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Implementation of Stewardship Programs in Hospitals: Systematic Review



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Abstract

Antimicrobial resistance is a pandemic issue affecting hospital patients. There are many studies showing what can be done to decrease the resistance of many microbes, but there is not one complete method. This review indicates the effective methods that can be used to prevent resistance from spreading in hospitals. The review was set to focus on antimicrobial resistance, misuse, and overuse of antimicrobials, what doctors are doing that influences resistance and stewardship programs. Articles published from 2008- 2018 were found using Web of Science, ScienceDirect, and PLOS. Out of the 15 articles found, 7 articles met the ideal selection criteria and were included in the review. All articles demonstrated the importance of antimicrobial resistance and provided ways in which resistance can be decreased. All studies reported the use of stewardship programs were necessary, but only three articles demonstrated its effectiveness. This review demonstrates a high need for antimicrobial stewardship programs to decrease the evolution of antimicrobial resistance. However, there is a problem with individual medical providers not complying to such programs due to the restrictions they say it creates. The results state otherwise and in fact demonstrate how a medical provider's behavior must change to provide significance on the implementation of successful stewardship programs.

Keywords: Antimicrobial resistance, Hospitals, Stewardship programs

Stewardship Programs in Hospitals

Introduction

Antimicrobial resistance is a growing pandemic that affects humans with transmissions being commonly spread through the air, skin, reproductive organs, and oral consumption. Antimicrobial resistance occurs when a microorganism builds resistance to a drug or medicine an individual intakes. A microorganism can attack drugs being consumed and spread resistance of this drug in specific areas of the human body. The drugs that an individual intakes are expected to kill the microorganism, but recently drugs haven't been effective, and with growing resistance, there is a great demand for new drugs to be formulated.

Such microbes cause infections that can lead to disease and mortality. One common microbe is methicillin-resistant *Staphylococcus aureus* (MRSA); it is a bacterium that is resistant to many kinds of antibiotics. Generally, it is a staph bacterium which appears on the skin or nose of a person. At first glance, it looks like a spider bite, but if the skin is cut an infection can grow and cause severe pain. People who are at risk are those who have direct contact with the infection, and those who have obtained the infection secondhand. MRSA is the result of long-term misuse of antibiotics and now is a growing issue worldwide.



STEWARDSHIP PROGRAMS IN HOSPITALS

Antibiotics can be misused in multiple ways such as using an inappropriate number of dosages, the length of dosage therapy, the lack of sanitation, or the lack of patient isolation in the hospital. In the United States, the Centers for Disease Control and Prevention (CDC, 2018) reported, "two in 100 people carry MRSA." Although there is no research providing a total number of incidence or mortality rate of MRSA in the United States, in Europe, there were more than 27,000 rates of incidence of MRSA and more than 5,000 deaths associated with it in 2007 (de Kraker, Marlieke E A, Davey, & Grundmann, 2011). The only way for someone to determine if they have MRSA is by going to the hospital to get an analysis. Even though it is wise to get an analysis in the hospital, people are still at risk of obtaining an infection or spreading the infection. The hospital is where many people get treated for infections, hence, as the CDC states, there are greater opportunities there to contract diseases that may be spreading due to the healthcare provider's lack of sanitation skills and environment. Many people seek medical help to relieve any sort of issues they may be dealing with, but recent research has shown that even hospitals are places where infection and diseases can spread. Therefore, the reason as to why people are obtaining diseases in hospitals is being examined in more detail. There is a lack of guidelines to help prevent infections from spreading in hospitals (Mutters, De Angelis, Restuccia, Di Muzio, Schouten, Huslcher, & Tacconelli, 2018).

STEWARDSHIP PROGRAMS IN HOSPITALS

Hospitals are one of the most important places that should be sanitized but aren't. The problem with sanitization is due to a lack of antibiotic stewardship, which stems from the fact that each medical provider has their own way of treating such patients and have their own opinions about proper patient treatment (Pulcini, William, Molinari, Davey, & Nathwani, 2011). Stewardship is the obligation of supervising and managing something that is, in this case, treating patients who have contracted a drug-resistant microbe, preventing the microbe from being spread, and decreasing the rate of incidence by following important protocols. Doctors understand the significance of antimicrobial resistance, but many do not worry about it during their daily shifts at the hospital even though they are contributing to the problem. A doctor can prescribe antibiotics to any patient regardless of the severity of the patient's case. Misuse or unnecessary use of the antibiotics is another reason as to why there is more resistance occurring for the many kinds of microorganisms (Alp, Kiran, Altun, Kalin, Coskun, Sungur, & Doganay, 2011). Once a patient obtains a resistant microbe, no drug can cure it immediately, therefore patients have longer bed-stays, and hospitals have higher morbidity and mortality rates (de Kraker et al., 2011).

STEWARDSHIP PROGRAMS IN HOSPITALS

One would assume that the case is different when viewing other countries, but research shows that each case is similar. This review will demonstrate the issues going on in hospitals to determine what doctors are doing to prevent antimicrobial resistance from spreading. The studies indicate a problem with the use and misuse of antibiotics, how healthcare workers are contributing to the issue, and what effective control doctors must do to prevent the problem from increasing. Doctors do not have restrictions and are very lenient when treating patients. The goal of the study is to demonstrate which antibiotic stewardships are the most effective at decreasing the rates of resistance and how well healthcare workers are at implementing the stewardships highly recommended by the researchers.

Methods

Online published articles from the years 2008 through 2018 were obtained. The articles were found in Web of Science, ScienceDirect, or PLOS. In Web of Science, advanced search was used to refine results and such terms were used: "antibiotic resistance" or "bacterial resistance" in ICUs or Hospitals. In Science Direct, the following terms were used: "antibiotic resistance" or "bacterial resistance" in ICUs or Hospitals and doctor technique* "antibiotic resistance" or "microbial resistance." In PLOS medicine, the following search was used: Doctor practice* "antibiotic resistance" or "bacterial resistance". In PLOS pathogens,

STEWARDSHIP PROGRAMS IN HOSPITALS

the following search was used: “antibiotic resistance” or “microbial resistance” in ICUs or Hospitals. For all the databases, the results were refined to have specific dates of “2008-2018” and the article type was always set as “research article”.

The articles were selected based on the data they demonstrated such as explaining antibiotic resistance being a problem in hospitals, finding a solution or prevention for antimicrobial resistance by implementing antimicrobial stewardship programs in hospitals, what doctors were doing that increased the issue, and how patients are being affected. It was important to obtain research articles from a variety of countries as it signifies antimicrobial resistance being a global problem. The studies that were not included had very specific bacterial classes, they did not mention hospitals, the focus was the type of infection the patients had, and the number of patients infected by such diseases. If it was missing information on how to prevent or solve the problem using antimicrobial stewardship programs, then the articles were not considered.

Results

There were fifteen articles in total that were obtained from ScienceDirect, PLOS pathogens, PLOS medicine, and Web of Science. Of the fifteen articles, seven were chosen that met the criteria needed and were reviewed in this research paper. The articles were divided into 2 sections: (1) the misuse and

STEWARDSHIP PROGRAMS IN HOSPITALS

overuse of antibiotics, and (2) Antimicrobial resistance stewardship recommendations.

In order for antimicrobial resistance to cease in hospitals, there must be guidelines implemented or a protocol that healthcare workers must follow. There are a couple of techniques researchers decided to use while researching hospitals. One of the techniques required the researchers to surveil a hospital for ten years to see what sort of susceptibilities were found.

Another article used cycling and mixing to improve the usage of antibiotics and determined whether there would be any sort of decrease in resistance. According to Abel (2014), cycling means, "scheduled changes of the predominant antibiotic in a whole ward or hospital," and mixing means, "the random assignment of patients to different antibiotics, such that at any given time point multiple antibiotics are employed in approximately equal proportions." The usage of antibiotics was tested to see which is the highest recommended treatment, the use of cycling was successful when the dosage was adjusted on a patient whom the bacterium was not multi-resistant to antibiotics. It was proven that cycling is not effective when a patient has a multi-resistant bacterium.

STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

Research Articles	Country research took place	Location of research	Population Size	Study Duration	Methods	Stewardship programs	Results
(A) Junior doctors' knowledge and perceptions of antibiotic resistance and prescribing: a survey in France and Scotland	Nice, France Dundee, Scotland	Centre Hospitalier Universitaire de Nice Service d'Infectiologie, Hôpital l'Archet 1, Route Saint Antoine de Ginestière Ninewells Hospital and Medical School, Dundee, UK	139 post-graduate doctors	5 months	Objective was to assess junior doctors' perceptions of their antibiotic prescribing practice and of bacterial resistance. Surveyed 190 post-graduate doctors still in training at two university teaching hospitals, in Nice (France) and Dundee (Scotland, UK).	Designed control interventions to minimize the spread of antimicrobial resistance and get a medical providers opinion on such actions.	139 doctors (73%) responded to the survey. Doctors were not willing to implement a stewardship program. They were aware of the pandemic issue but did not believe the hospital was affected with antimicrobial resistance. They lacked knowledge on how to treat patients, but were willing to have programs that can educate medical providers on how to treat infected patients.

STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

<p>(B) Changing pattern of antibiotic susceptibility in intensive care units: Ten years experience of a university hospital</p>	<p>Kayseri, Turkey</p>	<p>Erciyes University, Faculty of Medicine</p>	<p>21,104 patients</p>	<p>10 years</p>	<p>Ten years data of ICUs was evaluated retrospectively from surveillance forms. Microorganisms and their antibiotic resistance was recorded according to the years.</p>	<p>Suggested not implemented: Spread of resistant microorganisms can be prevented by effective infection control program. Isolation of the patient, effective hand hygiene, use of gloves and gowns and disinfection of environment and devices are infection control measures recommended for multi-drug resistant microorganism.</p>	<p>During the ten years, there was no consistent data. Some classes of antibiotics increased while others decreased, the reason for this was not studied. Antimicrobial use is the key driver of resistance. Antimicrobial use selects resistant mutant species and it allows the emergence of resistant pathogen in the gut flora.</p>
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STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

<p>(C) Cycling Empirical Antibiotic Therapy in Hospitals: Meta-Analysis and Models</p>	<p>Maas-tricht, The Netherlands, Zurich, Switzerland Boston, Massachusetts, United States</p>	<p>Brigham and Women's Hospital/Harvard Medical School University Hospital Zurich Maastricht University</p>	<p>1000 patients</p>	<p>10 years</p>	<p>Performed a quantitative pathogen-specific meta-analysis of clinical studies comparing cycling to standard practice.</p>	<p>Cycling and mixing of antibiotics for optimal treatment adjustments to decrease levels of resistance.</p>	<p>It has been shown that patient outcome is worse when being assigned to an ineffective initial treatment. At low levels of baseline resistance, clinical cycling reduced the total incidence rate of resistant infections substantially. Adjustable cycling is especially advantageous if multiple resistance has not risen to high frequencies yet but is likely to rise further.</p>
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STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

(D) Use of evidence-based recommendation in an antibiotic care bundle for the intensive care unit	Catania, Italy	Heidelberg University Hospital	142 patients	6 months	Identified evidence-based recommendations (EBRs) of appropriate antibiotic usage in the ICU.	Develop an easy-to-implement bundle for prescribing, testing the adherence, and applicability of the bundle in routine antibiotic management in ICU patients.	The ABC-Bundle is a novel tool to improve the delivery of appropriate antibiotic therapy to patients in the ICU that could be included in an antimicrobial stewardship program.
	Rome, Italy	University of Freiburg					
	Nijmegen, The Netherlands	Fondazione Policlinico Universitario A. Gemelli					
		University of Catania					
		Radboud University					
		Tübingen University Hospital					
		Verona University					

STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

<p>(E) Antibiotic resistance in common pathogens reinforces the need to minimize surgical site infections</p>	<p>Berlin, Germany</p>	<p>Charité Hospital</p>	<p>1 Hospital</p>	<p>N/A</p>	<p>N/A</p>	<p>Suggested, not implemented: Stewardship involves selecting an appropriate drug and optimizing its dose and duration to cure an infection. This minimizes toxicity and conditions for the selection of resistant bacterial strains. Preoperative skin preparation to prevent or minimize surgical site infections.</p>	<p>Antibiotics given sooner (except possibly for longer half-life agents such as metronidazole) are not effective, nor are agents that are given after the incision is closed. Careful preparation of the skin with an appropriate antiseptic is essential.</p>
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STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

<p>(F) Impact of hospital-wide infection rate, invasive procedures use, and antimicrobial consumption on bacterial resistance inside an intensive care unit</p>	<p>Porto Alegre, Brazil Rio Grande do Sul, Brazil</p>	<p>Univer- sidade Fed- eral do Rio Grande do Sul Hospital de Clínicas de Porto Alegre</p>	<p>N/A</p>	<p>30 mont hs</p>	<p>Determined the impact of hospital-wide antimicrobial consumption, invasive procedure use, and Hospital-Acquired Infections (HAIs) on antimicrobial resistance.</p>	<p>Finding a correlation between antimicrobial consumption and antimicrobial resistance.</p>	<p>Significant correlation between antimicrobial use and bacterial multi-resistance rates when antibiotic consumption for the whole hospital was considered.</p> <p>More than one-third of the multi-drug resistant bacteria rate in the ICU could be addressed through infection control measures implemented outside the unit.</p> <p>The finding underlines the relevance of implementing hospital-wide approaches to HAI surveillance and antimicrobial control.</p>
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STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

<p>(G) Implementing an antibiotic stewardship program at a long-term acute care hospital in Detroit, Michigan</p>	<p>Detroit, Michigan, United States</p>	<p>Detroit Medical Center-Wayne State University Kindred Hospital</p>	<p>88 patients</p>	<p>6 years</p>	<p>Team based: including an infectious diseases physician, an infection control practitioner, a microbiologist, and a clinical pharmacist. The stewardship was a 7-step pyramid approach derived from the Centers for Disease Control and Prevention's 12 Steps to Prevent Antimicrobial Resistance (AMR) Among Hospitalized Adults.</p>	<p>Implement successful stewardship program that decreases antimicrobial resistance and was sustainable.</p>	<p>65% of doctors strongly agreed that AMR was a national problem; however, only 38% strongly agreed that it was a problem at their own facility. This indicates that HCP are generally aware of the growing problem of AMR, but they often underestimate the magnitude of the problem at their own facility. Most HCP also believed that interactive health education combined with timely feedback and advice from local experts would be the best way to improve prescribing behavior.</p>
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STEWARDSHIP PROGRAMS IN HOSPITALS

Table 1: Overview of Studies

<p>(H) Infection control and antibiotic stewardship practices reported by south-eastern Mediterranean hospitals collaborating in the ARMed project</p>	<p>South-Eastern Mediterranean</p>	<p>Mater Dei Hospital Hacettepe University Hospital Charles Nicolle Ain Shams University Jordan University of Science and Technology Nicosia General Hospital St. George University Hospital</p>	<p>45 Hospitals</p>	<p>1 Year</p>	<p>Investigation through a structured questionnaire, which examines infection control and antibiotic stewardship practices in hospitals participating or collaborating with the Antibiotic Resistance Surveillance & Control in the Mediterranean Region (ARMed project).</p>	<p>To identify possible contributory factors to help design control interventions.</p>	<p>60% of respondents indicated that they faced situations of overcrowding (the available bed complement was insufficient to cope with demand). 26.7% of hospitals had a committee whose remit included advice on antibiotic use and/or possessed a published approved set of guidelines for antimicrobial prescribing. 56.3% of hospitals believed that this service was not regularly and 68.9% of hospitals reported no interaction with clinicians outside of the laboratory.</p>
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STEWARDSHIP PROGRAMS IN HOSPITALS

- A. Pulcini et al (2011). Gut flora: Complex community of microorganism that live in the digestive tract.
- B. Alp (2011) Half-life: The time it takes for a drug to decrease by half its plasma (blood) concentration.
- C. Abel et al (2014)
- D. Mutters et al (2018)
- E. Dohmen et al (2008) Antiseptic: Relating to or denoting substances that prevent the growth of disease-causing microorganism.
- F. Jacoby et al (2010)
- G. Mushtaq et al (2017)
- H. Borg et al (2008)

Misuse and Overuse of Antimicrobials

All the articles believe that antimicrobial resistance is an issue in hospitals and stated the importance of finding the appropriate usage for antimicrobials. Appropriate usage of antimicrobials is one way to decrease the development of resistance within a microorganism. According to Dohmen (2008), the increased use of antibiotics affects the flora in the gut and causes infections and resistance to travel to the gut because good flora is wiped out. Around 20%-50% of antibiotics are used incorrectly or unnecessarily because patients aren't aware of the harm antibiotic misuse results in. In 2010, a study by Jacoby calculated the total of two years of the consumption of antibiotics to be 38.2 defined daily doses, and for an ICU the total was 91.6 defined daily doses per 100 patient-days.

STEWARDSHIP PROGRAMS IN HOSPITALS

During this time, microbiologists also found nineteen different classes of bacteria in patients, totaling 1,490 separate incidences between patients. Most of the studies showed a correlation between antimicrobial use and bacterial multi-resistance in the hospital.

Antimicrobials are not being handled correctly. Excess amounts are being used and patients are not being given the correct antibiotics (Abel et al., 2014). There is a lack of sanitation in hospitals such as healthcare workers not washing their hands with alcohol, using cloth towels to wipe their hands, and not isolating the patients that are infected (Borg et al., 2008). Questionnaires regarding the knowledge of antimicrobials and antimicrobial resistance were given out to doctors and many answered that they did not feel confident when they stopped antibiotic therapy, planned the duration the patient will undergo the therapy, and the use of multiple drug therapies, but they did feel confident when they diagnosed patients (Pulcini et al., 2011). This lack of confidence when prescribing medication or drug doses to patients is another example of the misuse of antibiotics as doctors don't know the necessary time span to administer the drugs. This extended period of therapy or overuse is a common way for a bacterium to build resistance to the drug (Mutters et al., 2018).

STEWARDSHIP PROGRAMS IN HOSPITALS

Antimicrobial resistance stewardships

Antimicrobial resistance stewardships are not studied often nor implemented in hospitals. Many researchers highly recommend them, but doctors are not likely to use them. The seven articles which observed the significance of antimicrobial resistance had showcased different templates of what the appropriate stewardship program looked like; Table 1 shows in-detail steps or recommendations each article stated based on their results. Selecting the appropriate drug, and providing correct usage, is one way for doctors to prevent the spread of resistance. This means that doctors must be restricted or limited to performing certain treatments and instead consult with a microbiologist about effective treatments for the patient's unique infection. Restricting the use of the same antibiotic on different patients for a certain period must also be implemented in the hospital to decrease antimicrobial resistance (Abel et al., 2014).

Healthcare workers must also be aware and careful when working with ill patients because incorrect procedures can be damaging. Less than 50% of healthcare workers are not committed to controlling programs that involve effective hygienic routines that include handwashing, wearing gloves, gowns, or proper cleaning of used equipment (Alp et al., 2011). 95% of doctors in Dundee's (Scotland, UK) and Nice's (France) research hospital understand the

STEWARDSHIP PROGRAMS IN HOSPITALS

necessity of antimicrobial resistance, but only 63% believed it was a problem in clinical practice. Doctors prefer to be educated about the most effective ways to use antibiotics rather than being restricted to distributing them (Pulcini et al., 2011). Doctors are not likely to agree with restrictions, but the research shows that their lack of agreement is what is causing resistance to occur in hospitals.

Alternatively, clinicians accepted evidence-based recommendations (EBR) for appropriate use of antibiotics in ICUs (Mutters et al., 2018). There were ten EBRs presented, but only six became an antibiotic care bundle (ABC) that was used in the ICU. This bundle was highly recommended by clinicians and researchers but unfortunately, due to a lack of guidelines, the bundle was not used consistently by doctors with less than 85% of performance ratings. This information was not enough to provide an improvement to create an effective ABC bundle. Another form of stewardship is by educating medical providers to change their behavior towards antibiotic resistance (Mushtaq et al., 2017). Education sessions were bi-weekly and during the session, they targeted prescribers and informed them about the most effective antibiotic prescription practices stated by the CDC. This was an intro session to help them create optimal behaviors so policies could be translated and practiced in the hospital. The second phase of this session was based on the CDC's 12 Steps to Prevent Antimicrobial Resistance Among Hospitalized Adults. In the study, they created

STEWARDSHIP PROGRAMS IN HOSPITALS

a team consisting of an infectious disease physician, an infection control practitioner, a microbiologist, and a clinical pharmacist. Out of the twenty-six healthcare providers, only seventeen said that antibiotic resistance is a global issue, and sixteen agreed that antibiotic resistance was a problem in the hospital they worked in. Regardless of their opinions, the team continued to follow the guidelines stated by the CDC and due to such actions, the research was successful and considered sustainable.

Discussion

Antimicrobial resistance is a global issue in-and-out of hospitals. Regardless of the number of times patients get treated, resistance still grows including areas that should be safe from such problems: the hospital. There are several studies highlighting the significance of antibiotic resistance, but hospitals are not inclined to reach such measures to implement changes. The techniques such as antimicrobial cycling and EBRs are not recommended nor effective, as resistance is still evolving. There are many empirical studies being done that show positive results indicating antimicrobial resistance is declining when working with infected patients. The data demonstrates how big the issue is as mortality and morbidity rates are increasing in different parts of the world. In the year 2007, Europe alone had 8,000 resistant bacterium related deaths with 70 million dollars in excess costs. Antimicrobial stewardship will help contain

STEWARDSHIP PROGRAMS IN HOSPITALS

more than one-third of antibiotic resistant bacterium in hospitals and can potentially slow down the spread of many classes of microbes (Jacoby et al., 2010).

Antimicrobial stewardship is very important to prevent the spread of infections, but the lack of support prevents the stewardship from being implemented in hospitals. There are many conflicts researchers face when working with doctors, many do not listen to protocol nor use antibiotics as recommended. Doctors are confident when it comes to prescribing antibiotics, but not when stopping therapy, knowing how long to prescribe antimicrobials, or when treating patients with multiple antimicrobial treatments. This is a major problem because doctors have the freedom to prescribe and distribute antimicrobials freely, but do not use antimicrobials correctly. This is how resistance starts to spread in hospitals. Many studies have shown that misuse of antibiotics is a leading cause of resistance, but it keeps occurring in hospital environments. Researchers are essentially giving doctors all the answers on how to fix this problem, but doctors are simply ignoring their advice.

This indicates a gap between research and healthcare, so what can be done? The issue here is that medical providers are not willing to work with researchers to cease antibiotic resistance. There have been empirical studies done on the proper and improper use of antibiotics, antimicrobial care bundles

STEWARDSHIP PROGRAMS IN HOSPITALS

for use, the rates of mortality and morbidity, etc. This problem is significant as it demonstrates the need for more communication and willingness between researchers and doctors. Without a medical provider's help, the research done will not have enough clinical based evidence to be considered significant and until then, antibiotic resistance will keep evolving.

Limitations

This review had many limitations. First, the studies were all published in English and did not include unpublished work. Second, the data was not specific to infections or type of bacterium which may have affected results. The data was obtained from articles that did studies in different countries, which have also affected the results. The restriction to the search strategy prevented the opportunity of using other articles in relation to the topic. There were many topics amongst each research article, so there may be some inconsistencies with the data. Finally, the length of the research review affected the number of articles obtained.

Conclusion

In summary, it is important to implement antimicrobial stewardship programs in hospitals to reduce antimicrobial resistance. Not many healthcare workers are willing to comply to such programs because they see it as setting

STEWARDSHIP PROGRAMS IN HOSPITALS

restrictions on their work. Healthcare providers may also be knowledgeable about antibiotic resistance, but may not know how to treat infected patients accordingly. For that reason, antimicrobial stewardship programs must be implemented and more research must be done. There is plenty of research recommending and proving that stewardship programs are successful and significant, yet the healthcare workers are not implementing the recommendations enough to say stewardship programs are needed to decrease the spread of antimicrobial resistance.

Overall, further research must be done to demonstrate the effectiveness of stewardship programs. Through this review, it is important to notice that a doctor's behavior must change to a certain degree so stewardship programs can progress and show significance. It is strongly stated that the lack of guidelines is what leads to antimicrobial resistance growth. Such lack of guidelines includes medical providers not using proper sanitation skills, not isolating infected patients, not providing the correct drug or dosage of drugs, and not providing a correct form of therapy. Without the stewardship programs, antimicrobial resistance will continue spreading and evolving in hospitals globally.

STEWARDSHIP PROGRAMS IN HOSPITALS

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STEWARDSHIP PROGRAMS IN HOSPITALS

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