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EDITORIAL COMMENTARY

"Cultural" Variation in Antibiotic Prescribing: Have Regional Differences Had Their Day?

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Investigations going back to the mid-1990s have described regional variability in antibiotic prescribing in the United States (US) that cannot be explained by clinical differences, with the highest prescribing rates in the South [1–6]. Much attention has been paid to this finding, and for good reason. This variation suggests that some people are at risk of harm from unnecessary exposure to antibiotics. In addition, we all should be concerned about regions with higher rates of unnecessary antibiotic use. Antibiotic use causes antibiotic resistance and human-defined geographic regions are of no concern to microbes.

Variation in antibiotic use is found at every level in which investigators have looked: across patients, prescribers in the same practice, practices in the same small area, small areas in the same state, states in the same region, regions in the same country, and countries across the globe [7–9]. Documenting the existence of variation in antibiotic prescribing that cannot be explained by clinical need is a bedrock justification for stewardship interventions and policy. As explanations for these large regional differences in the US, authors often point to distinct influences: patient-level factors (expectations for antibiotics, health literacy, educational attainment, underlying comorbidities such as obesity, income, and race), clinician prescribing habits, and culture. However, we question the utility of the continued focus on variation in antibiotic prescribing by US Census Region and the suggestion to explore "cultural" differences among them to address antibiotic overuse.

In this issue of *Open Forum Infectious Diseases*, Bizune and colleagues contribute another study demonstrating regional variation in the volume and quality of antibiotic prescribing associated with outpatient visits in the US [10]. The authors used IBM MarketScan data to examine acute respiratory infection (ARI) visits to physician offices, retail clinics, urgent care clinics, and emergency departments, stratified by diagnoses for which antibiotics are always, sometimes, or rarely indicated. They found that clinicians prescribed antibiotics in 40% of ARI visits, more often in the South (43%) than the Midwest (41%), Northeast (37%), or the West (34%). Across regions, the antibiotic prescribing rate for always-indicated and sometimes-indicated diagnoses were roughly the same (about 58% to 69%) and lower for rarely indicated diagnoses (13% in the West, 16% in the Northeast and Midwest, and 18% in the South).

In multivariable modeling with the West as the referent, for always-indicated diagnoses, there were no differences; for sometimes-indicated diagnoses, the South and Northeast had significantly greater antibiotic prescribing; and for rarely indicated diagnoses, there was incrementally greater antibiotic prescribing in the Midwest, Northeast, and South. Examining antibiotic prescribing across both regions and appropriateness tiers with rarely indicated ARI visits in the West as the referent, there was significantly greater antibiotic prescribing in all tiers and all regions, particularly in the South.

Bizune and colleagues call for work addressing "the cultural factors that may be affecting regional differences," state that "qualitative research could also provide more insight into the cultural context and regional differences," and recommend that evidence-based interventions "be tailored to fit unique cultural needs."

However, invoking "culture" without clarification about its meaning obstructs actionability [11]. In popular use, "culture" typically refers to a bounded, consistent, and stable group of beliefs, symbols, and practices shared by one group in contrast to another. While

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Table 1. Hypothetical Clinical Encounter

Clinician
Dr Susan George is a general internist who is 1 year into a job at an urgent care clinic owned by a national corporate chain located in the city of a Southern state that uses a lot of antibiotics compared to other states in the US. Dr George grew up in the city, from a family with deep roots in the area. She completed her medical training plus a decade of primary care practice in a health system–affiliated clinic in a city in a Western state that uses far fewer antibiotics compared to other US states, but she wanted to move closer to her aging parents.
Dr George describes her mother, for as long as she can remember, as quick to see the local family doctor for any symptom and as a big believer in the power of medication to relieve discomfort, often saying "there is a pill for every ill." To this day there are bottles of leftover antibiotics in her parents' medicine cabinet. During training and her early career, Dr George grew to appreciate the harms of unnecessary antibiotic use, with 2 particularly memorable cases—a patient she cared for during residency who died of a multiply drug-resistant organism and a primary care patient with *Clostridioides difficile* infection–associated intestinal perforation acquired after taking clindamycin prescribed by a dentist.
Her prior employer, a large health system, had an advanced quality improvement infrastructure. Antibiotic stewardship was a system-wide goal, well-resourced, and a priority in Dr George's practice. She and her colleagues received individual antibiotic prescribing performance reports with peer comparison. They often discussed adopting a unified approach to antibiotic use, had electronic clinical decision support available to them, and took professional pride in delivering evidence-based care without sacrificing patient-centeredness.
Since moving back home, Dr George has found her new employer and clinic setting to be quite different. She does not know her colleagues well and there are not many opportunities for group discussion, clinic management is concerned about losing patients to competing urgent care practices in the city so incentivizes patient satisfaction scores, she is expected to see a much larger number of patients per day, there is limited antibiotic stewardship beyond infection-specific treatment guidelines, and the clinic has a very high volume of patients with comorbidities and poor access to primary care.
Patient
Frank Smith is a 50-year-old auto mechanic who recently started driving for an app-based ride share service at night to make ends meet given rising costs associated with inflation. He is a lifelong resident of the area with mild depression, hypertension, and chronic back pain.
Frank had a long-time primary care doctor who recently retired. While he has a new primary care nurse practitioner, Frank does not like her as much and has begun to find it very difficult to book an appointment through the practice's newly instituted automated phone tree. So, he frequently visits corporate urgent care clinics in town when he has a health problem.
Frank is a big believer in medical intervention, thinks of his body in mechanistic terms—as a car that needs fixing when broken—and is anxious when his ability to work is interrupted given increasing pressures he feels to provide for his family as "the man of the house." His old primary care doctor routinely prescribed antibiotics whenever Frank had respiratory symptoms, which always seemed to help him get better quickly without noticeable side effects.
Encounter
It is 4 PM on a Thursday before a long holiday weekend. Frank is currently experiencing a flare-up of his back pain plus a cold accompanied by a hacking cough. It is day 2 of his symptoms and he is frustrated. He is especially annoyed about the cough, which he feels will get in the way of taking advantage of an increased volume of ride share requests that will be more lucrative because of holiday weekend surge pricing. One of his coworkers at the auto body shop had a similar cold recently and mentioned how he got a Z-pak, which cleared up his symptoms fast. Frank decides to go to the corporate chain urgent care clinic to get antibiotics, so he'll feel better faster and get back on the road to earn money.
Frank is Dr George's last patient of a very long clinic day. This is the first time they are meeting each other. There is a respiratory viral infection going around the community, so she has recently seen multiple visits for people with symptoms just like Frank's, some of whom wanted antibiotics. In the morning she felt satisfied in that she was able to avoid prescribing unnecessary antibiotics for 2 patients who she thought wanted them. But as the day wears on and Dr George makes a number of difficult decisions and completes numerous burdensome administrative tasks, she enters Frank's exam room feeling tired and depleted.

Abbreviation: US, United States.

"culture" is often used in reference to large groups (eg, nations, generations, religions), smaller groups have attributes of culture (eg, organizations, neighborhoods). Social scientists have challenged the notion that culture forms neatly coherent and distinct wholes, arguing instead that culture is contradictory, loosely integrated, weakly bounded, and subject to constant change [12]. Culture is not entirely consistent or shared for a given group, or even within an individual [13]. Instead, people draw fluidly on different cultural elements that are part of their identity or life history depending on the context and social structure around them [14]. The influence of culture on individual behavior is complex.

"Cultural tailoring" of stewardship interventions to the 4 US Census Regions is probably of limited utility. Doing so assumes coherent and bounded Southern, Midwestern, Northeastern, or Western culture operate to shape antibiotic prescribing. Social science tells us this is unlikely. Even if one does exist, what is the mechanism by which regional culture influences antibiotic prescribing? Is accounting for regional culture in research and targeting it in interventions likely to make a difference in antibiotic use? Might other levels of culture, individual life experience, or more immediate contextual-structural factors play a bigger role in influencing antibiotic prescribing than a broad regional culture?

We urge adopting a nuanced view of culture in antibiotic stewardship research to explain variation in prescribing, to ensure focus on the places where intervening can make the most difference. Consider a hypothetical scenario between a clinician and patient in which a decision about antibiotics will occur (Table 1). This scenario paints a detailed picture of the multiple interacting social, cultural, contextual, and structural factors that could shape a clinician's decision to prescribe an antibiotic, a patient's care-seeking behavior, and expectations for an unnecessary antibiotic. Assume the scenario occurs in a Southern state with a high rate of antibiotic prescriptions compared to other states in the US [15]. While both physician and patient spent their formative years in the South, presumably influenced by a broad regional culture, their individual life history and more immediate, modifiable factors—organizational context, micro-level social dynamics, economic incentives—around the clinical encounter are likely exerting more influence (Table 2).

While we are enthusiastically supportive of considering context when implementing antibiotic stewardship

Table 2. Potential Influences on Decision Making

Dr George	• Family of origin culture ◦ Norms and beliefs about medication, illness, and health • Memorable personal experience ◦ First-hand experiences with the harm of antibiotics • Training environment ◦ Location in low antibiotic-utilizing state • Clinic culture and structure ◦ Quality improvement infrastructure and resources ◦ Leadership support for antibiotic stewardship ◦ Social interactions and peer support ◦ Availability and design of electronic clinical decision support ◦ Professional culture and identity ◦ Patient satisfaction scores incentivized because of clinic concerns about local competition ◦ Workload and staffing • Context of encounter ◦ Time of day ◦ Decision fatigue ◦ No prior relationship with the patient
Frank	• Gender culture ◦ Norms and beliefs about the body, medication, illness, and health ◦ Norms and beliefs about economic responsibility • Economic pressures ◦ Lack of covered sick leave ◦ Supplemental income via gig economy, lack of worker protections, and unpredictable degree of income ◦ Inflation and rising cost of living • Access to care ◦ Usability of appointment booking technology ◦ Change in relationship with primary care clinician • Memorable personal experience ◦ History of receiving antibiotics for similar symptoms • Social networks ◦ Prompts for antibiotics from others with similar symptoms

interventions [16], doing so requires a working logic model of how proposed intervention elements will work to change behavior. To this end, we agree with Bizune and colleagues when they suggest future work should focus on smaller geographic areas to generate a more nuanced understanding of the factors shaping variation in antibiotic use and to target stewardship interventions. For example, they highlight the Kentucky Antibiotic Awareness (KAA) campaign as an example of a tailored stewardship effort. While Kentucky is in the Southern US Census region, the KAA campaign was tailored to the structure of the state, not Southern "culture." State-level tailoring makes sense, especially when stewardship interventions involve techniques such as the provision of social norm feedback from a high-profile authority whose influence on prescribers operates via the state level (eg, licensing boards, departments of public health, state-wide payers such as Medicaid) [17].

Moving forward, we have three recommendations. First, investigators should be specific and clear about what they mean by "culture" when suggesting it as an explanation for observed geographic variation in antibiotic use. Second, research that seeks to use observed variation to tailor stewardship interventions should start with a working logic model to propose how implementation will address determinants of antibiotic overuse at multiple levels, including characteristics of the individuals involved, immediate contextual considerations, and larger sociostructural factors [18]. Third, investigators should retire their focus on the four US Census Regions when addressing variation in antibiotic prescribing. We should strive for more granularity in research on this topic by looking at smaller area variation to facilitate efficient policy- or intervention-targeting. Novel empirical strategies such as small area estimation or analyses that examine the migration of patients or clinicians from one region to another could be used to generate knowledge about the relative contribution of different factors to observed geographic variation in prescribing [19, 20]. While large area regional differences may be useful to point out what is possible, for addressing variability and designing interventions, regional differences have probably had their day.

Notes

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