implementation (Pulcini et al., 2017).

Participants expressed the opinion that effectiveness of ASP efforts would further benefit from narrowing focus to serious infections, extended spectrum beta-lactamase-producing organisms, or carbapenem- and vancomycin-resistant organisms (Fleming et al., 2015).

Social/Professional Role and Identity

Uncertainty around division of responsibilities between multiple infectious diseases professional groups was identified, but only in one study, and its participants ranked it as the least common barrier (Johannsson et al., 2011).

Goals

The selective reporting of AST results was reported to be hindered by a lack of support in current ASP guidelines (Pulcini et al., 2017). Studies also reported other higher priority initiatives competing with establishing and maintaining ASPs (Johannsson et al., 2011; Howard et al., 2015; Pulcini et al., 2017). Populations other than immunocompromised hosts having higher priority in antibiotic stewardship programmes, was considered to be an important barrier by antibiotic stewardship clinicians (Wolf et al., 2016).

Intentions

A lack of willingness to change behavior was felt to hinder ASP implementation efforts (Bryant, 2015).

Reinforcement

A lack of incentives to use selective reporting of AST was reported to impede its implementation (Pulcini et al., 2017).

Skills

It was felt that local professionals are generally lacking relevant skills (especially physicians' clinical microbiology skills) needed for the selective reporting of AST results (Pulcini et al., 2017).

Quantitative Summary

The most commonly reported (≥4 out of 8 studies) influences on ASP implementation were coded into the domain "*environmental context and resources*": problems with data and information systems (e.g., inadequate information technology, lack of dedicated information technology assistance, lack of good quality data and resources to utilize it), lack of key personnel (e.g., infectious disease clinicians, pharmacy staff, microbiologist) and inadequacy of financial resources. In addition, other higher priority initiatives hindering the implementation of ASPs were coded into the domain "*goals*") (**Table 1**).

Country Context

One paper in this review (Wolf et al., 2016) found no effect of continent when comparing North American and Australasian institutions. Another included paper (Howard et al., 2015) concluded that a lack of funding or personnel and a lack of information technology or ability to acquire data (all coded into the domain *"environmental context and resources"*), followed by prescriber opposition ("*social influences*") or other higher priorities ("*goals*") were the top barriers to implementing an ASP, uniformly across all continents except for Africa, for which information technology was ranked as the main barrier. In hospitals that planned to develop an ASP, the main barrier was a lack of funding, except in South America, where a lack of awareness on the part of the hospital administration ("*social influences*") that implies a lack of leadership from hospital administration, was the key barrier stated (Howard et al., 2015). "*Behavioural regulation"* strategies such as finalizing local guidelines on existing ASP efforts, developing processes for the implementation of ASP strategies and introducing an

electronic prescribing system to adjust prescribing patterns were key strategic enablers of ASPs suggested by the UK, but not Irish respondents (Fleming et al., 2015). Ring-fencing of financial resources ("*environmental context and resources*") and a need for microbiologist leadership ("*social influences*") were mentioned by respondents from Ireland, but not from the UK (Fleming et al., 2015).

DISCUSSION

In response to calls for improved understanding of contextual influences on the implementation of ASP in hospitals (World Health Organization, 2015; Davey et al., 2017; Hulscher and Prins, 2017), we conducted a systematic review of transnational studies on reported barriers and facilitators to implementation of ASP in hospitals. Except for one study, most of the data comes only from developed countries (North America, Europe and Australasia). Reported barriers and facilitators were coded using the TDF, a framework based on behavioral theories. None of the included studies used behavioral theory explicitly to identify barriers and facilitators, reiterating the problem of behavioral approaches being underutilized in antibiotic stewardship studies (Charani et al., 2011; Rawson et al., 2017) and highlighting the importance of efforts to enable their widespread use (Atkins et al., 2017). The most commonly reported influences on ASP implementation included problems with data and information systems, lack of key personnel and financial resources. Another commonly reported barrier was the effect of conflicting priority initiatives. Between-country differences in the order of importance of specific influences on ASP implementation efforts warrant further investigation.

The main methodological weakness of included studies concerned the methods used in these studies to identify barriers and facilitators. Five studies used a list of options for barriers compiled by study authors and three studies used open-ended questions, hence barriers and facilitators were not comprehensively captured. It is unclear to what extent methods of assessment affected types of reported barriers. Two of three studies with high scores on quality of measurement of barriers were strategy- and context-specific and this possibly enabled participants to recall specific episodes or information more accurately. There were difficulties with quality of reporting, including the use of vague wording, incomplete descriptions and limited space dedicated to reporting barriers and facilitators. Frontline hospital workers involved in ASPs were rarely represented.

The review itself has its strength and limitations. By using TDF, a well-operationalized, multi-level implementation determinant framework derived from theory, we synthesized generic learning from diverse studies on dissimilar, context-specific multi-component ASPs, which may be useful to research teams designing future large-scale evaluation efforts. Other frameworks promote knowledge synthesis about what works, where and why, across multiple contexts, such as the Consolidated Framework For Implementation Research (CFIR) (Damschroder et al., 2009). However, given all included studies involved interventions to change antibiotic prescribing behavior, a behavioral approach using TDF was a suitable means of providing a high level of elaboration for contextual influences related to both individual-level change (provider behavior) and collective-level constructs. With a recognized need for the use of behavioral theory approaches (Davey et al., 2017; Rzewuska et al., 2019), the high level of transparency in our reporting of the review methods enhances existing guidance (Atkins et al., 2017). For example, a user less familiar with the TDF may find it easier to apply it, by following the outputs from each step of the analytic process reported in this paper. A limitation of the review is that, although we searched several databases using a comprehensive search strategy, we included only research published in English. Hence, the findings may not generalize beyond English language contexts.

The scope of our review has important implications. First, antibiotic stewardship involves different "actors," including individuals (e.g., antibiotic prescribers), organizations and governments (Dyar et al., 2017). By focusing on hospital staff experiences with implementation of ASPs, we took a focused approach that is an organization level approach. Several factors are known to influence prescribing behavior in acute care hospital settings (Md Rezal et al., 2015), hence a need for understanding a context of antibiotic stewardship (Tamma et al., 2014). A methodological reason for taking a focused approach was that the framework method of analysis, thematic analysis and qualitative content analysis, involve categorization, which in turn requires data that is specified at a similar level (Gale et al., 2013). Second, we reasoned that there are qualities of the whole that cannot be reduced to the qualities of its parts and yet the nature of a part depends upon the whole in which it is embedded (Wagemans et al., 2012). As such we were interested in comparing multi-component ASPs ("whole") with individual ASP-supporting interventions ("parts"). However, we aimed in this work to learn about implementation of ASPs, as opposed to conceptualizing individual behavior change interventions ("parts"). For an example of "why" and "how" the TDF can increase clarity and help to operationalise the individual intervention elements, we refer a reader to another paper published by the authors (Duncan et al., 2020). At last, to fully address the remaining uncertainties surrounding the value of antibiotic stewardship, we advocate for robust large-scale participatory collaborative evaluation research (Grimshaw et al., 2019; Rzewuska et al., 2019). Finding a balance between full and consistent implementation across multiple contexts, while providing the flexibility for individual sites to adapt the intervention as needed, is a major task (Damschroder et al., 2009). Multinational trials will face the design challenge of setting minimum conditions addressing differences between countries that are likely to generate unintended influences (barriers and facilitators) on outcomes and, thus, potentially hinder the generalisability and transferability of results. Therefore, we reasoned that commonalities captured through transnational studies would inform us about a broad scope of circumstances and characteristics that should be considered when facing early methodological issues, such as defining the scope of the evaluation and selecting study sites (Bryce et al., 2005).

Country-level studies seem to be highlighting similar barriers. For example, quantitative analysis of data from three nationwide studies in the USA (Doron et al., 2013) and Australia (Chen et al., 2011; James et al., 2015) identified the same barriers as those reported in the current review. Chen and colleagues (Chen et al., 2011) concluded that barriers identified through quantitative and qualitative methods were alike. Overall, transnational studies were unlikely to use qualitative methods of data collection, which would seem to be more appropriate in the context of studies in which face-to-face methods of data collection are more feasible (Cotta et al., 2015; James et al., 2015).

Work presented in this review has the potential to inform local or regional initiatives to guide ASP implementation efforts. We have provided a detailed coding manual so that future initiatives may be informed by this behavioral approach.

There are several research implications of this review. There is an apparent need for a transnational mixed method study inclusive of low-, medium- and high-income countries, to identify barriers and facilitators to implementation of ASPs using a behavioral approach and to explore country, context and health systems differences. Assuming that optimizing ASP efforts may be effectively approached by addressing the commonly reported influences on ASP implementation, an appropriate next step is to identify strategies for optimizing ASPs that could, in turn, change prescribing behavior of frontline healthcare professionals. A wide range of behavior change approaches have been proposed, for example, education, persuasion, incentivisation, coercion, training, restriction, environmental restructuring, modeling or enablement (Michie et al., 2014).

CONCLUSIONS

Despite a substantial research effort, and many quality improvement initiatives, there is still a poor evidence base to identify barriers and facilitators for establishing and maintaining ASPs transnationally, even in developed countries where most data comes from, and thus a poor basis for optimizing these large-scale quality improvement efforts to address what is a globally important problem. The reviewed here evidence suggests that these efforts will likely require taking into account the possibility of issues around inadequacy of information systems, unavailability of key personnel and funding, and the competition from other priority initiatives. To provide comprehensive generalizable evidence on barriers and facilitators to establishing and maintaining ASPs, a prospective transnational mixed methods study with hospital staff using behavioral theory may be worthwhile. For this purpose, we suggest using implementation frameworks, for example TDF is well-suited to design ASP interventions to enhance implementation and CFIR evaluation of the implementation of a specific ASP in multi-level contexts. This work enhances the evidence base to inform guidance by taking a behavioral approach to identify influences on ASP uptake.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: EMBASE, MEDLINE.

AUTHOR CONTRIBUTIONS

MR, ED, and CR were involved in the conception and design of the review. MR and ED performed study selection, extracted data from the included studies, and critically appraised methodological quality of the included studies. MR, ED, and JF analyzed and interpreted the literature and drafted the manuscript. AM, KS, PD, JG, and CR revised the review critically for important intellectual content, contributed to data interpretation, and to the writing of the manuscript. All authors revised and approved the submission of the manuscript.

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Diagnosis Between Chaos and Control: Affect and Hospital Clinicians' and Older Adult Patients' Narratives of Urinary Tract Infections

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Research has observed that older adults are frequently overdiagnosed with urinary tract infection (UTI) and unnecessarily prescribed antibiotics in hospitals. In this article we explore the overlooked affective dimension of experiences of diagnosis and prescribing. Drawing on interviews with doctors, nurses and older adult patients ($n = 41$) on UTI diagnosis in two UK hospitals and Arthur Frank's work on illness narratives we identified two affective ways of experiencing diagnosis. Some clinicians and older adult patients articulated *chaos* narratives about being overwhelmed by contradictory evidence and events, doubting the repeated UTI diagnoses and courses of antibiotics but being unable to do anything about their concerns. Other clinicians and patients articulated *control* narratives about UTIs being frequently diagnosed and antibiotics prescribed to restore patients' health, echoing certainty and security, even if the processes described typically did not follow current guidance. We contend that analyzing the affective dimension offers conceptual insights that push forward sociological discussions on diagnosis as reflective or dogmatic in the context of the contradiction between acute care and chronic illnesses of old age. Our findings contribute practical ideas of why overdiagnosis and overprescribing happen in hospitals and complicate notions of patients pressuring for antibiotics. We also present methodological suggestions for analyzing *how* participants tell about their experiences in order to explore the typically not directly spoken affective dimension that influences thoughts and actions about diagnosis.

Keywords: affect, diagnosis, antibiotic prescribing, urinary tract infections, antimicrobial resistance, narrative analysis

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INTRODUCTION

Older adults frequently have bacteria in their urine without symptoms (asymptomatic bacteriuria), which should not be treated with antibiotics. Clinical guidance in the UK recommends that UTIs should be primarily diagnosed based on symptoms, such as pain when passing water, rather than presence of bacteria in urine identified by diagnostic tests, such as point-of-care urinary dipsticks or bacterial cultures (Scottish Intercollegiate Guidelines Network, 2012; Public Health England, 2018). However, international research has observed that this guidance is frequently not adhered to in hospitals (Pallin et al., 2014; Lee et al., 2015; Eyer et al., 2016) or care homes (Chambers et al., 2019) contributing to antimicrobial resistance (AMR).

Qualitative research has found that junior doctors' overdiagnosis of UTIs and unnecessary antibiotic prescribing in hospitals is driven by overreliance on laboratory results, risk aversion, difficulties in interpreting symptoms and perceived pressure from peers, patients, and families (Eyer et al., 2016). Research on antibiotic prescribing in general has found that doctors typically focus on the immediate risk of infection for their individual patients rather than the communal, future risk of AMR (Broom et al., 2014; Krockow et al., 2019). It has also been observed that antibiotics are prescribed to appease other staff, patients, and families in hospitals (Lewis and Tully, 2009; Charani et al., 2013), that there are problems in interaction between different staff, patients and clinical domains (Skodvin et al., 2017; Saukko et al., 2019), junior doctors are confused by contradictory advice (Mattick et al., 2014; Kajamaa et al., 2019) and that professional identities (Broom et al., 2016) and "off label" local cultures fuel prescribing (Caronia and Saglietti, 2017).

Previous studies resonate with medical sociological work on diagnosis, such as junior doctors' reflections on uncertainty and whether it relates to their lack of knowledge or uncertainties of medical knowledge itself (Fox, 1980), how junior doctors' decisions may not only be characterized by uncertainty but also by unreflective, learnt stock responses (Atkinson, 1984), different ways of using evidence by doctors (Timmermans and Angell, 2001), the contradictions between focusing on disease manifesting itself in pathology, such as laboratory results, and illness articulated through patients' descriptions of symptoms (Armstrong, 2011) and how clinicians do not necessarily follow guidelines but, for example, rely on their intuition and consider organizational issues (Carthey et al., 2011; Johannessen, 2017). The empirical and conceptual research illustrate different factors and approaches at play when clinicians encounter an ambiguous situation, such as a suspected UTI in an older adult. Our qualitative interviews with doctors, nurses and older adult patients in hospitals corroborated many of the previous observations. However, we contend that previous research has not considered the affective feelings (Massumi, 1995; Seigworth and Gregg, 2010), which underpin experiences of diagnosis and antibiotic prescribing.

The first author initially noticed that our interviews with clinicians and older adult patients gave off a sense of being overwhelmed by contradictory evidence, repeated UTI diagnosis, and antibiotics, having doubts about the procedures but being unable to act on the concerns. Other participants told about diagnosis and antibiotic use with a sense of certainty and security, even if the processes described did not follow current guidance. Participants did not directly tell about these affective experiences, such as saying that they were bewildered. Rather, the form of narratives in the interviews (*how* stories were told) brought to the fore the sense of being out of or in control. In making sense of these stories we drew on Arthur Frank's classic work on types of patients' illness narratives (Frank, 1995), arguing that UTI diagnosis and antibiotic prescribing for older adults could be experienced in terms of *chaos* and/or *control*.

We contend that analyzing the affective dimension offers conceptual insights that push forward sociological discussions on diagnosis as reflective or dogmatic in the context of the contradiction between acute care and chronic illnesses of old age. Our findings also contribute practical ideas of why overdiagnosis and overprescribing happen in hospitals and complicate notions of patients pressuring for antibiotics. We also present methodological suggestions for analyzing *how* participants tell about their experiences in order to explore the typically not directly spoken affective dimension that influences thoughts and actions about diagnosis.

DIAGNOSIS AND AFFECT

Classical sociological work on diagnosis in hospitals has focussed on junior doctors' experiences of reflecting on uncertainties of medical knowledge or evidence or relying on routine or dogmatic stock responses to clinical situations (Fox, 1980; Atkinson, 1984; Timmermans and Angell, 2001). Antibiotic prescribing decisions have been found to lean toward the dogmatic side of the equation and doctors have been observed to overprescribe focusing on the risk of infection (Broom et al., 2014). Nurses have been found to push for antibiotics seeing themselves as advocates for patients (Broom et al., 2016), and nurses have also been observed to follow internalized "mindlines" rather than guidelines in triage decisions (Johannessen, 2017), highlighting the fine balance between too strict following of either guidance or intuition.

Sociologists typically consider critical reflection more sensitive to the multi-faceted nature of medical decisions and patient experiences than unquestioning following of routines or guidance (Timmermans and Angell, 2001). However, reflection is a rational, solution-driven activity, even if it has been acknowledged that it can be accompanied by feelings of self-doubt (Fox, 1980). In our research we noticed that clinicians and older adult patients could have doubts about diagnosis or prescribing decisions, but these doubts did not necessarily lead to a different line of action but to a sense of unease. At the same time routine practices potentially leading to overdiagnosis were described with a sense of certainty. We contend that these observations point to a neglected affective dimension of diagnosis and prescribing that importantly influences decisions and renders them intelligible.

To capture the above mentioned feelings we use the term affect rather than emotion. It is not our intention to participate in debates about the currently fashionable interest in affect in social sciences (Wetherell, 2015). In psychology affect usually refers to a visceral layer of experience, whereas emotions are understood to be cognitively recognized states, such as sorrow or joy (Russell, 2003). We take the lead from post-structuralist work that sees affect as feelings that may or may not be cognitively and verbally articulated and that emerge from relations between people, events and things (Deleuze and Guattari, 1987; Massumi, 1995; Gregg and Seigworth, 2010).

The important thing here is that the sense of unease or security were not necessarily directly verbalized in the interviews but conveyed through the way in which events were described. To gauge this affective dimension we resorted to narrative analysis, which has been used in medical sociology and health services

research to bring to the fore the embodied and emotional dimension of experience often silenced in biomedical research. Early narrative research often focused on patients' emotional experiences (Hurwitz et al., 2008). Recent work, more directly pertinent to our research, has analyzed UK junior doctors' narratives on regulation of emotion (Lundin et al., 2018) and preparedness for practice (Monrouxe et al., 2018). Closest to our topic there is also research on junior doctors' narratives of antibiotic prescribing about feelings of being unsupported or given contradictory advice (Mattick et al., 2014; Kajamaa et al., 2019) as well as on nurses' narratives on their experiences of speaking up about safety concerns (Law and Chan, 2015).

Narrative analyses have drawn attention to clinicians' and patients' uncomfortable experiences, such as a sense of powerlessness, which influence clinical practice. However, the analyses mostly focus on the content of the narratives (*what* is being told) rather than the form (*how* is it being told) (Chatman, 1978). Form is the less obvious dimension of narrative, but it is saturated with meaning; for example, the classical research article, using a passive voice and a detached description, communicates authority, and objectivity. The scientific article illustrates how narrative forms frequently follow normative cultural scripts. Drawing on structuralism and phenomenology Frank (1995) argues that forms of illness narratives articulate both social scripts and not necessarily conscious embodied and emotional ways of relating to the world.

Frank (1995) delineates basic illness narratives, of which we will discuss two that resonated with our study. The first, restitution narrative rehashes the classical normative script of a patient falling ill and biomedicine heroically restoring his/her health; the order of events is linear, orderly and achieves closure. The second, chaos narrative is disorderly, events occur out of sequence and repetitively, the illness overwhelms the experience and there is no resolution to the situation. As indicated earlier the forms of narrative identified by Frank repeated in our interviews, highlighting the affective dimension of overdiagnosis and overprescribing that pushes forward discussions on reflexivity, dogmatism, adherence to guidance and why overdiagnosis happens.

METHODS

Our study explored processes of diagnosing and treating UTIs in older adults in two hospitals in the UK Midlands. After obtaining ethical approval from Healthcare Research Authority (IRAS 202255) we put posters about our research on the walls and published information on relevant staff e-newsletters. Afterwards a research nurses visited wards, handing out information packs and invitations to participate to: (i) healthcare staff involved in diagnosing UTIs in older adults and (ii) older adult patients (>70 year olds) who had been diagnosed with a UTI during their current hospitalization. Staff and patients who expressed an interest in taking part were contacted by an experienced qualitative researcher who arranged for an interview.

We recruited a total of 41 participants, including 27 healthcare staff, comprising of 13 nurses, 9 doctors, 3 healthcare assistants and 2 microbiologists, and 14 older adult patients. Most of the doctors (7) were junior doctors, who mostly perform initial UTI diagnosis. The doctors were recruited from both acute (A&E) and subacute wards, the patients and nursing staff were recruited from subacute wards, including older adults, orthopedics, stroke, and rehabilitation. The average age of the patients was 81 (range between 71 and 89) and they were all assessed by the research nurse to be cognitively capable of giving informed consent. Staff were asked to describe their job role, how diagnosing UTIs in older adults featured in their work, how they went about the diagnosis, their role in prescribing, perspectives on recovery, and any concerns they may have. Patients were asked to tell about being diagnosed with a UTI, experiences with treatment, prior experiences with UTIs and other health related issues and any concerns they may have. All bar one interviews with staff took place in a private room in the hospital, one in a clinician's home. Six patients were interviewed in the hospital, seven at home after discharge and one, who lived in another area, was interviewed by phone. The average length of the interviews was 24 min, ranging between 12 and 43 min; some interviews were short due to older adult patients in the hospital being frail and getting tired and some clinicians being busy. Most of the interviews were thus not in depth but short conversations carried out with clinicians over a break or with convalescing patients, which did not necessarily gauge significant amounts of background information but could capture the experiences of diagnosis and/or illness in the hospital environment.

The interviews were transcribed in verbatim. We first analyzed the interviews using the constant comparative method (Glaser, 1965) and observed that they featured two broad themes of "control" and "chaos." Following the principles of abductive analysis (Timmermans and Tavory, 2012) we brought Frank's (1995) work to bear on the material, reading back and forth between literature and material. The two broad themes were coded into subthemes, based on key moments in diagnosis e.g., symptom recognition, facilitated by the use of NVivo 10 qualitative software. A selection of transcripts was read by all members of the research team, and the coding scheme was developed building consensus within the team, including two clinical members who are not authors of this article. A previous article focused on the subthemes, discussing the different staff groups' and older adult patients' divergent understandings of the key stages of diagnosis leading to problems in "translation" (Saukko et al., 2019).

This article focuses on the broader themes of chaos and control, defined as affective states, characterized by (i) sense of being out of control, experience of contradictory events/perspectives, doubts about the righteousness of actions, and an inability to act on concerns, and (ii) sense of being in control, experience of orderly series of events, sense of "doing the right thing," and problems being solved. The sense of chaos and control was articulated through how the narratives were told. To systematically analyse these narrative forms we used insights from Frank (1995) and other work on narrative analysis (Chatman, 1978; Riessman Kohler, 1993; Stephens and Breheny, 2013) to discern three key aspects of the interviews: (i) how the teller positioned him or herself in relation to his/her and

others' actions, (ii) the coherence of the sequence of events and perspectives, and (iii) whether the story achieved closure or resolution. It should be noted that individual interviews could be dominated by either chaos or control narrative but interviews often shifted between the two.

In what follows we will first present the general characteristics of our material, then discuss the chaos narratives featuring in the interviews, and move on to discuss control narratives.

FINDINGS

The overall feature of our material was that the descriptions of processes of diagnosing UTIs and prescribing antibiotics for older adults did not typically follow the ideal proscriptions of clinical guidelines (Scottish Intercollegiate Guidelines Network, 2012), which was also corroborated by our parallel quantitative case series review of patient records (Rousham et al., 2019). The sense of chaos vis a vis the diagnostic process was most prominent in the junior doctors' and older adult patients' interviews and less common among nursing staff; the sense of control and certainty was most common in nurses' interviews and was less common in doctors' and patients accounts. In what follows we will present our findings through illustrative cases from doctors, patients, and nurses to capture the experiences of different groups. The cases have been selected to represent both intense and typical (often less clear) cases (Patton, 2015) seeking to do justice to the richness and nuances of the material. The names used are pseudonyms and some details have been modified to protect anonymity.

Diagnosis as Chaos

"Maybe It's a UTI"

First example of a chaos narrative is the description by Anthony, a junior doctor, of a typical situation of encountering UTIs:

> **So, when do you encounter UTIs—?**
> It crops up because I see quite a few patients in acute medical unit. They come in just feeling actually unwell and they can't tell you what's wrong with them as they're too confused sometimes, and then you have to somewhat think, "Oh, maybe this is an infection causing delirium and maybe it's UTI," which is one of the most common causes anyways. … Maybe the family says, "Oh, this patient she's been having like foul-smelling urine and pain, so maybe it's UTI." … The over 65 group, they're confused, they don't know where they are. They can't really explain what's going on. They sound like they have dysuria [pain when urinating] or maybe not, not too sure, and yeah, just think about UTI and then get all the investigations done and we think about and hope it is the UTI.

Anthony switches between the pronouns "I," the impersonal "you," use of passive voice and in the end evoking the collegial "we," fluctuating between owning and distancing himself from his actions and having and lacking agency. The older adult patients are referred to impersonally as "they," more as objects to be observed rather than subjects to be engaged with reference to vague illness (actually unwell), potential UTI symptoms (sound like they have dysuria, maybe not, not too sure), and cognitive impairment (cannot say what's wrong with them, they don't know where they are, what's going on). Anthony's narrative describes his unsure ("you gotta somewhat think") attempt to match the symptoms to a textbook diagnosis (maybe infection causing delirium) to justifying his actions with reference to ostensibly factual common sense (it is one of the most common causes). Characteristic of chaos narrative many contradictory events happen all at once (patient is unwell, families tell they may have dysuria, patients don't know where they are, investigations are done) and the narrative does not proceed in an orderly fashion and achieve a resolution or closure. The felicitous nature of diagnosis is left unclear with a query "maybe it's UTI" and "hope it's UTI" left hanging in the air, reflecting Anthony's doubts about the diagnostic process.

Anthony's interview could be read from the point of view of content of the narrative (what is told), corroborating that junior doctors find interpreting symptoms of UTI difficult (Eyer et al., 2016). The form of Anthony's interview, however, opens another affective and not directly verbalized perspective on the experience of UTI diagnosis. Similar to Mattick et al. (2014) analysis of junior doctors' antibiotic prescribing narratives, Anthony shifts between a position of knowing and not knowing in his interview. However, Anthony's narrative mainly communicates him being tugged and pulled into contradictory directions by different clues about older adult patients' symptoms. In an earlier part of the interview Anthony described similar series of events in interpreting inconclusive and contradictory diagnostic tests. Overall, his narrative gives off a sense of being overwhelmed by contradictory evidence and of being acutely aware that the default position of UTI diagnosis ("maybe/hope it's a UTI") is not necessarily the right one whilst being unable to do anything about it.

Catriona is a junior doctor working in a rehabilitation ward. At the start of the interview she describes processes of diagnosing UTIs in older adults echoing confidence and control, underlining how senior consultants had instructed her not to pay too much attention to urinary dipstick results. However, when describing processes of collecting urine samples, the form of her narrative changes:

> **Could you tell me about the urine collection … is it tricky with the older adults?**
> I'd say yes. A lot of the time I'll optimistically ask for a specimen and then I'll be told actually they're incontinent. Then when they're incontinent, then I will say can we dip the [continence] pad. Which probably isn't best practise, but it's the best we can do given the circumstances. …
> **How do you interpret the results against the fact that they've been taken from a pad?**
> … If I know it's been taken from the pad, I don't think it really changes the way that I would interpret it to be honest. I think I would interpret it the – I think I would – bear in mind it's been taken from the pad and probably it's not going to be as accurate as we would like it to be, because it's not the way it's intended to be used. I guess sometimes you have to make do with what you've got.

In this excerpt Catriona mainly uses the first person pronoun "I" articulating herself as the agent of actions. However, at the end of both paragraphs, where doubts about the righteousness of the procedure appear, she shifts into a collective "we" and passive voice, distancing herself from the actions and her own agency. In the second paragraph Catriona's narrative takes the form of thinking out loud which line of action she would be taking ("if I know," "I don't think," "I would … to be honest," "I think I would"), shifting between positions and articulating hesitancy. The narrative resembles bouncing off the walls in a blind alley until it becomes clear there is no way out or resolution, and Catriona concludes that diagnosing UTIs based on dipsticking urine taken from a continence pad is something one "has to make do with" even though she is acutely aware of this not being the ideal course of action.

The content of Catriona's interview corroborates qualitative and quantitative observations from hospitals care homes that urine samples are not often collected midstream (Schweizer et al., 2005; Pallin et al., 2014). However, the focus on narrative form and affect illustrates how a junior doctor's shifting around different scenarios in relation to urine collection and interpretation of results, concluding it is impossible to do it right.

The forms of junior doctors' narratives of diagnosing UTIs in older adults highlight the affective experience of being overwhelmed, faced with complex and/or impossible to solve situations, being ambivalent about the righteousness of one's actions and unable to do anything about it. The interviews articulate elements of uncertainty (Fox, 1980), routine practices (Atkinson, 1984), erring on the side of overinterpreting risk (Broom et al., 2014) and not adhering to guidelines (Carthey et al., 2011). However, these works on clinicians and diagnosis do not capture the experience of repeated and seriously doubted actions, which open another perspective on how overdiagnosis of UTIs in older adults and overprescribing of antibiotics happens in hospitals.

"Tablets for Something"

Older adult patients' interviews often articulated a sense of chaos amidst their frequently complex care. For example, Elena is in her late eighties, has heart failure, has recently been diagnosed with breast cancer and relates she has been repeatedly diagnosed with UTIs and describes how she was hospitalized during the latest episode of UTIs:

> I couldn't breathe anymore, and I pressed that button [home alarm] … and they sent the ambulance … and then they said I have to go to hospital. … And when I came there – I already had a water infection there, and they gave me something for it. And then they gave me something to breathe, you know, some tablets, antibiotics or something. … Then the ambulance brought me back again. … I got different tablets for two weeks from the hospital … Anyway, I got different tablets, but they took the water tablets away... And I don't know why … But then afterwards it might be they took it away and then maybe they'll bring it back again, we don't know. Because I've got a kidney infection as well …
>
> **Oh, so did the water infection go to your kidneys this time around?**
>
> No, the water infection, I had an x-ray in the hospital and they said I had water on the lungs. And that's why they gave me something for it, and then I think antibiotics.

Elena uses the first-person pronoun "I," relating her experience of events, and refers to clinicians impersonally as "they." Characteristic of chaos narrative Elena's account of events is repetitive, referring to "tablets," which are given, taken away and possibly brought back. Some of the tablets are possibly antibiotics ("or something"), some of them are for UTIs, others for other ailments, such as water in the lungs. The sequence of events in the narrative is blurred, many events happen all at once, it becomes difficult both for Elena and the reader/listener to make sense of what happens and in what order. There are multiple illnesses (breathing, UTIs, heart, lungs, kidney infection) and multiple treatments involved. All the events, illnesses, and treatments create a jumbled-up narrative and a strong sense of being overwhelmed amidst too many health-related things going on. Elena, the protagonist, is clearly not in control of the events, which are mainly driven by the impersonal clinicians, referred to as "they."

Elena's narrative illustrates the affective experience of being at the mercy of medical interventions happening to her. Her narrative exemplifies how co-morbidities or multiple illnesses and treatments of old age intermesh with the UTI diagnosis making them all blend into a chaotic, anxiety-riddled experience. Research on clinicians has reported that they perceive patients to "pressure" for antibiotics (Eyer et al., 2016). Elena's narrative did not indicate pressure, rather her narrative communicates a sense of being overwhelmed with her repeated diagnoses and medications. Elena's narrative is also indirectly critical of clinicians, who are referred to as an anonymous force ("they"), whose actions she observes without being able to fully understand them and not being given explanations.

Philip is in his early eighties, had experienced balance problems and several falls, which had been the original reason for his admission. He has been diagnosed with a UTI, at the time of the interview his hospitalization had prolonged, his UTI is unresolved and his balance problems continue to be investigated. He describes antibiotic prescribing for his UTI as follows:

> **How did they treat you for this water infection?**
> By medicine I think, tablets and that, trying to—
> **So it was tablets?**
> Yes. I'm on a lot of tablets, believe me (laughs).
> **Okay, just for this or just in general?**
> Yes, in general. I should be rattling by now all that I've had (laughs).
> **What kind of medicines do you take?**
> It's all tablets.
> **What's that for?**
> Don't ask me, my dear. I couldn't tell you. I know there was some – when I first came in there was water tablets and then I [was put on IV antibiotics].

Philip tells his story in first person, from his perspective, but refers to "tablets" in passive voice as "it's" and "there was" indicating he is not actively taking medications but they are being administered to him. Similar to Elena's narrative, the prescribing

of a "lot" of unspecified medications for various, unclear reasons repeat. Philip is not in control of events, he does not know exactly what medications he has been given. The narrative does not achieve a resolution, Philip's hospitalization, antibiotics/tablets, UTI, and balance problems all remain on-going. However, Philip articulates less urgent worry and dissatisfaction with care than Elena, he frames himself as having accepted a passive role and intersperses the interview with humor throughout even though he is frail and has to make an effort to speak during the interview.

Hospitalized older adults' experiences of UTI diagnosis have not, to our knowledge, been studied before. Clinicians have been observed to perceive patients and families to pressure for antibiotics for UTIs in hospitals (Eyer et al., 2016) and care homes (Chambers et al., 2019). However, rather than pressure for antibiotics our findings resonate with older adult experiences of taking multiple medicines (polypharmacy) in community has been found contradictory, often accepting of the necessity of medications but also having concerns and not understanding or being explained the purpose of different medications (Moen et al., 2009; Clyne et al., 2017). The narratives of our older adult patient participants highlight an affective experience of repeated UTI diagnoses, other illnesses, and medications, creating an undistinguishable amalgam of medical interventions which patients do not fully comprehend interlaced with greater or lesser amounts of worry.

Antibiotics and Dipsticks Again

An example of a nurse narrative structured by chaos is Elias' interview. He works on an older adults' ward and discusses how older adult patients often had repeated UTI diagnoses and courses of antibiotics, returning to the ward and the bacteria becoming resistant to antibiotics:

> **So, you see the same patients with recurrent UTIs?**
> Usually, yeah.
> **So how common is that, that they . . . come again?**
> As I've said, because they become resistant to treatment— Yeah. So, in the acute stage, again they will give strong antibiotics, like to which antibiotic they are responding. Some of them are still responsive, but it kind of takes a while before they get better. And then maybe, I could say, I think, they kind of become a carrier— What do they call that? They are harbouring the bacteria, but they are not symptomatic … So, any time they can flare up, if their body could not – if the immune system is low, is down. So, it can flare up again, then treat again with the kind of strong antibiotics and then come back again.

The interview is characterized by repetitive recurrence, characteristic of the chaos narrative of older adult patients being prescribed "strong antibiotics," how it takes patients longer to recover, until the bacteria becomes resistant to antibiotics and the patient is treated with another course of "strong antibiotics" and, yet again, returns to the hospital. The narrative has a strong sense of powerlessness, which is articulated through mainly use of passive tense, treatment decisions being made by an impersonal institutional agent, interspersed with occasional use of first person pronoun to indicate Elias' hesitant critical own view with "I think" "I could say."

Elias's narrative goes against observations of clinicians' behavior vis a vis inappropriate antibiotic prescribing in hospitals. It has been noted that doctors consider antimicrobial resistance an abstract threat in the future, whereas the risk of infection for their patients is more immediate and concrete (Broom et al., 2014). In Elias's narrative the risk of antimicrobial resistance is concrete, affecting nursing staff on the ground who witness bacteria colonizing older adult patients becoming resistant and returning to the ward with UTI diagnosis. Nurses have been observed to indirectly push for antibiotics, in the interest of the patients (Broom et al., 2016). However, Elias's narrative illustrated the difficult position of nurses that witness recurrent, potentially unnecessary prescribing of antibiotics without being able to do anything due to their position in the hospital hierarchy, which has been observed in narrative research on safety issues generally (Law and Chan, 2015). The narrative reflects the affective experience relentlessly repetitive antibiotic prescribing, powerlessness and urgency, almost despair.

Most interviews with nursing staff did not contain intense or prominent chaos narratives. The interviews often had parts where a confusing aspect of diagnosis were discussed but then the interview restored normality or control, as in the interview with Sonia, a healthcare assistant in an older adults ward:

> I think because we get a lot more dementia patients now, it can be very tricky. There are a lot more patients that have issues with ulcers and things and there are fluid balance charts and things like that, you know, fluid restriction because they get a lot water in the legs and things like that and that could cause you to wee a lot. So if they've got that, as well as the weeing a lot, and they're on a fluid restriction, sometimes it can be difficult. But the actual test isn't so difficult. So, you know, if you're suspicious, it's just a urine dip and you roughly get a good idea if something else is going on.

In the excerpt Sonia discusses patient care mostly in passive tense ("there are," "it can be") not implicating herself in the actions directly. She discusses various other conditions and symptoms typical in older adults (ulcers, fluid balance charts, fluid restriction, weeing a lot) that could confound UTI diagnosis and affect urination and (de)hydration. However, even if Sonia's interview has aspects of chaos narrative in terms of introducing contradictory series of events, it achieves closure through using a urinary dipstick.

The nurses' experiences of being overwhelmed by contradictory events is similar to those of doctors. However, nurses' narratives also illustrate the affective dimension of their powerlessness in the organizational structure as well as how the use of urinary dipsticks, which goes against clinical guidance, becomes a means to resolve a confounding and contradictory situation.

Narratives of Control

Whereas, the chaos narratives were characterized by a sense of events spinning out of control, in the control narratives the

narrators present themselves as in charge of the processes of UTI diagnosis.

"Every Patient Has a Urinalysis"

Anette is a senior nurse in an older adults' ward and describes her job as "making sure that the care that's being delivered is at a high standard, and that we're meeting all the measurements and the targets." So, she presents herself as in control of not only her work but of the overall care in the ward. She describes UTI diagnosis in older adults in terms of a routine sequence of procedures followed:

> Well every patient that comes onto the ward has a urinalysis, so on admission to the ward they'll have a urinalysis done. …
> **You mentioned urinalysis, how is that done?**
> Through a dipstick. Yeah, so their urine is dipsticked on arrival to the ward, and then obviously if they've got blood, or leukocytes then obviously that's escalated to the medics and then we automatically send a specimen away to the lab. … If it's positive then obviously a specimen is sent off, medics are involved; medics usually don't prescribe until they've actually got the result back from the microbiologist. But if the patient is symptomatic, got a temperature or just feeling generally unwell then they will prescribe, I think it's three or five days of trimethoprim. … because they've obviously, urosepsis and things like that, we've got to be careful of.

Anette mainly uses the passive voice, her narrative position observes events from a distanced, managerial perspective, different actors of the process are referred to in terms of professional groups as "staff," "patients," and "medics." She occasionally identifies herself with the nursing staff as "we," referring to sending specimens to the laboratory, changing to a more encompassing "we," including doctors, when referring to the need to be careful about sepsis. Anette's narrative presents diagnosis of UTIs in older adults proceeding in an orderly sequence; every patient is dipsticked on admission; if the dipstick is positive, samples are sent to the laboratory and if the patient is symptomatic or generally unwell, antibiotics are prescribed, to avoid sepsis. Anette's narrative gives off a sense of control and of doing the right thing. The diagnostic procedures described, however, are largely at odds with clinical guidelines, which recommend against the use of dipsticks in diagnosing older adults, on admission or otherwise.

Anette's orderly narrative with a resolution (Chatman, 1978) articulates an embodied, affective sense of control and order. The narrative illustrates how patterned processes of diagnosis, which conform to cultural scripts of biomedicine curing disease, lend them affective force.

The sense of control or straightforwardness was also echoed in descriptions of UTI symptoms, as illustrated by an account by Ellie, a nurse in a ward for older adults:

> **What alerts you to a UTI?**
> Okay, it may be that the patient is showing signs of confusion and they're not normally confused, so that would alert me that they may have a UTI. I'd want to rule that out first. So I'd get a urine sample, obs them, see if they've got a temperature, see if they're tachycardic, anything else away from the baseline, but get some urine for urinalysis, dip it and see and send off a specimen if they have – if it's a positive dip, so if they've got leucocytes, nitrates, protein, blood, anything out of the normal really.

In this excerpt Ellie uses first person pronoun, indicating her sense of agency. The answer does not echo as strong control as Anette's reply but—even if Ellie elsewhere in the interview acknowledges that UTI diagnosis in older adults may be "tricky" because of "comorbidities"—it presents identification of symptoms as a fairly simple, linear process of looking for confusion, taking temperature, dipping the urine, and sending a urine sample to the lab if the dip is positive.

Previous research has found nurses to push for antibiotics (Broom et al., 2016) and that doctors' may perceive nurses to pressure for antibiotic and prescribe to appease them (Charani et al., 2013; Eyer et al., 2016). The interviews by Anette and Ellie do not necessarily indicate active pushing; rather the descriptions of orderly UTI diagnosis, when they could lead to overdiagnosis, have a sense of being self-evident. The nurses' descriptions are similar to the junior doctors' "stock responses" observed by Atkinson (1984) but also highlight the affective confidence and certainty afforded by adhering to old practices that lend them force.

"Then I Was Treated"

Most older adult patient narratives had elements of chaos even if they also articulate a sense of control in part of the interview.

Joanne is in her seventies, and her interview is an unusually clear case of control narrative, Similar to Elena, Joanne has recurrent UTIs, which she relates to urine retention or "when I have a wee my bladder doesn't empty completely." She describes her hospitalization matter of factly of not being able to walk, being taken to hospital by ambulance and being treated for a UTI. Reflecting on the repeated UTIs, together with her husband in the room, she stated that she was not perturbed by recurrent UTIs:

> **Are the water infections a big bother?**
> Not really.
> **So they kind of come—**
> And go.
> **… How do you find the tablets?**
> All right.
> *She gets antibiotics.*
> Yeah, antibiotics.

Joanne's replies to questions are short, and she completes or corroborates the interjections by the interviewer and the husband. Joanne maintains that she is not overly concerned about the repeated UTI diagnoses and in the curd answers here as well as elsewhere in the interview she presents antibiotics as solving the problem. Joanne's narrative does not necessarily frame herself as in control, rather the narrative achieves resolution and UTIs are being controlled by antibiotics administered by healthcare professionals in recurrent, predictable manner, restoring normalcy in Joanne's life who comes across as a willing object of treatment.

Joanne's narrative suggests that she might be a patient who could expect antibiotics for her suspected recurring UTIs as suggested by clinician interviews (Eyer et al., 2016). However, Joanne's interview also illustrates the affective force of control and security afforded by the restitution narrative (Frank, 1995) that promises that biomedicine cures disease and restores health amidst repeated illnesses in old age.

Most, older adult patients' interviews mixed elements of chaos and control. For example, Alison, in her seventies, had undergone a rectal operation in the hospital when diagnosed with a UTI; after discharge she was diagnosed with a UTI again by her GP based on laboratory results, as she tells:

> They must have given me antibiotics. Yes, it did, but it [water infection] came back for some reason, but I'm not surprised because, excuse me saying it, I was on the toilet most of the time.
> Second time it [the urine] was cloudy, because I didn't see the first time because they tested it, but I certainly saw it the second time.
> **Yes, okay. So, it didn't hurt and you didn't run a temperature or anything like that?**
> No, not at all.
> **… Okay. So, when you had it [the urine] tested the second time, was that with your GP?**
> Yes.
> **Okay, so did they just suggest that you might want to have it done again or—?**
> Oh, yes, absolutely, and that's when I had it done again after taking antibiotics and it cleared.

Alison shifts between first person pronoun describing her actions ("I was on the toilet," "I saw the [urine]") and passive voice when describing diagnostic tests, treatments and the disease ("tested it," "treated it," "it came back") indicating her passivity in relation to medical interventions and agency in terms of observing them. In Allison account antibiotics are given, infection comes back, urine is tested, urine is cloudy, there is no pain and urine is tested again by GP, all having elements of chaos narrative where things happen repeatedly in a somewhat uncertain order and not always making sense. However, the narrative achieves closure as eventually antibiotics clear the infection, restoring, if not health (as rectal problems persist), at least curing infection.

The patients' control narratives highlight the affective sense of resolution afforded by antibiotics in the context of repeated chronic diseases of old age. However, as the two narratives illustrate, the intensity of this affect varies, Joanne clutching to the restorative powers of antibiotics, whereas for Alison treatment by antibiotics is simply accepted, highlighting that even if patients consider antibiotics a resolution they are not necessarily invested in them in equal measure.

Tradition and Counter-Tradition

The doctors' interviews often combined elements of control narrative and chaos narratives. Typically, doctors discussed UTI diagnosis in terms of being in charge of an uncomplicated process at some point in the interview but shifted into voicing doubts and contradictions at another point.

Anya is a junior doctor, who at the time of interview works in the rehabilitation ward but had recently worked in A&E. Much of her interview conforms to the control narrative. In answering one of the first questions on typical situations where UTI was diagnosed, Anya offers an orderly account:

> Typical situations will be patients coming with some sort of falls or infections and we do an in-depth to see if – we either think of chest or urinary, those are the causes most of the time. … So, once the patient comes up to acute medicine we do a urine dip and if it's positive for nitrites, leukocytes, we generally ask them to send it to the lab for culture and see if it's growing anything. If there are any signs of sepsis or white cell count is too high, CRP is high, patient is not clinically well, we start the patient on antibiotics anyway.

Anya uses the pronoun "we," evoking a narrative of a common collegial practice among (junior) doctors, rather than an individual one. She describes the process of UTI diagnosis in older adults as unproblematic, proceeding from identifying signs (falls), testing the urine with a urinary dipstick and prescribing antibiotics, if patients are unwell or there are any suspicion of sepsis. Anya's description follows the familiar sequence of events, repeating in many interviews with clinicians, of focusing on vague signs (falls), using urinary dipsticks for diagnosis, and prescribing antibiotics, when older adult patients are unwell. This sequence of events does not necessarily adhere to current clinical guidance. However, the coherent order of events and the closure brought to the narrative by antibiotics communicate a sense of control and certainty, Anya's story lets on that she is doing the right thing.

Stephen's interview is unusual in that even though it echoes control it does not repeat the restitution narrative (Frank, 1995), whereby curing disease brings closure to the story. Stephen is a senior consultant in a stroke ward and underlines throughout the interview that he does not diagnose UTIs in older adults based on identifying bacteria in urine:

> **What kind of alerts you to a UTI?**
> Preferably symptoms, new onset pain, discomfort and passing urine, passing urine more often, plus or minus fever. Then you might want to back it up with urine culture, but I wouldn't primarily diagnose it just on the basis of an E. coli urine culture coming back again because it's not necessarily right. It doesn't necessarily mean anything, to be honest. So preferably symptoms that the patient can describe and perhaps in association with fever and hopefully supported by a urine sample.
> Sometimes it can be difficult if you've got a patient who's had a stroke and can't talk to you, for instance, but I wouldn't assume that just because you've got E. coli in the urine that you've got a urinary tract infection requiring antibiotics.

Stephen uses passive voice when describing diagnostic practices ("you might," "it does not mean anything") indicating impersonality but uses first person pronoun "I" when emphasizing that he would not diagnose based on *E. coli* in urine, coming across as his personal perspective. Stephen shifts between reflecting on symptoms, acknowledging that identifying

symptoms is difficult with older adult patients who cannot talk after stroke. Despite reflections, the narrative is coherent; yet, it does not achieve the usual resolution of restitution narrative, whereby biomedicine cures disease but ends up a narrative underlining refraining from making UTI diagnosis based on laboratory results even if coherence creates an affective sense of control.

Like the nurses' control narratives of UTI diagnosis, junior doctors' descriptions may resemble the stock responses discussed by Atkinson (1984), illustrating the unreflective sense of doing the right thing, even if the practices could fuel antibiotic overprescribing. However, Stephen's narrative illustrates the possibility of coherent counter-narratives to diagnosing UTIs based on bacteria identified in urine, which may be afforded by his senior position.

DISCUSSION

We contend that our findings related to chaos and control narrative interlacing our participants' accounts make conceptual, practical and methodological contributions to understanding diagnosis in hospitals, especially diagnosing UTIs in older adults.

Conceptually, our study addresses the contention between health research, which typically considers adherence to evidence, such as clinical guidelines, in medicine important, and medical sociologists, who have expressed concerns that evidence may lead to "cook book" medicine that is not sensitive to the complexities of clinical situations and patient experiences (Timmermans and Angell, 2001). Research has found that clinicians may use evidence differently, more in cook book fashion or critically reflecting on it (Timmermans and Angell, 2001), ignore guidance when it contradicts their "feel for the game" (Broom et al., 2014) and find a balance between flexibility and rigidity in using guidelines (Johannessen, 2017). These observations further relate to a classical discussion on how clinicians respond to uncertainty in a reflective way (Fox, 1980) or resorting to stock responses (Atkinson, 1984; Broom et al., 2014) or both (Timmermans and Angell, 2001).

Our chaos and control narratives share features of reflective and stock responses to uncertainty, respectively, but they also complicate them. Reflection has been discussed as an intellectual questioning attitude open to different perspectives and possible actions (Timmermans and Angell, 2001) or as an almost existential experience of self-doubt (Fox, 1980). Whilst chaos narratives have aspects of critical reflection, they typically did not indicate opting for different lines of action but a sense of being overwhelmed by contradictory experiences and events. Doubts about diagnosis were not only the purview of doctors but also underpinned the narratives of nurses and older adult patients and articulated their powerlessness. The control aspects of narratives resemble clinicians' adherence to customary mindlines or stock responses (Atkinson, 1984; Johannessen, 2017), but they also illustrated the affective sense of control and order afforded by following customary practices that comfortingly promised to restore health. However, control narratives also became intelligible in relation to experiences of chaos, highlighting how urinary dipsticks and antibiotics became means of bringing order to and thwarting the chaos of overwhelming evidence and illnesses. At the same time, being control could also sometimes articulate a different, non-dogmatic line of action.

Clinicians and patients articulated affective experiences of chaos or control in particular in relation to two aspects of diagnosing UTIs in older adults. Chaos and control became prominent when clinicians and older adult patients' described contradictory evidence, such as vague signs and symptoms of "being unwell," and contradictory results of diagnostic tests, partly reflecting the tensions between the ostensibly objectively pathological evidence and the patient-centered subjective evidence of symptoms (Armstrong, 2011), confounded by new guidance. The other aspect provoking chaos and control narratives was aspects of caring for older adults, such as potential cognitive impairment, difficulties in understanding, and multiple illnesses and medications typical of old age. These issues of identifying and treating acute illnesses in old age boil down to the basic contradiction in hospital medicine identified by Strauss et al. (1987) that hospitals were originally geared toward treating acute illnesses and are poorly equipped to deal with chronic illnesses of old age they currently mostly cater for. The affective experiences of chaos and control were different ways of responding to the contradiction at the heart of acute model of hospital medicine, which led to the investigation of a suspected UTI in an older adult who was generally unwell.

The practical contribution of our study is the observation that the descriptions of how the diagnosis of a suspected UTI in an older adult proceeded was often very similar throughout our interviews and similar to quantitative and qualitative descriptions (Pallin et al., 2014; Eyer et al., 2016), the difference being the affective sense of doubt or certainty underpinning the accounts. Older adult patient views of UTI diagnosis have not, to our knowledge, been investigated, and our findings highlight that patients' experiences may articulate a sense of bewilderment with repeated UTI diagnoses and courses of antibiotics rather than pressuring for antibiotics, as indicated by clinician accounts (Charani et al., 2013; Eyer et al., 2016). Eventually the different affective experiences are likely to complicate communication and cooperation between staff groups and patients, an important component of suboptimal antibiotics prescribing (Lewis and Tully, 2009; Charani et al., 2013; Skodvin et al., 2017; Saukko et al., 2019). This is especially the case as junior doctors' and nurses' perspectives were often different, junior doctors doubting the diagnostic processes more often, perhaps due to a more reflexive occupational disposition (Fox, 1980; Timmermans and Angell, 2001) and higher awareness of new guidance. Efforts to reduce inappropriate antibiotic prescribing in hospitals have mostly focused on top-down education of clinicians (Davey et al., 2017). Whilst these interventions have been mostly effective (Davey et al., 2017) they focus on cognitive change and do not often involve patients. Our findings suggest that there is a rarely examined or acknowledged affective underlay that shapes clinicians' and patients' understandings and actions vis a vis diagnosis and antibiotic prescribing. To address this affective dimension would likely require a more conversational and cooperative approach to improving diagnosis and prescribing

to enable the often unspoken insecurities and securities to be discussed.

Finally, our study also offers methodological insights on how to analyse the important affective dimension of experience through forms of narratives. The favored method for analyzing interviews in medical sociology is thematic analysis. Thematic analysis is flexible but focuses on *what* people tell rather than *how* they tell about their experiences. Our study offers ideas on how to analyse the way in which individuals position themselves in relation to unfolding events, whether the sequence of events is orderly and whether the story achieves resolution or closure. These elements highlight the not directly spoken way in which people position themselves as in charge of or at the mercy of events and whether they are indirectly doubting or certain about their or others' actions. Considering these often unspoken aspects of experience could shed new conceptual and practical light on why overdiagnosis and overprescribing happens.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Health Research Authority (IRAS 202255). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

ER and PS designed the study, contributed to analysis, and writing of the manuscript. PS led the qualitative data collection and analysis, and writing of the manuscript. All authors contributed to the article and approved the submitted version.

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Prescribing Antibiotics in Rural China: The Influence of Capital on Clinical Realities

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Primary care clinicians in rural China are required to balance their immediate duty of care to their patients with patient expectations for antibiotics, financial pressures, and their wider responsibilities to public health. The clinicians in our sample appear to make greater efforts in managing immediate clinical risks and personal reputation than in considering the long-term consequences of their actions as potentially contributing to antimicrobial resistance. This paper employs Bourdieu's theory of capital to examine the perspectives and practices of Chinese primary care clinicians prescribing antibiotics at low-level health facilities in rural Anhui province, China. We examine the institutional context and clinical realities of these rural health facilities and identify how these influence the way clinicians utilize antibiotics in the management of common upper respiratory tract infections. Confronted with various official regulations and institutional pressures to generate revenues, informants' desire to maintain good relations with patients coupled with their concerns for patient safety result in tensions between their professional knowledge of "rational" antibiotic use and their actual prescribing practices. Informants often deferred responsibility for antimicrobial stewardship to the government or upper echelons of the healthcare system and drew on the powerful public discourse of "*suzhi*" (human quality) to legitimize their liberal prescribing of antibiotics in an imagined socioeconomic hierarchy. The demands of both practitioners' and patients' social, cultural, and economic forms of capital help to explain patterns of antibiotic prescribing in rural Chinese health facilities.

Keywords: antibiotic resistance, AMR, clinical practice, rural China, cultural capital, social capital, economic capital

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INTRODUCTION

Pathogenic resistance to antimicrobials (AMR) is widely acknowledged as a key global health challenge (World Health Organization, 2012, 2015; United Nations, 2016). Antibiotic resistance poses a particularly severe threat in China, a leading consumer of antibiotics in humans, agriculture, and livestock, with high rates of antibiotic resistance, and in 2018, it was projected to have the highest mortality rates in the world from AMR by 2050 (The Center for Disease Dynamics Economics Policy, 2018). In order to mitigate this threat, it is imperative to understand all the factors influencing the development of antibiotic resistance in China at this time.

Since antimicrobial resistance begins to evolve as soon as new antibiotics begin to be used, the push to develop new antimicrobials is not likely to resolve AMR. Many drivers of AMR

are anthropogenic, and as Smith (2015, p. 1–2) argues: "The conditions promoting the biological mechanisms of antimicrobial resistance are deeply social, shaped by cultural, political, and economic processes. Although the mechanism for antimicrobial resistance is biological, adherence to antimicrobial stewardship is fundamentally social [and] as a social challenge it demands social solution[s]." Thus, if AMR is ultimately an outcome of clinical praxis, as well as embodied dispositions influenced by the social, cultural, and economic capital forming the habitus of particular groups[1], then studies that foster an understanding of these sociocultural drivers could potentially identify and guide the changes needed to effectively manage AMR.

Individual practices are structured by the medical and broader social systems in which these individuals work, while their practices reciprocally shape these systems. According to Bourdieu (1986), "It is in fact impossible to account for the structure and functioning of the social world unless one reintroduces capital." Stated simply, forms of capital accumulate and distinguish one's place and one's assigned value in a given social hierarchy according to what one knows, who one knows, and what one owns.

Bourdieu's theory of capital has been used to analyze a range of healthcare issues including health inequalities (Pinxten and Lievens, 2014), health achievement (Meinert, 2004), healthcare provider choice (Collyer et al., 2015), maternal practices (McKeever and Miller, 2004), medical elites (McDonald, 2014), and medical education (Brosnan, 2011). Broom et al. (2014, 2017, 2018, 2020), Broom and Doron (2020) have specifically used Bourdieu's framing of the role and production of social capital and habitus to unpack the complex antibiotic prescribing behaviors of physicians. They argue that "antibiotic decisions are relational and negotiated, and tied to patient expectations as well as the lay-expert dynamics that influence these" (Broom et al., 2014, p. 82). They conclude that antibiotic prescribing is particular to the acquisition of social capital through the habitus of a given context, regardless of best practices or therapeutic guidelines.

To better understand the complex relationships between the myriad social drivers influencing human antibiotic use in rural China, we build on and expand Broom's use of Bourdieu to this work by unpacking the prescribing behaviors of clinicians in six rural health facilities—three village clinics (VCs) and three township health centers (THC)—in three counties of Anhui province, China. We interpret the use of antibiotics by VC and THC doctors for patients presenting with symptoms of upper respiratory tract infections (RTIs) as an outcome of their negotiations of cultural, social, and economic capital[2]. We examine both doctors' and patients' social, economic, and institutional positioning in China's health systems and their influence on antibiotic prescribing.

[1] *Habitus* is Bourdieu's conception of the physical embodiment of social and cultural capital manifested through physical actions and activities.

[2] For a full discussion of the forms of capital, see: Bourdieu (1986) *The Forms of Capital*.

METHODS AND SETTINGS

The findings presented here draw on direct observation, semi-structured interviews, and informal conversations with a sample of village doctors and township level physicians in three counties of Anhui Province, China (referred to here as Sites 1, 2, and 3), between January 2017 and June 2018. This qualitative research was part of a wider interdisciplinary study investigating pathways to antibiotic use and antibiotic resistance in clinical and community settings in rural Anhui province, details of which are reported elsewhere (Zhao et al., 2019). In each county, one THC and one VC were selected for patient recruitment and direct observation of the clinical encounter.

Like most rural primary healthcare units in China, both THCs and VCs provide walk-in clinics for outpatients with no appointment system or triage, although THCs also have inpatient wards. THCs are the healthcare units at the bottom of the state health system hierarchy and are literally referred to in Chinese as the "Hygiene Hall" (*Weisheng Yuan*, 卫生院). After the SARS epidemic in 2003, THCs were officially designated to manage public health in rural areas by incorporating local VCs into the healthcare system. VCs are subcontracted to carry out public health functions, such as vaccination on behalf of the THC, which the THC manages, in addition to overseeing the public health activities and records of VCs. There is a ratio of between 3 and 6 VCs per THC[3].

The three VCs studied are diverse in terms of their staff numbers, division of labor, and their use of electronic and paper information systems. For example, three doctors work in Site 1 VC. All three provide patient consultations and use electronic patient records. By contrast, site 2 VC has four staff members whose roles differ and include a senior doctor, who is officially retired but has returned to work and undertakes most patient consultations; his younger brother, who is the VC director and cashier and who also inputs the electronic patient records; a third staff member who acts as the in-house pharmacist; and a fourth doctor who mainly undertakes home visits. Patient volume and staffing likewise vary across the three THCs studied. Two serve as the central health facilities for the local town (*zhen zhongxin yiyuan,* 镇中心医院) and receive a large number of outpatients every year. Site 1 THC has two outpatient doctors, one of whom is trained in traditional Chinese medicine (TCM), while the other is biomedically trained. Site 2 THC employs nine doctors in total, of which seven doctors staff inpatient wards and outpatient clinics in rotation. Site 3 THC is smaller and quieter than the other two, with three doctors available for outpatient consultations.

Unlike the predominantly biomedically trained physicians who work in THCs, VCs are overseen by so-called village doctors (*cunyi*, 村医), a carry-over of the minimally trained community health workers formerly known as barefoot doctors (*chijiao yisheng,* 赤脚医生) during the Maoist period. Barefoot doctors were often the only health workers in the local level brigade health units that were dissolved under the economic reforms of Deng Xiaoping in the 1980's (Hu et al., 2017). Although,

[3] For further details of China's primary health care system, see, for example, Li et al. (2017) and Duckett (2012).

since the 1990's, village doctors have been required to complete a minimum of 2–3 years of specialist medical education in order to practice, they have not passed the examination to obtain a license to practice as an assistant physician and therefore do not have the same social standing as trained physicians (*Ibid.*)[4].

Data Collection and Analysis

From the six healthcare facilities participating in this study, a total of 21 village doctors and township physicians were observed during their daily consultations with patients, all but 2 of whom were followed up for semi-structured interviews toward the end of the 4th month of observation in each site. A topic guide was drafted for the interviews, which was then piloted in Site 1 and revised for Sites 2 and 3. To protect confidentiality, each informant interview was anonymized via a study ID. Verbal informed consent was obtained before clinical observation and at the beginning of each interview.

All VC informants held the Certificate of Village Practitioner, issued by the local County Health Commission. Thirteen informants had received training in a 2 or 3-year vocational health college (*weixiao*, 卫校), of which nine were trained solely in biomedicine (*linchuang zhenduan*, 临床诊断), three were trained in traditional Chinese medicine (*zhong yi*, 中医), and one informant had received both biomedical and TCM training (1-1-20170704). Three village doctors reported that they had no formal health training but had apprenticed with family members or been taught via correspondence courses (2-2-20180124). **Table 1** provides a summary of the demographics of the sample.

The majority of interviews were audio-recorded and transcribed by the research team. Anonymized transcripts and observation notes were stored and coded in the software package NVivo 11 (4 from site 1; 13 from site 2; 4 from site 3). Thematic analysis, as described by Charmaz (2006) and Boyatzis (1998), was performed. Themes were also analyzed according to a theoretical framework employing Bourdieu's concepts of social, cultural, and economic capital. A list of coding labels was developed through a process of inductive coding. Ethical approval was obtained from the Anhui Medical University Research Ethics Committee.

RESULTS: UNCERTAINTY AND RISK IN ANTIBIOTIC PRESCRIBING

This study reveals multiple factors that influenced antibiotic prescribing in our sample of medical practitioners. Several informants discussed clinical uncertainty (*bu queding*, 不确定) as a primary reason for prescribing antibiotics. Clinical uncertainty was frequently mentioned as a common issue that clinicians face in rural Chinese primary care settings when deciding upon treatments. This uncertainty is an outcome of two challenges: correct differential diagnosis of the overall category of infection and the ability to distinguish the specific type of pathogen present.

A majority of informants described using broad treatments due to the difficulty in differentiating between bacterial and viral infections. One informant noted:

> As a clinician, I think that if you aren't sure, then all you can do is choose to use both types [of medicine] together. Because if you can't confirm what [the pathogen] is, and if you only use, say, antibiotics (*kangsheng su,* 抗生素), [that is] anti-inflammatories (*xiaoyan yao,* 消炎药), when in fact it is a viral infection (*bingdu ganran,* 病毒感染), then you won't have good results. So all you can do is use the two together in combination (1-2-4).

Here, the clinician refers to "antibiotics" (*kangsheng su)* and "anti-inflammatories" (*xiaoyan yao*) as the same thing, in addition to being medicines that do not work for viral infection. Informants commonly claimed that when they were unable to make a definitive diagnosis of bacterial or viral infection; they would need to prescribe both antibiotics *and* antivirals, a practice that was frequently observed in the clinics. They rationalized that, thereby, they could be certain that at least one of these two types of medicines would work for patients. Informants attributed the difficulty of a precise diagnosis to a lack of laboratory support in rural primary care settings. Thus, when unable to differentiate between the type of pathogen causing an infection, the practice of prescribing both antiviral and antibacterial medicines was widespread and regarded as normal, despite informants' knowledge that antibiotics are for use in bacterial infections and are ineffective for viral infections, which often include upper respiratory tract infections.

A second type of clinical uncertainty demonstrated by informants was in distinguishing the exact type of bacteria causing infection. Township clinic informants reported, and were frequently observed, using blood tests and chest x-rays as proxy diagnostic tools. However, since only microbiological cultures, which are not available on site, can identify the specific group of bacteria causing infection, informants pointed out that they are unable to determine accurately whether to prescribe broad-spectrum or narrow-spectrum antibiotics. As one THC informant noted:

> If you aren't certain which type of microbial infection (*xijun ganran,* 细菌感染) it is, then it is generally agreed that you should use broad-spectrum antibiotics (*guangpu kangsheng su,* 广谱抗生素); sometimes combining two or three is definitely a bit better. Why do I say a bit better? Because you aren't certain which type of antibiotics (*kangsheng su*) is better for the infection in question (2-1-20180201).

Faced with such inexact methods of identification, several informants spoke candidly that in such cases they would prescribe at least two broad-spectrum antibiotics, such as amoxicillin or cephalosporin (*toubao,* 头孢), along with another type of antibiotic. Informants revealed a rationale that two broad-spectrum antibiotics would deal with more than one group of bacteria, or bacteria located at two or more locations in the body, such as the throat and chest. Another informant (2-1-20180201) described this therapeutic goal as encircling the pathogenic agent, or literally "to form a large enclosure around the pathogen,"

[4]For example, village doctors are not included as health professionals in formal Chinese health statistics (Hu et al., 2017:7).

TABLE 1 | Summary of sample demographics.

Dataset	**Site 1**		**Site 2**		**Site 3**		**Total**	
Clinician Interviewed	4		11		4		19	
	VC	THC	VC	THC	VC	THC	VC	THC
	2	2	3	8	1	3	6	13

Sex		
Female	**Male**	**Total**
2	17	19

Number of Years in Practice				
10–15 years	15–20 years	20–30 years	30–40 years	Over 40 years
2	2	11	1	3

Formal medical training in clinical medicine (临床医学专业): 2–3 years in Secondary Vocational Health College (literally Hygiene College, *Zhongzhuan* or *Dazhuan Weixiao* 中专大专卫校)

Secondary vocational medical school			**No formal medical training**	**Unknown**
13			3	3
Specializes in biomedicine (*xiyi*)	Specializes in TCM (*zhongyi*)	Specializes in both biomedicine and TCM		
10	4	1		

whereby several types of antimicrobials are combined in order to broadly treat any infection, regardless of the actual pathogenic agent. Several informants reported to employ such strategies to derive a sense of certainty that they were making efforts to fight all probable causes of infection. This pattern of prescribing is officially labeled "combined use of medicine" (*lianhe yongyao,*联合用药) and is perceived by informants to more reliably treat all possible causative pathogens, despite the fact that the use of "combination medicine" is widely associated with the development of AMR and has been explicitly banned by official guidelines in recent years specifically for this reason (National Health Commission of the People's Republic of China, 2015, Document No. 43).

However, clinical uncertainty was not the only driver of frequent antibiotic prescribing in our sample. Several informants discussed the benefits of using antibiotics to reduce risk, both to the patient and to their professional reputation. One informant considered it justifiable to prescribe antibiotics in some cases in order to avoid "medical risk" (*yiliao fengxian,* 医疗风险), in situations where "antibiotics can be used" (*[kangsheng su] keyong bukeyong,* "[抗生素] 可用可不用"), such as "when the patient has a viral infection, and [the patient] is in good physical condition or has good immunity. Then in the first two days, it is OK not to use antibiotics" (2-1-20180115). This informant estimates that the number of cases where there is "no necessity for antibiotics" accounts for 20–30% of the THC antibiotic prescriptions. Yet, he felt that "even if antibiotics are used for 10% [of these cases], it cannot be regarded as [drug] abuse (*lanyong,*滥用), as medical risk is present. The Health Ministry told us not to use antibiotics." However, the frontline clinicians, depending on the extent of their medical expertise, would often use antibiotics in order to "prevent risk" [to both clinicians' reputations and patient's health] (*fangfan fengxian,* 防范风险).

> If [the] clinician's medical capability is poor and they've got no guts, then they use it. As long as there are no allergies to the antibiotic, we use it. Every [doctor] is using it anyway (2-1-20180115).

Interestingly, this informant is deeply critical of what he sees as "antibiotic abuse" by his colleagues at the health service unit where he works. He stressed this occurs at the "lowest level" (*diceng*, 底层) primary care unit and implies that these clinicians lack the medical skills and courage to treat patients effectively, without relying on antibiotics. He and other informants suggest that "frontline clinicians," such as his colleagues, may use antibiotics to minimize the potential risks they perceive; of being accused by patients for having failed to prescribe antibiotics in case of serious infection. Two other informants (2-1-20180201; 2-1-20180131) similarly mentioned that they couldn't risk putting their patients' well-being in any immediate danger, as their first reason for prescribing antibiotics.

The perception of using antibiotics for risk reduction also provides a rationale for their prophylactic use but creates conflicts for doctors in demonstrating appropriate practice. One THC informant commented:

> Some doctors have to think about safety, right? This is preventive use, because I don't know yet if there is new infection, so I use a little bit of antibiotics first (2-1-20180201).

This informant perceives that he is demonstrating his concern for patient safety with his prophylactic use of antibiotics. By

stressing that he would use only "a little bit" of antibiotics, however, he also attempts to demonstrate his awareness of the policy limiting antibiotic use, while simultaneously diminishing the clinical significance of his practice as having an impact on antibiotic resistance.

Greater clinical risk is associated with the perceived vulnerability of some patients, particularly of the elderly and children. When patients' symptoms initially indicate viral infection at the time of consultation, informants report being concerned that the viral infection may develop into a bacterial infection with serious complications, such as pneumonia. One doctor reported that he "would rather" use antibiotics prophylactically for those whom he perceives to be more vulnerable: "A child's situation can change rapidly in a short period of time" (2-1-20180131).

Another circumstance that prompts clinicians to prescribe antibiotics for "preventive use" is for night-time emergencies at THCs, when neither blood tests nor x-rays are available to support a diagnosis. One THC doctor states:

> We might use some [antibiotic] when it's not clear whether something is a viral or bacterial infection, because you can't do a blood test in the evening or especially in emergency situations where there isn't the time. At night you don't actually know what the cause is. Perhaps we may as well use antibiotics (*kangsheng su*), but the ones we use are usually not the type that require a skin test. For example, in the evening we might use levofloxacin, [a broad spectrum antibiotic] (2-1-20180131).

While informants emphasized patient safety as a rationale for prescribing in situations of clinical uncertainty, antibiotics are regarded as quick and effective by both patients and doctors. Furthermore, informants worry that they will lose their clientele if they do not prescribe, or if they are more cautious in prescribing antibiotics than other local doctors.

However, it needs to be emphasized that these uncertainties resulting in greater antibiotic use are not unique to health workers in rural China. For example, among physicians in Australia, Broom et al. (2014, p. 84) identified that all of their informants reported to prefer to err on the side of overuse of antibiotics to reduce immediate risks to patients. "Overtreatment utilizing broad-spectrum [antibiotics], prescribing prophylactic antibiotics, or beginning antibiotics without a clear rationale was viewed as situated within a sense of risk that overtreatment was more favorable than the potential for adverse immediate patient outcomes. In many respects this was about peer perspective and reputational risk." Furthermore, distinguishing between types of infection has been identified as a challenge common to primary care clinicians[5] across many settings including the UK, Australia, and North America (Lock and Nguyen, 2010; Cabral et al., 2015; Podolsky, 2015; Broom et al., 2020). Such ambiguities problematize the popular construction of a pure biomedicine that is globally practiced in a hegemonic manner and that somehow exists outside of time, place, and social influence.

UNPACKING SOCIAL DRIVERS OF ANTIBIOTIC PRESCRIBING

The previous section describes when and how antibiotics and related technologies are employed by informants and how these practices and decisions are understood and rationalized by practitioners. This section considers the wider social and institutional contexts for these decisions among informants from both THCs and VCs and interprets our findings with reference to Bourdieu's theory of capital.

The Cultural, Economic, and Social Capital of Practitioners

Simply put, cultural capital is the social distinction acquired through the embodiment of social values and assets, as reflected in what one knows, how that knowledge was acquired, and the extent to which social values, skills, knowledge, and taste are embodied (Pinxten and Lievens, 2014). Whereas, social capital can be understood as the resources and social status acquired via one's social relationships, as exemplified in the proverbial "Old Boy's Club." Social capital is particularly central to Chinese social relations, where success and status are portrayed as a direct outcome of the strength of one's connections or *guanxi* (關係). The concept of *guanxi*, which dates to Confucian doctrine, is enacted through one's mutual commitments and reciprocity in social relations, and is similar to the transcultural role of gift giving—as the crossing of a threshold marking entry into social relationships—as described by Mauss (2002). Social hierarchy is also determined by material assets that are convertible into money, or economic capital. Hence, cultural and economic capital are closely linked with the social capital of *guanxi*, and these three forms of capital intersect and mutually determine one another.

The structure of healthcare in China reflects an embedded hierarchy of cultural and social capital in which the rural VC and its village doctors are positioned at the bottom of this hierarchy, with THCs considered only one step above. Public trust in higher-level health facilities is a reflection of the assignment of cultural capital to the better-qualified staff working in the upper strata of the healthcare system by both the lay public and health workers. Informants from both VCs and THCs denigrated their own lower-tier health facilities by referring to working "down below here," "down here in the village," and "at the bottom level." One of the female VC informants with over 20 years of medical experience stated: "I feel like the frog at the bottom of the well." She and her colleagues considered themselves to have markedly little influence and importance from their position as workers in lower-tier health facilities. Several other informants mentioned the lack of opportunities for further professional training to improve their qualifications, pointing to their limited medical experience and limited expertise in the health system. In this instance, limited cultural capital not only restricts the capacity

[5]This lack of differentiation is equally problematic among the lay public in the west. For example, Lock and Nguyen (2010:4-5) identify that though "Canadians believe that antibiotics are effective against viruses, two-thirds of Canadians report that they have a clear understanding of when and how antibiotics should be taken."

to influence others, but also limits access to the means to increase one's cultural capital.

Social capital is also relevant to antibiotic prescribing practices because of its potential impact on clinical knowledge, uncertainty, and treatment decision-making. Village doctors reported that they face greater clinical uncertainty—and thereby need to prescribe more antibiotics in order to reduce patient risk—than their counterparts in higher-tier hospitals. When asked what could be done to tackle antimicrobial resistance, one THC informant spoke about rural clinicians' low "social status" (*shehui diwei*, 社会地位):

> The social status of the base-level doctors is low. You are in contact with people who are suffering from bitterness and difficulties and who usually do not have [*sic.*] a good mood. Communication with them can easily lead to medical disputes. If the medical treatment works to their recovery, your job is done, but if it doesn't work, you will be blamed (2-1-20180115).

Thus, for village doctors, prescribing antibiotics may serve to cope with insecurities they experience due to their position at the bottom of the healthcare hierarchy. However, social rank not only is based on a health worker's education, professional status, or career development, but also extends to, and derives from, their access to material resources. For example, in addition to a lack of access to newer-generation antibiotics, informants stated that the medicines available at the "lower-tier facility" were characterized as "medicine of low taste, low grade, inadequate" and "not worth much money" (*bu zhiqian*, 不值钱) (2-1-20180115). Informants commonly differentiated between rural health facilities and upper-level hospitals beyond THCs, which were considered "more advanced" (*gaoji*, 高级), and stocked with "newer antibiotics" (2-1-20180115). Hence, in this instance, we can see the intersection of social, cultural, and economic capital.

Medical materials were not limited to pharmaceuticals but also include access to testing equipment. The example of one village doctor who commented that she could afford to set up blood testing equipment at her clinic demonstrates the mutually determining character of different forms of capital. This doctor commented that offering blood tests could have generated extra revenue for the clinic, but she decided against the purchase, "because people would trust the test results from the township heath center more [than from my village clinic]" (1-3-31). Instead, she commonly sends patients with a fever to the THC for a blood test.

Furthermore, the generation of economic capital was also a factor impacting treatment decisions and the extensive use of medical materials. The 2009 National Essential Medicines Scheme (NEMS) prohibited any increase above the retail price paid to the manufacturer of essential medicines, and was implemented to counteract the long-standing problem of marking up the prices of medicines (procured wholesale) for retail sale to patients in order to generate profit for health facilities and their staff. VC and THC doctors in Anhui province can only prescribe medicines from the *Anhui Provincial List of Essential Medicines*, and a general concern voiced by informants was that the antibiotics on the list are older-generation drugs that are no longer effective. This policy change resulted in a significant loss of income for village and township doctors and has generated its own perverse economic incentives. To make up for the loss in revenues from mark-ups on pharmaceuticals, doctors have found other means to generate income, including prescribing unnecessary diagnostic tests.

TABLE 2 | Tests ordered for the 638 patients observed at THCs.

Types of test	Blood test	X-ray
Carried out	160	107
Not carried out	13	6
Subtotal	173	113

These diagnostic tests were understood by informants as essential to their professional survival. For example, one THC director spoke of his ambition to purchase more test equipment to be housed in his new health center building: "the money made from carrying out tests for patients is 100% income, as the investment in the test machine is a one-off." During site observation, we noted that ∼30% of RTI patients with common symptoms were given tests, such as blood tests and X-rays, as presented in **Table 2**. Thus, although doctors emphasized the use of these tests for guiding antibiotic prescribing in our interviews, neither of these tests reliably indicate the presence of bacterial infection, though economic incentivization may be another, possibly more significant, driver. Given the pressures placed on health workers to generate revenue for their health facilities, doctors are incentivized to order diagnostic tests irrespective of clinical need.

The same issues may help to account for the pervasive use of intravenous administration of drugs. One doctor (2-1-20180115) mentioned that generating revenue for his THC was one of three major pressures for him to prescribe the use of intravenous drips, albeit often using TCM formulae, which are not part of the Essential Medicine List, and thereby can be "marked up." He describes this practice as his compromise both for patients who do not require any antibiotics but who demand "drip" treatment and for his hospital demanding increased revenues. The same compromise was mentioned by other informants for patients who demand antibiotics and are provided to them, irrespective of their diagnosis.

The ambiguous employment status of VC doctors who are not directly state-salaried, the relatively meager basic salary of THC doctors and the pressures placed on them to generate income for their health facility, and the complex and sometimes lengthy process for obtaining medical insurance reimbursement, all act as direct or indirect economic drivers in treatment decisions[6].

Regardless of conflicting social pressures placed on health workers, the bottom line for many informants is practicing in a manner that ensures their economic survival. Clearly,

[6]The vast majority (over 99%) of villagers in all three of our sites were members of the NACMIS (New Agricultural Cooperative Medical Insurance Scheme, *xin nong he*, 新农合). VCs and THCs have to work with NRCMIS, but the process of insurance reimbursement for a patient's medical care is not straightforward and cannot be covered here (see Bernardi and Miani, 2014).

the social, cultural, and economic capital of the practitioner interact in complex ways to influence antibiotic prescribing practices. However, the social and cultural capital *of patients* also influence prescribing practices. By refusing patient expectations and demands, informants identify that they risk being overlooked in the local healthcare provider market, which they perceive as the fault of their patients' "low human quality" and poor medical literacy.

The Cultural and Social Capital of Patients

Doctors' prescribing behaviors are not only related to their own cultural and social capital, but are influenced by their perceptions of their patients to be lacking cultural capital. In general, informants described patients as having "*di suzhi,*" literally low or poor human quality. *Suzhi'* (素质) is a popular Chinese concept that groups people into hierarchies according to their level of self-cultivation, education, and personal achievement, which is embodied in their behavior. Informants referred to patients with *di suzhi* in derogatory terms and emphasized the difficulty in refusing such patients' demands for antibiotics.

One informant offered:

> Here in the countryside [patients] are not as civilized (*wenmin*, 文明) as those in the cities. They just come in to demand strong or good water [IV drips] and what can you say to these rough people? (1-3-31).

Several other informants made similar comments, emphasizing their patients' lack of civil behavior or medical knowledge due to residing in a rural area. For example, one informant remarked on when he would refuse patients' requests for antibiotics:

> Those with wider knowledge and more education know about [drug resistance], and I will mostly explain [my rationale] to them. But there are some difficult people; they simply come in to say they want antibiotics. I'll explain at most twice [before giving what they ask for]. What if he [the patient] has a bacterial infection? It will backfire on me. Some villagers are particularly stupid and stubborn (2-2-21).

Referring to patients who come in to ask specifically for antibiotics (*xiaoyan yao*, 消炎药), another informant stated:

> This is about culture. They are not very highly cultured. Very culturally refined people would not do this [i.e., demand antibiotics]. Rural people believe a more expensive drug is a good drug. People in the countryside think that a higher price is equated with a better drug. More accomplished people, people with more self-cultivation, don't want to take a lot of anti-inflammatories (2-2-201802).

Again, rural patients are portrayed here as lacking cultural capital and as ignorant of the potential consequences of taking many antibiotics. This familiar scenario of blaming the patient for being an ignorant "other" is a form of alterity that has been afforded to the privileged and those proclaiming expertise across many periods and contexts, but in this case, it frees the health worker from accountability or the need to take responsibility for their own prescribing practices. Here, clinicians are using their patients' lack of cultural capital as an excuse for frequent prescribing of antibiotics.

Language is also an important indicator of cultural capital that was emphasized by informants. The terminology for antibiotics used in patient–clinician encounters is an important influence on patients' understanding and use of antibiotics, as we describe elsewhere (Lambert et al., 2019). In consulting with patients, a majority of informants were observed to use the term *xiaoyan yao* (literally translated as anti-inflammation medicine) to refer to antibiotics, such as amoxicillin and cephalosporin. When queried, one clinician explained:

> The commoners won't understand if I say *kangsheng su* (抗生素), the technical term for antibiotic. They do not know the term *kangsheng su*. They only know *xiaoyan yao*. These rural folks talk about *xiaoyan yao* out of habit (1-2-15).

Similarly, an in-house pharmacist commented:

> *Xiaoyan yao* is local dialect (lit. 'earthy language'). Between clinicians, we cannot say *xiaoyan yao*. We need to speak formally. In fact, [the patients] use it to mean antibiotics. But if I say "*kangsheng su*," the patient won't understand. So we need to speak a simple language with them, and discuss *xiaoyan yao*. But if we talk with other doctors using the term *xiaoyan yao*, we would be laughed at (2-2-180131).

A village doctor echoes that he generally would use the term *kangsheng su*, rather than *xiaoyan yao*, with people whose educational level is junior college or higher, whereas "It's pointless to talk about it with ordinary commoners" (2-2-201802). Through this narrative of the "ignorant patient," doctors perpetuate misunderstandings of the drug and its inappropriate use by using the vernacular term with patients, thereby thwarting the possibility for altering the patient's understanding. This is particularly problematic in China, where patients commonly purchase antibiotics in retail pharmacies without a prescription by seeking the more general category of anti-inflammatories (*xiaoyan yao*).

Patients are *othered* by doctors not only according to their lack of cultural capital (concerning what they don't know), but also according to the cultural and social capital derived from where they live and who they know. Some informants suggest that exposure to the city seems to increase people's "self-cultivation" and medical knowledge:

> Young people are better if they have been working as migrants in the city. Otherwise, [there is] no point explaining drug resistance to them, they won't understand (2-2-21).

The implication here is that patients have different inherent qualities based on where they live, though every patient is obliged to take responsibility for their own well-being. By characterizing patients this way, informants, again, appear to shift responsibility for antibiotic prescribing decisions away from themselves and onto the patient.

Rural migrant workers, or the so-called *nongmin gong* (农民工), are commonly portrayed as peasants of *di suzhi* (low

human quality) who carry disease and have often been blamed by both the lay public and the medical community in China for the spread of diseases such as HIV/AIDS and tuberculosis into urban areas. This narrative is perpetuated even though the majority of migrant workers are young and healthy and despite the fact that the epidemiological evidence clearly contradicts this narrative (Hesketh et al., 2006; Wang et al., 2007; Gong et al., 2012; Mou et al., 2013). Informants portrayed migrant workers as adding to their difficulty in making treatment decisions. For example, one doctor discussed how massive rural-to-urban migration affects his work:

> Many families here are from "left-behind" households, with young parents working as migrants away in the city [while grandparents look after the preschoolers or school-age children]. Few of them demonstrate filial piety (*xiao*, 孝) [being supportive of elderly parents' healthcare] (2-1-20180115).

This doctor went on to discuss how young adult siblings fight over who should pay the medical fees of their elderly parents' and how clinicians often become an easy target for blame in such disputes. Other informants spoke of bearing the brunt if any social problems arise, claiming that rural doctors serve as scapegoats, literally "cannon fodder" (*dang pao hui*, 当炮灰) (2-1-20180115).

Yet, despite their disparagement of patients' low cultural capital, rural doctors are highly dependent on their patients' social capital to maintain their own livelihoods. Perceived or actual poor care would potentially result in significant loss of clientele through reputational damage in rural communities with strong social networks. Thus, in order to avoid patient disputes and "medical trouble" (*yi'nao*, 医闹), health workers feel obliged to do whatever is necessary to appease the patient and their family, particularly to avoid the cost of financial compensation to patients to settle legal medical disputes. Village doctors are particularly vulnerable to such legal action since they are not fully incorporated into the national healthcare system and essentially operate as licensed private practitioners. Private practitioners are more exposed to risks of litigation in this system and are liable to pay any compensation to patients out of their own pockets if there are any medical accidents. One village doctor (1-3-31) claimed to take notes of all her patients' allergies in her record book and to be able to remember almost all by heart, despite not keeping formal patient records other than recording the medicines prescribed to new patients. Similarly, by prescribing antibiotics, clinicians claim they are demonstrating their concern for their patient's health and the need to protect them from potential further complications, even though they are simultaneously protecting their own livelihoods and economic capital, as well as maintaining their own local social capital.

CONCLUSION

This research has examined the clinical, social, and economic influences on antibiotic prescribing that clinicians face every day while working at the lowest levels of health facilities in rural Anhui Province, China. A marked gap has been identified between informants' understanding of what antibiotics are for and how, in practice, they are prescribed on a daily basis. Uncertainty in diagnosis and treatment, due to either lack of knowledge or of material resources, and the need to engage in "safe practice" both result from, and are a potential threat to, informants' cultural, social, and economic capital. Health workers' perception and practice of safety is often contradictory and requires a contorted logic in an attempt to fulfill the conflicting demands of capital. In addition to interacting in a complex and unpredictable environment, these drivers of clinical practice are dynamic and changing, particularly in the Chinese context where healthcare policies may markedly change every few years.

Our study clearly has limitations, in part due to the sensitive nature of this research in China at this time. For example, probing financial incentives as a driver for informant prescribing is difficult, particularly since a number of official policies have been launched to reduce the potential of personal and institutional financial gains from medical treatment. We are also aware that informants' characterizations of the ignorance of their patients may be influenced by the interviewing situation, in which practitioners who are being questioned about their clinical practices may, in defense, emphasize their own knowledge to justify their prescribing decisions. Sample size also restricts the representativeness of these data and opportunities to conduct extended ethnographic research beyond the clinic settings were restricted due, again, to sensitivities regarding the conduct of this research in rural areas. Overall, identifying how the overuse of antibiotics and the increasing risk of AMR may best be mitigated in the context of medical institutional hierarchies will benefit from further empirical research. Despite these limitations, we provide new insights into the powerful sociocultural, economic, and institutional drivers that shape antibiotic prescribing, in addition to a fresh analytic approach that demonstrates that prescribing practices cannot be explained solely by reference to individually modifiable forms of behavior.

Our work largely corroborates, but goes beyond, the key findings of Broom et al. (2014) in which maintaining forms of capital often outweighed adherence to clinical guidelines, including antimicrobial stewardship, in the very different setting of Australian hospitals. Although our findings align with the conclusion that clinicians are placed "in the complex position of abiding by obligations and responsibilities (to patients, peers, institutional structures, profit, recovery) while also navigating the values of scientific rigor and efficacy (a complex balance of social capital (networks), cultural capital (reputation), and professional capital)" (Broom et al., 2017, p. 2003), previous research has largely focused only on the influence of social capital. In this paper, we have attempted to further develop the use of Bourdieu's concept of capital to examine clinician antibiotic prescribing practices by also considering cultural and economic forms of capital as particularly salient in this setting and thereby offer a valuable and original perspective for better understanding the sociocultural factors impacting AMR.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

This study involving human participants was reviewed and approved by Anhui Medical University Ethics Committee. Participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HL, CC, PK, and MC planned and designed the interview topic guides. MC conducted interviews in all field sites, coded all interview transcripts, translated the quotes, and drafted the first manuscript version. PK contributed the theoretical framework. All authors contributed to the data analysis and reviewed and revised the final version of the manuscript.

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