OUTPATIENT BEHAVIORS AND PERCEPTIONS THAT INFLUENCE ADHERENCE TO PROPER ANTIBIOTIC STEWARSHIP PRACTICES: INDICATIONS FOR FUTURE INTERVENTION DEVELOPMENT

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A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Public Health in the Department of Health Policy and Management in the Gillings School of Global Public Health.

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ABSTRACT

Lisa C. Strader: Outpatient Behaviors and Perceptions that Influence Adherence to Proper Antibiotic Stewardship Practices: Indications for Future Intervention Development
(Under the direction of Leah Devlin)

Since their introduction in the late 1920s, antibiotics have had a positive impact on human health by reducing morbidity and mortality from infectious diseases and injuries. Antibiotics have allowed many elective surgeries to take place such as hip replacements, hernia repair, kidney stone removal, and other exploratory surgeries. Yet, fifteen years after the discovery of penicillin, antibiotic-resistant organisms were identified. Over the last 20 years, a rise in the number of antibiotic-resistant strains of bacteria represents a serious threat to humans, animals, and environmental health in the United States and globally.

In the United States, most antibiotic expenditures result from prescribing in outpatient settings. Improving poor antibiotic consumption practices by educating prescribers and patients, developing new antibiotics, and ensuring proper antibiotic prescribing, is a national priority. However, less attention is currently focused on outpatient settings. The purpose of this study was to explore the knowledge, beliefs, and perceptions among patients and community members that drive inappropriate antibiotic practices in outpatient populations.

The Health Belief Model was employed to study factors that facilitate or impede individual outpatient adherence to antibiotic prescription guidelines and the knowledge and perceptions that determine whether a patient will follow proper antibiotic stewardship guidelines. Focus groups were convened to explore in greater detail the constructs, drivers, and subjective influences that guide outpatient use of antibiotics and to inform the development of an online survey. The survey was divided into six sections: 1) demographics, 2) healthy and

unhealthy behaviors, 3) illness and healthcare visits, 4) vaccinations and antibacterial products, 5) antibiotic knowledge, and 6) 5-point Likert scale questions focused on knowledge, beliefs, and perceptions.

Three themes were identified for use in future development of antibiotic stewardship intervention programs: 1) how humans contribute to antibiotic resistance, 2) how antibiotic-resistant infections are transmitted, and 3) what perceived susceptibility has the best chance of influencing change.

To my daughters, Brenda and Nery, and my granddaughter, Allison.
Find your passion and pursue it – the best way to do great work is to love what you do.

To all those working in public health, never think that what you do doesn't make a difference.
Great things happen one small step at a time.

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LIST OF ABBREVIATIONS

AB	Antibiotic
ABR	Antibiotic resistance
AMR	Antimicrobial resistance
CARB	Combatting antibiotic-resistant bacteria
CBA	Controlled before and after trial
CDC	Centers for Disease Control and Prevention
CEDI	Community-engaged dissemination and implementation
CNP	Certified nurse practitioner
COVID	Coronavirus disease
CRCT	Cluster randomized control trial
CTSA	Clinical and Translational Science Awards
GP	General practitioner
HBM	Health Belief Model
IRB	Institutional review board
ITS	Interrupted time series
MD	Doctor of Medicine
MeSH	Medical subject headings
NAP	National Action Plan
NC	North Carolina
NIH	National Institutes of Health
PA	Physician assistant
PACCARB	Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
PA	Physician assistant
PI	Principal investigator

RCT	Randomized control trial
RN	Registered nurse
UNC-CH	University of North Carolina at Chapel Hill
USA	United States Government
WHO	World Health Organization

CHAPTER 1: INTRODUCTION

Statement of the Issue

Since their introduction in the late 1920s, antibiotics have had a positive impact on human health by reducing morbidity and mortality from infectious diseases and injuries allowing medical procedures such as organ transplants and open-heart surgery to take place (Hutchings, 2019). Antibiotic agents kill or inhibit the growth of bacteria that cause diseases such as pneumonia, tuberculosis, cholera, and food borne illnesses. Other major microorganisms that cause disease in humans, but are not susceptible to antibiotics, are viruses (e.g., chickenpox, shingles, and HIV, COVID), fungi (e.g., ringworm) and protozoa (e.g., malaria).

Antibiotic resistance results from bacteria that are able to survive and grow in the presence of an antibacterial agent, either because the concentration of antibiotic is insufficient to kill the bacteria (also called acquired resistance) or as a result of mutation or transfer of resistant genes between species of bacteria (Sabtu, 2015). The Centers for Disease Control and Prevention (CDC) reported in November 2019 that antibiotic-resistant bacteria in the U.S. results in at least 2.8 million infections and 35,000 deaths each year, excluding the bacterium *Clostridioides difficile* (*C. difficile*) (CDC, 2019). Further, CDC estimates that *C. difficile*, which is not typically resistant to antibiotics but usually occurs in people who have taken antibiotics, results in an additional 3 million infections and brings the annual death total to 48,000 per year (CDC, 2019). Increasingly, there also is concern about the limited number of antimicrobials used to treat *C. difficile* infection. The 2019 CDC report does not estimate the financial cost of antibiotic-resistant infections nationally. However, the 2013 Antibiotic Resistance Threats in the United States report estimated $20 billion in excess health care costs, loss in worker

productivity as high as $35 billion, and an additional 8 million more hospital days per year was reported in 2011 by the Infectious Disease Society of America (Dadgostar, 2019; Infectious Diseases Society of America [IDSA], 2011; CDC, 2013).

As an ever-growing number of bacterial strains become antibiotic-resistant, it may become impossible to treat some diseases or may require postponement or cancellation of certain surgical procedures. Recently, some strains of bacteria have been found to respond to only one or two antibiotics (Brunning, 2014). In this case, the antibiotic that is the last known effective antibacterial agent against a specific strain of bacteria is called a "drug of last resort" (Brunning, 2014).

Antibiotic resistance is a One Health[1] concern – we are all connected (World Health Organization, 2017; McEwen &Collignon, 2018). When antibiotics are used by people and in animals, it causes side effects and increased resistance (CDC, 2022b). When they are used in crops, for example, to fight blight and bacterial disease, this can result in reduced food production (Stockwell & Duffy). Use of antibiotics in one of the three groups has the potential to affect the other two because of our shared environment. A One Health approach where we all work together is needed for us to have the biggest impact on antibiotic resistance. The United States and other global organizations, such as the World Health Organization and the United Nations, have developed public health campaigns focused on the prudent use of antibiotics and are collaborating to slow the development of antibiotic resistance and mitigate its impact on global morbidity and mortality (CDC, 2021c).

Recognized as a threat to U.S. public health and the economy, antibiotic resistance was the focal point of the President's 2014 Executive Order where a commitment was made to "reduce the emergence and spread of antibiotic-resistant bacteria and help ensure the continued

[1]One Health is an integrated, unifying approach to balance and optimize the health of people, animals, and the environment. It is particularly important to prevent, predict, detect, and respond to global health threats such as the COVID-19 pandemic (WHO, 2017).

availability of effective therapeutics for the treatment of bacterial infections" (Secretary, W.H.P., 2016; Obama, 2014; CDC, 2021c). A 2014 plan released by the U.S. White House, *National Strategy for Combating Antibiotic-Resistant Bacteria*, focused on 1) slowing the emergence of resistant bacteria and preventing the spread of resistant infections; 2) strengthening national One-Health surveillance; 3) advancing development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria; 4) accelerating basic and applied research and development for new antibiotics, therapeutics, and vaccines; and 5) improving international collaboration and capacity for antibiotic-resistant prevention, surveillance, control, and antibiotic research and development (House, W., 2014).

The Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB), established in September 2015 and focused on combatting the rise in antibiotic-resistant bacteria, hosted a series of public meetings between 2016 and 2021 in which they established priority areas and corresponding recommendations, reviewed the current landscape, and finalized the priority areas for the 2020-2025 iteration of the National Action Plan on CARB (Assistant Secretary for Health, 2022).

Background

In 1945, approximately 15 years after the discovery of penicillin by Alexander Fleming, he noted that penicillin-resistant organisms had begun to appear (Sternbach & Varon, 1992; Rammelkamp & Maxon, 1942). A rise in the number of antibiotic-resistant strains of bacteria over the last 20 years represents a serious threat to public health and the economy in the United States (U.S.) and the rest of the world.

The Centers for Disease Control and Prevention (CDC) released its first AR Threats Report in 2013 describing the burden of antibiotic-resistant infections in the U.S. In the report, they noted that more than two million people were infected and at least 23,000 died each year due to antibiotic resistant (ABR) infections. As a result of new and improved data, the estimates

were found to be an underrepresentation and were revised to more than 2.6 million antibiotic-resistant infections and nearly 44,000 deaths each year.

In 2015, informed by the CDC report, the U.S. Government (USG) developed a National Strategy and National Action Plan (NAP) for Combating Antibiotic-Resistant Bacteria (CARB) that provided a domestic and international approach to "detect, prevent, and control illness and death related to antibiotic-resistant infections over five years (2015-2020)" (House, W., 2015) When implemented, the plan's One Health approach was effective in reducing the number of deaths by 18% overall and by 30% in hospitals since the first ABR Threats Report was released in 2013 (CDC, 2019). However, antibiotic resistance continues to be a threat to health in the U.S. and more work needs to be done (CDC, 2019).

The CDC's November 2019 Antibiotic Resistance Threats report, its second, estimates more than 2.8 million antibiotic-resistant infections, and more than 35,000 deaths occur each year (CDC, 2019). The report also includes a list of urgent threats including Carbapenem-resistant *Acinetobacter*, *Candida auris*, *Clostridioides difficile*, Carbapenem-resistant *Enterobacteriaceae*, and drug-resistant *Neisseria gonorrhoeae* (CDC, 2019). The report also identifies 11 serious threats and 2 concerning threats (CDC, 2019).

The emergence and spread of antibiotic-resistant bacteria combined with an increased use of antibiotics in humans and in animal husbandry now pose a serious global health threat of increasing concern in humans, animals, and environmental health. In addition to the risk of patients potentially having to delay surgeries, antibiotic treatment may not be available as protection against infection for those receiving dialysis, organ transplants, and chemotherapy (CDC, 2019).

To combat overprescribing of antibiotics in outpatient settings, the U.S. called for a 50% reduction in inappropriate outpatient antibiotic use in the 2015 National Action Plan for Combating Antibiotic-Resistant Bacteria (House, 2015). Although there seems to be a small reduction in inappropriate prescribing, particularly in infants and children, data in the last three

to four years indicates that overall rates of inappropriate prescribing remain in the 28-30% range (Zetts, et. al., 2018; Buehrle & Clancy, 2021). Annually CDC reports on total outpatient antibiotic prescriptions. In 2019, 765 antibiotic prescriptions per 1000 persons were dispensed in the U.S. (CDC, 2021a). The figures were 613 and 636 antibiotic prescriptions per 1000 persons in 2020 and 2021, respectively (CDC, 2021b; CDC, 2022a).

To reduce inappropriate prescribing in the outpatient domain, human antibiotic stewardship programs have focused on prescribers and pharmacists (Meeker, et. al., 2016; Zetts, et. al., 2018; Dobson, et. al., 2017; Klepser, et. al., 2017). Patients and communities are rarely the focus of antibiotic stewardship programs. With more than 60% of antibiotic expenditures and prescribing in the U.S. occurring in outpatient settings (Talkington, et. al., 2016; Zetts, et. al., 2018; Klepser, et. al., 2017), comprehensive outpatient programs should also emphasize both patients and communities. This study provides an opportunity to understand and identify ways to address poor antibiotic stewardship practices in these two groups.

CHAPTER 2: LITERATURE REVIEW

Based on a Cochrane review of antibiotic prescribing practices (Arnold & Straus, 2005), a PubMed (MEDLINE) literature search was conducted from April 20, 2011, through April 17, 2016, limited to English language human studies. The following search terms were used:

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"Drug Resistance, Microbial"[Mesh] AND ("Health Education"[Mesh] OR "Controlled Before-After Studies"[Mesh] OR "Interrupted Time Series Analysis"[Mesh] OR "Health Promotion"[Mesh] OR "Historically Controlled Study"[Mesh] OR "Non-Randomized Controlled Trials as Topic"[Mesh] OR "Evidence-Based Practice"[Mesh] OR "Controlled Clinical Trial"[Publication Type]) AND ("2011/04/20"[PDat] : "2016/04/17"[PDat] AND "humans"[MeSH Terms] AND English[lang]
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Figure 1: MeSH Search Term

Studies were included if they 1) evaluated an intervention in an outpatient setting whose aim was to reduce antibiotic resistance; 2) assessed and reported data on antibiotic use or prescribing before and after the intervention; and 3) were a randomized control trial (RCT), cluster randomized control trial (CRCT), controlled before and after trial (CBA), or interrupted time series (ITS). Reasons for study exclusion are identified in Figure 1.

Findings

The literature search identified 429 citations, 74 of which were considered within the scope of this effort based on title and abstract review. Full text review of the 74 citations led to the further exclusion of 66, resulting in 8 citations that met the eligibility criteria for the study (1 CRCT, 3 RCT/RT, 1 ITS, 3 CBA) (Figure 2, Table 1).

All but one of the eight trials were conducted in Europe, representing 5 countries – 2 in Portugal, 2 in the United Kingdom, and 1 each in France, Greece, and Norway. The final study was conducted in Australia. Three of the study interventions focused on prescribers/general practitioners (GPs), two on students, one on patients, one on parents and the remaining study

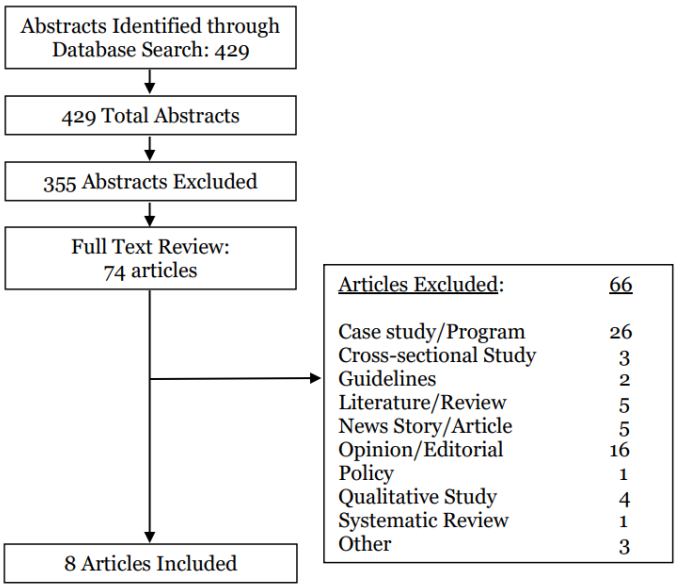


Figure 2: Summary of Literature Search and Review

had a combined focus on parents and children (families). Five of the studies employed an education intervention, one a supportive program, and two a combination of education and support. All five education programs incorporated some form of lecture (e.g., presentation, peer education, slide/science show, or seminar). Four of the five incorporated interactive learning (e.g., labs, interactive stalls, group discussion), two of the five distributed written leaflets or flyers, and one of the five distributed small incentives to group practices with continuing education credits to practice GPs. Two trials provided supportive feedback to GPs/clinicians on prescribing practices and 1 delivered a motivational seminar that included a discussion on problem solving skills. As a primary outcome, four trials reported on intervention effectiveness in increasing knowledge, three on prescribing rates (one of these combined with cost, one combined with consumption), and one on consumption alone. The average intervention exposure was 17.88 weeks with a range of 1 – 104 weeks.

Table 1: Summary of Studies

Study	Country & Age	Study Design (sample size)	Intervention Strategy (study goal)	Time Frame	Assessment	Outcome	Limitations	Risk of Bias
Azevedo (2013)	Portugal 14-16 yrs	Pre/Post Test; convenience sample from 2 schools (82 total students; 37 from school D.M.II and 45 from C.C.B.)	Teaching activity including a slide show presentation and a 90-minute discussion. (Assess knowledge of 9th graders in 2 schools on use of antibiotics; determine efficacy of teaching intervention in improving students' knowledge of antibiotic use)	2 months	Unmatched pre/post questionnaire	Mixed - number of correct answers increased in the post-test. Some of the measures, regarding the types of illnesses that antibiotics are effective against, were statistically different between pre- and post-test, primarily.	• Convenience sample does not allow matching pre/post responses • Generalizability	Moderate
Fonseca (2012)	Portugal 15-17 yrs	Pre/Post Test; students self-selected/responses were anonymous (42 high school students)	Students participated in 3 interactive lectures, 6 wet lab activities, selected from a menu of 21 options. (Increase student understanding on antibiotic use and resistance as a result of participation in program; impact of the project on the participants' interest about the topics addresssed and their procedural competencies)	1 week	Questionnaire, observation, and activity reports	Encouraging - all pre-post test quesitons had significant ($p<0.05$) improvements. Participants reported enjoying participating ($p<0.001$) and program contributed to increasing curiosity about the topic ($p<0.001$).	• Participants self-selected • Program implemented during summer school (less formal setting) which can positively impact interest. • Used open-ended questions with potential for coding bias	Moderate (sampling, coding)
Gjelstad (2013)	Norway 48.3 yrs in interventio n 49.7 yrs in control	CRCT[a] Stratified by regions (5) & randomized (382 general practitioners in 79 pre-existing medical education groups)	Intervention participants received 2 visits from peer educators - 1) guidelines and relevant research presented; 2) feedback from reports on their own prescribing habits from previous year. Regional 1-day seminars offered as a supplement post-intervention. Control received different intervention on non-antibiotic prescribing practices for older patients >70 yrs) (Assess effects of education intervention in general practice to: 1) reduce prescription rates for acute respiratory tract infection; 2) reduce broad spectrum antibiotic use)	1-2 months between first and second session Additional data capture on prescribing practices 1-year post-intervention	Specially designed software program captured 1-yr restrospective data from practitioners' electronic medical records system.	Mixed - prescribing rates decreased slightly in intervention arm and increased in the control arm. Based on group means, prescriptions per 1000 patients increased in both arms at the episode level.	• Education groups are dynamic • Peer instructors (acadmic detailers) received common training but differing personalities may have influenced effect • Data did not distinguish between primary and secondary treatment contacts potentially underestimating antibiotic rates • No follow-up data available for practitioners that dropped out of the study	Low (potential differences in peer education delivery; potential bias towards null resulting from non-distinction between primary/secon dary treatment)

Study	Country & Age	Study Design (sample size)	Intervention Strategy (study goal)	Time Frame	Assessment	Outcome	Limitations	Risk of Bias
Hernandez-Santiago (2015)	Scotland 47 (mean)	Interrupted Time Series (408,058) regional residents)	Guidelines/Education/Feedback: prescribing guidelines; written & pharmacist facilitate education; audit & feedback of practice prescribing rates against target; small financial incentive to practices; professional development credits for GPs. (Reduce patient antimicrobial prescribing rates)	24 months 8 years of prescribing data obtained post-intervention	Anonymized, linked demographic & prescribing data obtained from National Health Service electronic data sets. Pre- and Post- (6, 12, 24 mos) intervention	*Mixed - total 4C prescribing appears to decline; no change in non-4C prescribing. There appears to be an increase in doxycycline, nitrofurantoin, and trimethoprim prescribing; and a decrease in macrolide prescribing. *No obvious change in total antibiotic prescribing. Intervention likely prompted antibiotic substitutions to more closely align with guidelines.	• Other interventions took place at same time (e.g., hospital antimicrobial use) • Cannot confirm causality	Moderate
Lecky (2014)	United Kingdom –	Pre/Post intervention evaluation	Family science show (3 minute presentation +5 interactive stalls) based on the 8-module e-Bug education program presented across two weeks in the summer at a holiday resort. (Examine effectiveness of program to improve parent and child knowledge of antibiotic use and existence)	Assessment immediately following intervention	Questionnaire (5 sections matching stall topics) piloted for readability and understanding at a different resort than intervention resort	Encouraging - overall increase of 25% in antibiotic knowledge from pre-test.	• Study participants likely come from same demographic area so generalizability to larger population is not possible • Study participants also self-selected, potential affecting generalizability • No control group	High
Le Corvoisier (2013)	France –	3-arm prospective RCT[b] of general practitioners (GPs). Control group received no specific information on antbiotic prescribing; Intervention 1 received 2-day didactic educational seminar; Intervention 2 received same as I1 plus 1-day additional seminar focused on problem solving strategies	Seminar consisting of small group discussions and plenary sessions; second intervention group received same as first plus an additional 7 hr motivational seminar with problem solving strategies. (Effectiveness of educational seminar on presecribing as measured by change in proportion of antibiotic prescriptions; change in related costs. Plus secondary outcomes)	2-3 days Follow-up 1x/yr for 3 yrs	2 months of general practitioner prescription data extracted from National Health Insurance System database and analyzed - collected at baseline and during same months for follow-up every year for 3 yrs.	Significant decrease in proportion of prescriptions containing antibiotic observed in intervention group ($P<0.001$); increase observed for same measure in control group ($P<0.01$). Between group difference was significant ($P<0.001$). Cost analysis showed decrease in antibiotic prescription was associated with significant reduction in antibiotic prescription costs in intervention vs. controls ($P<0.001$). Prescribing modifications sustained for up to 30 months post-intervention.	• Study not designed to analyze patient outcome, on prescriber behavior • 30 GPs randomly assigned to intervention groups could not attend seminar so were excluded from analysis	Low (positive - randomized, oversampled; negative - uncertain if 30 intervention GPs that did not attend seminar were different from controls)

Study	Country & Age	Study Design (sample size)	Intervention Strategy (study goal)	Time Frame	Assessment	Outcome	Limitations	Risk of Bias
Northey (2015)	Australia –	RT[c] Patrons of 3 pharmacies assigned to Intervention or Control based on random ballot. (34 patients presenting at pharmacy with prescription for antibiotic; 2 withdrew and 6 lost to follow-up)	Pharmacy staff provide patient education about antibiotic resistance and distribute a leaflet on same and how to manage symptioms of respiratory infection. Control group received a Consumer Medicines Information leaflet and no education. (Assess effectiveness of involving community pharmacy staff in patient education about antibiotic resistance, thus improving antibiotic use and knowledge)	1 month	Demographic and knowledge survey completed by patients while waiting for randomization. Second survey administered via phone one month after intervention.	Significant increase in antibiotic knowledge in intervention group (P=0.008)	• Small sample size • Pharmacies were from one region - generalizability is limited	Moderate (researcher aware of patients' allocation to intervention/control
Plachoura (2014)	Greece –	RT[c] (772 parents of children in nursing care or primary school; physicians; 30/151 dentists)	Pamphlet distributed to parents, followed by 17 2-hour educational meetings (Q&A forum) on proper use of antibiotics in all major municipalities in a district, beginning with a lecture by an infectious disease physician. Primary care physicians in the district received a lecture followed by 4 interactive sessions on case management; 5 meetings were held with primary care physicians in care centers; meetings were also held with dentists. Control group included remaining Peloponnese districts and national rates. (Decrease antibiotic consumption for upper respiratory tract infections during winter months in the intervention group)	Winter months over 2 yrs	Parent completed pre-intervention questionnaire on experience and perception of antibiotics. Data on antibiotic consumption obtained from IMS Health Holdings Inc. (only data on antibitiotics prescribed for respiratory tract infections were included)	No reduction in antibiotic prescription rate; significant difference in type of antibiotics prescribed in the two groups. (Intervention district had an increase in the use of Amoxycillin and Penicillin and a decrease in use of macrolides, 2nd generation cephalosporins, fluoroquinolones and amoxicillin clavulanate; neighboring control districts saw the opposite in specific type of antibiotic consumption. This reflects a more rational use of non-broad spectrum antimicrobials.) Post-campaign, antibiotic use reverted to previous levels.	• Comparisons on months before/after intervention do not account for seasonality • Data only available for limited time points, preventing time-series analysis	Moderate (bias towards increased participation of parents and physicians familiar with correct antibiotics use)

Discussion

This systematic review supplements the review by Ranji, et. al. (2008), "Interventions to reduce unnecessary antibiotic prescribing: a systematic review and quantitative analysis," and provides updated information from April 2011 to April 2016 on the interventions used to reduce unnecessary antibiotic prescribing. Several quality improvement strategies were found to increase knowledge of antibiotic resistance among patients and prescribers and to reduce unnecessary prescribing of antibiotics. Although several of the studies reported significant findings, no one strategy was identified as being superior and most interventions involved a combination of strategies.

Despite the lack of a strong prevention strategy rising to the top, there were several approaches that showed promise. The Fonseca, et. al. (2012) and Lecky, et. al. (2014) studies demonstrated an increase in AMR knowledge in students and families, respectively, using hands-on approaches. In the Fonseca study, high school students participated in à la carte activities such as preparing presentations on bacterial cells at different growth stages, analysis of scientific papers, and culturing bacteria from samples collected in agar plates (petri dish with growth medium) from door handles, cell phones, keyboards, and participant's hands, etc. The Lecky study included activities based on a successful British interactive science show (e-Bug) where study participants engage in tasks such as attempting to wash away a fluorescent powder from their hands using water alone or soap and water, and an activity where an acid/base color change titration demonstrates the importance of finishing your course of antibiotics. Gjelstad, et. al. (2013) and Northey, et. al. (2015) utilized peer educators and professionals (pharmacists), respectively, to provide information on AMR that resulted in an increase in AMR knowledge. Finally, Plachouras, et. al. (2014) and Hernandez-Santiago, et. al. (2015) observed an increase in proper antibiotic selection based on guidelines provided to physicians.

Data Quality

Seven of the eight studies reviewed were from European countries and as a result, the information available on participant visits to physicians, that is drawn from centralized national health systems, is more readily accessible compared to similar data in the U.S. This allows the researchers to be confident that prescribing information is comprehensive. However, this does not contribute to the confidence of results from studies whose goal was to increase knowledge.

European Union countries have well-established national and international surveillance systems for AMR as compared to the U.S. where programs are less mature but growing because of COVID. As a result, findings from countries with a centralized system may not be generalizable to a U.S. population. Australia on the other hand, whose system is funded and administered by several levels of government but also supported by private health insurance (50%), is like the U.S. system versus those countries located in Europe (Tikkanen, et. al., 2020).

Generalizability of Studies

Several studies used convenience or self-selected participants, potentially resulting in selection bias. For example, in one study, participants were temporary residents of a summer resort resulting in possible homogeneity among the study participants. Because of this, generalizability to a larger, more heterogeneous group is limited. Further, because study participation was anonymous in many of the studies, matching of pre- and post-assessment data was unachievable. This reduced the amount of information available on participants that completed the study versus those that were lost to follow-up.

Study Design and Sample Size

Regarding study design, one study was conducted in an environment where more than one intervention was taking place. Consequently, causality cannot be established without additional research. Several other studies were designed as pre- and post-assessments and although controlled before and after studies were included in the review, a control group would strengthen the idea that the intervention (independent variable) was in fact, responsible for the

changes seen in the studies. Moreover, a control group (i.e., multi-arm trial) can aid in identification of program components that are most effective and with which populations.

Except for three studies, most had small sample sizes (generally < 100), again leading to questions of generalizability. Interestingly, two of the studies with large sample sizes (408,058 regional residents in Hernandez-Santiago, et. al., (2015); 772 parents, 111 physicians, and 30 dentists in Plachouras, et, al., (2014)) saw an increase in specific classes of antibiotic prescribing and a reduction in other classes. The researchers questioned whether this was a result of adjustments made by prescribers to follow specific antibiotic prescribing guidelines or an artifact of the study.

Limitations and Conclusions

Several limitations of this study merit discussion. First, the number of studies included was small and as a result, there was insufficient sample size to conduct detailed analysis and discussion on cross-study effects and potential confounding. Further, synthesizing results with such a small sample size requires broad categorization of study outcomes and limitations. Although beyond the scope of this effort, combining these additional studies with the original Ranji, et. al. (2008) review would provide increased sample size and therefore, more definitive results. This review was limited to studies conducted in outpatient settings and as such, generalizability to other settings is not assured without further research. The combination of multiple intervention components and populations of the studies reviewed here do not allow researchers to ascertain which components are most effective and with which specific populations.

Interventions focused on reducing antibiotic prescribing for non-bacterial infections and those focused on increasing knowledge of antibiotic resistance and proper antibiotic use can have an impact in limited populations. Based on this review, peer and professional educators, prescribing guidelines, and hands-on interventions, such as those used in the Plachouras, et. al. (2014) and Lecky, et. al. (2014) studies and described above, may prove to have merit for

increasing AMR awareness and improving antibiotic prescribing in outpatient settings in the U.S. The confidence, long-term effect, and generalizability of such improvements are unknown. Future research should identify key drivers of patient and prescriber behavior and incorporate sufficiently sized trials over longer periods of time with participant randomization to provide conclusive information on which antibiotic stewardship intervention components, or combination of components, are most effective and with which populations. Also, robust evaluation studies should be incorporated so that anomalies such as the one found in previous reviews where prescribing for some antibiotic classes increased while others decreased, can be understood. An evaluation would also contribute to assigning proper causality where multiple intervention components are involved.

In October 2022, the literature review was repeated using the same MeSH search term with an updated date range of April 18, 2016, through October 31, 2022. Few (less than 5) additional antibiotic resistance intervention studies were identified. There continues to be a dearth of studies focused on an outpatient setting with most interventions focused on reducing antibiotic prescribing.

CHAPTER 3: METHODOLOGY

The nature of antibiotic resistance is that as new antibiotics are introduced, bacteria resistant to that antibiotic will develop shortly thereafter (Sternbach & Varon, 1992; Rammelkamp & Maxon, 1942). Therefore, the ABR crisis requires sustained intervention that includes efforts to improve poor antibiotic consumption practices by educating prescribers and patients, develop new antibiotics, and ensure proper antibiotic prescribing (e.g., right drug, proper dose, for an appropriate duration, when needed). In recent years, global efforts to identify and implement strategies to control the rising antibiotic resistance trend have increased (CDC, 2019; WHO, 2014; Obama, 2014; House, 2014; House, 2015; Dobson, et. al., 2017). A growing focus of these intervention strategies is the outpatient setting, where overuse of antibiotics is pervasive. At the outpatient level, increased antibiotic stewardship offers an increased likelihood of stemming resistance (Klepser, et. al., 2017; Zetts, et. al., 2018) and has the potential to extend the effectiveness of antibiotics approved for human use and slow the loss of antibiotic efficacy.

The 2020-2025 National Action Plan for Combating Antibiotic-Resistant Bacteria outlines numerous objective and milestones. Under Goal 1, Objective 2 prioritizes an action to "Engage the public and other stakeholders to develop, expand, and increase national and State education, training, and communication campaigns focused on using antibiotics responsibly, stopping the spread of antibiotic resistance, and preventing infections and life-threatening conditions like sepsis" (Federal Task Force on Combating Antibiotic-Resistant Bacteria, 2020).

This study was designed to collect information on outpatient knowledge, beliefs, and practices to guide the development of interventions to improve outpatient stewardship practices that will change the trajectory of antibiotic resistance and improve public health.

Conceptual Framework

Social and behavioral science theories allow researchers to analyze human behavior. These theories facilitate the understanding of past behavior and aid scientists in predicting future behavior. By providing a systematic way to understand people's actions, theories assist health researchers in moving beyond feelings or instincts toward an understanding of behaviors that are the foundation for developing and evaluating effective behavioral interventions (Glanz, 1997). These theories have been used to design health studies and interventions that impact health behaviors in areas such as TB and HIV/STD medication adherence, vaccination uptake, injury prevention, and exercise and healthy eating (Glanz, et. al., 2015).

This study used the Health Belief Model (HBM) as a framework to understand outpatient perceptions and knowledge that influence antibiotic stewardship practices. The HBM was also used to identify barriers, facilitators, and modifying factors affecting antibiotic prescription adherence.

The Health Belief Model (HBM) was developed in the 1950's as a tool to explain why U.S. Public Health Service medical screening and prevention programs for tuberculosis, cervical cancer, and dental disease, among others, were not successful (Rosenstock, 1974; Strecher & Rosenstock, 1997). The theory is one of the most widely used in health promotion and health education today (Janz & Becker, 1984).

The HBM model theorizes that people's beliefs about whether they are or are not at risk of acquiring a disease or health problem and their perception of the benefits of taking precautions to avoid it, influence their readiness to take action (Rosenstock, 1974; Strecher & Rosenstock, 1997). The HBM is centered on four constructs and, through a series of statements, measures: 1) perceived susceptibility and perceived severity, 2) perceived benefits and perceived barriers, 3) cues to action, and 4) self-efficacy. The HBM model by Janz and Becker, including the addition of self-efficacy, is presented in Figure 3.

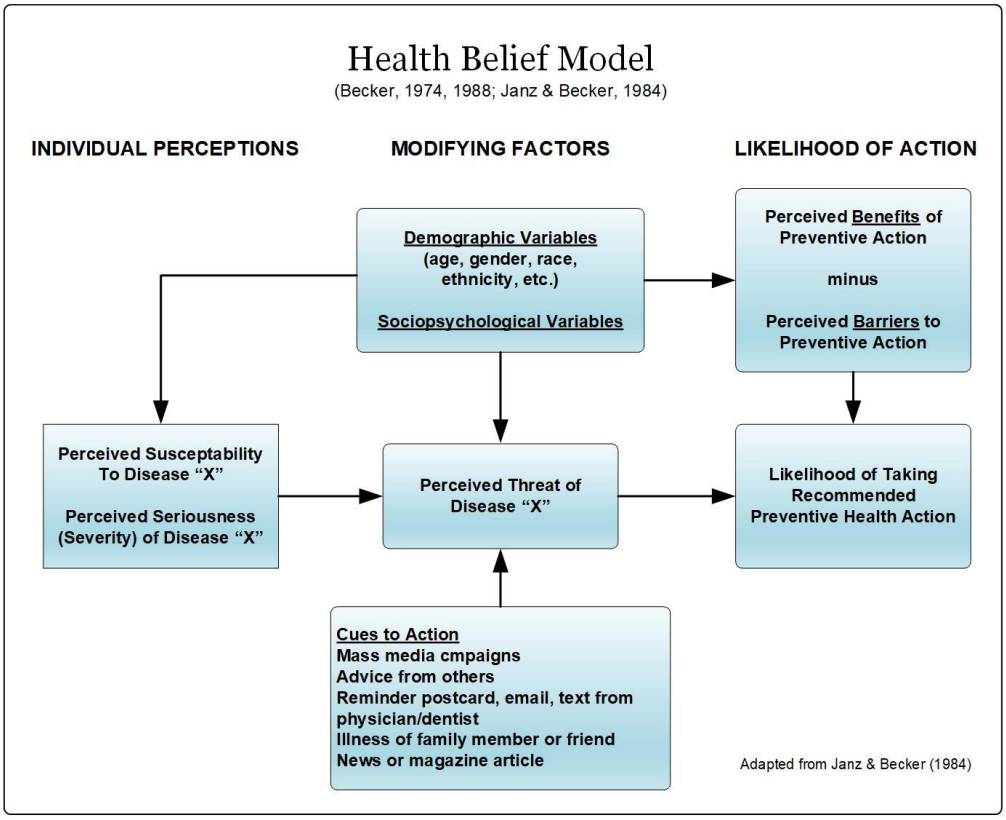


Figure 3: Conceptual Framework Model

More recently, the HBM has been used to understand hospitalized patients' (i.e., inpatient) and physician perceptions about antibiotic resistance and to prevent antibiotic resistance in healthcare settings such as hospitals and acute care facilities (Heid, et. al., 2016; Bush-Knapp, et. al., 2007). Key inpatient antibiotic resistance themes identified include: 1) a reduced perception of susceptibility to antibiotic-resistant infections when there was a high degree of trust in the patient's physician, 2) lack of understanding of how the ABR mechanism contributes to low perceived susceptibility, and 3) patients felt they should have a role in ensuring the appropriate use of antibiotics, however, the level of their involvement varied.

Given the successful adaptation of the HBM framework to study ABR in acute care settings with physicians and hospital patients, the HBM was selected for this study as a sound theoretical framework to assess the factors that drive individual outpatient adherence to prescription guidelines and good antibiotic stewardship practices.

Study Design

The purpose of this study was to identify factors that facilitate or impede individual (e.g., patient, parent of patient) adherence to antibiotic stewardship guidelines and to understand what encourages outpatients to or discourages them from requesting an antibiotic when not medically necessary. More specifically, the study was designed to answer the following questions:

1. What behavioral, normative, and control factors facilitate or impede individual outpatient adherence to antibiotic prescription guidelines?
2. What patient perceptions and preferences determine whether a patient will follow prescriber instructions?

The study used an exploratory mixed methods design, as described by Cresswell (2014). Applying this study design, qualitative data was collected and analyzed to inform the development of a quantitative survey instrument. Both the qualitative and quantitative data collection was guided by the HBM constructs.

The focus groups, conducted with 18 participants in seven separate sessions, served two primary purposes: it allowed the researcher to explore in greater detail the constructs, drivers, and subjective influences that guide outpatient use of antibiotics, and it identified areas of focus for the online survey.

A structured, close-ended survey, adapted from validated questionnaires, was refined based on the focus group results and informed by the HBM constructs. The survey was divided into six sections: 1) demographics, 2) healthy and unhealthy behaviors, 3) illness and healthcare visits, 4) vaccinations and antibacterial products, 5) antibiotic knowledge, and 6) 5-point Likert scale questions focused on knowledge, beliefs, and perceptions. The online survey was completed by 327 participants.

Population of Interest

Individuals visiting outpatient clinics and receiving antibiotic prescriptions in the U.S. are culturally diverse, with a broad age range and the potential for a variety of medical conditions. The decision was made to refine the population to a manageable group for analysis and generalizability.

The Affordable Care Act requires plans and issuers that offer dependent child coverage to make the coverage available until a child reaches the age of 26, regardless of marital status. At the other end of the spectrum, individuals become eligible for Medicare health insurance at age 65, unless they have a disability. To reduce the impact that older adults and younger children who may have more health conditions requiring more frequent antibiotics, adult females and males, ages 26-64 with no current, reported medical condition were recruited for the study. Additional criteria for inclusion in the study included individuals who spoke English and had access to the internet. Criteria for exclusion included individuals that lived outside of the United States, had a health or medical condition, or were unable to provide consent.

ResearchMatch, a nonprofit program funded by the National Institutes of Health (NIH) through a Clinical and Translational Science Award (CTSA), is a national registry available at no cost that connects volunteers with researchers in the United States (Harris, et. al., 2012). Volunteers provide general demographic information including contact information, date of birth, height, weight, gender, race, ethnicity, and tobacco use. With approximately 142,000 nationwide volunteers, of whom 34% or 48,280 report no medical condition, and the information available on each participant, the decision was made to use ResearchMatch to recruit participants for both the qualitative and quantitative phases of the study.

Sample Size

Focus Group Participants

The goal in identifying the number of focus groups and individuals participating in each was to ensure enough participants to understand individual perceptions and beliefs and to

obtain sufficient data to guide the refinement of the online survey. As many groups and participants increase the risk of repetitive data and require additional resources, an initial goal of 20-24 individuals was identified for recruitment.

The goal in composing each group was to have enough participants, balancing homogeneity and diversity, to encourage sharing within the group as well as allow for contrasting opinions. To accomplish this, the researcher planned to assign participants to a group based on their gender and age. However, a total of 24 participants, particularly with difficulties in scheduling, made it difficult to match participants.

In the end, after 18 individuals participated across seven focus groups, no new information was being collected so data collection was concluded.

Online Survey Participants

For the online survey, a sample size was calculated to allow for comparison of internal consistency between measures and a comparison of linear variables (e.g., demographic characteristics and antibiotic resistance constructs) using a standard regression analysis for population correlation ρ (see Table 2) (Arifin, 2018) Using an online sample size calculator, estimates were calculated for various levels of power, effect size, and significance (Arifin, 2022).

Table 2: Survey Sample Size Estimates

Sample Size Estimate: Correlation			
Power	**Correlation (effect size)**	**Significance Level**	**Sample Size (per group)**
80% (0.80)	Small (0.2)	95% (0.05)	194
	Moderate (0.5)		29
	Large (0.8)		10
85% (0.85)	Small (0.2)	95% (0.05)	222
	Moderate (0.5)		33
	Large (0.8)		11
90% (0.90)	Small (0.2)	95% (0.05)	259
	Moderate (0.5)		38
	Large (0.8)		12
95% (0.95)	Small (0.2)	95% (0.05)	319
	Moderate (0.5)		46
	Large (0.8)		14

Based on these calculations, a sample of 320 online survey participants was determined to be sufficient to detect a moderate effect size in all cases.

Ethics and Confidentiality

A request for Institutional Review Board (IRB) approval was submitted to the Office of Human Research Ethics at the University of North Carolina on May 5, 2020, and an exemption was granted on June 2, 2020 (see Appendix A). As a precaution, the registry "uses a clearinghouse model that blocks identifying information on a researcher's screen until the volunteer specifically gives approval to be contacted for a specific study" (Harris, et. al., 2012). Therefore, UNC's IRB exemption was submitted to ResearchMatch with a request to access the research database. Requests for access to ResearchMatch are automatically routed to the researcher's institution consortium liaison (a UNC employee) for confirmation and approval. The time span during which the registry can be accessed by a researcher corresponds to the study's IRB approval period. The first query for potential focus group participants was submitted to ResearchMatch on July 6, 2020, and the last survey participant query was on July 21, 2022.

Data Collection

Information on antibiotic behaviors, beliefs, and knowledge was collected sequentially using both qualitative and quantitative data collection. A list of potential participants was randomly selected using ResearchMatch and invited to participate, first in the focus groups and then in a randomly selected separate group for the online survey. ResearchMatch samples without replacement so once an individual is selected and accepts participation in a focus group, the individual is not eligible and will not appear in the sample pool for the online surveys.

All individuals who participated in this study were contacted via the ResearchMatch program. Several queries were submitted through the ResearchMatch program using study inclusion/exclusion criteria. The program generated a list containing general characteristics (e.g., gender, age, race, state, etc.) of potential matches. The researcher reviewed and approved

the lists. The program then sent the identified individuals an automated email with the study description and a message informing them that a researcher from UNC – Chapel Hill was interested in contacting them about a potential study. Interested individuals provided approval to share their contact information with the researcher. Using the list of interested individuals, the researcher emailed additional study details and information about the study consent process. The message sent to potential participants is found in Appendix B.

Those that met the inclusion criteria and agreed to participate completed an online consent form (see Appendix C for the focus group consent and Appendix F for the survey consent). Basic demographic information was gathered from ResearchMatch on focus group participants before participation. Survey participants completed demographic questions during survey administration. The sequence of data collection was completed as follows: collection and analysis of focus group data then online survey design, collection, and data analysis.

Focus Group Activities

After random selection via ResearchMatch, seven to ten potential participants were invited to take part in each 60-minute focus group session. As part of the invitation, individuals were informed that the purpose of the focus group was to help researchers understand how antibiotics are prescribed and used, and what individual behaviors and habits might improve or worsen antibiotic resistance. Those that agreed to participate were consented electronically and sent a confirmation email (see Appendix D) with the date, time, and a group-specific Zoom access link (audio only). An additional reminder was sent to participants two days before the scheduled group.

Focus groups were conducted from October 8, 2020 – August 23, 2021. All focus groups were conducted and recorded using the Zoom™ conferencing platform and transcribed into Microsoft® Word 365. After confirming written consent at the start of the session, focus group participants were reminded that the session was being audio recorded for transcription. The focus group moderator (researcher) followed a discussion guide (see Appendix E) that had been

previously pretested with 3 individuals meeting inclusion/exclusion criteria. The guide outlined the ground rules of the session and the questions to be asked and included pre-established probes. Focus group participants were encouraged to ask questions at the beginning of the session and as the session proceeded if they needed clarification. Both open-ended and semi-structured questions were asked of participants during the 60-minute sessions. Each session ended with a thank you to all participants and a reminder to keep responses confidential.

Immediately following each focus group, session recordings were transcribed, and the resulting transcript was compared with the original audio for quality and accuracy.

Survey Activities

The survey was developed and administered using Qualtrics®[XM] software (Provo, UT). The draft survey containing 99 questions was pilot tested, and minor changes were made to several questions to simplify the language and provide clarity. Seventeen queries, each requesting random identification of 1500 individuals meeting the study inclusion/exclusion criteria, were submitted to ResearchMatch. Like the focus groups, individuals randomly selected by ResearchMatch were provided a description of the study and invited to participate. Of the 25,500 initial queries, 608 individuals accepted the invitation and were provided with a personalized link to the Qualtrics survey.

Participant consent was obtained electronically prior to beginning the survey. The survey was active for seven weeks and participants completed surveys from June 14 – August 3, 2022. See Appendix G for a copy of the survey.

Data Analysis

Qualitative Analysis

Transcribed focus group sessions were reviewed to identify themes and to compare session responses across groups. Themes were coded and weighted by frequency of mention and correlation to HBM constructs. Themes and corresponding quotes were grouped for review and summation.

Quantitative Analysis

After the survey was closed, responses were exported to a Microsoft Excel spreadsheet and to SAS for analysis. Data were reviewed and participants who had completed less than 50% of the survey (n=9, 3%) were removed. One participant completed 66% of the survey, missing most of the Likert scale questions. No responses were modified, and missing data was not inputted. All analyses were based on complete cases.

Quantitative data were summarized using descriptive statistics derived from Microsoft® Excel 365 (Redmond, WA). All other statistical analyses were conducted using SAS® 9.4 software (Cary, NC). An antibacterial stewardship knowledge score was computed for each participant by summing the number of correct responses to knowledge-related questions (possible scores range from 0 to 14). For example, a "True" response to "Bacteria can become resistant to antibiotics" would contribute one point to the knowledge score. See Figure 4 for a distribution of knowledge scores. Similarly, a measure of self-reported healthy behavior was constructed using responses to questions regarding substance use, exercise, healthcare visits, and vaccination status (possible scores range from 0 to 16). See Figure 5 for a distribution of self-reported healthy behavior scores.

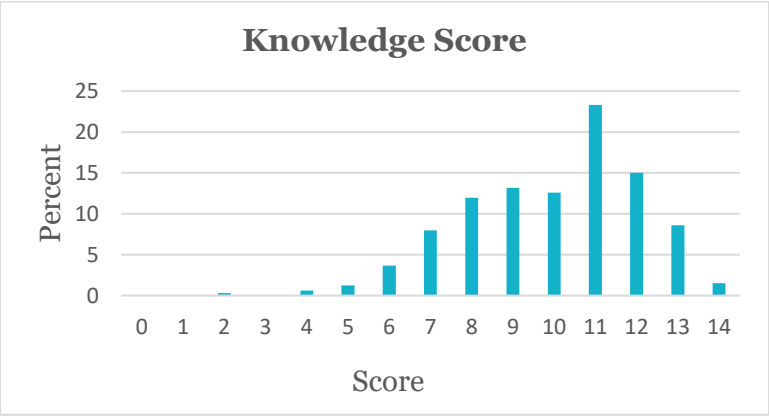


Figure 4: Distribution of Knowledge Score

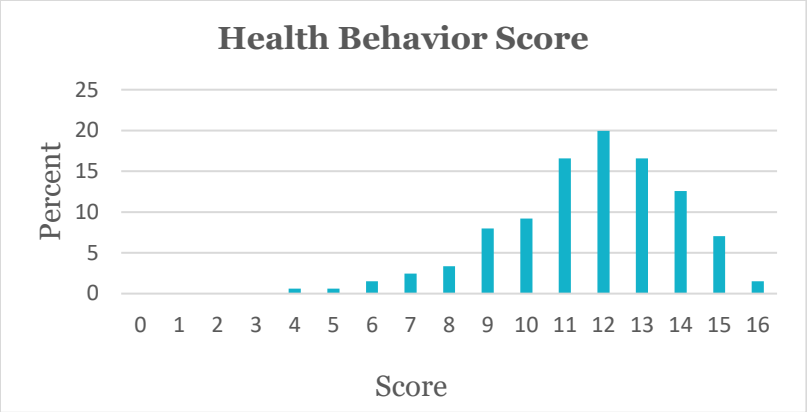


Figure 5: Distribution of Health Behavior Score

Within each health behavior model construct, survey items were summarized individually and in aggregate. Pairwise correlations between items within each construct were calculated. Cronbach α (1951) statistic was computed for each construct by assigning a numeric rank to Likert scale responses (e.g., 1=strongly disagree to 5=strongly agree) and are reported in Table 3 (Cronbach, 1951). Survey items phrased in the negative were reverse coded. When a set of survey items designed to measure a construct resulted in Cronbach α below 0.7, factor analysis was employed to identify potential latent structures. The latent class of items producing the best alpha was reported. When the number of survey items made factor analysis prohibitive, a "leave-one-out" approach was employed, and the single item resulting in best improvement to alpha was dropped.

Table 3: Reliability Statistics for HBM Constructs

Construct	Cronbach α
Barrier	0.495
Benefit	0.602
Cues to action	0.367[1]
Self-efficacy	0.566[2]
Severity	0.704
Susceptibility	0.827

1 Value obtained after removing one item from construct.

2 Based on the latent class of items identified via factor analysis that produced the highest α.

For four of the constructs, internal consistency was acceptable for all measures within the construct. For the constructs cues to action and self-efficacy, the measures did not have acceptable internal consistency; from the former (cues), one item was removed and for the latter (self-efficacy), factor analysis was conducted to extract maximum common variance from all measures. Following this, three of the six constructs (barrier, cues to action, and self-efficacy) did not meet the threshold of 0.6-0.7 for an acceptable level of reliability but were retained for analysis. To improve internal consistency in the future, additional measures could be added to the constructs where there were small numbers of measures (barrier=4 measures, cues=2, and self-efficacy=3).

To assess relationships between survey items, constructs, and derived score variables, a series of generalized linear models (McCullagh & Nelder, 1989) were fitted. All models were adjusted for confounders (educational attainment, age, region, marital/partnered status, parent/nonparent status, and any recent healthcare encounter). Linear regression models were employed for health behavior score and Likert-scale survey item outcomes. The tenability of the normality assumption was assessed graphically (via q-q plots). Negative binomial regression was used to model the number of prescriptions (a right-skewed count variable). Point estimates, 95% confidence intervals and *p*-values for all model terms are reported. A *p*-value of $<.05$ was considered significant.

CHAPTER 4: RESULTS

Focus Groups

Eighteen individuals randomly selected via ResearchMatch participated in one of seven focus groups conducted on the Zoom™ conferencing platform. Demographic characteristics of the focus group population sample are presented in Table 4. The average age of participants was 43 years, and the median age was 41 years. Fourteen (78%) of the individuals were female, 15 were white (83%) and 17 were non-Hispanic (94%). Participants were generally dispersed across the United States with six (33%) in the West, five (28%) in the Midwest, four (22%) in the Northeast, and three (17%) in the Southeast. There were no participants from the Southwest region. The group discussions were designed to assist researchers in understanding how individuals are prescribed and take antibiotics, and what antibiotic stewardship behaviors could improve or exacerbate antibiotic resistance. Focus group data was used to refine an online questionnaire administered nationwide.

Antibiotic Stewardship Knowledge

Participant knowledge on what antibiotics are used for, how to take them, and what to take them for, was largely correct as demonstrated here:

> "I'm quite scared of them. . .my understanding is that the antibiotic resistance, it's a type of bacteria that doesn't respond to the usual antibiotics that are commercially available, so it might require a custom medicine or something to get rid of it or there might not even be a medicine to treat it at all."

> "For viral stuff they're ineffective. . .if it's the flu, you want Tamiflu not amoxicillin or Augmentin."

> "I'm aware that you only take it for bacterial type infection, and you don't want to take them any more than you have to."

> "By MRSA, do you mean Methicillin-resistant Staphylococcus aureus? Yeah, the C Diff, and Clostridium difficile, the MRSA and all those things. . .tuberculosis, I think

> generally, virtually every strain of tuberculosis is somewhat antibiotic-resistant now. I'm very familiar with those."
>
> "Yes, so antibiotic resistance, or if something has developed antibiotic resistance, it no longer can be killed by a specific antibiotic and so I know there's kind of a super resistant ones where all of the different, it's developed that resistance to all the, most of the available antibiotics."

Most of the individuals across the groups were aware that you can take antibiotics for bacterial infections and not for viral infections. This may be attributed to participants from ResearchMatch being primarily employed by universities or in health care settings (see employment demographics of survey participants in Table 4). There was mixed knowledge about how to take antibiotics and how to prevent an ABR infection; however, some participants noted that preventative measure for the recent COVID pandemic (e.g., masking, physical distancing) would likely be applicable to preventing ABR infections.

Experiences with Antibiotics

Most of the focus group participants had some experience taking antibiotics themselves or with a family member taking antibiotics.

> "I did have to take them probably about just about two years ago now. And I always, I always complete them because I know that's very. . .well, they always say it's very important. I always complete them."
>
> "I have not taken antibiotics much in my life. I've been fairly healthy, thankfully. I think I've only taken them once that I can recall, one time in college."

Those that experienced negative side effects had strong feelings about taking antibiotics in the future. The following are representative responses:

> "Unfortunately, they didn't give me one that was strong enough and that just compounded the issue. . .and I had to take the antibiotics, a lot longer in the end, because then they had to give me a stronger one."
>
> "I have four boys and my wife. And so, in our family, the kids when they were smaller, you know, went through ear infection after ear infection after ear infection. I was trying to find somebody who'd sell me amoxicillin by the 55-gallon drum."
>
> "Amoxicillin, you're throwing out a word that scares the living wits out of me because it really did a number on the kids. I think that was the one that did a number on one of the kid's stomach and luckily, we didn't have to after, again, our second child had a lot of ear infections. And from there on out, we didn't have to do too much with antibiotics"

Some participants talked about avoiding antibiotics and most drugs, if possible.

Leftover Prescription Antibiotics

We know that participants don't always finish prescriptions, either because they feel better and decide not to complete the prescription or because they experience side effects that make it difficult to complete the prescription (McNulty, 2007). For this reason, participants were asked what they do if there are leftover antibiotics after finishing a prescription.

> "If it was one or two, I would probably just throw them away."
>
> "I keep them. I know I keep them in case I ever need them. I don't share them with anybody, but I keep them."
>
> "The couple of times that I have had an adverse reaction, honestly, they go in my fridge, they sit there for about a year, with all the cat antibiotics and stuff of that nature. And then about once a year, I go through and I do a purge and I will admit, I am a horrible person, I throw them in the trash."
>
> "I feel like I've had leftovers before and just kind of discarded them, because as I mentioned before, I usually feel better. . .before the end, before I ran out and so there's usually been extras. I just threw them away, didn't really share them with anybody, but just discarded them."
>
> "I have always finished my antibiotics. If I've had medicine, I've thrown them in the garbage, but I probably should flush them down the toilet now that you asked the question."
>
> "If I have [leftover] pills, I flush them down the toilet."

Participants generally responded that they would throw them away or flush them. One or two talked about disposing of them at drop off sites such as drug stores or police departments because of the risk antibiotics pose to the public water supply when flushed down the toilet or when liquid antibiotics are rinsed down the sink. Upon hearing about drop off sites, participants who were not previously familiar with them talked about finding their local drop off site next time they need to dispose of antibiotics.

Antibiotic Resistance Education Programs

The CDC has been working to educate and inform the public about the appropriate use of antibiotics. An early campaign, "Get Smart: Know When Antibiotics Work," launched in 1995

and formed the axis around a program in which state-based, non-profit and for-profit organizations participated (APUA, 2013). A “Get Smart About Antibiotics” week was introduced and promoted with various activities. The week corresponded with other international antibiotic awareness days in Australia, Canada, and the European Union.

In 2003, the CDC launched a new campaign, “Be Antibiotics Aware: Smart Use, Best Care,” to promote awareness and proper antibiotic use (CDC, 2003). Despite the regular annual awareness weeks and the resources and education provided to patients, healthcare professionals, and state health departments, none of the focus group participants could remember seeing any antibiotic resistance campaigns in the doctor’s office or elsewhere. When asked if they had seen handouts or displays in the doctor’s office about antibiotic resistance, they answered:

> “I just can't recall seeing any but that doesn't mean any. . .that doesn't mean they weren't there.”
>
> “I'll be honest, I usually go through the drive thru to pick up my prescription, so I don't recall seeing anything. My doctor doesn't really have that kind of stuff put up in his waiting room.”
>
> “Negative. I've never heard that.”

Although tailored for patients, their colleagues, family, and friends, and for health care professionals, it is not clear whether there is good uptake of the program and its corresponding materials. This might be a resource that could be explored further and encourage use of CDC “Be Antibiotics Aware” campaign material, graphics, and videos by physician practices and pharmacies to reach patients and the wider community.

Important Antibiotic Focus

All participants had an opinion when asked what the most important issue was related to antibiotics. A sample of responses include:

> “To me it’s understanding why they're used, when they're used and doing, following the purpose of them. You know, you don't get a triangle and use that as a substitute for a wheel. It just won't work.”

> "I would like to hope that there are fewer and fewer people who go to the doctor and demand antibiotics, at this point in time. As I say, my brother-in-law and sister-in-law were people that did do it in the past. I'd like to think that they don't do it anymore."

> "Knowing to take the full dose of them, especially if you're a provider or your pharmacy doesn't make that clear. Just, you know, knowing to take a full dose because if not, then it could add to the resistance."

> "Just to take them when they're absolutely necessary. Because without doubt, antibiotics can treat a lot of diseases that like, you know, people were dying before the discovery of, before they discovered antibiotics. But nowadays, they are overprescribed obviously, in some part of the world more than others."

Most agreed that a primary focus of an antibiotic stewardship program should be to take antibiotics only when necessary and to take them as prescribed. One individual summarized it as, "They [antibiotics] should not be abused or the bacteria is going to beat us because they're going to get stronger."

Finally, one participant provided a notable point that best describes the issue of antibiotic resistance: "I certainly see the antibiotics as one of those medicines that has probably made modern life possible in the past 50 years, and if we lose them then we might have a significant population collapse. And I don't think that's hyperbole."

The focus groups presented an opportunity to hear how representatives from the target population view antibiotic stewardship practices, resistance, and perceptions. The qualitative data was used to refine the online survey. Some questions with similar themes, measuring the same construct were removed. In addition, a question was added asking participants about their experience in healthcare, to control for potential confounding, after noticing a larger number of focus group participants that had a healthcare background.

Survey

Of the 608-survey links sent to ResearchMatch individuals expressing interest, 348 (57%) opened the link and of those, 335 (96%) provided responses. Of the 335 participants, 326 (97%) completed 50% or more of the survey and were included in the analyses (eight participants did not progress beyond the consent form; one participant each only completed

25% and 66% of the survey). The demographic characteristics of the survey population sample are presented in Table 4. Among the remaining 326 participants, the median age was 38 years (range 26-64). Two-hundred fifty-two (252) of the survey participants were female (78%), 265 self-identified as white (84%) and 289 were non-Hispanic (88%). One-hundred one (31%) were in the Southeastern United States, with 80 (25%) in the Midwest, 66 (20%) in the Northeast and 63 (20%) in the West, and 13 (4%) in the Southwest.

The participants were highly educated with 88% having a degree (4% associate, 35% bachelor, 48% graduate). The largest percentage of participants were married (58%) or living with a partner (10%), with the next largest group being single (23%). Half of the participants had one or more children (51%). Eighty-seven percent (87%) of the participants were employed, with 61% working 40 or more hours per week and 26% working 1-39 hours per week. The remaining non-employed participants were either retired (6%), not looking for work (5%), looking for work (2%) or disabled (< 1%). Interestingly, 28% of the participants identified as a current or previous healthcare worker (MD, RN, CNP, PA, home care, or hospital administrator) which is higher than the general population, of which approximately 10% of U.S. workers were employed as health care technicians and practitioners in 2019, according to the U.S. Census Bureau (Laughlin, et. al., 2021).

Antibiotic Stewardship and Risk Behaviors

When queried, 80% (n=261) of survey participants had seen a health care provider in the last 12 months and 14% (n=36) of those had seen the provider five or more times during the period. Approximately 72% of the participants had been prescribed an antibiotic in the last 12 months. Eighty percent (80%) of participants correctly acknowledged that antibiotics do not help reduce cold and flu symptoms, but only 70% agreed that the way that <u>others</u> use antibiotics

Table 4: Demographic Characteristics of Participants

Characteristic		Focus Groups Total = 18		Survey Total = 327	
		N	%	N	%
Age	26-35	6	33.3	134	41.1
	36-45	4	22.2	80	24.54
	46-55	4	22.2	58	17.79
	56-64	4	22.2	54	16.56
	Total	18	100.0	326	100.0
Gender	Female	14	77.8	252	77.06
	Male	4	22.2	75	22.94
	Total	18	100.0	327	100.0
Race	White	15	83.3	265	84.1
	Black or African American	0	0.0	26	8.3
	American Indian or Alaska Native	0	0.0	2	0.6
	Asian	1	5.6	14	4.4
	Native Hawaiian or Pacific Islander	0	0.0	0	0
	Other	2	11.1	6	1.9
	Prefer not to say	N/A	N/A	2	0.6
	Total	18	100.0	315	100.0
Ethnicity	Not Hispanic/Latino	17	94.4	289	88.4
	Hispanic/Latino	1	5.6	36	11.0
	Unknown	N/A	N/A	1	0.3
	Prefer not to say	N/A	N/A	1	0.3
	Total	18	100.0	327	100.0
Region	Northeast	4	22.2	66	20.4
	Midwest	5	27.8	80	24.8
	Southeast	3	16.7	101	31.3
	Southwest	0	0.0	13	4.0
	West	6	33.3	63	19.5
	Total	18	100.0	323	100.0
Education	Less than high school			0	0.0
	Some high school (no diploma/GED)			1	0.3
	High school diploma or GED			10	3.1
	Some college, no degree			29	8.9
	Associate degree			16	4.9
	Bachelor's degree			115	35.2
	Graduate degree			156	47.7
	Total			327	100.0
Marital Status	Married			188	57.5
	Living with partner			33	10.1
	Widowed			4	1.2
	Divorced			23	7.0
	Separated			3	0.9
	Never married			76	23.2
	Total			327	100.0
Number of Children	0			159	48.9
	1			37	11.4
	2			85	26.2
	3			27	8.3
	4			13	4.0
	5			4	1.2
	Total			325	100.0
Healthcare Worker	No			234	72.0
	Yes			91	28.0
	Total			325	100.0

affects their chance of getting an antibiotic-resistant infection, with even less (18%) agreeing that how they use antibiotics affects others' chance of getting an antibiotic-resistant infection.

Further, 78% agreed with the statement, "People can become resistant to antibiotics" when, in fact, it is the "Bacteria [that] can become resistant to antibiotics" (95% agreed). An individual's perceived impact on other individuals was low, with only 25% recognizing that antibiotic resistance can spread from person to person. See Table 5 for additional information on survey participants' antibiotic stewardship knowledge and perceptions.

Table 5: Participant Knowledge and Perceptions about Antibiotics and Resistance

Knowledge and Perceptions	True		False		Don't know	
	N	%	N	%	N	%
The body fights mild infections on its own without antibiotics.	315	96.9	6	1.8	4	1.2
Antibiotics help reduce cold and flu symptoms.	50	15.3	261	80.1	15	4.6
Antibiotics help reduce symptoms of strep throat, whooping cough, and urniary tract infection.	282	86.8	29	8.9	14	4.3
Skipping one or two doses of an antibiotic does not contribute to antibiotic resistance.	35	10.7	226	69.3	65	19.9
How other people use antibiotics doesn't affect my chance of getting antibiotic resistant infections.	61	18.8	230	70.8	34	10.5
People can become resistant to antibiotics.	252	77.5	51	15.7	22	6.8
Antibiotic resistance can spread from animals to humans.	104	32.0	64	19.7	157	48.3
To reduce the risk of resistance, antibiotics should be stopped immediately when the individual feels better.	24	7.4	292	89.6	10	3.1
How I use antibiotics doesn't affect other people's chance of getting antibiotic resistant infections.	58	17.8	230	70.8	37	11.4
Bacteria can become resistant to antibiotics.	308	94.5	6	1.8	12	3.7
Antibiotic resistance can spread from person to person.	80	24.6	144	44.3	101	31.1
People should keep leftover or unused antibiotics for the next time they are sick.	18	5.5	298	91.4	10	3.1
It is okay to share antibiotics with family or friends when they are sick with the same symptoms.	16	4.9	305	93.6	5	1.5
If taken too often, antibiotics are less likely to work in the future.	269	82.5	24	7.4	33	10.1
I know someone such as a family member or friend who has experienced antibiotic resistant infection (for example, C. Diff or MRSA).	121	37.1	177	54.3	28	8.6
I know if I need antibiotics before I see my doctor.	67	20.6	215	66.2	43	13.2
It is my right to ask for an antibiotic from my doctor.	159	48.8	112	34.4	55	16.9
I would change doctors if my doctor didn't prescribe an antibiotic when I ask for one.	18	5.5	266	81.6	42	12.9
I would rather take an antibiotic that I may not need than wait to see if I get better without it.	34	10.4	268	82.2	24	7.4
I trust my doctor when they tell me I don't need antibiotics.	300	92.0	9	2.8	17	5.2

When it comes to the potential impact of antibiotic resistance on an individual or their family, 71% agreed/strongly agreed that the thought of getting an antibiotic-resistant infection scared them. Sixty-five percent (65%) agreed/strongly agreed that if they got an ABR infection,

they might die and 73% agreed/strongly agreed that if they got an ABR infection, their family would be negatively affected.

It was unclear whether participants lacked knowledge, motivation or desire when addressing their capacity to make an impact on ABR. Thirty-two percent (32%) of survey participants agreed/strongly agreed and 45% were neutral (neither agree nor disagree) that they could help with the ABR problem. Only 45% agreed/strongly agreed that they feel they must help with the ABR problem when reading about it on the internet. At the same time, 75% acknowledged they could go without an antibiotic prescription if their doctor told them how to deal with their symptoms. Connecting potential impact of ABRs and an interest in helping with the right tools or steps might aid in the fight against ABR infections.

Regression Analysis

Regression analysis was used to identify potential relationships between the survey variables. Both the knowledge and healthy behavior models have been previously defined in the data analysis section. First, a linear regression was conducted to determine if greater antibiotic stewardship knowledge could be used to predict self-reported healthy behavior. Data suggest that a higher antibacterial stewardship knowledge score was associated with a slightly larger number of self-reported healthy behaviors, while controlling for the effect of confounders, p = .0017 (see Table 6). So that, on average, for every one-unit increase in knowledge score, the value of health behavior score increased by 0.18.

Next, a linear regression was conducted to determine if the participant's level of belief that medical experts would solve the ABR problem was associated with the idea that if sick, they could "tough it out" without an antibiotic prescription. Here, data suggest a higher level of belief that experts will solve the ABR problem is associated with a lower belief that the participant can tough it out without an antibiotic, while controlling for the effect of confounders, p = <.001 (see Table 7). So that, on average, for every one-unit increase in the participant's belief that medical

Table 6: Effect of Level of Knowledge on Health Behavior

Variable	Estimate	95% Confidence Interval	p-value
Intercept	11.02	(10.20, 11.84)	<.0001
Knowledge score	0.18	(0.07, 0.29)	0.0017
Bachelor's degree or higher education	1.37	(0.73, 2.00)	<.0001
Age	0.04	(0.02, 0.06)	0.0001
Partnered	0.50	(-0.03, 1.03)	0.0631
Has children	-0.68	(-1.19, -0.17)	0.0086
Northeast region*	0.34	(-0.31, 0.99)	0.3006
Midwest region*	0.07	(-0.55, 0.69)	0.8249
Southwest region*	-0.28	(-1.48, 0.93)	0.6522
West region*	0.32	(-0.35, 0.98)	0.3458
Been to provider in past 12 months	-0.85	(-1.43, -0.28)	0.0037

* Reference category is Southeast region.

experts will solve the ABR problem (on the Likert scale), the value of the participant's self-reported ability to go without an antibiotic prescription (on the Likert scale) decreased by 0.22.

Table 7: Effect of Degree of Belief Experts will Solve ABR Problems on Ability to Tough it Out Without Antibiotic

Variable	Estimate	95% Confidence Interval	p-value
Intercept	3.55	(3.17, 3.93)	<.0001
Degree of belief that experts will solve the problem of antibiotic resistance	-0.22	(-0.33, -0.11)	0.0001
Bachelor's degree or higher education	0.09	(-0.20, 0.38)	0.5480
Age	0.01	(-0.00, 0.02)	0.1573
Partnered	-0.01	(-0.25, 0.23)	0.9345
Has children	-0.09	(-0.32, 0.15)	0.4620
Northeast region*	0.10	(-0.20, 0.39)	0.5260
Midwest region*	0.37	(0.09, 0.66)	0.0108
Southwest region*	0.04	(-0.51, 0.59)	0.8880
West region*	0.29	(-0.01, 0.60)	0.0596
Been to provider in past 12 months	0.21	(-0.05, 0.48)	0.1084

* Reference category is Northeast region.

Several other regressions were conducted including:

- Effect of Level of Concern about Getting an ABR Infection on Health Behavior
- Effect of Level of Knowledge on Number of Antibiotic Prescriptions in the Last 12 Months

- Effect of Being Able to go Without AB Prescription if Deal with Symptoms on Number of Antibiotic Prescriptions in the Last 12 Months
- Effect of Perceived Susceptibility to ABR Infection on Number of Antibiotic Prescriptions in the Last 12 Months
- Effect of Participant's Degree of Belief that Experts will Solve the ABR Problem Before it Becomes too Serious on Their Perceived Ability to Help with the ABR Problem

Corresponding tables have been included in Appendix H. However, for these variable pairs, no strong and statistically significant correlations were observed. With the amount of data available from this study, further analyses could be conducted to identify potential additional correlations between variables.

Beliefs and Perceptions

A series of 5-point Likert scale questions was included in the online survey to capture information on people's beliefs and perceptions about health, antibiotic resistance, and the risk of acquiring an antibiotic-resistant infection. Twenty-five of the questions used a scale from strongly disagree to strongly agree. The frequency of responses assessing who is at risk of acquiring an ABR infection, how the infections are spread, and what encourages/discourages proper antibiotic stewardship are included in Figures 6 through 15.

Most participants, as noted in Figure 6, were aware that bacteria become resistant to antibiotics (95%, n=308) [correct=true]; however, 78% (n=252) also thought that people become resistant to antibiotics [correct=false], with 16% (n=51) disagreeing and 7% (n=22) who were not sure. A third of participants (see Figure 7) agreed that ABR infections can spread from animals to humans (32%, n=104) [correct=true], but 20% (n=64) disagreed and 48% (n=157) were not sure. This leaves room for additional education of patients and the community about how ABRs are spread and how they are not. Educational programs, similar to the CDC's "Be Antbiotics Aware" program, that incorporate materials such as posters, brochures, and handouts from physicians when prescribing an antibiotic or from pharmacists when receiving one, have potential to reach patients.

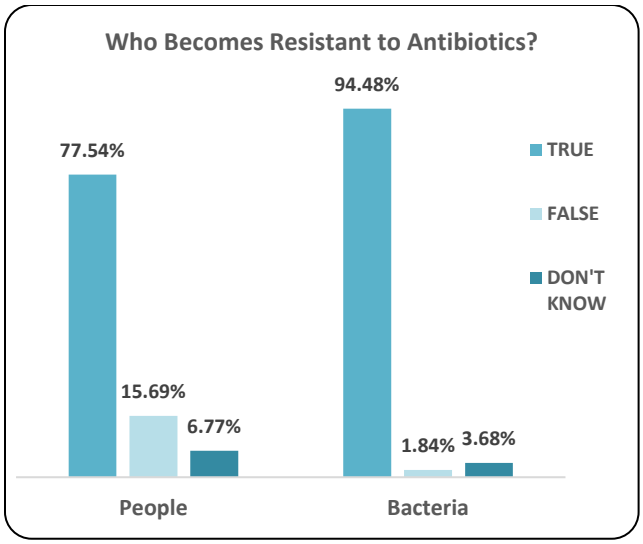


Figure 6: Resistance to Antibiotics

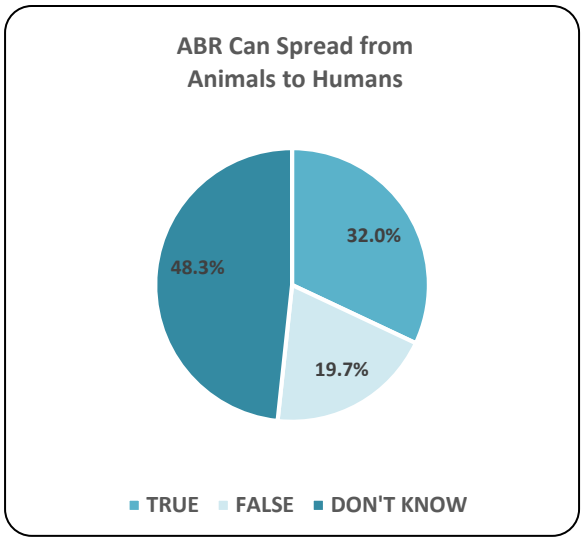
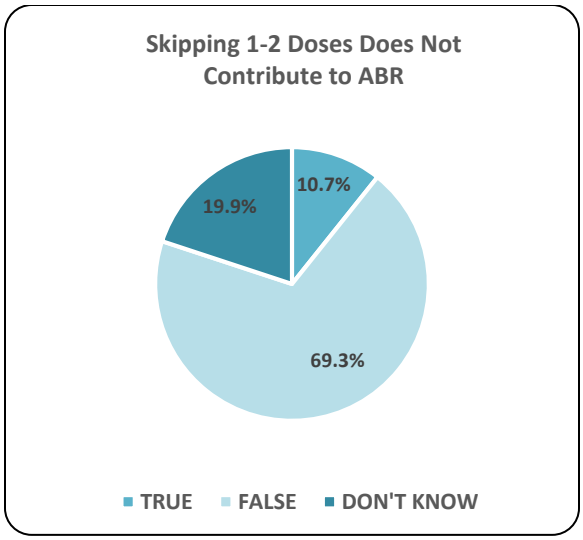


Figure 7: ABR Spread from Animals to Humans

Like the misconceptions on the spread of ABR infections, participants' perceptions on how resistant bacteria occur were less clear. Figure 8 shows that 69% (n=226) of study participants correctly disagreed that skipping 1-2 doses of antibiotics does not contribute to ABR infection [correct=disagree]. The remaining participants that answered this question either agreed (11%, n=35) that skipping doses does not contribute to ABR infection or were not sure (20%, n=65). Next, in Figure 9, 60% (n=195) said that they did not throw away leftover antibiotics when they had them but 40% (n=128) agreed that they did throw leftover antibiotics away. During the focus groups discussions, some participants noted that they flushed them down the toilet and others said they threw them away. A couple of focus group participants shared with their groups that they take leftover prescriptions to proper disposal locations (e.g., drug store or police stations that accept leftovers a couple of times a year). Their fellow group participants were eager to hear about this method of disposing of leftover prescriptions and asked many questions so that they could use these locations in the future. It seems that there is also an opportunity to provide information on proper antibiotic disposal to patients and the larger communities.



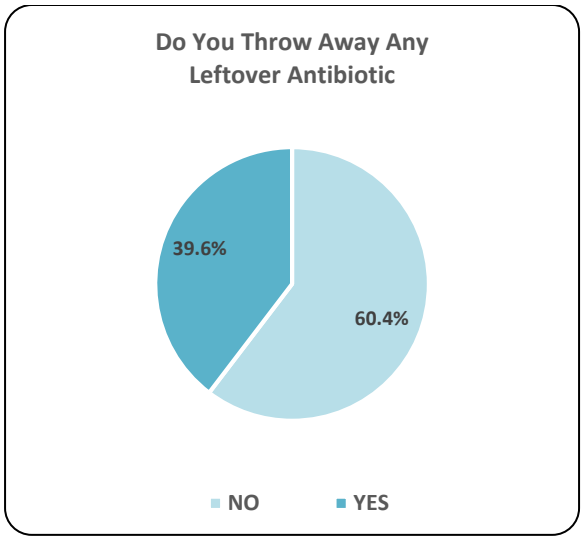
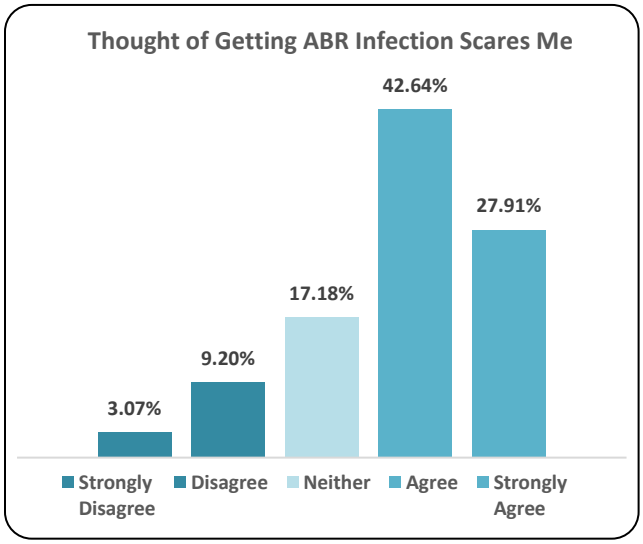


Figure 8: Skipping Antibiotic Doses ***Figure 9: Disposing of Antibiotics***

The next two questions relate to the awareness of ABR infections and to the impact that has on participants. Figure 10 shows that 71% of survey participants either agreed (43%, n=139) or strongly agreed (28%, n=91) that the thought of getting an ABR infection scared them, with only 12% disagreeing (9%, n=30) or strongly disagreeing (3%, n=10); 17% (n=56) neither agreed nor disagreed. In Figure 11, 54% (n=177) of survey participants reported that they did not know



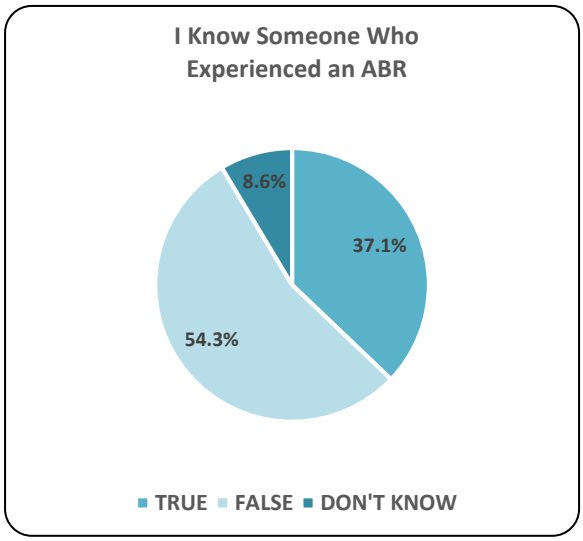
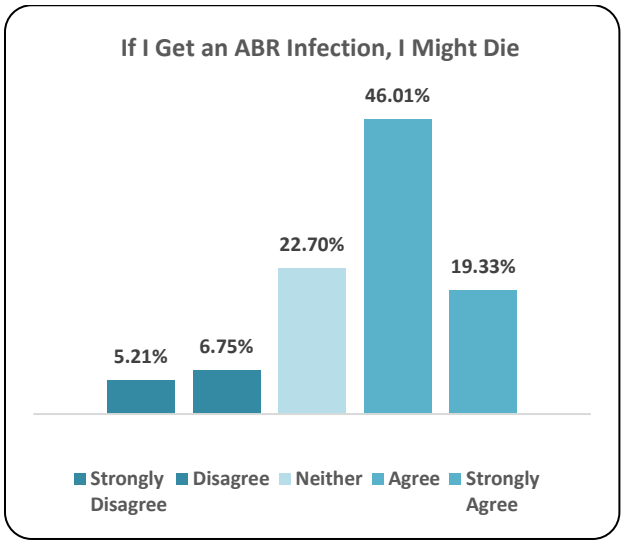


Figure 10: Fear of Antibiotic-Resistant Infection ***Figure 11: Others with ABR Infection***

someone who had experienced an ABR infection, whereas 37% (n=121) said they did know someone and 9% (n=28) were not sure. The number of individuals who did know someone with

an ABR infection may be inflated since a higher number of survey participants than the average population were associated with a healthcare profession. Using the Health Belief Model as an explanatory framework, it appears that a higher number of participants recognize the risk of acquiring an ABR infection and this perceived susceptibility may be used when developing future interventions, stimulating action by patients to prevent risk.

Where perceived susceptibility was observed in Figure 10, Figures 12 and 13 indicate potential perceived severity if an ABR infection is acquired. Figure 12 shows that 65% of survey participants either agreed (46%, n=150) or strongly agreed (19%, n=63) that if they were to contract an ABR infection, they might die, with 12% either disagreeing (7%, n=22) or strongly disagreeing (5%, n=17); 23% (n=74) neither agreed nor disagreed. Seventy-three percent (73%) of study participants either agreed (49%, n=160) or strongly agreed (24%, n=78) that if they



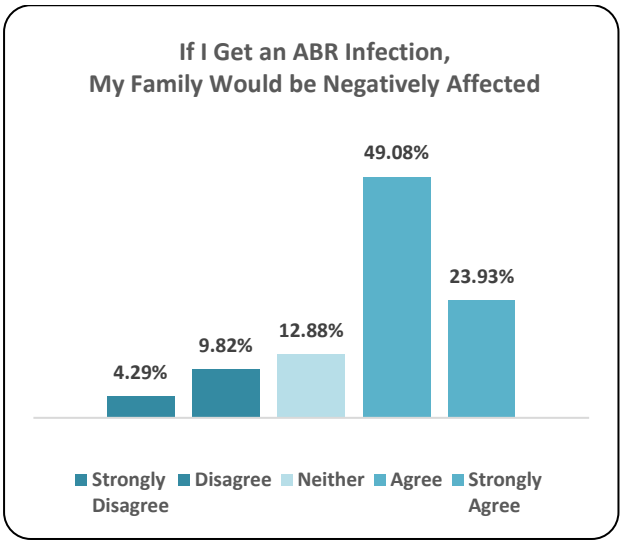
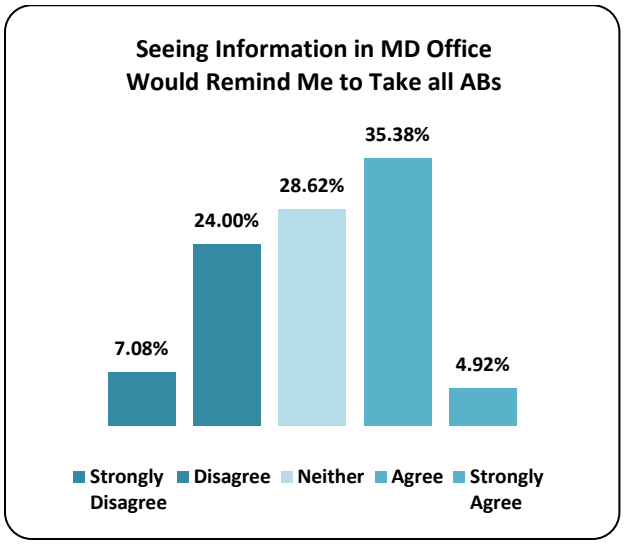


Figure 12: Consequence of ABR Infection ***Figure 13: Impact on Family***

were to contract an ABR infection, their family might be affected, whereas 14% either disagreed (10%, n=32) or strongly disagreed (4%, n=14); 13% (n=42) neither agreed nor disagreed (see Figure 13). Since perceived severity can be influenced by many factors such as medical consequences (e.g., death or amputation if an ABR infection is untreated) and social consequences (e.g., loss of job, inability to support family), it is unclear what each participant

considered when responding to the questions. Therefore, these two perceptions could benefit from additional research to further understand what consequences influence an individual's perceived severity.

Based on focus group and survey responses, it was unclear if participants had been exposed to education programs such as "Be Antibiotics Aware" and had not seen them or if they had not been exposed. The expectation is that CDC pilot tested the materials but information on the development and testing of the toolkit components was not available online. CDC continues to make the educational materials available in their partner toolkit and promote knowledge and understanding during the annual antibiotic awareness week in November each year. Using the toolkit components in future interventions and educational programs could be valuable and reduce the cost of developing all new material.



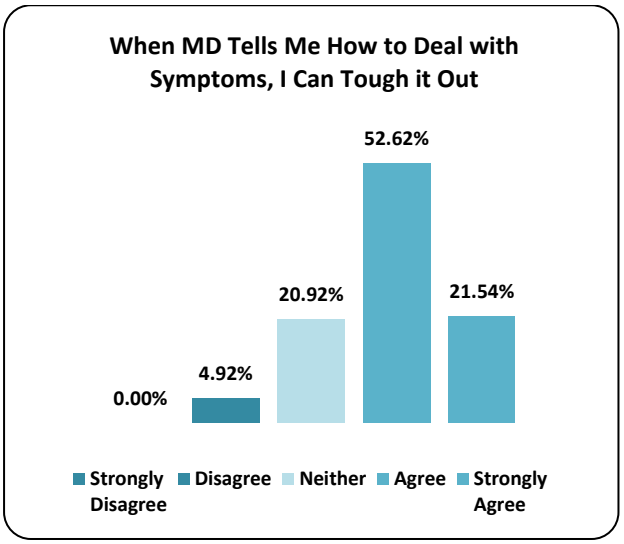


Figure 14: Impact of Education Program ***Figure 15: Dealing with Symptoms of Illness***

Figure 14 shows that 40% of survey participants agreed (35%, n=115) or strongly agreed (5%, n=16) that seeing information such as the "Be Antibiotics Aware" campaign in their physician's office would encourage them to complete a course of antibiotics. Almost a third (31%) of participants disagreed (24%, n=78) or strongly disagreed (7%, n=23); 29% (93) neither agreed nor disagreed. What is unclear is whether the 35% of participants that agreed or strongly

agreed would have completed the full course of antibiotics regardless of exposure to the campaign or if the campaign would have no impact. Further data is needed if this were to be considered for inclusion in a future intervention.

One area that may be valuable in reducing ABR is providing patients with clear information on how to deal with symptoms when their diagnosis does not necessitate an antibiotic prescription. In Figure 15, we see that 74% of survey participants either agreed (53%, n=171) or strongly agreed (22%, n=70) that they could go without an antibiotic if the physician provided information on how to deal with their symptoms. Based on the literature, it is increasingly the case that prescriber's perceptions that patients or parents of patients expect to receive an antibiotic is not tied to patient satisfaction when no prescription is provided (Dobson, et. al., 2017; Klepser, et. al., 2017; Zetts, et. al., 2018). This is another area for further exploration when developing future interventions to reduce ABR infections.

Discussion

The overuse of antibiotics and antimicrobials leading to antibiotic-resistant infections is a serious concern for global health and the economy. As observed in Chapter 1, outpatient prescribing accounts for more than 60% of antibiotic use in humans. Although research on outpatient antibiotic stewardship has expanded in recent years, there continues to be room for greater understanding of the problem and the development of approaches to improve outpatient antibiotic stewardship.

Exploring outpatient antibiotic resistance knowledge, beliefs, and perceptions through the lens of the HBM provided an opportunity to understand how an individual perceives their risk of contracting an ABR infection, what actions, if taken, could reduce that risk, and what motivates them or discourages them from taking action. What the HBM cannot explain are individual habits, social motivation, economic factors, and equal/unequal access to information that may exist or influence behavior.

During all phases of the study (e.g., focus groups, survey development, data analysis, etc.), valuable information was obtained. The literature review sought to understand what successful individual education programs and interventions exist to address ABR in outpatient settings. Although several programs addressed prescriber and pharmacist outpatient practices, few were found to focus on patients and communities overall. Furthermore, none were theory-based.

By using theory to design this study, it allowed deeper explanations and interpretation of seemingly disparate data. It also allowed a richer analysis of the data, beyond just descriptive analysis. Using the HBM provided the framework to allow a more rigorous and credible way to identify new insights into understanding antibiotic use in outpatient settings.

With the incorporation of focus groups, important insight was gleaned from the sample population to clarify what was meaningful and not meaningful, and how they felt or thought about topics related to ABR. Group participants were aware of the existence of good bacteria and bad bacteria. They also knew that if you take antibiotics often, they were less likely to work in the future and knew how ABR occurred. Group participants, generally, felt engaged by prescribers in their treatment plan and were okay if their doctor told them they did not need an antibiotic prescription. This suggests group participants were knowledgeable about antibiotic resistance and the risks to the general population; however, they did not consider their family members to be at a similar level of risk. About half the group participants disagreed that there was a chance their family members could get an ABR infection. Likewise, approximately one-fifth of the group participants felt that ABR would not affect their community. One approach to increasing good antibiotic stewardship practices might be to appeal to individual's concern about their family and community. Using this information and other focus group results, survey questions were developed and refined to test assumptions and determine what approaches might be used to change outpatient behavior.

Data was collected, analyzed, and interpreted from the online survey to augment information obtained from focus groups participants. Three themes were identified that are worth exploring as potential intervention topics or for use in educational programs.

- *How antibiotic resistance happens* – specifically, how humans contribute to antibiotic resistance. Study participants understood that misuse and overuse of antibiotics accelerates resistance. However, they appeared not to recognize their own contributions to antibiotic resistance and the potential impact on those close to them. They did not understand that others' use of ABs or their use of ABs could affect others or their own chances of contracting an ABR infection. Although participants conveyed an understanding that overprescribing and use in animal agriculture contributes to resistance, there is room to expand outpatient knowledge and attempt to reduce resistance in outpatient populations.
- *The ways in which resistant bacteria are transmitted* – The majority were not aware or were unsure that ABR can spread from person to person or from animals to humans. Wearing masks and using hand sanitizer during the coronavirus pandemic has raised awareness as to the ways that infections can spread. Taking advantage of COVID-19 synergies, complementary efforts to boost ABR knowledge and awareness could result in greater impact. Survey data demonstrated that an increase in participants' level of knowledge can lead to greater positive health behaviors. The value of information and increased knowledge are essential for prevention and control of ABR.
- *Concern for family as motivation* – In reviewing responses to the survey questions about individual risk of acquiring an ABR infection and various health conditions versus risk of family members, participants minimized their own risk and quantified the potential risk to family members higher than their own. A focus on the benefits of taking action to protect yourself and your family from the threat of infection is likely

to be a strong motivator for this population. Various stages of lifecycle such as being single or married with no children versus adults with children will require different messaging and methods of disseminating information. For example, a parent with a young child might need specific information for dealing with their children's illness as an alternative to antibiotics, provided by the pediatrician's office. Whereas an adult with no children might find a one-page flyer with antibiotic stewardship information that they pick up at their local pharmacy or have access to at work is sufficient.

Moving forward, continued research into understanding antibiotic use and how to reduce ABR in outpatient settings in a timely, cost-efficient, and effective manner is needed. This study is one step in that effort and results can be used as a foundation to help develop, pilot test, and employ intervention programs to educate individuals on the risks of unnecessary antibiotic use.

Limitations

Limitations of this study include a study population that was, in general, highly educated with a larger percentage than the general population that had a background in healthcare. Furthermore, participants were selected via convenience sampling, which limits generalizability. Although the sample size was sufficient to compare two variables using linear regression, there were not sufficient sample participants to match some of the general population's demographic characteristics, including region, gender, and race/ethnicity.

Although five to eight potential focus group participants were selected and invited to each session so that four to six individuals would ultimately participate, some sessions only included two individuals because of last-minute cancellations and no-shows. The small focus groups may have limited the range of experiences during the session or in some cases, been dominated by one individual. Consequently, the moderator continually worked to create an atmosphere of inclusion during the session.

The online survey limitations may have included non-response and recall bias. Both the survey and the focus groups could have introduced social desirability or conformity bias. Moreover, survey questions were adapted from similar questions found in the literature but were not validated for this study. Finally, given the nature of the questions (e.g., knowledge, beliefs, perceptions), question order may have influenced responses.

Despite these limitations, the study findings can provide valuable information in the understanding of outpatient knowledge and beliefs about antibiotic resistance.

CHAPTER 5: PLAN FOR CHANGE

Antibiotic use, both inpatient and outpatient, along with antibiotic use in agriculture, are the primary drivers of antibiotic resistance development (CDC, 2019; Sabtu, et. al., 2015). U.S. and global efforts are focused on slowing the emergence and spread of resistant bacteria by implementing antibiotic stewardship programs across all healthcare settings. Findings from this study identified several areas from the outpatient setting, particularly focused on patients themselves, where tailored stewardship programs could support efforts to reduce overuse and misuse of antibiotics.

As noted in Chapter 4, stewardship programs that engage participants and increase knowledge in two areas, 1) how antibiotic resistance occurs, and 2) how antibiotic-resistant bacteria are transmitted, have the potential to result in reductions in the development of antibiotic resistance and transmission of ABR infections in outpatient settings. Furthermore, a multifaceted approach drawing on perceived susceptibility by an individual for their loved one's risk of acquiring ABR infections could be a path for increasing uptake of outpatient-focused antibiotic stewardship programs.

Community engagement is a valuable tool for implementing and accelerating the uptake of research findings in a real-world setting. To guide the development and roll-out of a stewardship intervention program in an outpatient setting, a community-engaged dissemination and implementation (CEDI) approach will be followed. The CEDI model engages stakeholders with diverse perspectives and experiences to help tailor study results to local population context. The following CEDI guided dissemination plan was developed.

Step 0: Additional Analysis and Publish Results

A rich data set was compiled during the conduct of this small study. The statistical analysis plan was completed, and results have led to additional queries that can be explored, including additional regression analysis between antibiotic use, knowledge, and demographic variables. It is likely that these analyses will lead to supplemental information for educational/intervention program development.

A study results manuscript will be developed and submitted for publication. Separate focus group and survey manuscripts could be developed.

Step 1: Engage Community Partners

Community partners will be selected and recruited to advise the research team. These partners will be identified from among the audience for whom the intervention program is developed. Once convened, study information including aims and results will be shared with the community partners. Sufficient time will be allocated for this phase since understanding the HBM conceptual framework, study data and the interpretation of results is vital for program success. The team will establish goals and a timeline to guide program development and delivery.

Next, using the HBM constructs (e.g., perceived susceptibility, perceived barriers, etc.) as a model, team members will identify an approach and develop core elements of the intervention program to ensure outpatient engagement. The intervention program should be well-conceptualized to aid in delivery and uptake and have sufficient resources to implement. This includes not only financial resources, but also consultants or individuals with appropriate expertise such as graphic designer, community organizations, and partners where the intervention program will be delivered.

Step 2: Identify Resources

There are several sources of funding for ABR research. In addition to NIH, there are several foundations that fund antimicrobial resistance efforts include the Robert Wood Johnson

Foundation, Burroughs Wellcome, and PEW Charitable Trusts. A post-doctoral fellowship might be an additional opportunity to develop and implement antibiotic stewardship programs.

Step 3: Develop and Finalize Program and Delivery Mechanism

Guided by the core elements identified in the previous step, appropriate messages will be developed, and fact-based information gathered, keeping in mind who the target population is, what key messages are most important, and how to increase acceptability and adoption among the target population. Existing materials and media (e.g., videos, fact sheets, brochures, etc.) such as the "Be Antibiotics Aware" toolkit will be evaluated and incorporated. Where appropriate material is not available, it will be developed. Since the outpatient population is diverse, one approach may not be sufficient. Therefore, data such as gender, race/ethnicity, and age will be considered. For example, older populations such as those approaching retirement may not be comfortable using smart phone whereas the younger generations have spent most of their lives using technology. Therefore, age-appropriate material with tailored messages and designs for different delivery mechanisms may be needed.

Next, appropriate venues for delivering the program will be identified. For example, will program implementation be conducted at doctor's offices, schools, gyms, soccer fields, or other suitable locations? Again, different population characteristics may reach different outpatient populations.

Step 4: Pilot Test Program Intervention

All parts of the intervention program will be pilot tested using actual target populations. Evaluations will be conducted on message content, tailoring, material design, delivery tools such as signs or fact sheets, whether uptake was successful, and any feedback provided by those delivering the intervention as well as the recipients or target population(s). Program adaptations will be made to incorporate feedback. A second, smaller pilot test may be considered, depending on the amount and level of modification needed. Once the intervention program is final, the toolkit will be assembled, and training and delivery material developed.

Step 5: Train Delivery Champions

Community partners and intervention delivery champions will receive training to get to know the target population and the program being implemented. The training agenda will include modules on expectations, how to accomplish those expectations, what not to do, what to do if an emergency arises, and maintaining confidentiality. Training will be interactive and include didactic sessions, group exercises, and role play. Each trainee will be evaluated to ensure they were able to understand the program components and deliver the intervention.

Step 6: Implementation

Step 7: Evaluate and Determine Program's Future

Based on the program core elements and specific measurable objectives, the antibiotic stewardship intervention program will be evaluated for impact and effectiveness. Some evaluation questions might include:

1) Did the program reach the appropriate population (outpatient individuals)?
2) Was there a change in knowledge, beliefs, or perceptions of antibiotic resistance that will lead to a reduction in the development and spread of antibiotic resistance?
3) Are there any lessons learned that might be incorporated in future programs?
4) If the program did not meet the objectives, should it be sunsetted or adapted?

Explore Other Potential Change Prospects

The study documented here has valuable data and can be further mined for additional results that might benefit the intervention program and/or additional antibiotic resistance reduction programs. Additional correlations can be explored, and study results can be submitted to an appropriate journal for consideration. Additionally, results can be adapted to a policy brief and submitted for publication in a journal such as *Health Affairs*.

If found to be successful, the intervention program toolkit could be shared with key public health stakeholders in local health departments to aid in development and refinement of local and state plans to address ABR.

Conferences are an additional way to distribute study results and recommendations. Abstracts will be submitted for presentation at professional meetings and conferences such as

the annual IDWeek Annual meeting (http://idweek.org) and a National Association of County & City Health Officials (NACCHO) annual meeting (http://www.nacchoannual.org/home). Additional local conferences include the North Carolina Public Health Leaders' Conference (sponsored by the North Caroline Public Health Association) and the Triangle Global Health Consortium Annual Conference.

By exploring opportunities to share study results and implementing a plan for change, research becomes more accessible to communities and can benefit the populations who are most directly impacted by the research results.

APPENDIX A: IRB APPROVAL

To: Lisa Strader and Leah Devlin
Health Policy and Management Operations

From: Office of Human Research Ethics

Date: 6/02/2020
RE: Notice of IRB Exemption
Exemption Category: 2.Survey, interview, public observation
Study #: 17-0846

Study Title: Outpatient Behaviors and Practices Influencing Adherence to Proper Antibiotic Stewardship Practices: Indications for Future Intervention Development

This submission, Reference ID 291570, has been reviewed by the Office of Human Research Ethics and was determined to be exempt from further review according to the regulatory category cited above under 45 CFR 46.104.

Study Description:

Purpose: The purpose of this study is to identify and address factors that facilitate and/or impede individual (e.g., patient, parent of patient) adherence to antibiotic stewardship guidelines and to understand what encourages outpatients to or discourages them from requesting an antibiotic when not medically necessary.

Participants: Participants being recruited nationally from ResearchMatch.org for this study include adult females and males, age 26-64 with no current, reported medical conditions. In the first phase, a maximum of 24 individuals will be recruited in groups of 4-6 for a total of 3-4 focus groups. Next, 250-300 individuals will be recruited to participate by taking an online survey.

Procedures (methods): The Health Belief Model (HBM) will be used as a framework for understanding the perceptions, modifying factors, and likelihood of taking action from the perspective of outpatients in order to identify the multiple factors that influence individual compliance with antibiotic stewardship practices. The HBM also will be used to understand barriers and facilitators affecting antibiotic prescription adherence (e.g., completion of all prescribed antibiotics; individuals requesting antibiotics when not medically necessary).

I propose that an examination of the factors associated with antibiotic stewardship practices using the HBM will result in information that can be used to develop effective interventions to strengthen positive stewardship practices and discourage unnecessary antibiotic consumption at the individual outpatient level. The findings from this study can inform future intervention efforts to increase adherence to antibiotic guidelines in target populations.

Summary of changes approved with this submission:

ResearchMatch requires a recruitment contact message approved by the IRB. I am attaching a draft message for both Focus Groups and the Survey. This is an addition to the previously submitted application.

Submission Regulatory and other findings:

As a reminder, although the UNC-Chapel Hill OHRE/IRB may have approved or made a determination that this study can commence, at this time UNC-Chapel Hill in response to direction from the UNC System Office has reduced campus activity significantly due to the COVID-19 outbreak. All human subject research activities are expected to follow all institutional and UNC Health policies, including those that may limit direct contact of participants. If you need to modify or alter your study design due to COVID-19 in order to conduct your research activities, please submit a modification and advise in the "Cover page" that this is "COVID-19 Related".

Investigator's Responsibilities:

If your study protocol changes in such a way that exempt status would no longer apply, you should contact the above IRB before making the changes. There is no need to inform the IRB about changes in study personnel. However, be aware that you are responsible for ensuring that all members of the research team who interact with subjects or their identifiable data complete the required human subjects training, typically completing the relevant CITI modules.

The IRB will maintain records for this study for 3 years, at which time you will be contacted about the status of the study.

The current data security level determination is Level II. Any changes in the data security level need to be discussed with the relevant IT official. If data security level II and III, consult with your IT official to develop a data security plan. Data security is ultimately the responsibility of the Principal Investigator.

Please be aware that approval may still be required from other relevant authorities or "gatekeepers" (e.g., school principals, facility directors, custodians of records), even though the project has determined to be exempt.

IRB Informational Message - please do not use email REPLY to this address RB Informational Message - please do not use email REPLY to this address

APPENDIX B: RESEARCHMATCH CONTACT MESSAGES

The following message is sent via ResearchMatch to identify registrants interested in participating.

FOCUS GROUPS
Fifteen years after penicillin was first discovered, scientists began seeing penicillin-resistant bacteria. A rise in antibiotic resistance over the last 10 years represents a threat to public health and the economy in the United States and the rest of the world.

A graduate student at the University of North Carolina at Chapel Hill is conducting a research study to understand how individuals take antibiotics, if they follow antibiotic prescription guidelines, and what encourages someone to, or discourages them from requesting an antibiotic from their doctor.

We are emailing to ask if you would like to help us by participating in a focus group. The focus group discussion will take approximately one hour and will take place online. You and 4-5 other individuals will talk with a researcher about your experience with antibiotics – taking them, asking for them, and how you take them. Participation is completely voluntary, and your responses will be labeled with a code that does not include your name or any other direct identifier.

You may be eligible for this study if:

- You are between 26-64 years old
- You are not diagnosed with a health or medical condition (not reported in ResearchMatch)
- You live in the United States of America
- You speak English
- You have internet access

If you are interested in hearing more about this study, please click "yes" so that a study team member may contact you.

Thank you for your time.

SURVEY
NOTE - Substitute for paragraph 3 above (all other paragraphs remain the same)

We are emailing to ask if you would like to help us by completing a survey. The survey will take about 30 minutes to complete and will ask about your experiences with antibiotics – taking them, asking for them, and how you take them. We estimate that approximately 300 individuals will take part in this study. Participation is completely voluntary, and your responses will be anonymous.

APPENDIX C: CONSENT FORM – FOCUS GROUP PARTICIPANTS

Title of Study:	Outpatient Behaviors and Practices Influencing Adherence to Proper Antibiotic Stewardship Practices: Indications for Future Intervention Development
Institution:	University of North Carolina at Chapel Hill
Principle Investigator (PI):	Lisa Strader, MPH Phone Number: (919) 966-8333 Email: lstrader@unc.edu

STUDY PURPOSE

Antibiotics kill or restrict the growth of bacteria that can cause diseases such as pneumonia, some sexually transmitted infections (STIs), and food borne illnesses such as E. coli. Over the last 10 years, the number of antibiotic-resistant strains of bacteria have grown and this represents a threat to public health and the economy in the United States (U.S.). In the U.S. for example, antibiotic-resistant bacteria cause at least two million illnesses and 23,000 deaths each year. This can result in $20 - 35 billion in excess health care costs, loss in worker productivity as high as $35 billion, and can add 8 million more hospital days per year. The majority of increased antibiotic health costs are due to improper prescribing or patient non-compliance with prescription instructions in outpatient settings (where medical care or treatment does not require an overnight stay in a hospital or medical facility).

This research study was planned to help researchers understand how antibiotics are prescribed and used, and what individual behaviors and habits might improve or worsen antibiotic resistance. You are invited to take part in a *web-based focus group* to help researchers understand 1) what factors make it easy or difficult for individuals visiting the doctor to follow antibiotic prescription guidelines, and 2) what factors encourage or discourage outpatients from requesting an antibiotic when it is not medically necessary.

PROCEDURES

You were identified as one of 24 potential focus group participants for this research study because you have registered at ResearchMatch.com. You are being asked to participate because you are between the ages of 26-64, do not have a diagnosed medical condition, and speak English. Joining the research study is voluntary. You may choose not to participate or to withdraw your consent to be in the study, for any reason, without penalty. If you decide to join the research study, you will participate in a one-time 45–60-minute online group discussion with 4 – 6 other individuals. A moderator will ask several questions such as what you know about antibiotics and how they work, how you ask for or get prescribed an antibiotic, how you take antibiotics when you have a prescription. No questions will be directed to you individually, but instead will be posed to the group. You may choose to respond or not respond at any point during the discussion. You may choose to withdraw from the study at any time.

As approved by the University of North Carolina's Institutional Review Board, this focus group will be audio-recorded, and a note-taker will be present. The recordings are used to accurately capture the information you and others provide; however, your responses will remain confidential, and no names will be included in the final report.

Please note that there are no right or wrong answers to focus group questions. Researchers want to hear many different viewpoints and would like everyone to contribute their thoughts. Out of

respect, we ask that you refrain from interrupting others, as everyone will have a chance to respond. Feel free to be honest even when your responses are not the same as those of other group members.

BENEFITS AND RISKS
Research is designed to benefit society by gaining new knowledge. Your participation will help us learn more about what individuals know about antibiotic resistance and how individuals make decisions when it comes to taking or requesting an antibiotic from a doctor. You will not benefit personally from being in this research study. No risks are anticipated beyond those experienced during an average conversation.

COST AND INCENTIVES
It will not cost you anything to be in this research study. Upon completion of your participation in the focus group, you will be entered into a drawing to win a $20 gift card. The drawing will be held [enter date]. The estimated odds of winning the drawing are 1 in 24.

CONFIDENTIALITY
Should you choose to participate, you will be asked to respect the privacy of other focus group members by not disclosing any information discussed during the session. Every effort will be made to protect your identity as a participant in this research study. You will not be identified in any report or publication of this research study or its results. Your name will not appear on any transcripts; instead, you will be given a code number. The list which matches names to code numbers will be kept in a locked file cabinet. After the focus group recording has been transcribed, the recording will be destroyed, and the list of names and numbers will also be destroyed.

CONTACT
You have the right to ask, and have answered, any questions you may have about this research. If you have any questions or concerns about the research study or your rights as a participant, contact the researcher listed on the first page of this form. You may also contact the Institutional Review Board at (919) 966-3113 or irb_subjects@unc.edu.

ELECTRONIC CONSENT
Please select your choice below. You may print a copy of this consent form for your records. Clicking on the "Agree" button indicates that

- You have read the above information
- You voluntarily agree to participate
- You are 18 years of age or older

☐ Agree

☐ Disagree

Full Name: _____

APPENDIX D: FOCUS GROUP CONFIRMATION LETTER

Online Focus Group Confirmation

[date]

Subject: Participation in Research Focus Group – understanding how antibiotics are prescribed and used by individuals

Dear _____,

Thank you for your willingness to participate in the online focus group. As we communicated to you earlier, we would like to hear about your experiences with antibiotics. You will be in a group with 4-5 other individuals and your responses to the questions will be kept anonymous. At the end of your participation, you will be entered into a drawing to win a $20 gift card. The drawing will be held [enter date] and the estimated odds of winning the drawing are 1 in 24. The date, time, and internet access information are provided below.

DATE February 15, 2020 [example]
TIME 9:00 am – 10:00 am [example]
ZOOM INTERNET ACCESS INFORAMTION http://unc.zoom.us/x/xxxxxxxxx
TELEPHONE NUMBER (xxx) xxx-xxxx

If you need additional information or will not be able to participate for any reason, please call [name] at [phone number]. Otherwise, we look forward to talking with you.

Sincerely,

Lisa Strader
Principal Investigator
Email: lstrader@unc.edu

APPENDIX E: FOCUS GROUP DISCUSSION GUIDE

Facilitator's welcome, introduction and instructions to participants

Welcome and thank you for volunteering to take part in this focus group. You have been asked to participate because your point of view is important. We realize you are busy, and we appreciate your time.

Introduction

This focus group discussion is designed to understand your current thoughts and your experience with antibiotics – taking them, asking for them, and how you take them. The focus group discussion will take no more than one hour. As a reminder, we will be recording the session so that we can make sure we capture your thoughts correctly. Unless there are objections, I am going to begin the recording now. (If no objection, begin recording)

Anonymity

Despite being recorded, I would like to assure you that the discussion will be anonymous. The recording will be kept safely in a password-protected file until it is transcribed word for word, then the recording will be destroyed. The transcribed notes of the focus group will contain no information that would allow individual participants to be linked to specific statements. You should try to answer and comment as accurately and truthfully as possible. Additionally, I and the other focus group participants would appreciate it if you would avoid discussing the comments of other group members outside the focus group. If there are any questions or discussions that you do not wish to answer or participate in, you do not have to do so; however please try to answer and be as involved as much as possible.

Ground rules

- The most important rule is that only one person speaks at a time. There may be a temptation to jump in when someone is talking but please wait until they have finished. And remember that we are recording, so to make sure your input is clear, it's best to only have one person speak at a time.
- There are no right or wrong answers.
- You do not have to speak in any particular order. My role as moderator is to guide the discussion. Talk to each other.
- When you do have something to say, please do so. There are several of you in the group and it is important that I obtain views of each of you.
- You do not have to agree with the views of other people in the group, but we ask that you listen respectfully as others share their views.
- Please turn off your cell phones. If you cannot turn it off and you must take a call, please do so as quietly as possible and rejoin us as quickly as you can.
- Does anyone have any questions? (provide answers)
- OK, let's begin

Warm up

First, I'd like everyone to introduce themselves. Can you tell us your first name only, no last names?

General:

☐ Do you "regularly" participate in healthy behaviors?
If yes, what behaviors do you participate in?
- □ How often?
- □ Why do you consider these healthy?
- □ Example behaviors may include exercising, eating lots of fruits and vegetables.

If no, why not?

Introductory question

I am going to give you a couple of minutes to think about your experience with antibiotics – taking them, asking your doctor for an antibiotic prescription for yourself or your child or other family member, finishing the prescription, and anything else. Is anyone willing to begin by sharing his or her experience?

Guiding questions

Knowledge and awareness:

☐ For what kind of infections can you take an antibiotic?
- □ Are antibiotics good to treat colds, the flu, strep throat?
- □ Do antibiotics fight against viruses such as the flu or coronavirus (COVID-19)?
- □ For what other conditions can you use antibiotics?

Practices:

Receiving and taking antibiotics

☐ Can you describe a "typical" appointment with your doctor?
- □ Does s/he come in and ask you questions for example?
- □ Is there back and forth discussion?

☐ How much does your doctor listen to you?
- □ Does s/he explain things?

☐ How often does your doctor ask you what you think about a treatment plan (e.g., prescription, additional tests, etc.)?

☐ When your doctor prescribes an antibiotic, does s/he explain why you are getting the prescription?
- □ For what disease/condition?

☐ Does s/he explain to you how often you should take the prescription and for how long?
- □ Number of times a day?
- □ How many days?

If no, how do you know how to take the prescription?
Do you
- □ . . .read the bottle?
- □ . . .ask the pharmacist?
- □ . . .something else? What?

☐ What do you do if your doctor says you (or your child) don't need an antibiotic?

☐ When you do get an antibiotic prescription, do you ever have any leftover pills in an antibiotic prescription? If so, what do you do with them?
- □ Save the rest for later?
- □ Share antibiotics with a family member or friend if they start to feel sick?

Susceptibility

☐ We know that some diseases can build up a resistance to antibiotics, called antibiotic resistance, and that the resistant infections can spread from human to human. Have you ever heard about antibiotic-resistant infections. . .people getting them in hospitals, nursing homes, or gyms? Can you explain what an antibiotic-resistant infection is?

Have you ever heard of
- □ drug-resistant tuberculosis?
- □ MRSA (staph or staphylococcus aureus)?
- □ C. diff (clostridium difficile)?

☐ How could antibiotic resistance affect people in your community?

☐ How could antibiotic resistance affect your family?

☐ What is the chance that you or a family member will get an antibiotic-resistant infection?

☐ Are there ways YOU can keep from getting an antibiotic-resistant infection?

☐ What do you think YOU can do to stop antibiotic resistance from happening/getting worse?

Cues to action

☐ Have you ever seen a handout or display in your doctor's office about antibiotics resistance?
- □ Have you ever heard about or seen a program called "Be Antibiotics Aware"?
- □ Any other antibiotic programs?

☐ Do you ever feel pressure to get an antibiotic for yourself or your child? From whom do you feel pressure?
- □ My boss, coworkers, husband/wife?
- □ Childcare center or child's school?

Concluding questions

☐ Of all the things we have discussed today, what would you say are the most important issues when it comes to antibiotics?

☐ Are there any questions I did not ask that I should have?

Conclusion: Thank you for participating. This has been a very productive discussion. Your opinions will be a valuable asset to the study. I hope you have found the discussion interesting as well.

I would like to remind you that any comments from the discussion and the resulting report will be anonymous, and I would like to remind you not to discuss others' comments outside this focus group. Thank you.

Potential probes:

- ☐ Would you explain further?
- ☐ Would you give an example?
- ☐ Tell me more about _____.
- ☐ When you say _____, what exactly do you mean?
- ☐ So, are you saying [paraphrase the response]?
- ☐ How would you describe _____.
- ☐ What was most important about that situation?
- ☐ What is it about _____ that you prefer/like/dislike?
- ☐ What was going through your mind when that happened?
- ☐ Can you share your reasons for that decision?
- ☐ What if _____?
- ☐ [Silence]

APPENDIX F: CONSENT FORM – SURVEY PARTICIPANTS

Title of Study:	Outpatient Behaviors and Practices Influencing Adherence to Proper Antibiotic Stewardship Practices: Indications for Future Intervention Development
Institution:	University of North Carolina at Chapel Hill
Principle Investigator (PI):	Lisa Strader, MPH Phone Number: (919) 966-8333 Email: lstrader@unc.edu

STUDY PURPOSE

Antibiotics kill or restrict the growth of bacteria that can cause diseases such as pneumonia, some sexually transmitted infections (STIs), and food borne illnesses such as E. coli. Over the last 10 years, the number of antibiotic-resistant strains of bacteria have grown and this represents a threat to public health and the economy in the United States (U.S.). In the U.S. for example, antibiotic-resistant bacteria cause at least two million illnesses and 23,000 deaths each year. This can result in $20 - 35 billion in excess health care costs, loss in worker productivity as high as $35 billion, and can add 8 million more hospital days per year. The majority of increased antibiotic health costs are due to improper prescribing or patient non-compliance with prescription instructions in outpatient settings (where medical care or treatment does not require an overnight stay in a hospital or medical facility).

This research study was planned to help researchers understand how antibiotics are prescribed and used, and what individual behaviors and habits might improve or worsen antibiotic resistance. You are invited to participate in a *web-based online survey* to help researchers understand 1) what factors make it easy or difficult for individuals visiting the doctor to follow antibiotic prescription guidelines, and 2) what factors encourage or discourage outpatients from requesting an antibiotic when it is not medically necessary.

PROCEDURES

You were identified as one of 300 potential survey participants for this research study because you have registered at ResearchMatch.com. You are being asked to participate because you are between the ages of 26-64, do not have a diagnosed medical condition, and speak English. Joining the research study is voluntary. You may choose not to participate or to withdraw your consent to be in the study, for any reason, without penalty. If you decide to join the research study, you will be asked to complete a short (20-30 minute) survey online on your computer. You may choose to skip any of the questions and may exit the survey at any time. You may choose to withdraw from the study at any time.

BENEFITS AND RISKS
Research is designed to benefit society by gaining new knowledge. Your participation will help us learn more about what individuals know about antibiotic resistance and how individuals make decisions when it comes to taking or requesting an antibiotic from a doctor. You will not benefit personally from being in this research study. No risks are anticipated beyond those experienced during an average conversation.

COSTS AND INCENTIVES
It will not cost you anything to be in this research study. Upon completion of the survey, you will be entered into a drawing to win one of four (4) $20 gift cards. The drawing will be held [enter date]. The estimated odds of winning the drawing depend on the number of study participants that complete a survey but are estimated to be 1 in 75.

CONFIDENTIALITY
Should you choose to participate, your survey answers will be stored initially with Qualtrics.com in a password protected electronic format. Qualtrics does not collect identifying information such as your name, email address, or IP address. Therefore, your responses will remain anonymous. No one will be able to identify you or your answers, and no one will know whether or not you participated in the research study. Data will later be downloaded and stored in password protected files. You will not be identified, and your name will not appear in any report or publication of this study or its results.

CONTACT
You have the right to ask, and have answered, any questions you may have about this research. If you have any questions or concerns about the study or your rights as a participant, contact the researcher listed on the first page of this form. You may also contact the Institutional Review Board at (919) 966-3113 or irb_subjects@unc.edu.

ELECTRONIC CONSENT
Please select your choice below. You may print a copy of this consent form for your records. Clicking on the "Agree" button indicates that

- You have read the above information
- You voluntarily agree to participate
- You are 18 years of age or older

☐ Agree

☐ Disagree

Full Name: _____

APPENDIX G: ONLINE SURVEY

Exploring Individual's Experiences with Health and Antibiotics
Online Survey (administered via Qualtrics)

Question	Resp. Code	Response Options	Skip/Action
INTRODUCTION: Thank you for agreeing to participate in this 10–15-minute online survey. Your responses are voluntary and anonymous and will help researchers understand how antibiotics are prescribed and used. Data collected will be analyzed together and all individual responses will remain confidential. **The following questions ask about your background and health. Please answer each question as accurately as possible by selecting the appropriate response.**			
The following questions ask about your background and health. Please answer each question as accurately as possible by selecting the appropriate response.			
1. What is your current age?		26-64 (pull down list)	If outside range, "Thank you for your interest; however, participation is limited to individuals aged 26-64."
2. What was your gender at birth?	1 2	☐ Female ☐ Male	
3. What is your gender identity?	1 2 3 4 5	☐ Female ☐ Male ☐ Transgender ☐ None of these ☐ Refused	
4. What is your marital status?	1 2 3 4 5 6	☐ Married ☐ Living with partner ☐ Widowed ☐ Divorced ☐ Separated ☐ Never married	
5. How many children do you have?		(2 characters)	If 0, skip to #6

5a/b/c/etc. (for each child) How old are your children? (child 1, child 2, etc.)	1 2 3 4 5 6	☐ ≤ 12 months ☐ 13-36 months ☐ 4-8 years ☐ 9-12 years ☐ 13-16 years ☐ 17 or older	Ask age for each child identified in #5
6. What is the highest level of education you have completed?	1 2 3 4 5 6 7	☐ Less than high school ☐ Some high school (no diploma or GED) ☐ High school diploma or equivalent (GED) ☐ Some college, no degree ☐ Associates degree ☐ Bachelor's degree ☐ Graduate degree	
7. Which of the following describes your race? (check all that apply)	1 2 3 4 5 6 7	☐ White ☐ Black or African American ☐ Asian ☐ Native Hawaiian or Other Pacific Islander ☐ American Indian or Alaska Native ☐ Other ☐ Refused	
8. Are you of Hispanic/Latino ethnicity (origin)?	1 2 3 4	☐ Yes ☐ No ☐ Unknown ☐ Refused	
9. In what state do you currently live?		Alabama to Wyoming (pull down list)	

10. What is your current employment status?	1 2 3 4 5 6	☐ Employed, working 1-39 hours per week ☐ Employed, working 40 or more hours per week ☐ Not employed, looking for work ☐ Not employed, NOT looking for work ☐ Retired ☐ Disabled, not able to work	
11. Are you a healthcare worker (for example, MD, RN, homecare, hospital administrator)	1 2	☐ Yes ☐ No	
12. How would you describe your overall health?	1 2 3 4	☐ Excellent ☐ Good ☐ Fair ☐ Poor	
13. How would you describe your eating habits?	1 2 3 4	☐ Excellent ☐ Good ☐ Fair ☐ Poor	
14. Have you ever used tobacco?	1 2	☐ Yes ☐ No	If no, skip to #15
14a. Do you currently use tobacco products (for example, cigarettes, cigars, pipes, vape)?	1 2	☐ Yes ☐ No	If no, skip to #15
14b. How long have you used tobacco products (for example, cigarettes, cigars, pipes, vape)?	1 2 3 4 5	☐ Less than 6 months ☐ More than 6 months but less than a year ☐ 1-5 years ☐ 5-10 years ☐ Greater than 10 years	
15. How often do you have a drink containing alcohol?	1 2 3 4 5	☐ Never ☐ Monthly or less ☐ 2 to 4 times a month ☐ 2 to 3 times a week ☐ 4 or more times a week	If never, skip to #16

15a. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 2 3 4 5	☐ 1 or 2 ☐ 3 or 4 ☐ 5 or 6 ☐ 7 to 9 ☐ 10 or more	
16. In the last 12 months, have you seen a doctor, or other health care provider (for example, physician's assistant or nurse practitioner)?	1 2	☐ Yes ☐ No	If no, skip to #17
16a. In the last 12 months, how often have you seen a doctor or other health care provider (for example, physician's assistant or nurse practitioner)?	1 2 3 4 5 6	☐ None ☐ 1-2 times ☐ 3-4 times ☐ 5-6 times ☐ More than 6 times ☐ Not sure	
17. In the last 12 months, have you been prescribed an antibiotic by a doctor, dentist, physician's assistant, or nurse practitioner?	1 2	☐ Yes ☐ No	If no, skip to #18
17a. In the last 12 months, how often has a physician, physician's assistant, or nurse practitioner prescribed you an antibiotic?	1 2 3 4 5 6	☐ None ☐ 1-2 times ☐ 3-4 times ☐ 5-6 times ☐ More than 6 times ☐ Not sure	
18. In the last 12 months, how often have you had an upper respiratory tract infection (for example, a cold, sinus infection, tonsillitis, middle ear or throat)?	1 2 3 4 5 6	☐ None ☐ 1-2 times ☐ 3-4 times ☐ 5-6 times ☐ More than 6 times ☐ Not sure	
19. In the last 12 months, how often have you had bronchitis or pneumonia?	1 2 3 4 5 6	☐ None ☐ 1-2 times ☐ 3-4 times ☐ 5-6 times ☐ More than 6 times ☐ Not sure	

20. In the last 12 months, how often have you had a bladder or urinary tract infection?	1 2 3 4 5 6	☐ None ☐ 1-2 times ☐ 3-4 times ☐ 5-6 times ☐ More than 6 times ☐ Not sure	
21. Do you regularly take vitamins or health supplements?	1 2	☐ Yes ☐ No	
22. How many days per week do you typically exercise?		0-7 (pull down list)	
23. Prior to March 2020 (start of coronavirus pandemic), did you regularly buy antibacterial products such as antibacterial soap or hand sanitizer such as Purell?	1 2	☐ Yes ☐ No	
23a. These days, do you regularly buy antibacterial products such as antibacterial soap or hand sanitizer such as Purell?	1 2	☐ Yes ☐ No	
24. Have you ever been vaccinated against the flu (influenza)?	1 2 3	☐ Yes ☐ No ☐ Note sure	If no or not sure, skip to #26
24a. How often do you get vaccinated against the flu (influenza)?	1 2 3 4	☐ Every year ☐ On average, every other year ☐ On average, every third year or less ☐ Note sure	
25. Have you ever received a COVID-19 vaccine?	1 2 3	☐ Yes ☐ No ☐ Not sure	If no or not sure, skip to #27
25a. Did you receive a vaccine product that requires only one does or two doses?	1 2 3	☐ One dose ☐ Two doses ☐ I don't know	
25b. How many doses of a COVID-19 vaccine have you received?		1-4 (pull down list)	

26. Have you heard of the term antibiotic resistance?	1 2	☐ Yes ☐ No	
27. Have you ever heard of the following infections?	1 2 3 4	☐ MRSA (Methicillin-resistant Staphylococcus aureus ☐ C. Diff (Clostridium difficile) ☐ MDR TB (Multi-drug resistant tuberculosis) ☐ Other _____	Check all that apply
The following section contains statements about health and antibiotics. Read each statement and select whether you think the statement is true, false, or you don't know.			
28. The body fights mild infections on its own without antibiotics	1 2 3	☐ True ☐ False ☐ Don't know	
29. Antibiotics help reduce cold or flu symptoms	1 2 3	☐ True ☐ False ☐ Don't know	
30. Antibiotics help reduce symptoms of strep throat, whooping cough, or urinary tract infection	1 2 3	☐ True ☐ False ☐ Don't know	
31. Skipping one or two doses of an antibiotic does not contribute to the development of antibiotic resistance	1 2 3	☐ True ☐ False ☐ Don't know	
32. How other people use antibiotics doesn't affect my chance of getting antibiotic-resistant infections	1 2 3	☐ True ☐ False ☐ Don't know	
33. People can become resistant to antibiotics	1 2 3	☐ True ☐ False ☐ Don't know	
34. Antibiotic resistance can spread from animals to humans	1 2 3	☐ True ☐ False ☐ Don't know	
35. To reduce the risk of resistance, antibiotics should be stopped immediately when the individual feels better	1 2 3	☐ True ☐ False ☐ Don't know	

36. How I use antibiotics doesn't affect other people's chance of getting antibiotic-resistant infections	1 2 3	☐ True ☐ False ☐ Don't know	
37. Bacteria can become resistant to antibiotics	1 2 3	☐ True ☐ False ☐ Don't know	
38. Antibiotic resistance can spread from person to person	1 2 3	☐ True ☐ False ☐ Don't know	
39. I know if I need antibiotics before I see my doctor	1 2 3	☐ True ☐ False ☐ Don't know	
40. It is my right to ask for an antibiotic from my doctor	1 2 3	☐ True ☐ False ☐ Don't know	
41. I would change doctors if my doctor didn't prescribe antibiotics when I ask for one	1 2 3	☐ True ☐ False ☐ Don't know	
42. I would rather take an antibiotic that I may not need than wait to see if I get better without it	1 2 3	☐ True ☐ False ☐ Don't know	
43. I trust my doctor when they tell me I do not need antibiotics	1 2 3	☐ True ☐ False ☐ Don't know	
44. People should keep leftover or unused antibiotics for the next time they are sick	1 2 3	☐ True ☐ False ☐ Don't know	
45. It is okay to share antibiotics with family or friends when they are sick with the same symptoms	1 2 3	☐ True ☐ False ☐ Don't know	
46. If taken too often, antibiotics are less likely to work in the future	1 2 3	☐ True ☐ False ☐ Don't know	

The next section has potential situations that could happen when taking antibiotics. Read each item and select Yes or No to indicate if you would take the action or not.			
47. A doctor prescribes an antibiotic for you. After taking 2-3 doses you start to feel better			
47a. Do you stop taking the rest of the prescription?	1 2	☐ Yes ☐ No	
47b. Do you save the remaining antibiotics for the next time you get sick?	1 2	☐ Yes ☐ No	
47c. Do you throw away the remaining, leftover medicine?	1 2	☐ Yes ☐ No	
47d. Do you give the leftover antibiotics to your family or friend if they get sick?	1 2	☐ Yes ☐ No	
47e. Do you complete the full course of antibiotic?	1 2	☐ Yes ☐ No	
48. Do you know anyone such as a family member or friend who has experienced an antibiotic-resistant infection (for example, C. difficile or C. diff, Staphylococcus aureus or MRSA)?	1 2	☐ Yes ☐ No	
Indicate how strongly you are concerned or not concerned about the following statements by selecting a response from among those ranging from NOT AT ALL CONCERNED to EXTREMELY CONCERNED. We are interested in how you think or feel RIGHT NOW as you complete this next set of questions.			
49. Some people are quite concerned about health, while others are not as concerned. How concerned are you about your own health?	1 2 3 4 5	☐ Not at all concerned ☐ Slightly concerned ☐ Moderately concerned ☐ Very concerned ☐ Extremely concerned	

50. How concerned are you about the chance of getting sick?	1 2 3 4 5	☐ Not at all concerned ☐ Slightly concerned ☐ Moderately concerned ☐ Very concerned ☐ Extremely concerned	
51. How concerned are you about the impact a serious health condition could have on your ability to work?	1 2 3 4 5	☐ Not at all concerned ☐ Slightly concerned ☐ Moderately concerned ☐ Very concerned ☐ Extremely concerned	

Indicate how strongly you agree or disagree with the following statements by selecting a response between EXTREMELY UNLIKELY and ESTREMELY LIKELY. The closer your selection is to one end or the other signifies the strength of your agreement or disagreement. If you don't agree or disagree with a statement, select the response in the middle. We are interested in how you think or feel RIGHT NOW as you complete the next set of questions.

52. How likely is it that <u>you</u> could get one of these illnesses? For example, how much chance is there that you could ever get pneumonia?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
52a. Strep throat?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
52b. Diabetes?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
52c. Antibiotic-resistant infection?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	

53. How likely is it that one of <u>your family members</u> could get one of these illnesses? For example, how likely is it that a family member could ever get pneumonia?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
53a. Strep throat?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
53b. Diabetes?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
53c. Antibiotic-resistant infection?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
54. How likely are you to get an antibiotic-resistant infection compared to others your age?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	
55. How likely is it that an antibiotic-resistant infection could affect your community?	1 2 3 4 5	☐ Extremely unlikely ☐ Unlikely ☐ Neutral ☐ Likely ☐ Extremely likely	

Indicate how strongly you agree or disagree with the following statements by selecting a response between STRONGLY DISAGREE and STRONGLY AGREE. The closer your selection is to one end or the other signifies the strength of your agreement or disagreement. If you neither agree nor disagree with a statement, select the response in the middle. We are interested in how you think or feel RIGHT NOW as you fill out the questionnaire.

56. The thought of getting an antibiotic-resistant infection scares me.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
57. There is no need to worry about antibiotic-resistant infections because scientists will discover new treatments.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
58. Treating an antibiotic-resistant infection may take a long time, for example, six weeks or more.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
59. If I got an antibiotic-resistant infection, I might die.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
60. If I got an antibiotic-resistant infection, my family would be negatively affected.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
61. Antibiotic resistance is not an important or serious public health issue.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
62. Taking antibiotics correctly will help me not worry about antibiotic-resistant infections.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	

63. Not asking for an antibiotic if my doctor says I don't need one will help protect me from antibiotic-resistant infections.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
64. Following the antibiotic prescription instructions will keep me and my family safe from serious infections in the future.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
65. I don't understand how to take my antibiotics.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
66. I don't trust my doctor to know when I need an antibiotic prescription.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
67. There is not much that people like me can do about antibiotic-resistant infections.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
68. Medical experts will solve the problem of antibiotic resistance before it becomes too serious.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
69. I trust my doctor, so I don't need to worry about antibiotic-resistant infections.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	

70. A doctor who does not prescribe antibiotics when the patient thinks that they are needed, is not a good doctor.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
71. If I think I need an antibiotic, I tell the doctor about symptoms, for example, green or yellow mucus that I know will get me an antibiotic prescription.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
72. I can tough it out if the doctor says I don't need an antibiotic.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
73. As long as I eat right, exercise, and take care of myself, I don't need to worry about getting an antibiotic-resistant infection.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
74. When I read about antibiotic resistance on the internet, I feel I can help with the problem.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
75. When my doctor prescribes an antibiotic, s/he or the nurse explains how to take the medicine and for how long.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
76. My boss, significant other, or someone important in my life encourages me to get an antibiotic so I feel better soon.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	

77. Seeing information in my doctor's office such as signs or brochures reminds me to take all my antibiotics.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
78. When my doctor tells me how to deal with my symptoms, for example, fever or cough, I'm able to go without an antibiotic prescription.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	
79. When I read about antibiotic resistance on the internet, I feel I must help with the problem.	1 2 3 4 5	☐ Strongly disagree ☐ Disagree ☐ Undecided ☐ Agree ☐ Strongly agree	

Source: Adapted and assembled from Maiman, et. al., 1977; Vallin, et. al., 2016; Afzal Khan, et. al., 2013; Sievers, et. al., 2014; Byrne, et. al., 2019.

APPENDIX H: ADDITIONAL LOGISTIC REGRESSION TABLES

Table 8: Effect of Level of Concern about Getting an ABR Infection on Health Behavior

Variable	Estimate	95% Confidence Interval	p-value
Intercept	10.88	(10.05, 11.71)	<.0001
Level of concern about antibacterial resistant infection*	0.09	(-0.15, 0.32)	0.4645
Bachelor's degree or higher education	1.61	(0.98, 2.24)	<.0001
Age	0.04	(0.02, 0.06)	<.0001
Partnered	0.57	(0.02, 1.11)	0.0413
Has children	-0.72	(-1.24, -0.21)	0.0062
Northeast region**	0.30	(-0.36, 0.96)	0.3684
Midwest region**	0.07	(-0.56, 0.71)	0.8199
Southwest region**	-0.25	(-1.48, 0.98)	0.6897
West region**	0.37	(-0.30, 1.05)	0.2783
Been to provider in past 12 months	-0.90	(-1.49, -0.32)	0.0025

* Based on the question, "The thought of getting an antibiotic-resistant infection scares me."

** Reference category is Southeast region.

Table 9: Effect of Level of Knowledge on Number of Antibiotic Prescriptions in the Last 12 Months

Variable	Estimate	95% Confidence Interval	p-value
Intercept	-1.72	(-2.52, -0.92)	<.0001
Knowledge score	-0.08	(-0.17, 0.02)	0.1042
Bachelor's degree or higher education	-0.17	(-0.71, 0.37)	0.5342
Age	-0.04	(-0.06, -0.02)	0.0001
Partnered	-0.27	(-0.75, 0.21)	0.2759
Has children	0.50	(0.00, 0.99)	0.0486
Northeast region*	-0.03	(-0.59, 0.54)	0.9277
Midwest region*	0.02	(-0.52, 0.55)	0.9454
Southwest region*	0.22	(-0.75, 1.19)	0.6544
West region*	-0.32	(-0.95, 0.31)	0.3168
Been to provider in past 12 months	0.80	(0.18, 1.42)	0.0114
Dispersion	0.38	(0.09, 1.49)	–

* Reference category is Southeast region.

Table 10: Effect of Being Able to go Without AB Prescription if Deal with Symptoms on Number of Antibiotic Prescriptions in the Last 12 Months

Variable	Estimate	95% Confidence Interval	p-value
Intercept	-1.67	(-2.48, -0.87)	<.0001
Can go without antibiotic if deal with symptoms	-0.15	(-0.41, 0.10)	0.2424
Bachelor's degree or higher education	-0.23	(-0.76, 0.30)	0.3883
Age	-0.04	(-0.06, -0.02)	<.0001
Partnered	-0.30	(-0.78, 0.18)	0.2182
Has children	0.54	(0.05, 1.03)	0.0319
Northeast region**	-0.01	(-0.58, 0.56)	0.9725
Midwest region**	0.00	(-0.54, 0.54)	0.9911
Southwest region**	0.27	(-0.70, 1.25)	0.5838
West region**	-0.37	(-1.00, 0.26)	0.2477
Been to provider in past 12 months	0.82	(0.20, 1.44)	0.01
Dispersion	0.41	(0.11, 1.49)	–

* Based on the question, "When my doctor tells me how to deal with my symptoms, for example, fever or cough, I'm able to go without an antibiotic prescription."

** Reference category is Southeast region.

Table 11: Effect of Perceived Susceptibility to ABR Infection on Number of Antibiotic Prescriptions in the Last 12 Months

Variable	Estimate	95% Confidence Interval	p-value
Intercept	-1.34	(-2.84, 0.16)	0.0794
Perceived susceptibility	0.16	(-0.28, 0.60)	0.4829
Perceived severity	-0.23	(-0.55, 0.09)	0.1585
Bachelor's degree or higher education	-0.23	(-0.76, 0.29)	0.3852
Age	-0.04	(-0.06, -0.02)	0.0002
Partnered	-0.27	(-0.76, 0.22)	0.2766
Has children	0.53	(0.04, 1.03)	0.0358
Northeast region*	0.01	(-0.56, 0.58)	0.9663
Midwest region*	0.03	(-0.51, 0.57)	0.9105
Southwest region*	0.27	(-0.70, 1.24)	0.5820
West region*	-0.38	(-1.01, 0.25)	0.2338
Been to provider in past 12 months	0.79	(0.16, 1.42)	0.0139
Dispersion	0.38	(0.10, 1.50)	–

* Reference category is Southeast region.

Table 12: Effect of Participant's Degree of Belief that Experts will Solve the ABR Problem Before it Becomes too Serious on Their Perceived Ability to Help with the ABR Problem

Variable	Estimate	95% Confidence Interval	p-value
Intercept	2.96	(2.60, 3.32)	<.0001
Degree of belief that experts will solve the problem of antibiotic resistance	0.03	(-0.07, 0.14)	0.5491
Bachelor's degree or higher education	0.20	(-0.08, 0.47)	0.1563
Age	0.01	(-0.00, 0.01)	0.2117
Partnered	0.01	(-0.21, 0.24)	0.8984
Has children	0.02	(-0.20, 0.24)	0.8613
Northeast region*	0.22	(-0.06, 0.51)	0.1271
Midwest region*	0.02	(-0.25, 0.29)	0.8748
Southwest region*	0.45	(-0.08, 0.97)	0.0960
West region*	0.32	(0.03, 0.61)	0.0300
Been to provider in past 12 months	-0.23	(-0.48, 0.02)	0.0683

* Reference category is Southeast region.

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