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Antimicrobial Stewardship and its Effects on Resistant Organisms

by

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Abstract

Antimicrobial stewardship has been found to have an impact on resistant organisms, but it has been unclear the importance of how strong those recommendations should be and if more strict or numerous guidelines equals fewer or less resistant organisms. “Antimicrobial stewardship (AMS), an organizational or system-wide health-care strategy, is designed to promote, improve, monitor, and evaluate the rational use of antimicrobials to preserve their future effectiveness, along with the promotion and protection of public health. (Majumder et al., 2020)” In reviewing recent peer-reviewed research it can be shown that medical facilities that utilize antimicrobial stewardship guidelines when prescribing antibiotics have less infections that do not respond to antimicrobial therapy. The aim of this review was to look for a trend between the amount of AMS guidelines and the number of resistant infections within medical facilities, and although there can’t be a specific trend-line drawn, there can be inferences made between facilities that do and do not practice AMS. It is up to those within the medical community to utilize best practices, study peer-reviewed literature, and speak with infectious disease professionals to make the decision on whether a situation is appropriate for antibiotic utilization.

Keywords: antimicrobial stewardship, antibiotic, resistance

Antimicrobial Stewardship and its Effects on Resistant Organisms

Introduction

Antibiotics have been around for almost 100 years and during that same time, bacteria and other organisms have started developing resistance to the drugs to stay alive. It is up to the medical community to keep an eye on patterns in resistance and stewardship practices to adapt and do the least harm to patients and the community. Recent evidence from the Center for Disease Control and Prevention (CDC) suggests that more than half of all hospital prescriptions for antimicrobial treatments were not congruent with recommended prescribing practices (CDC, 2020). See Figure 1.

Statement of the Problem

As antibiotic prescribing increases so does the opportunity for microorganisms to become more resistant. To reduce the number of drug-resistant organisms, many medical facilities have antibiotic stewardship in place. These suggestions or policies are not followed the same in all facilities, leading to varying success in slowing the progress of resistance. It is important to note the latest evidence-based practice regarding the effect of antibiotic stewardship on the progression of antibiotic resistance.

Research Question

Is there a correlation between the amount of antibiotic stewardship rules and the number of resistant infections?

Anticipated Results

There is likely an inverse relationship between stricter antibiotic stewardship rules and the number of drug-resistant infections up to a point of diminishing return in any given medical setting. If this is true it should aid providers in seeing the importance of antimicrobial stewardship practices.

Methods

A comprehensive literature review was completed to research facets of antibiotic stewardship to delineate the subtleties between resistant organisms and the antibiotic stewardship programs associated with them. The literature review was performed utilizing the electronic search database PubMed. Using keywords and MeSH terminology, literature was sought that could explain concepts behind the research question and for research studies that included the topic. Terms searched included "antimicrobial resistance"; "antibiotic resistance"; "resistance"; "resistant"; "antibiotic;" and "antimicrobial stewardship." Additional filters were applied to limit results to the past five years, written in English, and involving only human subjects. A final filter was applied that gave only meta-analyses, clinical trials, or randomized controlled trials. A total of 26 results were found, of which 16 were thrown out due to being off topic, and a final 10 were used for the literature review.

Literature Review

Antibiotic Resistance Through the Years

Antibiotic resistance happens when microbes have or develop the capability to thrive in the presence of drugs specifically meant to stop them from flourishing. When these bacteria continue to live in that environment, they are more difficult to treat which leads to a cascade of increasing illness and death. According to the global epidemiological surveillance networks European Anti-microbial Resistance Surveillance Network (EARS-Net) and Central Asia and Eastern European Surveillance of Anti-microbial Resistance (CAESAR), throughout the last decade, prevalence of antibiotic-resistant strains of bacteria have increased (Christaki et al., 2020). Mechanisms of resistance are understood by scientists, but the trends can be highly variable and difficult to predict, which is why it is extremely important to know the history and evolution of antibiotics, microbes, and antimicrobial resistance.

Penicillin was the first antibiotic discovered in 1928 by Alexander Fleming and was used with widespread success during World War II. *Staphylococcus* strains shortly thereafter utilized their resistance mechanisms, specifically penicillinase, to skirt past penicillin to the dismay of healthcare workers (Christaki et al., 2020). Luckily there were other antibiotics in the pipeline being researched and developed that would hopefully be utilized to overcome this resistance. Methicillin, vancomycin, and tetracycline were developed in the 1950s to treat infections resistant to penicillin and within the span of ten years, scientists had found microbes that were resistant to all three of those antibiotics as well (Christaki et al., 2020). Between 1960 and 1980 the pharmaceutical industry developed a vast array of new antibiotics that were efficacious and in front of the resistance of their intended target. However, bacteria were able to catch up to this when new medications began to decline and after the 1980s, bacterial infections due to multi-drug resistance have wreaked havoc worldwide (Christaki et al., 2020).

The ability of bacteria to resist antimicrobial agents occurs through intrinsic, acquired, or adaptive means. Intrinsic resistance occurs because of the inherent properties of the bacterium (Christaki et al., 2020). Acquired resistance happens when a previously sensitive bacterium acquires a resistance mechanism via mutation or horizontal gene transfer through an exogenous source (Christaki et al., 2020). Horizontal gene transfer has three mechanisms that include: transformation in which free DNA is taken up, transduction which involves a bacteriophage transferring genetic contents, and conjugation, which involves plasmid transfer through direct contact with another bacterium (Christaki et al., 2020). Finally, adaptive resistance happens because of an environmental stressor in which modulations in gene expression occur, but only transiently (Christaki et al., 2020).

Mechanisms of antibiotic resistance can be explained as to how a bacterium can survive in the presence of an antibiotic meant to get rid of it. This resistance is usually the result of antibiotic destruction, antibiotic modification, reduced antibiotic accumulation, target alterations which include target replacement, target site mutations, target site enzyme alterations, target site protection, target overproduction, or target bypass, or global adaptation (Christaki et al., 2020).

There is no doubt that the widespread use of antibiotics in recent times has led to dramatic highs in antimicrobial resistance, but the molecular pathways responsible for resistance have been around since ancient times. We have been able to gather that some inhibitors did not appear specifically to help bacteria survive but to also help in different functions like cell signaling, quorum sensing, and biofilm development (Christaki et al., 2020). Additionally, penicillinases were around prior to the extensive use of penicillin, and beta-lactamases have been found within the soil of very remote areas (Christaki et al., 2020). Under low antibiotic strains it is the bacteria that can survive which are selected, but some antibiotics modulate the expression of virulence factors which can increase frequency (Christaki et al., 2020). There is a hypothesis that since antibiotic development, natural selection happened, and resistance spread faster than before antibiotics (Christaki et al., 2020).

Within the soil of our environment there is a group of organisms referred to as Actinomycetes which produce specific metabolites that are in fact antibiotics (Perry et al., 2016). These metabolites have enabled science to develop streptomycin, erythromycin, vancomycin, tetracycline, and chloramphenicol (Perry et al., 2016). In addition to producing natural antibiotics, Actinomycetes are resistant to those chemicals they produce. However, a good number of bacteria carry other forms of resistance thought to be incorporated into their genome via horizontal gene transfer (Perry et al., 2016). This group of resistance genes, along with those found in healthcare settings and within humans is collectively known as the antibiotic resistome (Perry et al., 2016).

To determine whether resistance to antibiotics was present prior to its advent we need to find viable bacteria that were around before 1928 (Perry et al., 2016). Researchers have done just that in several geologic locations throughout the world: in permafrost in the Canadian High North, Siberian permafrost, the gut microbiome of a pre-Columbian Andean mummy in Peru, medieval monasteries, and a Soldier killed in World War I (Perry et al., 2016). All the bacteria found in these places have shown antibiotic resistance, leading to proof that the resistome is at least 30,000 years old (Perry et al., 2016). Going beyond that information, researchers can extrapolate divergence times from fossil records and determine evolutionary age to specific genes. Using the Grishin equation: $q=ln(1+2D)/2D$ with q the average fraction of unchanged residues and D being distance, the last common ancestor of the compared sequences can be determined (Perry et al., 2016). Using isopenicillin-N synthase as a genetic marker, it was calculated that it has been 370 million years since bacteria transferred genes to a fungus (Perry et al., 2016). Erythromycin was calculated to be approximately 880 +/- 134 million years old by using a specific set of 18 sequences (Perry et al., 2016). The last common ancestor of daptomycin was identified as being 30 =/- 0.2 million years (Perry et al., 2016). Resistance genes themselves were also given approximate ages with B1 + B2 subclass metallo-beta-lactamases being around one billion years old (Perry et al., 2016). Most significantly the B3 subclass of beta-lactamases was dated to 2.2 billion years ago, which was prior to the split between gram-positive and gram-negative bacteria (Perry et al., 2016).

Antibiotic Overuse

Empiric use of broad-spectrum antibiotics within intensive care units prior to identification of infectious agents is seen all too often. One international prevalence study found that as many as 70% of all ICU patients get prescribed at least one antibiotic (Denny et al., 2020). In these cases, antibiotics can be lifesaving if needed, but often these patients are put at risk of antibiotic-associated adverse events instead. This could include adverse drug events, secondary opportunistic infection, or antimicrobial resistance (Denny et al., 2020). An ideal solution would be that the initiation of antibiotics would be withheld until the ICU provider was confident that an infection is present. A narrative review was conducted by Denny et al., (2020) to ascertain how antibiotic initiation could be avoided within the high-stakes environment of the ICU.

Currently, microbiological culture of suspected infection is the reference standard for confirmation of infection, but growth and identification of bacterial and fungal cultures can take over 24 hours (Denny et al., 2020). Along with occasional invasive sampling techniques, possible contamination, as well as patient deterioration while results are confirmed, the current best method has very distinct drawbacks. In one study, 28-49% of patients who presented with a differential list that included sepsis had negative cultures (Denny et al., 2020). In these scenarios, if nothing else were done for the patient besides initiating an antibiotic, too much time would have been wasted waiting for culture results.

On the other side of the spectrum in dealing with critical ICU patients is a watch and wait strategy that involves withholding antibiotics until they are proven necessary. Inappropriate initiation of antibiotics has been proven to be an independent risk factor for mortality within the ICU (Denny et al., 2020). Bloos et al. conducted a large prospective observational study that found no mortality benefit from initiation of antibiotic therapy within the first hour of organ dysfunction (Denny et al., 2020). However, inadequate source control showed an increase in 28-day mortality ranging from 26.7-42.9% (Denny et al., 2020). The authors thus hypothesize that the importance of timeliness of antimicrobial initiation might be overemphasized and a more nuanced approach involving brief delays in antibiotic therapy to allow for source recognition and control, as well as ensuring appropriate antibiotic prescription may be valid (Denny et al., 2020).

Future clinicians will likely have rapid testing instrumentation to help guide their diagnoses, but presently we must continue to utilize all clinical, laboratory, and radiological findings to optimize management of infected and non-infected patients (Denny et al., 2020). Shared decision-making lies at the heart of good patient outcomes as we are not living in a world with rapid point-of-care diagnostics yet (Denny et al., 2020). Until then, it is important to continue to research and identify the safety associated with antibiotic initiation or withholding.

In an editorial for the Annals of Internal Medicine, Dr. Barbara E. Jones implores readers to look at their own antimicrobial stewardship citing myriad improper antibiotic prescriptions for viral respiratory infections (Jones & Samore, 2017). Citing a cohort study by Silverman et al, of the 185,014 patients seen by 8,990 providers for acute respiratory infection, 46% were given an antibiotic (Jones & Samore, 2017). Additionally, many were broad-spectrum antibiotics which are not recommended for first-line therapy (Jones & Samore, 2017). Getting into demographics of this study, she found more patients received antibiotics from mid or late-career providers, those who had high patient loads, and those who attended school outside the United States or Canada (Jones & Samore, 2017).

Dr. Jones points out the difficulty with breaking long-standing habits and that many learned practices that are shared between providers and trainees resist change (Jones & Samore, 2017). She argues that social networks, to include the attitudes and behaviors of colleagues, can be a powerful motivator toward change (Jones & Samore, 2017). One major contributing factor in good antimicrobial stewardship is ensuring that providers are agreeable to changing their prescribing practices and that they agree antibiotics should only be used if they are potentially beneficial (Jones & Samore, 2017). Physicians and other clinicians must be at the forefront of this change and the preservation of antibiotics that can be utilized with benefit to patients depend on them.

Antimicrobial Stewardship Programs at a Glance

What is antimicrobial stewardship and why should we care about it? Put plainly and succinctly, "Antimicrobial stewardship (AMS), an organizational or system-wide health-care strategy, is designed to promote, improve, monitor, and evaluate the rational use of antimicrobials to preserve their future effectiveness, along with the promotion and protection of public health (Majumder et al., 2020)." Another definition refers to it as "an organizational or healthcare-system-wide approach for fostering and monitoring judicious use of antimicrobials to preserve their effectiveness (Majumder et al., 2020)." The Infectious Diseases Society of America came up with the concept of antimicrobial stewardship in 2007 calling it "organized interpositions with the premise of improving antimicrobial use when selecting the appropriate agents, the correct dose, route of administration, and the duration of therapy without prejudicing patient outcomes (Majumder et al., 2020).” Antimicrobial stewardship has three main strategies which include: (1) improving patient care and outcomes through optimal therapy, (2) reducing antimicrobial use leading to less resistance, and (3) lowering antibiotic cost (Majumder et al., 2020).

Numbers and Statistics in Antimicrobial Stewardship

From 2005-2014, Gulliford et al., (2019) conducted a parallel-group, cluster randomized controlled trial among 79 general practices within the United Kingdom Clinical Practice Research Datalink to create and evaluate interventions for antimicrobial stewardship within primary care and to evaluate how safely they could reduce antibiotic use in respiratory infections. At the same time, a population-based cohort study in 610 Clinical Practice Research Datalink general practices was conducted that did not receive trial interventions (Gulliford et al., 2019). The specific interventions within the trial group included webinars and monthly data reports on their antibiotic prescriptions as well as antibiotic prescription algorithms to help in their decision-making (Gulliford et al., 2019). The measured outcome for the trial was antibiotic prescription rates for respiratory tract infections over a 12-month period (Gulliford et al., 2019). This outcome was used instead of inappropriate prescriptions because it is already known that there are many inappropriate prescriptions, so this study sought to gather altogether different data.

The intervention group included electronic health records of 323,155 patient-years and the control group contained 259,520 patient-years (Gulliford et al., 2019). Within the intervention group, 98.7 antibiotic prescriptions per 1000 patient-years were recorded (total of 31,907 prescriptions), while the control group included 107.6 prescriptions per 1000 patient-years (total of 27,923 prescriptions) (Gulliford et al., 2019). The adjusted rate ratio for antibiotic prescribing was 0.88 with a 95% confidence interval of 0.78-0.99 (*p*=0.040). The trial showed no evidence that there was an effect in children <15, which had a risk ratio of 0.96 and confidence interval of 0.82-1.12, or in adults >/= 85 years, whose risk ratio was 0.97 and confidence interval of 0.79-1.18 (Gulliford et al., 2019). In adults between 15-84 years, antibiotic prescribing was reduced (risk ratio of 0.84, 95% CI 0.75-0.95), equating to one less antibiotic prescription per 62 (95% CI of 40-200 patients) patients per year (Gulliford et al., 2019). This study did find that antibiotic prescriptions for respiratory tract infections could be reduced through electronic interventions for adults, but not for those <15 or >84 years of age (Gulliford et al., 2019). One major limitation with this study is that the data was found within electronic health records which may not always be current or contain all information about that patient (Gulliford et al., 2019). The authors conclude that future strategies in antimicrobial stewardship should involve stratified interventions that are designed for specific age groups as well as research regarding the safety and efficacy of limiting the antibiotic prescriptions are both needed (Gulliford et al., 2019).

A systematic review and meta-analysis of feedback and audits within intensive care units was conducted with mortality as an outcome (Lindsay et al., 2019). 11 studies met the authors' inclusion criteria to evaluate antibiotic use with mortality as the outcome within the study (Lindsay et al., 2019). They were declared as uncontrolled before-after studies for that outcome. The studies included variable antibiotic stewardship interventions, frequency of feedback, and study durations (Lindsay et al., 2019). The pooled relative risk for mortality within intensive-care units was 1.03 with a 95% confidence interval of 0.93-1.14 (Lindsay et al., 2019). A single study within the meta-analysis found almost identical mortality in baseline periods compared to the intervention period (14.5% and 14.6%) (Lindsay et al., 2019). It was difficult, however, to discern a good pattern, and there was no association found between less antibiotic use and either higher or lower rates of mortality (Lindsay et al., 2019). It was concluded that using audits and feedback did not change mortality associated with antimicrobial stewardship (Lindsay et al., 2019). With all the factors considered for these studies and a lack of adjustment for variables, overall, there is very low internal validity and a high risk of bias from unmeasured confounders, unreported co-interventions, regression to the mean, and maturation of seasonal effects (Lindsay et al., 2019). Future research needs to use a standardized approach in collecting data, analyzing, and reporting outcome data to make meta-analysis of the studies' outcomes easier to interpret.

Dr. Philip Sloane and colleagues performed a two-year quality improvement trial with two arms that included standardized antibiotic stewardship programs (Sloane et al., 2020). They wanted to discern if antibiotic prescriptions within nursing homes could be reduced using a multi-component antibiotic stewardship program that was implemented by providers and nursing staff (Sloane et al., 2020). They also sought whether the implementation was more effective within a nursing home chain or within a medical provider group, which were the two arms of the trial (Sloane et al., 2020). The study utilized 27 nursing homes in North Carolina to measure antibiotic prescription rates per 1000 resident-days overall and by type of infection, urine test ordering rates, and *C. difficile* and MRSA infection incidence (Sloane et al., 2020).

Specifically, the antibiotic stewardship intervention program included training modules for staff, posters, algorithms, guidelines for communication, quarterly information briefs, annual quality improvement reports, information brochures for residents and their families, and free continuing education credits (Sloane et al., 2020). Results of the trial discovered that systemic antibiotic prescribing rates decreased from baseline by 18% at the 12-month mark with an incident rate ratio of 0.82 and 95% confidence interval of 0.69-0.98 and p=0.029, and 23% at 24 months, with an incident rate ratio of 0.77 and 95% confidence interval of 0.65-0.90 and p=0.001 (Sloane et al., 2020). There was a 10% increase in the proportion of residents in the medical provider arm that was associated with a 4% decrease in prescribing, with an incident rate ratio of 0.96 and 95% confidence interval of 0.92-0.99 (Sloane et al., 2020). There were no statistically significant changes in *C. difficile* or MRSA infection incidence, hospitalizations, or hospital re-admissions (Sloane et al., 2020). There were also no adverse events recorded from not prescribing antibiotics (Sloane et al., 2020). The authors concluded that antibiotic stewardship programs can be successful in community nursing homes with either arm of implementation and that the ability to significantly reduce antibiotic prescribing for at least two years is achievable (Sloane et al., 2020). Finally, involvement from nursing home medical directors is an important element to garner success in this type of program (Sloane et al., 2020).

Edward Stenehjem and his colleagues conducted a study in 2014 using a cluster-randomized intervention assessing how effective the implementation of antimicrobial stewardship programs were within 15 small Intermountain Healthcare hospitals (Stenehjem et al., 2018). The hospitals were randomly assigned 1 of 3 antibiotic stewardship programs of increasing intensity (Stenehjem et al., 2018). Program 1 were given basic stewardship education and tools, an infectious disease hotline, and antibiotic use data (Stenehjem et al., 2018). Program 2 received all Program 1 tools plus advanced education, feedback for certain antibiotics, and local antibiotic restrictions (Stenehjem et al., 2018). Program 3 received all Program 2 tools, feedback on most antibiotics, an infectious disease clinician-approved restricted antibiotics list, plus reviewed microbiology lab results (Stenehjem et al., 2018). Using mixed models, changes in total and broad-spectrum antimicrobial use within and between programs were evaluated (Stenehjem et al., 2018). Program 1 and 2 hospitals showed no reduction in antibiotic use during the intervention period compared to the baseline (Stenehjem et al., 2018). Program 3 facilities did show reductions in total antibiotic use (RR, 0.89; CI, 0.80-0.99) and broad-spectrum antibiotic use (RR, 0.76; CI, 0.63-0.91) during the intervention compared to the baseline period (Stenehjem et al., 2018). The magnitude of effects comparison between programs displayed a trend toward Program 3, but it was not statistically significant (Stenehjem et al., 2018). The study concluded that an intense antimicrobial stewardship program policy can reduce total and broad-spectrum antibiotic use (Stenehjem et al., 2018).

Where Do We Go From Here?

The means by which we currently understand and treat antibiotic-resistant and multi-drug resistant strains of bacteria can be slow and ineffective. Antibiotic stewardship and infection prevention and control measures moving into the future therefore must not only consider where we are but also where we will likely be. A meta-analysis performed on 66 publications indicated that the prevalence of extended-spectrum beta-lactamase producing *Enterobacteriaceae* colonization was currently around 14% (with 95% confidence interval 9-20%), with an estimated increase of 5.38% annually (Bassetti et al., 2017). Other important gram-negative bacteria that have proven to develop resistance and cause morbidity and mortality include carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Enterobacteriaceae*, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and *Acinetobacter baumannii (Bassetti et al., 2017)*. Of equal or greater concern for some in the medical community is the gray line that is vanishing between community and healthcare-acquired infections. One reason behind this is the dramatic increase in CA-MRSA worldwide with a transfer of HA-MRSA clones to communities at the same time (Bassetti et al., 2017).

New or improved diagnostic testing capabilities and anti-infective agents or treatments appear to be the way that science is moving forward to combat resistant organisms (Bassetti et al., 2017). Matrix-assisted laser desorption ionization-time of flight mass spectrometry, rapid immunochromatography, molecular biology, automated time-lapse microscopy, and PCR/electrospray ionization-mass spectrometry platform all show promise in reducing the time of microbial identification and antibiotic susceptibility testing (Bassetti et al., 2017). Although these solutions aren't currently utilized on a large scale due to cost, they could eventually be used to directly analyze clinical samples at the bedside (Bassetti et al., 2017).

Antibiotics are currently the mainstay of infection control worldwide but there are some groups in the science community using novel concepts to fight microbial infection and resistance (Bassetti et al., 2017). Our intestinal microbiota itself is resistant to sustained colonization of exogenous microbes in a way that we do not fully understand, but this information could be used toward the development of promising multi-drug resistant treatments (Bassetti et al., 2017). Phage therapy is another means by which we can potentially rid individuals of their infective organisms (Bassetti et al., 2017). This is performed by using viruses that only target very specific bacteria and either directly lyse the bacterial cell or incorporate specific DNA to be replicated so more phages can be released (Bassetti et al., 2017). This concept could provide a good complement to antibiotic therapy because it is highly specific and there are no broad-spectrum phages that attack bacteria (Bassetti et al., 2017). Other tools in the microbiologist's arsenal include antibodies, vaccines, anti-virulence therapy, and anti-microbial peptides (Bassetti et al., 2017). With all these novel and high-tech methods of identifying and eliminating virulent bacteria, prevention does and will continue to hold high esteem in the medical community and it should not be discounted in favor of efficacious treatment (Bassetti et al., 2017).

Discussion

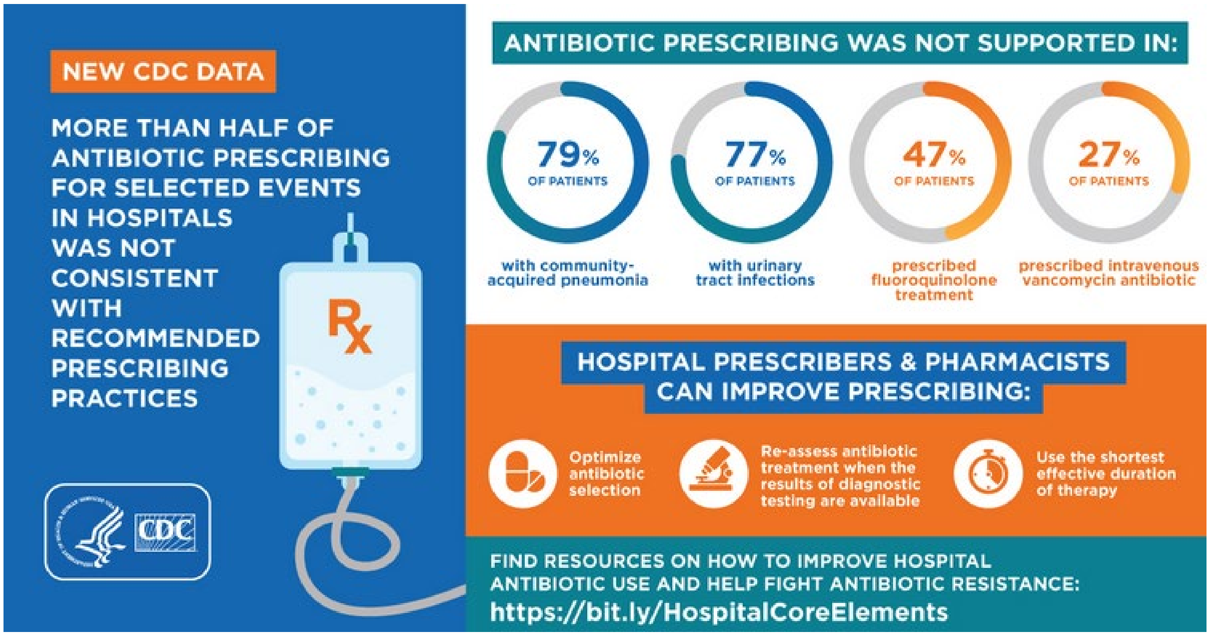
Although the specific research question has gone unanswered, we can still extrapolate the literature review information and statistics to useable and proven suggestions. There were no sliding scales of number or degree of antimicrobial stewardship rules utilized within the research studies, so a linear relationship cannot be drawn between the two variables quantitatively. However, it was shown clearly that qualitative results demonstrated that those facilities that had AMS guidelines in place had fewer resistant organisms to deal with than those with no such guidelines. Future research into varying levels of AMS guidelines and suggestions could potentially give better insight into my specific research question, answering if there is a benefit up to a point of diminishing return.

Historically, antibiotics were prescribed with no regard for the long-term negative effects, and now we are suffering from those well-meant, but detrimental decisions. There are currently five “urgent threats” put out by the CDC that include the top pathogens that pose a threat due to antibiotic resistance. These include carbapenem-resistant *Acinetobacter*, carbapenem-resistant *Enterobacteriaceae* (CRE), *Candida auris*, drug-resistant *Neisseria gonorrhoeae*, and drug-resistant *Clostridioides difficile*. These threats do change through time depending on their level of detrimental effects and how prevalent they are. That being said, those in practice have taken these threats seriously and minimized their incidence but must continue to do so to keep them from taking mention on this list.

Applicability to Clinical Practice

It is known that the number of antibiotic-resistant infections has increased dramatically in the recent past due partly to the overprescribing of antibiotics and lack of antimicrobial stewardship among providers. Patients that receive antibiotic prescriptions may not necessarily need them for their illness, and therefore may be unknowingly adding to the possibility of creating resistant organisms. The number one rule of being a healthcare provider is to do no harm, which has and will continue to happen if antibiotics are used haphazardly. The difficult and perhaps ironic part about resistant organisms wreaking havoc is that providers may be unaware that their actions could be contributing to this. It is important for all health care professionals to take action learning about the adverse events that can occur with the prescribing of antibiotics.

Figure 1: (CDC, 2020)



NEW CDC DATA

MORE THAN HALF OF ANTIBIOTIC PRESCRIBING FOR SELECTED EVENTS IN HOSPITALS WAS NOT CONSISTENT WITH RECOMMENDED PRESCRIBING PRACTICES

ANTIBIOTIC PRESCRIBING WAS NOT SUPPORTED IN:

79% OF PATIENTS	77% OF PATIENTS	47% OF PATIENTS	27% OF PATIENTS
with community-acquired pneumonia	with urinary tract infections	prescribed fluoroquinolone treatment	prescribed intravenous vancomycin antibiotic

HOSPITAL PRESCRIBERS & PHARMACISTS CAN IMPROVE PRESCRIBING:

- Optimize antibiotic selection
- Re-assess antibiotic treatment when the results of diagnostic testing are available
- Use the shortest effective duration of therapy

FIND RESOURCES ON HOW TO IMPROVE HOSPITAL ANTIBIOTIC USE AND HELP FIGHT ANTIBIOTIC RESISTANCE:
https://bit.ly/HospitalCoreElements

References

Bassetti, M., Poulakou, G., Ruppe, E., Bouza, E., Van Hal, S. J., & Brink, A. (2017). Antimicrobial resistance in the next 30 years, humankind, bugs and drugs: a visionary approach. *Intensive Care Med*, *43*(10), 1464-1475. https://doi.org/10.1007/s00134-017-4878-x

CDC. (2020). *Antibiotic/Antimicrobial Resistance (AR/AMR)*. Centers for Disease Control and Prevention. https://www.cdc.gov/drugresistance/index.html

Christaki, E., Marcou, M., & Tofarides, A. (2020). Antimicrobial Resistance in Bacteria: Mechanisms, Evolution, and Persistence. *J Mol Evol*, *88*(1), 26-40. https://doi.org/10.1007/s00239-019-09914-3

Denny, K. J., De Waele, J., Laupland, K. B., Harris, P. N. A., & Lipman, J. (2020). When not to start antibiotics: avoiding antibiotic overuse in the intensive care unit. *Clin Microbiol Infect*, *26*(1), 35-40. https://doi.org/10.1016/j.cmi.2019.07.007

Gulliford, M. C., Juszczyk, D., Prevost, A. T., Soames, J., McDermott, L., Sultana, K., . . . Charlton, J. (2019). Electronically delivered interventions to reduce antibiotic prescribing for respiratory infections in primary care: cluster RCT using electronic health records and cohort study. *Health Technol Assess*, *23*(11), 1-70. https://doi.org/10.3310/hta23110

Jones, B. E., & Samore, M. H. (2017). Antibiotic Overuse: Clinicians Are the Solution. *Ann Intern Med*, *166*(11), 844-845. https://doi.org/10.7326/m17-1061

Lindsay, P. J., Rohailla, S., Taggart, L. R., Lightfoot, D., Havey, T., Daneman, N., . . . Muller, M. P. (2019). Antimicrobial Stewardship and Intensive Care Unit Mortality: A Systematic Review. *Clin Infect Dis*, *68*(5), 748-756. https://doi.org/10.1093/cid/ciy550

Majumder, M. A. A., Rahman, S., Cohall, D., Bharatha, A., Singh, K., Haque, M., & Gittens-St Hilaire, M. (2020). Antimicrobial Stewardship: Fighting Antimicrobial Resistance and Protecting Global Public Health. *Infect Drug Resist*, *13*, 4713-4738. https://doi.org/10.2147/idr.s290835

Perry, J., Waglechner, N., & Wright, G. (2016). The Prehistory of Antibiotic Resistance. *Cold Spring Harb Perspect Med*, *6*(6). https://doi.org/10.1101/cshperspect.a025197

Sloane, P. D., Zimmerman, S., Ward, K., Kistler, C. E., Paone, D., Weber, D. J., . . . Preisser, J. S. (2020). A 2-Year Pragmatic Trial of Antibiotic Stewardship in 27 Community Nursing Homes. *J Am Geriatr Soc*, *68*(1), 46-54. https://doi.org/10.1111/jgs.16059

Stenehjem, E., Hersh, A. L., Buckel, W. R., Jones, P., Sheng, X., Evans, R. S., . . . Pavia, A. T. (2018). Impact of Implementing Antibiotic Stewardship Programs in 15 Small Hospitals: A Cluster-Randomized Intervention. *Clin Infect Dis*, *67*(4), 525-532. https://doi.org/10.1093/cid/ciy155