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Effectiveness of Educational and Behavioral Models in the Reduction of Inappropriate Antibiotic Prescribing in United States Health Delivery Settings

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Abstract:

Inappropriate antibiotic prescribing represents the most avoidable cause of resistance to antimicrobial drugs (CDC, 2015). As prevention constitutes the core principles of public health, any intervention addressing inappropriate antibiotic prescribing is susceptible of improving the health outcomes of communities as well as reducing the risk of resistance capable of inducing the worsening of the antimicrobial pandemic. Policymakers and public health leaders implemented several measures to tackle antibiotic resistance. Among those, we can mention educational training and behavioral interventions using either clinical decision support system, intrapersonal or interpersonal models to support changes in antibiotic prescribing. This project consisted of a systematic narrative review of seven studies describing interventions implemented to undertake the problem of inappropriate antibiotic prescribing in the United States (US). I focused on conducting a qualitative analysis of selected peer-reviewed papers. The purpose was to evaluate these different interventions and proceed to a comparative analysis that would permit us identifying the most efficient method to address this public health problem. Seven US experimental study designs evaluating educational and behavioral approaches were retained (Metlay 2016; Gonzales 2013; Gerber 2013; Meeker 2016; Mc Ginn 2015; Meeker 2014; Mainous 2013). All interventions from each selected study produced a distinct improvement in the reduction of inappropriate antibiotic rate for acute respiratory tract infections (ARTI). The decrease in antibiotic prescribing was considered the main favorable outcome described in the studies indicating a potential reduction in the risk of antibiotic resistance. Despite the encouraging findings from the systematic review, further investigations are needed to depict intervention that will be able to reduce inappropriate prescribing in hospitals and ambulatory health practices in the United States.

Introduction/Background

According to the Center for Disease Control and Prevention (CDC), antibiotic resistance approximately caused 2,049,442 diseases and 23,000 deaths on a yearly basis (CDC, 2015). Antibiotic resistance is defined as the capacity of bacteria to resist the effects of antibiotics which used to treat them. This issue constitutes one of the greatest global health problem affecting every single country. The spread of antibiotic prescribing worldwide exacerbated the number of antibiotic resistance cases. The exponential intake of antibiotics contributes to the overuse of these medications triggering resistance to their therapeutic effect.

Burden of antibiotic resistance

The Center for Medicaid and Medicare Services (CMS) stated the national health expenditures (NHE) was $ 3.2 trillion in 2015. This estimate represented an augmentation of more than five percent compared to the previous year. The endless debate to reduce national budget deficits and the difficulty to obtain sufficient funds to keep various health promotion and social empowerment programs justified the urgency to find effective methods to tackle this issue.

Antibiotic resistance represents a major public health concern considering the huge financial burden it created. To illustrate this significant financial load, Watkins, & Bonomo (2016) affirmed that antibiotic resistance cost the United States $55 billion annually. A closer look at this number revealed about $ 20 billion in term of health care cost and $ 35 billion for productivity loss. Golkar, Bagasra, & Pace (2014) went further by revealing that “medical cost per patient with an antibiotic resistant infection range from $18,588 to $29,069.” By contrast, CDC (2015) showed the average health expenditures in the United States was $ 9,523. A closer look at these statistical data showed that antibiotic resistance doubled and even tripled the healthcare burden per capita in the United States. The difference between these two measures displayed an enormous discrepancy illustrating the enormous impact of antibiotic resistance on the healthcare system.

The difficulty in treating patients who developed resistance to antibiotics worsened the expenditures as well. When medications are ineffective, patients tend to develop serious complications, increasing hospital length of stay as well as additional tests and treatment cost. This situation is alarming since the average medical expenses per capita is already exorbitant. The immense financial burden induced by antibiotic resistance justified the urgency to find credible solutions to tackle antibiotic resistance.

Mechanism of antibiotic resistance

Various mechanisms could cause resistance to antibiotics. Some medicines need to adhere to a target site called receptor on the bacteria wall to neutralize the microbe. An alteration of the target site might cause the antibiotic to become inefficient.

Bacteria can undergo some genetic mutations allowing them to produce metabolic products capable of inactivating drugs. These metabolites could incorporate the molecular drug and destroy or stopped the antibiotic.

Another common mechanism of antibiotic is related to the bacterial membrane. Some antibiotics must cross the microbial membrane to neutralize the genetic material. The alteration of the microbial pathogen can decrease the intracellular antibiotic accumulation by reducing their permeability or augmenting the efflux of antibiotics.

These antimicrobial medications are divided into various groups. These types of antibiotics differed from each other by their molecular structure or their mechanism of action (Blair, 2015).

Preventable causes of antibiotic resistance

The issue of antibiotic resistance existed more than 75 years ago. The first resistance was identified in the 1940s with the penicillin-resistant Staphylococcus aureus. Over the years, the issue escalated with other resistant organisms as long as antibiotic treatment expanded. Many causes such as overuse, inappropriate prescribing, and availability of new antibiotics have been identified as responsible for the growing burden of antibiotic resistance. (CDC, 2013; Ventola, 2015).

Antibiotic overuse consists in the intake of antibacterial drugs not appropriate to the pathogenic agent. In some cases, this overuse occurs because of the prescribers' lack of training. Most of the time, it is due to the deficit of knowledge regarding the latest treatment guidelines.

The lack of availability of new drugs in the market tends to increase the likelihood of antibiotic resistance. Nowadays, we observe a proliferation of new medicines targeting chronic diseases such as cancer, cardiovascular illnesses. By contrast, pharmaceutical companies are reducing their effort to create new drugs. The main reason is the lack of profit antimicrobial drugs generate, compare to medications for chronic health conditions. Infections treatment usually take weeks and rarely months to be treated. On the other hand, cancer or heart disease care lasts years obliging the patients or their health insurance companies to spend thousands of dollars. Clinical trials in the United States are burdensome, and these companies are eager to invest in products that would help them compensate their expenses. This choice is so unfortunate because microorganisms are increasingly becoming more resistant to old antibiotics. Studies on new antimicrobial drugs are imperative to attempt a reduction of resistance. With the advocacy of many public health leaders, we hope pharmaceutical companies will start investing more on new antibiotics.

Inappropriate antibiotic prescribing

The inappropriate antibiotic prescribing is defined by "any unnecessary use and improper selection, dosing and duration of antibiotics" (CDC, 2016). According to the federal agency mentioned above, inappropriate antibiotic prescribing represents the most preventable cause of antibiotic resistance. CDC identified several causes increasing the likelihood of inaccurate prescribing among providers and patients. The agency denoted, in its most recent study on inappropriate prescribing, that "perceived patient expectations, concern for misdiagnoses, time pressure," absence of behavioral incentives and old prescribing habits constituted major risk factors of inappropriate antibiotic prescribing. Sometimes, providers' misperception of their prescribing pattern could induce antibiotic resistance.

Venugopalan (2016) revealed that "while other practitioners overprescribe antibiotics, they did not feel that their prescribing habit was a problem." By denying their practice was facing the issue of inappropriate antibiotic prescribing, these providers contributed to the worsening of antibiotic resistance.

Acute respiratory tract infections (ARTI) and inappropriate antibiotic prescribing

According to Harris (2016), ARTIs represent the leading cause of antibiotic prescribing in adults. Acute bronchitis, common cold, pharyngitis, rhinosinusitis constitute the primary health conditions labeled under ARTIs. Most of these respiratory illnesses are often caused by a viral agent that is insensitive to antibiotics. Harris continued by revealing that even for bacterial rhinosinusitis, the use of

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antibiotics was barely helpful in some cases. Unsurprisingly, ARTIs represent the primary source of inappropriate antibiotic prescribing in hospitals and ambulatory settings (CDC, 2016).

Despite this evidence, various studies showed providers were more prone to prescribe antibiotics for these infections raising the likelihood of inappropriate prescribing. One of the main reason behind this situation is the fact that patients and even prescribers are more likely to expect to receive antibiotics regardless the nature of infections (Broniatowski, 2014). Additionally, the ease of transmission of such health conditions augments their incidence and the risk of antibiotic resistance (Magill, 2014). Fauci & Marston, (2014) illustrated the gravity of inappropriate prescribing in the treatment of viral respiratory infections when they stated that" almost 75% of US adults seeking treatment for acute bronchitis, mostly caused by a virus, are prescribed antibiotics."

Educational training and inappropriate antibiotic prescribing

CDC (2016) believed that reducing providers 'knowledge deficit and behavioral barriers" would increase appropriate antibiotic prescribing. CDC stated that the failure of providers to adapt their practice to the latest prescribing guidelines was to blame as one of the leading factors of inappropriate antibiotic prescribing. Thus, a strategy based on the training of clinicians was considered as potential intervention capable of reducing inappropriate antibiotic rate. The American Board of Internal Medicine regularly reviewed the plan of care of diseases, particularly infectious illnesses.

Fortunately, various studies revealed antimicrobial stewardship program (ASP) showed an amelioration of health outcomes and a diminution of antibiotic resistance as well as the healthcare burden. The Infectious Disease Society of America defined ASP as" coordinated interventions designed to improve and measure the appropriate use of antimicrobials." CDC, through his program "Get Smart," praised the impact of ASP on the reduction of antibiotic resistance with the propagation of informational session explaining to clinicians and patients the use of proper antimicrobial drug regimen, dose, duration of therapy, and route of administration. ASP minimizes toxicity and other adverse events, reduce the costs of health care for infections, and limit the selection of antimicrobial-resistant strains. The United Hospital Fund (2016) realized that ASP could diminish the burden of antibiotic resistance by "improving outcomes, and decreased in overall healthcare cost." A major strength of ASP is the capability to reduce inappropriateness of antibiotic use by educational training of providers. The systematic review included educational interventions from selected research conducted in different the United States health care settings. The review of these studies will assess the degree of effectiveness of the strategies to reduce inappropriate antibiotic utilization.

Behavioral interventions

Behavioral intervention refers to any approach based on psychosocial theories related to intrapersonal, interpersonal models at the individual, societal, organizational, community or governmental level (Glantz, 2008). In the context of my project, behavioral intervention aims to improve the quality of care and to decrease negative behavior susceptible of increasing the chance of developing antibiotic resistance.

The perception of patients to receive antibiotics regardless the origin of the infection had been documented as influencing providers' prescribing habit. Cals (2014) estimated that communication training could change the behavior of prescribers, reducing antibiotic overuse for respiratory infections. Additionally, several strategies using intrapersonal, interpersonal, and other behavioral models have been tested in some healthcare delivery systems. Recently, researchers denoted planning interventions at the organizational level could bring significant change in health behavior of the targeted population by constant exposure to psychological prompts.

The capstone project would analyze the results of selected behavioral interventions to determine their effectiveness by depicting the methodology of each selected studies and investigate the correlation between their results and the characteristics of each factor involved in the study.

Problem Statement

Many researchers conducted several studies on antibiotic prescribing by published guidelines with a focus on inappropriateness. CDC (2016) stated that "44 percent of outpatient antibiotic prescriptions are written to treat patients with acute respiratory conditions, and half of these outpatient prescriptions are unnecessary. "This assertion is alarming since overexposure of the human body to antibiotics is more likely to induce tolerance to these medications that would eventually evolve into resistance.

Inappropriate antibiotic prescribing represents the most avoidable cause of resistance to antimicrobial drugs (CDC, 2015). This could be explained by the fact that licensed prescribers (Physicians, Nurse Practitioners, and Physician-Assistants) are relatively easy to target, and already possessed sufficient knowledge that would make an educational or behavioral intervention less challenging than trying an approach focusing on patients and the communities as a whole. Furthermore, clinicians can

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contribute to the education of their patients once they received the most updated antibiotic prescribing guidelines. Besides, by prescribing and teaching their patients on the importance to follow the selected medications, they may reduce their reluctance to be compliant. As prevention constitutes the core principles of public health, any intervention addressing inappropriate antibiotic prescribing is susceptible of improving the health outcomes of communities as well as reducing the risk of resistance capable of inducing the worsening of the antimicrobial pandemic. Hospitals in the United States have been using various methods to overcome the inaccurate prescribing of antibiotics. Often, these health delivery settings are financially limited and cannot dedicate resources to combat antibiotic overuse and activities as economically feasible to figure out the most efficient measure for their settings.

Aware of this growing pandemic, policymakers and public health leaders implemented several measures to tackle antibiotic resistance such as antibiotic stewardship, patient education. Among those, we can mention educational training and behavioral interventions using either clinical decision support system or intrapersonal or interpersonal models to support a change in antibiotic prescribing.

Although several studies described several attempts to reduce inappropriate antibiotic prescribing in the United States, it is not clear there is a single approach that would show a higher potential to reduce this public health issue. This Capstone Project will evaluate peer-reviewed papers treating educational and behavioral intervention against inappropriate antibiotic prescribing to depict the most effective intervention capable of providing meaningful results while minimizing the cost of its implementation.

<u>Research Question- Objectives of the Study</u>

Few researchers conducted a systematic review of recent methods implemented in the United States delivery system to tackle the issue. Knowing that systematic reviews allow the comparative analysis of various interventions as well as investigating their effectiveness, I decided to use that study design to address the following question: which approach is more likely to diminish the issue of inappropriate antibiotic prescribing of acute respiratory infections in hospital and ambulatory settings in the United States?

I considered educational and behavioral models as the interventions of interest for my systematic review. This decision was motivated by the fact that several papers showed these approaches could reduce antibiotic resistance.

This Capstone Project is investigating the effectiveness of both interventions by selecting several studies targeting different health delivery systems from various regions in the United States.

I emphasized on ARI since they are highly prevalent in healthcare settings. Moreover, physicians were prone to prescribe antibiotics to these health conditions often caused by viruses which are insensitive to them. For these two reasons, the systematic review should be able to provide a significant generalizability to the outcome of the project.

I hope this systematic review will describe the most efficient approach capable of reducing inappropriate antibiotic prescribing. Consequently, the Capstone Project will lessen the likelihood of antibiotic resistance and allow the healthcare system of the United States to reduce drastically billions of dollars and attenuate patient harm.

Methodology

The purpose of this Capstone was to evaluate these different interventions and proceed to a comparative analysis that would permit us identifying the most efficient method to address this public health problem. I reviewed several studies related to approaches used to reduce inappropriate antibiotics prescribing. This project consisted of a systematic narrative review of seven studies describing interventions implemented to undertake the issue of inappropriate antibiotic prescribing in the United States.

Type of interventions

The systematic review incorporated these approaches listed below:

- Educational materials for clinicians: printed, electronic or audiovisual materials that target the health care professional. Metlay (2016), Gonzales (2013).
- Educational meetings: health professionals attending lectures or training courses. Gerber (2013), Meeker (2014).
- Audit and feedback: any summary of clinical performance of health care over a specified period provided to the healthcare professional. Gerber (2013).
- Reminders: verbal, written or electronic information intended to prompt a health care provider to recall information. Mc Ginn (2015); Mainous (2013).
- Behavioral interventions such as peer comparison, suggested alternatives, accountable justifications. Meeker (2016).

These strategies could be classified in two categories following Davey et al. (2013) methodology. The first set of intervention called "persuasive" method sought the reduction of inappropriate antibiotic prescribing through educational training or behavioral techniques. By contrast, the second type of intervention named restrictive strategy is

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characterized by the implementation of some form of constraint preventing prescribers the ability to include specific antibiotics in their medication order.

Search strategy

I ran a thorough search through Medline, Cochrane, and other American peer-reviewed sources such as the Journal of the American Medical Association (JAMA) and the Infectious Disease Society of America (IDSA) to detect these selected studies.

I performed an initial screening by reading the title and abstracts of pre-selected articles. I excluded all peer-reviewed papers that described mainly the causes or the impact of inappropriate prescribing but ignored the interventions implemented to address that issue.

Type of outcomes measured:

The primary outcomes measured were:

- The level of antibiotic prescriptions for patients with acute respiratory infections (ARI) whose providers were exposed to educational and behavioral interventions compared to those included in control groups. (Metlay, 2016; Gonzales, 2013; Gerber, 2013).
- The level of antibiotic prescriptions for patients with ARI whose providers were exposed to behavioral interventions compared to those included in control groups. (Mc Ginn, 2015; Meeker, 2016; Mainous, 2013; Meeker, 2014).
- The adjusted and non-adjusted inappropriate antibiotic prescribing rate between providers exposed to the intervention and the control group.

The secondary outcomes depicted were:

- Broad-spectrum antibiotic prescribing rate (Mainous, 2013).
- Rapid Streptococcal test order rate (Mc Ginn, 2015).

Study selection

I selected and reviewed ten studies describing strategies implemented by healthcare delivery systems to promote appropriate antibiotic prescribing. Based on specific criteria, three of them were excluded. The following criteria utilized for the systematic review are listed below:

1) First, all studies should occur in the United States. This principle was crucial since the objectives of the project target the improvement of antibiotic prescribing in the United States. Additionally, this choice reduced the risk of internal validity that would occur when comparing the same intervention for two different healthcare systems with their measurements.
2) Secondly, I limited the selection of these studies to published papers from 2012 to date. Considering the dynamic progression of healthcare, it would have been detrimental to our research to incorporate interventions older than five years old since the emergence of new prescribing guidelines, and more performing delivery systems rendered obsolete the accuracy of the results previously published before 2010.
3) Third, all selected articles were subject to experimental studies. These designs were mostly randomized controlled and clustered randomized trials. Researchers have better control of independent and third variables making it easier for them to reduce the risk of random and systematic errors.
4) Fourth, I purposely chose acute respiratory infections as the primary focus of the interventions. The literature review showed viral respiratory infections was among the leading causes of inappropriate antibiotic prescribing. Thus, selecting interventions to improve appropriate prescribing for these health conditions would significantly diminish antibiotic resistance.
5) Fifth, the participants were mostly providers (Attending Physicians, Residents, Nurse Practitioners, and Physician Assistants). Prescribers who worked in long-term care facilities such as nursing homes were not targeted by the systematic review. I voluntarily excluded studies that focused solely on patients. The reason behind this exclusion was prescribers constitute the most important stakeholders capable of reducing significantly inappropriate antibiotic intake since they possess a professional license to order such medications.

Once I determined the set of studies for the systematic review; I proceeded to their classification using different criteria. First, I grouped them according to the type of intervention: educational or behavioral approaches.

An educational intervention was defined by any method that allows individuals to acquire scientific knowledge that will improve their awareness, professional skills, or ability to perform their current work or to make healthy choices to enhance their well-being (CDC, 2015)

A behavioral intervention refers to psychosocial theories based on intrapersonal, interpersonal models at the individual, societal, organizational, community or governmental level (Glantz, 2008)

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I split the seven papers into three groups. Cluster randomized controlled trials (cRCTs), randomized control trials (RCTs), and quasi-experimental designs. (Table1)

The patient population consisted of children and adults treated for ARTIs in the United States.

The purpose of classifying the selected papers by intervention and type of experimental designs was to obtain a comparative analysis of their results and to determine their impact on the outcomes of the studies.

Assessment risk of bias in included studies

I used the Cochrane Collaboration's tool to estimate the possibility of bias. (Higgins, 2011) This tool used these six standard criteria (adequate sequence generation, concealment of allocation, blinded or objective assessment of personnel and primary outcomes, adequately addressed incomplete outcome data, freedom from selective reporting, freedom from another type of bias). A brief definition of each criterion explained the importance of the Cochrane Collaboration's tool for improving the quality of measurement of the review.

The adequate sequence generation assures a random assignment of subjects into intervention and control groups. Thus, it reduces the risk of selection bias and occurs at the beginning of the trial before the distribution of participants into different groups.

The concealment of allocation happens at the start of a study and minimizes selection bias as well. It reinforced the previous Cochrane criteria by strengthening the random assignment by preventing "the selection of who to recruit" as well as keeping the change of order.

The blinding of participants and personnel targets the elimination of performance bias. This criterion is important because it reduces the influence of the subjects and researchers' expectations on the outcomes. The blinding of results decreases detection bias diminishing the likelihood for the measurements to be affected by the "knowledge of intervention received."

The incomplete outcome of data refers to the creation of a systematic difference due to withdrawals. A high rate of withdrawals can threaten the validity of the study since those who quit the study may have had a different outcome.

Freedom for selective reporting decreases reporting bias by preventing results not to be incompletely reported due to researchers own expectations.

Data synthesis

I conducted a narrative synthesis of the results collected from the selected studies. I evaluated the studies based on their quality, designs, type of interventions, settings. Additionally, I performed an analysis of the theoretical basis of the approaches as well as their respective results.

Results

Description of studies

The effectiveness of educational and behavioral strategies used healthcare delivery systems to reduce inappropriate antibiotic prescribing.

Search result

Based on the criteria, seven studies were retained (Metlay 2016; Gonzales 2013; Gerber 2013; Meeker 2016; Mc Ginn 2015; Meeker 2014; Mainous 2013).

The remaining three papers (Kelly 2017, Camins 2009, Vinnard 2012) were excluded. Several reasons explained these exclusions. For instance, Vinnard et al. (2017) used only an observational study design to perform their research which made the paper ineligible for my capstone project. Regarding Camins, the published date of the peer-reviewed article failed to fall within the five-year window of the condition for inclusion. Although Kelly et al. paper covered an intervention acting against the inappropriate antibiotic prescribing, it did not use any epidemiological design and was essentially a report paper publishing the result of an ASP program.

Geographical location of the study

At least four of the selected studies (Gerber, 2013; Gonzales, 2013; Mc Ginn, 2015; Meeker, 2016) targeted providers working in health care facilities located in the Northeastern region of the United States and two others (Meekers,2014 & 2016) using participants operating in Southern California. The remaining studies targeted population living in urban areas.

Interventions

Although the selected studies focused on educational and behavioral approaches, the interventions were diverse and multidimensional.

Some studies used a multifaceted educational purpose. Several peer-reviewed papers revealed that a significant number of providers were not aware of the latest prescribing guidelines. Moved by this situation, Metlay et al. (2016) constructed an educational approach that permitted the participants to access the most recent prescribing updates. Metlay described a strategy including a combination of behavioral and pedagogical models. The Predisposing

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Reinforcing and Enabling Constructs in Educational Diagnosis and Evaluation (PRECEDE) constituted the fundamental basis of this intervention. The researchers utilized the four phases of PRECEDE to conduct their research. The initial phase, stating the desired result, focused on principles of appropriate antibiotic intake for ARTIs. Constant exposure to educational posters and distribution of brochures were documented as possible successful health promotion approach for PRECEDE. The authors utilized this evidence-based model to verify its possible replication in the fight against inappropriate antibiotic prescribing. Use of educational slides displaying evidence of appropriate prescribing for acute bronchitis represented the core of the provider educational intervention. These informational sessions were based on the CDC Get Smart Program.

Gonzales et al. (2013) used PRECEDE as well to evaluate the effectiveness of two informational support methods conducted in Pennsylvania. Their methodology consisted in three "arms cRCTs. These groups are respectively printed decision support (PDS), computer-based decision support (CDS) and a control arm. Each of them was assigned eleven primary care sites. The researchers conducted three separate experimental design as well as a comparative analysis of the results. PDS was tested in eleven health care systems where informational brochures on appropriate antibiotic prescribing were distributed to patients. CDS offered the availability of educational materials capable of inspiring the targeted providers to take the proper medical decisions in the treatment of respiratory symptoms (cough, dyspnea).

A third study evaluating educational intervention by using c RCT was conducted by Gerber et al. (2013). The primary objective of these researchers was to investigate the effectiveness of an ASP intervention on antibiotic prescribing for pediatric patients suffering from ARTIs. To increase the internal validity of the study, Gerber et al. excluded children with prior antibiotic use, chronic illnesses, and antibiotic-related allergies. The intervention consisted of an on-site session of an hour to clinicians working in eighteen primary care practices located in Pennsylvania and New Jersey. Additionally, the researchers conducted a personalized audit and feedback for "guideline-based antibiotic prescribing rate for the healthcare settings. Clinicians from control practices were neither exposed to the educational training nor the feedback.

Mc Ginn et al. (2015) used RCT to evaluate the impact of a behavioral intervention based on electronic clinical decision support tool coupled with the implementation of a point of care. Like all selected studies of the capstone project, this intervention was related to the treatment of ARTIs. (Figure 1)

Mc Ginn conducted an RCT in two ambulatory primary care practices in New York City recruiting physicians, residents, and nurse practitioners. The study encompassed two phases. The first step described the development and usability testing of the CPR tool, and the second one consisting of the assessment of the CPR's effectiveness in the reduction of risk of inaccurate antibiotic prescribing. The providers included in the intervention group attended a one -hour session where they were explained the latest guidelines related to the treatment of streptococcal pharyngitis and pneumonia. The researchers followed the outcome of "patient encounters with the study providers" and processed to the data collection through EHR for the intervention period. (Figure 1)

Meeker et al. (2016) used a c RCT to evaluate the effectiveness of a multifaceted behavioral intervention. The evaluation consisted of measuring the prescribing antibiotic rate among cases of "antibiotic-inappropriate ARTIs." Meeker et al. targeted clinicians working in 49 primary care practices using three EHRs from two renowned health delivery systems located in Massachusetts and California. Each of them comprises 22 practices. These prescribers received an invitation via email asking them to attend an online educational module presenting the latest guidelines related to ARTIs treatment. The primary study outcome was the prescribing antibiotic rate for antibiotic-inappropriate acute respiratory tract infection visits.

The main criteria for inclusion for Meeker were: patients 18 years or older, enrollment of both clinicians and practices, and visit occurrence "during the 18-month baseline and 18-month intervention period". The primary cause of exclusion was related to patients with comorbidities.

Three types of behavioral interventions were used by Meeker. The first strategy was the suggested alternative. It consisted of a computer-based system that would buzz the prescriber stating" antibiotics are indicated for this ARTIs diagnosis. Please consider the following prescriptions, treatments, and materials to help your patient."

The second behavioral method was accountable justification. It was characterized by a prompt requesting providers to furnish explanation justifying the prescription of a particular antibiotic against ARTIs. Moreover, the system warned the providers their justifications would appear on the patient's chart.

The last intervention was peer-comparison that allowed the ranking of prescribers from the higher to the lowest antibiotic prescribing rate through email. Those with the lowest number were called co-workers.

Other selected studies investigated the effectiveness of behavioral interventions against inappropriate antibiotic prescribing using RCT. For instance, Meeker et al. (2014) examined the effectiveness of a behavioral "nudge" based

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on the social cognitive theory. The researchers used five outpatient settings from the Los Angeles area to conduct their investigation. The study focused mainly on patients diagnosed with ARTI. The strategy consisted of a letter displaying poster-sized commitment letters in examination rooms for 12 weeks. According to Meeker "these letters, featuring clinician photographs and signatures, stated their willingness to avoid inappropriate antibiotic prescribing."By using this method, the authors hoped to figure out a successful approach for reducing inappropriate antibiotic prescribing.

Mainous (2013) conducted a quasi-experimental study to evaluate the impact of CDSS on antibiotic prescribing for ARTIs. Seventy United States healthcare delivery systems were selected among the Practice Partner Research Network (PPRNet). Among these health centers, nine were put in the intervention group and the remaining ones in the control group. PPRNet's health centers use an electronic health record (EHR)-based software that collects patient data and medical billing. The researchers "used" PPRNet to vehiculate a CDSS including the latest antibiotic prescribing guidelines. According to Mainous this CDSS possessed a" template that helps the provider in deciding on the appropriate diagnosis. Once a diagnosis has been made, the CDSS includes prompts about appropriate antibiotic use, and, when necessary, recommended first-line antibiotics." To increase the adherence of participants to the study and to reduce the loss to follow-up, Mainous et al. initiated multi-interventions encouraging providers to adopt the CDSS. The primary outcome of the study was to evaluate the level of inappropriate antibiotic among PPRNet patients who were diagnosed with ARI. The researchers used two methods: assessing the effectiveness of the intervention by dividing the number of ARI episodes where antibiotic use is appropriate by the total number of ARI episodes with an antibiotic prescription. The other measurement used the ratio corresponding to the number of ARI episodes for which antibiotics are inappropriate by the total number of ARI episodes.

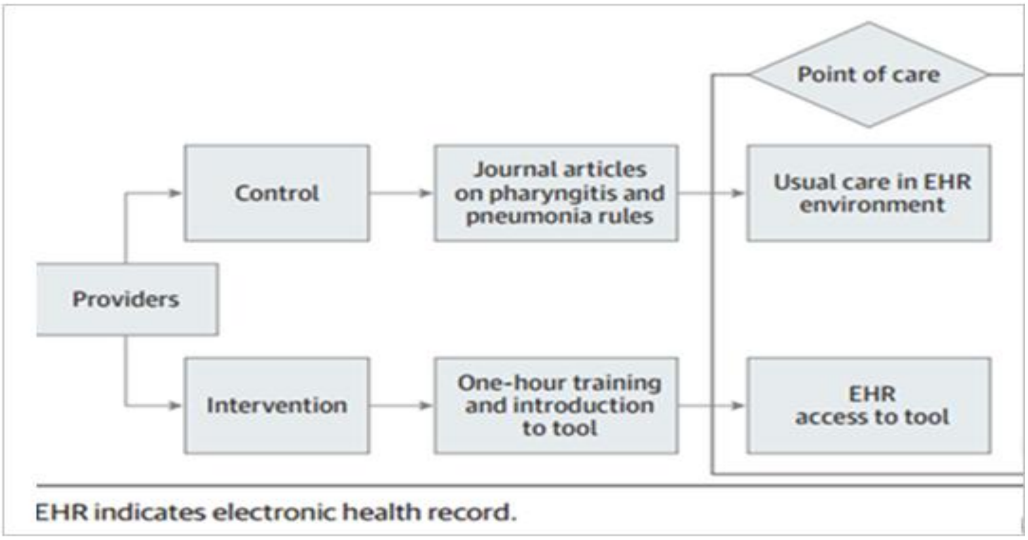

Figure 1 Study activities for Healthcare Providers for Control and Intervention group (Mc Ginn, 2015)

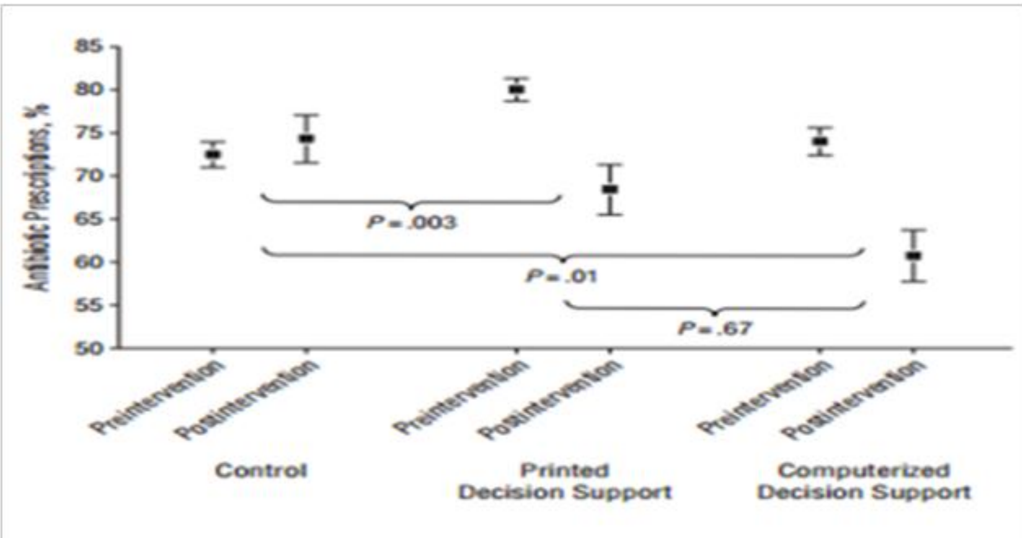

Figure 2 Effect of CDS and PDS on antibiotic prescription rates for patients diagnosed with acute bronchitis (Gonzales, 2013)

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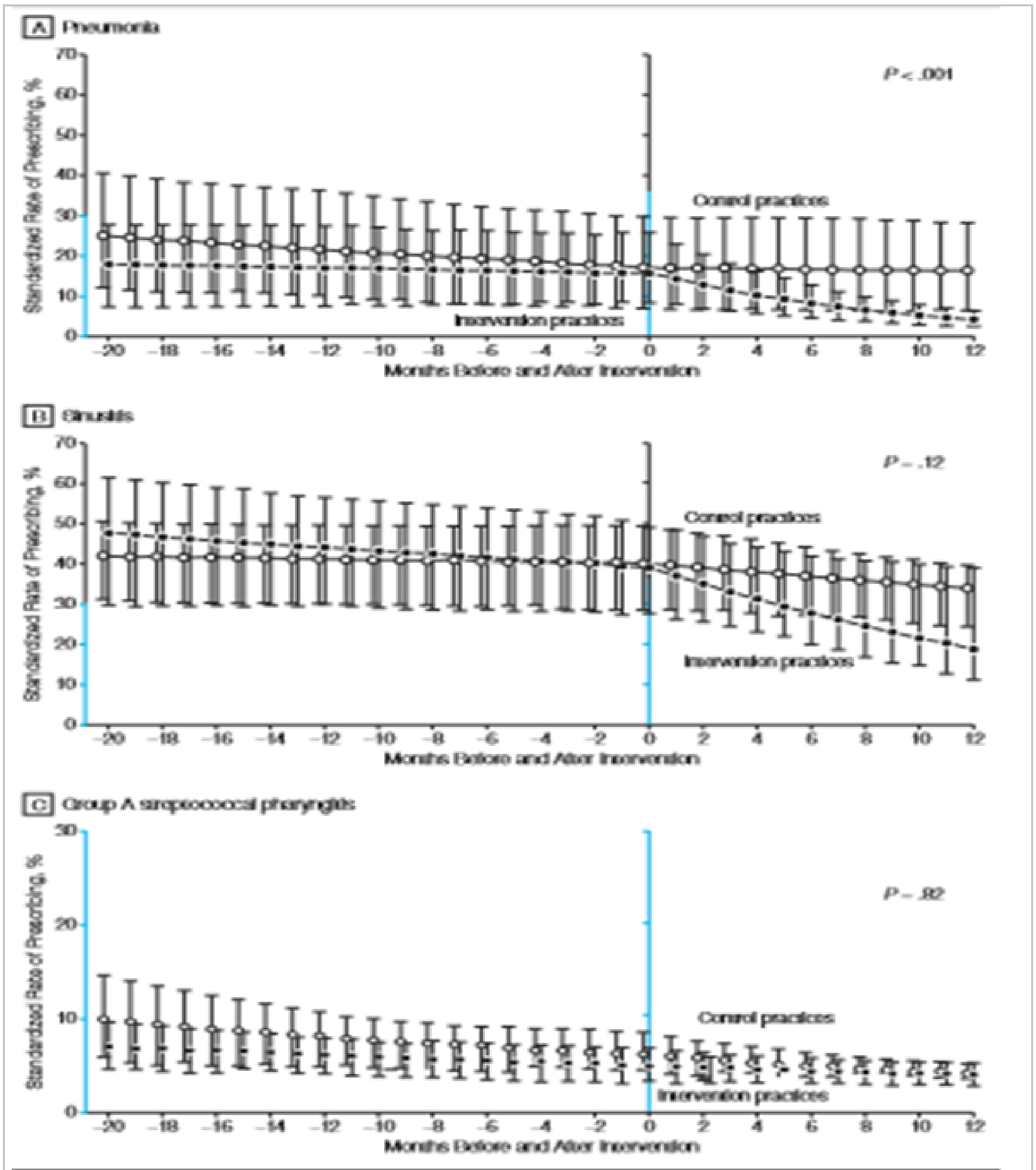

The estimate of interest (and associated *P* value) is the treatment × time interaction term, representing the relative changes in trajectories before and during the intervention. Error bars indicate 95% CIs. Y-axis in blue indicates range 0% to 30%.

Figure 3 Standardized Rates of Broad-Spectrum Antibiotic Prescribing at Acute Care Office Visits by Specific Acute Respiratory Tract Infection (Gerber, 2013)

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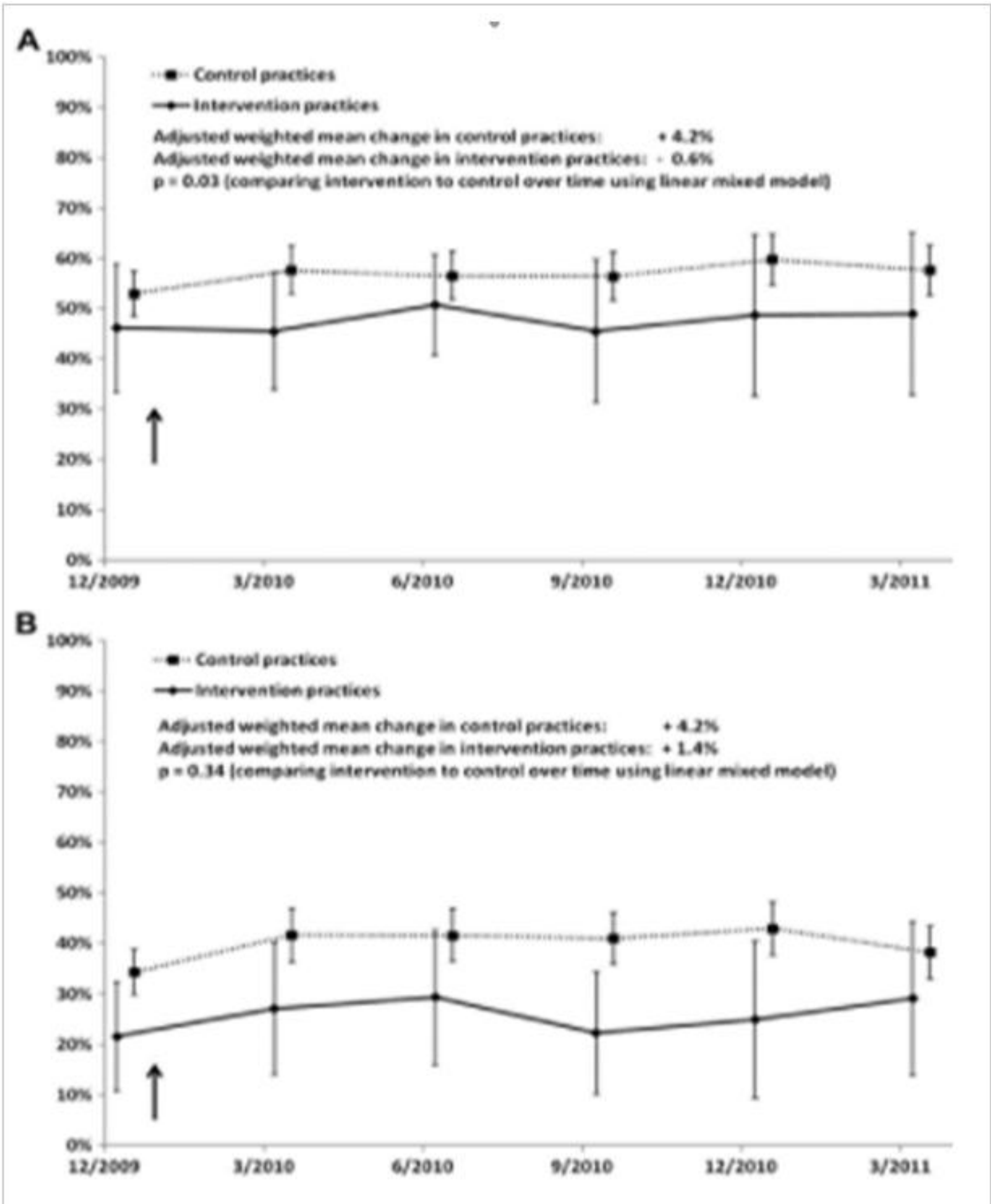

Figure 4 Comparison of intervention and control practices 'inappropriate prescribing over time between adult (A) and pediatric (B) (Mainous, 2013)

Table1: Classification by interventions and study designs

Authors	**Interventions**	**Study Designs**	**Main approach**	**Health settings**
Metlay, 2016	Educational	Cluster RCT	Informational slides Reprints materials on appropriate prescribing.	Veteran Health Center. US Urban areas
Gonzales, 2013	Educational	Cluster RCT	Printed decision support	Primary Care ambulatory settings.
Gerber, 2013	Educational	Cluster RCT	1 hour Education session Audit and feedback	Pediatrics ambulatory settings
Meeker. 2016	Behavioral	Cluster RCT	Suggested alternatives Accountable justifications Peer Comparison	Hospital settings
Mc Ginn. 2015	Behavioral	RCT	Clinical Decision Support System	Primary Care ambulatory practices
Meeker. 2014	Behavioral	RCT	Commitment Letter to providers containing antibiotic guidelines	Primary Care ambulatory settings
Mainous, 2013	Behavioral	Quasi-experimental	Clinical Decision Support System	Hospital and ambulatory settings in the United States

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Table 2: Site-specific levels of antibiotic prescription for patients diagnosed with URI and acute bronchitis at control and intervention sites. (Metlay, 2016)

	Visits Prescribed Antibiotic (95% CI), %			
Site	**Year 1 Unadjusted**	**Year 2 Unadjusted**	**Year 1 Adjusted[*]**	**Year 2 Adjusted[*]**
Control[†]				
Control 1	33.9 (25.2-42.7)	39.8 (30.4-49.3)	34.9 (27.8-42.8)	39.8 (30.9-49.4)
Control 2	44.4 (33.0-55.9)	52.8 (42.4-63.2)	46.2 (35.0-57.9)	53.5 (43.9-62.9)
Control 3	33.7 (24.3-43.0)	29.2 (20.1-38.3)	33.8 (25.2-43.6)	29.1 (20.7-39.3)
Control 4	36.4 (27.4-45.4)	24.1 (16.4-31.9)	35.6 (27.0-45.2)	25.7 (11.9-34.8)
Control 5	77.9 (69.9-85.9)	75.0 (66.5-83.5)	72.9 (61.1-82.1)	68.4 (57.9-77.4)
Control 6	27.6 (18.7-36.4)	28.7 (20.7-36.7)	26.6 (16.9-39.3)	30.1 (20.5-41.7)
Control 7	55.1 (46.1-64.1)	58.1 (48.7-67.5)	55.5 (43.6-66.8)	61.0 (48.7-72.0)
Intervention				
Intervention 1	38.8 (28.1-49.4)	32.9 (22.1-43.7)	36.6 (25.7-49.0)	31.4 (21.6-43.1
Intervention 2	50.9 (41.4-60.5)	28.8 (18.8-38.7)	50.5 (38.8-62.1)	26.6 (18.7-36.5)
Intervention 3	77.9 (71.2-84.5)	62.8 (53.4-72.1)	71.7 (62.2-79.6)	54.6 (41.1-67.5)
Intervention 4	45.5 (33.4-57.5)	55.3 (45.3-65.4)	46.0 (28.1-64.9)	56.7 (37.4-74.1)
Intervention 5	75.4 (67.9-82.9)	60.9 (52.5-69.4)	78.5 (70.2-85.0)	62.7 (49.5-74.2)
Intervention 6	77.4 (69.7-85.0)	59.0 (50.1-67.9)	73.8 (59.8-84.2)	53.5 (34.7-71.5)
Intervention 7	53.7 (44.3-63.1)	48.3 (40.2-56.4)	50.4 (39.6-61.2)	53.0 (38.0-67.5)
Intervention 8	17.9 (9.7-26.1)	28.7 (19.9-37.5)	15.4 (9.3-24.5)	24.2 (17.3-32.9)

*Adjusted percentages are estimated from alternating logistic regression models, controlling for provider type, recorded temperature at visit, current patient smoking history, patient sex, and VA/non-VA sites.

†One of the original 8 control sites dropped out of the trial before data collection was initiated in year 1.

Table 3 Antibiotic and Test Orders by Providers Randomization Status (Mc Ginn, 2015)

	No./Total No. (%)						
Variable	Intervention (n = 586)	Control (n = 586)	Absolute Risk Difference	Relative Risk (95% CI)[a]	*P* Value	Age-Adjusted Relative Risk (95% CI)	*P* Value for Age-Adjusted Relative Risk
Total CPR visits[b]							
Pharyngitis	374	224	...	...	...	...	...
Pneumonia	212	174	...	...	...	...	...
Antibiotic orders[c]	171/586 (29.2)	153/398 (38.4)	9.2	0.73 (0.58-0.92)	.008	0.74 (0.60-0.92)	.008
Pharyngitis	56/374 (15.0)	44/224 (19.6)	4.6	0.77 (0.53-1.11)	.16	0.76 (0.53-1.10)	.15
Pneumonia	115/212 (54.2)	109/174 (62.6)	8.3	0.79 (0.64-0.97)	.03	0.79 (0.64-0.98)	.03
Rapid streptococcal tests	109/374 (29.1)	93/224 (41.5)	12.1	0.75 (0.58-0.97)	.03	0.75 (0.58-0.97)	.03
Pharyngitis throat culture orders	76/374 (20.3)	50/224 (22.3)	2.0	0.55 (0.35-0.86)	.01	0.54 (0.18-1.64)	.28
Chest radiograph orders	45/212 (21.2)	36/174 (20.7)	0.1	0.89 (0.55-1.46)	.65	0.98 (0.60-1.62)	.95

Abbreviations: ellipsis, not applicable; CPR, integrated clinical prediction rule.

[a] Risk ratios, CIs, and *P* values are calculated from a generalized estimating equation log-binomial model adjusting for clustering of orders or visits by provider and using robust standard error estimators.

[b] Total visits with patients having pharyngitis or pneumonia seen by enrolled providers according to randomization status and disease.

[c] Counts for orders analyzed and presented here represent total visits in which at least 1 antibiotic order was placed.

Table 4 Interventions effects on primary and secondary outcomes (Meeker, 2016)

	Accountable justifications	Suggested alternatives	Peer comparisons	Clinician's prior year prescribing rate (per 10 % increase)
	Odd ratios (95 % confidence intervals) for antibiotic prescribing			
Antibiotic for non-antibiotic appropriate ARI diagnoses (primary outcome)	0.98 (0.42–2.29)	0.68 (0.29–1.58)	0.45 (0.18–1.11)	1.57 (1.15–2.13)*
Antibiotic for potentially antibiotic appropriate ARI diagnoses	0.77 (0.42–1.41)	0.57 (0.31–1.05)	1.14 (0.59–2.19)	1.71 (1.23–2.36)*
Antibiotic for other ARIs diagnoses or symptoms of interest	1.29 (0.92–1.80)	0.62 (0.44–0.89)**	0.70 (0.48–1.02)	1.40 (1.25–1.57)**
Antibiotic for all three combined	1.05 (0.80–1.39)	0.72 (0.54–0.96)***	0.73 (0.53–0.995)****	1.64 (1.45–1.84)***

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Table 5 Time Trends in Inappropriate Prescribing Rate by Group (Meeker, 2014)

Group	Inappropriate Prescribing Rate, % 6 to 10 Months Prior to Intervention	3 to 6 Months Prior to Intervention	0 to 3 Months Prior to Intervention	Intervention Period
Control	46.2	44.9	37.3	48.8
Intervention	46.4	50.6	40.4	36.0
Difference	0.2	5.7	3.1	12.8

Findings

Metlay (2016) stated that "the primary measure of effect was the percentage of visits for upper respiratory tract infections and acute bronchitis that were treated with antibiotics." Secondary outcomes were determined by the satisfaction and return visit rate of the patients treated for ARTIs. The prescribing antibiotic rate was obtained by the number of ARTI patients who were prescribed antibiotics divided by the total number of ARTI patients.The researchers used logistic regression models to adjust for provider type, recorded temperature at visits, patient smoking history, types of health sites (Veterans versus non-Veterans health delivery systems).

Table 2 displayed a comparison between antibiotic prescription rates for control and intervention sites. At first, the authors followed the prescribing antibiotic rate trend for two years using unadjusted results. Then, after adjustment of the results, he performed the same follow up for a couple of years to eliminate possible effects of confounders, mediators or effect modifiers. Every health center within the intervention group showed a decrease in the prescribing rate during the second-year post training while an opposite pattern was observed for most control sites. Even after adjustment, the prescribing antibiotic rate displayed the same trend as for the unadjusted results worsening the discrepancy of prescribing antibiotic rate between intervention and control sites.

With the PDS strategy utilized by Metlay, the intervention sites started showing a decrease of 10 % in their antibiotic prescription in the second year while the control sites displayed an increase of 0.5%. The adjusted antibiotic prescription level for upper respiratory tract infection/acute bronchitis visits was 47% for control sites and 52% for intervention sites in year 1. Antibiotic prescriptions at control sites increased by 0.5% between year 1 and year 2 (95% confidence interval 3% to 5%) and at intervention sites decreased by 10% (95% confidence interval 18% to 2%).

The second educational intervention reviewed in this project followed the same pattern as the first one. To obtain this result, Gonzales et al. (2013) utilized a logistic regression model to preserve the validity of the findings by limiting possible alterations of third variables such as clinicians and patients characteristics, smoking status, and abnormal vital signs. The authors investigated clinician prescribing behavior change by monitoring any variation in antibiotic prescribing. As a precaution to avoid altering the validity of the findings, the researchers limited this analysis to providers with at least ten patients during each study period. Thus, this restriction comprised 31 out of 68 PDS prescribers, 26 out of 41 CDS prescribers, and 27 out of 46 control prescribers.

Gonzales (2013) displayed a reduction of antibiotic prescribing from 80 % to 68.3% for the PDS group. Regarding the CDS process, the authors observed a similar decrease from 74% to 60%. For 33% of these providers, the decline in prescribing was even higher (-20%). On the other hand, the control sites showed a mild increase of antibiotic prescribing from 72.4% to 74.3% (Figure 2).

The third educational intervention depicted by Gerber consisted in an hour training session on the latest prescribing guidelines for ARTIs. A generalized linear model was used to perform a pre-post comparison of antibiotic prescribing. This comparative analysis evaluated the impact of the educational training on these three respiratory conditions: pneumonia, sinusitis, and Group A Streptococcal pharyngitis. The group of providers who benefited from that approach displayed a decrease in broad-spectrum antibiotic order from 26.8% to 14.6% (absolute difference 12. 2%). The difference of differences (DOD) between the absolute differences between the intervention and control sites in term of prescribing rate was 6.7%.

Gerber revealed the same pattern when he stated: "off-guideline prescribing for children with pneumonia decreased from 15.7% to 4.2% among intervention practices compared with 17.1% to 16.3% in controls (DOD, 10.7%; P.001)." Although a similar pattern was observed for acute sinusitis and viral infections prescribing, the statically nonsignificant p-value invalidate these correlations.(Figure 3)

The behavioral studies showed some significant findings resulting in the reduction of inappropriate prescribing. Mc Ginn employed t-tests and chi-square tests to perform an

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adequate comparison between intervention and control groups' results. These measure of associations (absolute risk difference, relative risk ratio) of antibiotic prescribing in the intervention group versus the control group were used to assess the impact of this behavioral intervention on the arms of the study. Mc Ginn stated that the "providers in the intervention group were significantly less likely to order antibiotics than the control group (age-adjusted relative risk, 0.74; 95% CI, 0.60-0.92). The absolute risk of the intervention was 9.2%, and the number needed to treat was 10.8." The results of the study revealed that the intervention group was less likely to prescribe antibiotics than the control group (age-adjusted relative risk, 0.74; 95% CI, 0.60-0.92). The absolute risk of the intervention and the number needed to treat were respectively 9.2 % and 10.8. The same pattern could be observed for the order rapid streptococcal tests compared with the control group (relative risk, 0.75; 95% CI, 0.58-0.97; P = .03). (Table 3).

Meeker et al. (2016) investigated separately the effectiveness of three behavioral interventions against inappropriate antibiotic prescribing as well as the probable effect of combining two of these methods together to assess its impact. Randomization of practices in a 2 x 2 x 2 design was used to reduce the effect of possible confounders and effect modifiers. While the number of patients augmented between eighteen months, pre-intervention to eighteen months post-intervention, the prescribing antibiotic rate showed an absolute difference of (-11%) from pre-intervention to eighteen months post-intervention. This finding denoted a significant decline in prescribing antibiotic rate. Only two out of the three behavioral methods showed a statistically significant reduction in antibiotic prescribing rate" accountable justification (DOD, -7.0% [95% CI, -9.1% to -2.9%]; P < .001); and for peer comparison (DOD, -5.2% [95% CI, -6.9% to -1.6%]; P < .001). However, when the researchers tried to combine these interventions to assess their effectiveness, the results showed a nonstatistical significance interaction. (Table 4)

Meeker (2014) displayed the effect of poster-sized commitment letters in examination rooms after exposing providers to the target group. The authors conducted an analysis based on the EHR system used by the selected health centers. With a mixed logistic model, the researchers were able to adjust for age, sex, insurance status and obtained a "predicted inappropriate antibiotic prescribing rate." This measurement was determined by the number of ARTI patients who were prescribed inappropriately antibiotics divided by the total number of prescribing among the same pool of participants Regarding the inappropriate prescribing rate, an absolute difference of (-12%) between the intervention and control groups occurred. (Table 5) This result suggested a decline of more than ten percent of inappropriate prescribing following the exposure of providers to the poster-sized commitment letters.

The last selected study was related to a computer-based tool reflecting the latest treatment guidelines for ARTIs. Mainous (2013) investigated the impact of a CDSS integrated into an (EHR) on appropriate prescribing in primary care settings. Inappropriate antibiotic prescribing among ARI patients, and broad-spectrum antibiotic use constituted the primary and secondary outcomes of the study respectively. The outcomes were measured every three months. Mainous used linear mixed model for statistical analysis to evaluate the impact of his approach o intervention and control groups. In adult patients, the proportion of ARTIs episodes with inappropriate antibiotic prescribing reduced to a significantly greater degree among adult patients in intervention practices than among those in control practices (0.6% vs. +4.2%, p¼0.03), a trend which was not seen among pediatric patients (+1.4% vs. +4.2%, p¼0.34). Utilization of broad-spectrum antibiotics diminished as well after the intervention "for both adult (-16.6%vs, p<0.0001) and pediatric patients (-19.7%, p<0.0001)." (Figure 4)

Risk of bias in included studies

All selected studies displayed a low risk of allocation concealment and random sequence generation. Randomization is a major characteristic of most designs. The random process used to distribute participants into the intervention and control groups minimized the possibility of having allocation concealment and the sequence generation biases.

Blinding was a major source of bias for three out of the seven selected studies. For Metlay (2016), Gonzales (2013), and Mainous (2013), clinicians who were aware of the objectives of the study might not provide the performance that would reflect the effect of the intervention on their prescribing habit. Gonzales evoked the possibility that some prescribers might have changed diagnostic codes to more antibiotic-appropriate codes, thus creating an erroneous evaluation of the impact of the educational intervention. Additionally, Gonzales believed the results of the study could have been different if the follow-up of the participants was a little bit longer.

Selective reporting bias was possibly a significant risk for Metlay (2016), Gonzales (2013) and Mainous (2013). Metlay used 16 health centers in their study. However, fourteen hospitals in the area contacted by the researcher rejected the offer to take part of the study when they had an idea about the possible outcome of the project. For the same reason mentioned above, Gonzales 'study possessed a high risk of selective reporting since some clinicians could alter the diagnostic code to some health conditions that were

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easier to handle compared to other respiratory infections. According to Mainous, some participants might be more oriented to limit antibiotic use changing the accuracy of the findings. In the note section: Characteristics of selected studies, we could see a summary of the risk assessment of bias for each research design. This list would be critical in the qualitative analysis of the results of our Capstone project.

Discussion

Summary of primary results:

Based on the results, all interventions from each selected study produced a distinct improvement in the reduction of inappropriate antibiotic rate for ARTIs. Each study used the measurement of specific outcomes to investigate the impact of their strategies on appropriate prescribing. The decrease in antibiotic prescribing was considered the main favorable outcome described in the studies indicating a reduction in the risk of antibiotic resistance. Blair (2015) found overexposure on antibiotics as one of the primary causes of antibiotic resistance. Using educational approaches to tackle the issue, Metlay (2016), Gonzales (2013) and Gerber (2013) demonstrated the exposure of prescribers to informational sessions could reduce the risk of antibiotic resistance by diminishing the prescribing antibiotic rate. These three studies used ambulatory and hospital settings, pediatric or adult (veterans hospitals) population to display the same pattern: a decline in prescribing rate. Each educational intervention denoted a decrease in antibiotic prescribing of at least 10 %. For Gonzales and Gerber the reduction reached even 20% for some cases.

By contrast, the control group observed an opposite pattern with an increase in prescribing. This discrepancy enhanced the evidence that these interventions could reduce inappropriate prescribing. These findings are encouraging because it confirmed the positive impact of educational interventions on the reduction of antibiotic resistance.

The behavioral studies displayed the same pattern as the aforementioned educational interventions. Despite the differences between the behavioral strategies, they revealed the same reduction in antibiotic prescribing. This systematic review presented results showing the impact of interventions at the organizational level. A decrease in the prescribing antibiotic rate of more than 15% among the intervention group revealed how effective these strategies could be in the diminution of antibiotic misuse. However, the combination of various behavioral interventions does not automatically induce a greater decrease of antibiotic prescribing. By investigating if the combination of accountable justification, peer comparisons, and suggested alternatives could trigger a higher reduction in the prescribing rate than each separately, Meeker et al. (2016) discovered the results were not statistically significant.

Similar to the educational interventions of the Captone Project, Mc Ginn (2015), Meeker (2016), Mainous (2013), and Meeker (2014) showed an increase in the prescribing antibiotic rate among the control groups over time. The major contrast between intervention and control groups illustrated the positive impact of these methods on appropriate antibiotic prescribing.

The systematic review revealed that regardless the nature of the interventions (persuasive or restrictive), the result was quite similar. Persuasive strategies such as informational sessions provided to clinicians extended knowledge about the latest guidelines reducing the use of inappropriate antibiotics. Interventions such as those displayed by Metlay (2016), Gerber (2013), Gonzales (2013) used educational training of providers to fight antibiotic resistance. Some behavioral interventions denoted a strong strategy as well. Mc Ginn (2015) used an electronic decision support system that created various options for the clinician to choose the right plan of care.

Other behavioral interventions relied preferably on the restrictive approach. Meeker (2016) tested three different strategies (suggested alternatives, peer comparison, and accountable justifications) in a single study. The strategies above used prompts or psychological stimulus to encourage prescribers to follow the appropriate plan of care. For instance, accountable justification required providers to produce meaningful explanations to their prescribing to obtain the system approval. By publishing a list of “top performers,” peer comparison probably created a fear that their reputation and self-esteem could be affected by being labeled as bad clinicians.

Knowing the enormous burden caused by this public health issue, expansion of these educational and behavioral approaches to every health center nationwide could drastically change the pattern of antimicrobial resistance. However, further investigation is needed to determine a single intervention that will be the most cost-effective strategy to decrease inappropriate antibiotic prescribing. That would diminish this current public health issue drastically while avoiding a significant financial burden to implement this approach.

Limitations

The Capstone Project presented several limitations. The sample size of some of the selected studies was not broad enough to sustain an external validity of their particular findings. For instance, Meeker et al. (2016) admitted their study displayed a small number of participants. Mc Ginn et al. (2015) affirmed their subjects were recruited from a

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single health clinic. Gerber (2013) not only conducted its study in one facility but limited the target health centers to pediatric hospitals raising this interrogation on the replication of the same findings in adult care settings. In both cases, the limited sample reduces the generalizability of the studies.

Another limitation consisted in the short duration of the follow-up of some of the selected papers. For instance, Gonzales evoked the possibility that a longer follow-up might have presented a different outcome He argued that the study lasted about four months and there was no guarantee that a follow-up of a year or more could have produced the same results.

Another issue is the inability to identify the impact of each component of the interventions in the reduction of inappropriate antibiotic prescribing. For Gerber (2013), Mc Ginn (2015), Gonzales (2013), Meeker (2014 & 2016), the inability to determine the level of influence of each component of the interventions such as patient and clinician training, rendered it difficult to monitor the contribution of each of them to the outcomes. The selected papers did not use the same type of health practices. It is, in fact, difficult to conduct an effective comparative analysis of an intervention between hospitals and ambulatory settings since they both disclose major differences. The use of various types of EHR worsened the inability to determine the most effective approach to these seven studies to tackle inappropriate antibiotic prescribing.

The variation of the targeted prescribers among the selected studies constituted a severe limitation. Some papers included young physicians in training in their sample while the others do not have such category of clinicians in their practice settings. Some studies included Physician-Assistants as well as Nurse Practitioners. Although the findings denoted an encouraging result with the reduction of prescribing antibiotic rate for ARTIs, the outcomes might have been different for some studies if they included less experienced prescribers. An attempt to compare the results of post-intervention prescribing for each category of prescribers might have provided extensive information about the impact of the level of medical expertise on appropriate antibiotic prescribing.

At least one of the selected studies did not adjust the findings to some socio-determinant factors of the patients the prescribers assisted during the intervention. Metlay et al. (2016) admitted they did not know if the results they obtained were only correlated to the intervention and not have any link with the race, socio-economic status of the affected patients. Mc Kee (1999) and Planta (2003) admitted patients who are facing financial hardship were less likely to be compliant with the prescribed medications regardless of the accuracy of the prescribing. The fact that low SES demographic groups are often uninsured augmented their risk to try other " drugs" coming from the black market. These poor patients might be tempted to seek antibiotics imported from third-world countries to try to treat themselves.

The geographical location matter as well. Most studies were conducted mostly in metropolitan areas except for Gonzales (2013). The latter enrolled clinicians from small or medium-size rural practices which usually deserve a pool of patients different from the major urban areas. Rural populations in the United States tend to be racially and ethnically less diverse than those in the urban areas. Thus, the impact of educational interventions on the outcome of antibiotic resistance could have been different.

Conclusion

In conclusion, this Capstone Project gathered seven studies using educational and behavioral approaches to tackle inappropriate antibiotic prescribing. Patient with ARTIs constituted one of the main criteria since these health conditions were mostly of viral origin. The selected studies occurred in rural and urban areas, pediatric and adult health settings. The systematic review collected papers treating interventions that targeted inpatient and ambulatory settings. Despite these differences, all studies revealed a statistically significant decrease in prescribing antibiotic rate for adults suffering ARTIs. Regardless the nature of the intervention, persuasive or restrictive, educational and behavioral interventions findings showed between 10 to 20% reduction of antibiotic prescribing. Broad-spectrum antibiotic use showed a similar decline as well.The inclusion of confounders and effect modifiers did not modify the outcomes of the studies and suggested a high certainty in term of effectiveness of behavioral and educational approaches.

The results were encouraging since a significant portion of ARTIs is caused by a viral agent. This systematic review will undoubtedly contribute to the diminution of antibiotic overuse and inaccurate prescribing knowing that antibiotics are not effective against viral infections. Thus, it is safe to believe that educational and behavioral approaches were necessary since antibiotic resistance represented the major consequence of inappropriate prescribing.

However, the Capstone Project failed to identify the most efficient intervention among the seven selected studies. This inability to determine the best approach could be explained by the large difference between the interventions. First, the seven peer- reviewed papers did not use the same health delivery settings. Secondly, some clinics included only Physicians in the study while others added Nurse Practitioners and Physician Assistants. Additionally, some studies included residents(doctors in training) among the

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targeted prescribers. The heterogeneity of the pool of participants makes it difficult to be quite certain that an intervention is more efficient than the others based on the findings. Furthermore, the small number of registered prescribers and health delivery settings created a lack of generalizability.

Despite those limitations, this systematic review is more likely to contribute to the reduction of Multi-Drug Resistant Organism (MDRO). This project may inspire public health leaders to actively advocate for an additional study that will select a large sample of providers who will be followed for a longer period. The adjustment of most confounding factors and effect modifiers will improve the validity and the generalizability of the results. Additional research is needed: an investigation of the degree of a proven successful intervention against inappropriate prescribing on patients living in poverty-stricken communities in the United States would be a tremendous interest in the assessment of the effectiveness of educational and behavioral approaches.

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References

[1] Blair, J.M., Webber, M.A., Baylay, A.J., Ogbolu, D.O., & Piddock, L. J. (2015). Molecular mechanisms of antibiotic resistance**.** *Nature Review Microbiology 13 (1), 42-51.*

[2] Broniatowski, D. A., Klein, E. Y., & Reyna, V. F. (2014). Germs Are Germs, and Why Not Take a Risk? Patients' Expectations for Prescribing Antibiotics in an Inner-City Emergency Department. Retrieved from doi: 10.1177/0272989X14553472.

[3] Brown, E., Charani, E., Fenelon, L., Gould, I.M., Holmes, A., & Wilcox, M. (2013). Interventions to improve antibiotic prescribing practices for hospital inpatients (Review). *Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD003543*. doi: 10.1002/14651858.CD003543.pub3.

[4] Camins, B.C., King, M.D., Wells, J.B., Googe, H.L., Patel, M., & Blumberg, H.M. (2009). Impact of an antimicrobial utilization program on antimicrobial use at a large teaching hospital: a randomized controlled trial. *Infection Control Hospital Epidemiology* 30 (10),931-938. Retrieved from doi: 10.1086/605924.

[5] CDC. (2015). Get Smart about antibiotics. Retrieved from CDC: www.cdc.gov/getsmart/community/materials-references/print-materials/index.html.

[6] CDC. (2014, September). Antibiotic Resistance: "Get Smart about Antibiotics". Retrieved from: Centers for Disease Control and Prevention: www.cdc.gov.

[7] CDC. (2014). Get Smart About Antibiotics. Retrieved from Centers for Disease Control: http://www.cdc.gov/getsmart.

[8] Center for Medicaid and Medicare Services. https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/nhe-fact-sheet.html

[9] Chow, A,. Benniger, M., Brook, I., Brozek, Ellie, J.C., & File, T. (2015). IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults. Retrieve from: doi: 10.1093/cid/cir1043.

[10] Davey, P., Marwick, C.A., Scott C.L., Charani E., McNeil K., Brown E., Gould, I.M, Ramsay, C.R., Michie S. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD003543. doi: 10.1002/14651858.CD003543.pub4.

[11] Donnely, J. P., Baddley, J. W., & Wang, H. E. (2013). Antibiotic Utilization For Acute Respiratory Tract Infections In United States Emergency Departments. Retrieved from doi: 10.1128/AAC.02039-13.

[12] Faucy, A. S., & Marston, I.D. (2014). The perpetual challenge of antimicrobial resistance. *Journal of the American Medical Association 311 (8), 1853-1854.*

[13] File, T.M., Srinivasan, A., & Bartlett, J. G. (2014). Antimicrobial stewardship: importance for the patient and public health**.** *Clinical Infection Disease, 59 (3), s693-s696.*

[14] Fleming-Dutra, K., Hersh, A. L., Shapiro, D. J., Bartoces, M., Hicks, L. (2016). Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *Journal of American Medical Association* 315(17), 1864-1873. Retrieved from doi:10.1001/jama.2016.4151.

[15] Haddix, A.C., Teutsch, S.M., & Corso, P.S. (2003). Prevention effectiveness: a guide to decision analysis and economic evaluation. *Oxford University Press, 345-357.*

[16] Harris, A.M., Hicks, L. A., & Qaseem, A. (2016). Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care from the American College of Physicians, CDC. *Annals of Internal Medicine, 2016.* 164425-434. Retrieved from doi: 10.7326/M15-1840www.annals.org.

[17] Higgins, P, Atman, Gotzche, P., Juni, P., Sterne, J. (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomized trials Systematic. *British Medical Journal* 343. Retrieved from doi: 10.1136/bmj.d5928.

[18] Kelly, A.A., Jones, M.M., Echevarria, K.L., Kralovic, S. M., Samore, M.H., & Neuhauser, M.M. (2017). A Report of the Efforts of the Veterans Health Administration National Antimicrobial Stewardship Initiative. *Infection Control Hospital Epidemiology* 38 (5) 513-520. Retrieved from doi: 10.1017/ice.2016.328. Epub 2017.

[19] Llor, C., Bjerrum, L., Munck, A., Cots, J. M., Hernandez, S., & Moragas, A. (2014). Access to point-of-care tests reduces the prescription of antibiotics among antibiotic-requesting subjects with respiratory tract infections. *Respiratory Care 59 (12), 1918-1923*. Retrieved from doi: 10.4187/respcare.03275.

[20] Macfarlane, J., Holmes, W., Macfarlane, R., & Britten, N. (1997) Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study. *British Medical Journal 315, 1211–1214*.

[21] McKee MD, Mills L, Mainous AG III. Antibiotic use for the treatment of upper respiratory infections in a diverse community. *J Fam Pract.* 1999; 48: 993–6.

[22] Moody, J., Cosgrove, S. A., Russel, O., Septimus, E., & Trivedi, K. Antimicrobial Stewardship: A Collaborative Partnership between Infection Preventionists and Healthcare Epidemiologists. Retrieved from doi: 10.1086/665037.

[23] Planta, M. B. (2007). The Role of Poverty in Antimicrobial Resistance. *American Board of Family Medicine*, 20, 6533- 6539. Retrieved from doi: 10.3122/jabfm.2007.06.0700019J.

[24] Smith, R.A., Mintaka, N.M., & Read, A.F. (2015). Antibiotic-resistance: a primer and call to action. Retrieved from doi: 10.1080/10410236.2014.943634.

[25] Ventola, C. L. (2015). The antibiotic resistance crisis: part 1: causes and threats. P. & T, 40Administration of a survey to evaluate the attitudes of house staff physicians towards antimicrobial resistance and the antimicrobial stewardship program at a community teaching hospital.

[26] Venugopalan, V., Trustman, N., Manning, N., Hashem, N., & Hidayat, L. (2016) Administration of a survey to evaluate the attitudes of house staff physicians towards antimicrobial resistance and the antimicrobial stewardship programme at a community teaching hospital. *Journal of Global Antibiotic Resistance (4), 21-27.* Retrieved from: https://doi.org/10.1016/j.jgar.2016.01.004.

[27] Vinnard, C., Linkin, D.R., Localio, A.R., Leonard, C.E., Teal, V.L., & Hennessy, S. (2013). Effectiveness of interventions in reducing antibiotic use for upper respiratory infections in ambulatory care practices. *Population Health Management* 16 (1), 22-27. Retrieved from: doi: 10.1089/pop.2012.0025. Epub. 2012 Oct 3.

[28] Watkins, R., & Bonomo, R. (2015). Overview: Global and Local Impact of Antibiotic Resistance. *Infectious Disease Clinic 30 (2),* 313-322. Retrieved from: http://dx.doi.org/10.1016/j.idc.2016.02.001.

[29] Glantz, K., Rimer, B.K., & Viswanath, K. (2008). *Health behavior and health education: theory, research, and practice*. 4th ed. Published by Jossey-Bass A Wiley Imprint 989 Market Street, San Francisco, CA 94103-1741.

[30] Tonkin-Crine, S., Wang, K., Van Hecke, O., Roberts, N. W., McCullough, A. & Del Mar, C. B. (2016). Clinician-targeted interventions to reduce antibiotic prescribing for acute respiratory infections in primary care: an overview of systematic reviews. Retrieved from doi: 10.1002/14651858.CD012252.

Table 6: Cochrane risk of bias in selected studies Metlay, 2016

Methods	**Cluster RCT**
Participants	PROVIDERS: Emergency physicians, physician-assistants, emergency nurses. Patients treated for acute respiratory infections. CLINICAL PROBLEM: ATB prescription rate. SETTING: 8 U.S. Veteran and 8 U.S. Non-veteran Hospitals.
Interventions	Provider educational intervention based on 4h-training session o appropriate ATB use. Patients intervention based on waiting room posters, and brochures incorporated messages that are part of CDC Get Smart.
Outcomes	PRESCRIBING: Decrease antibiotic prescribing for ARTIs
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk
Allocation concealment	Low risk
Blinding of participants and personnel	Moderate risk
Blinding of outcome assessment (subjective data)	High risk
Blinding of outcome assessment (objective data)	Low risk
Incomplete outcome data Other bias	High risk Low risk
Selective reporting	High risk: Although we selected our participating sites according to a national survey of all academic EDs and VA medical centers, not all sites were willing to participate, 14 potentially limiting the generalizability of the study results.
Similar baseline characteristics	Low risk
Adequate protection against contamination.	Low risk

Table 7: Gonzales, 2013

Methods	**Cluster RCT**
Participants	PROVIDERS: Emergency physicians, physician-assistants, emergency nurses. CLINICAL PROBLEM: ATB prescription rate for ARTIs SETTING: 8 U.S. Veteran and 8 U.S. Non-veteran Hosp.
Interventions	PDS educational brochures distribution CDS for prescribers.
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk
Allocation concealment	Low risk
Blinding of participants and personnel	High risk: physician bias by changing diagnostic codes to more antibiotic-appropriate codes
Blinding of outcome assessment (subjective data)	High-risk: different possible outcome if longer follow-up
Blinding of outcome assessment (objective data)	Moderate risk: inability to assess the individual impact of each component
Incomplete outcome data	High-risk: same as blinding of participants
Selective reporting	High risk
Similar baseline characteristics	Low risk
Adequate protection against contamination.	Low risk
Adequate protection against contamination	Low risk

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Table 8: Gerber, 2013

Methods	**Cluster RCT**
Participants	PROVIDERS: Attending physicians, physician-assistants, emergency nurses. From pediatric settings Patients treated for acute respiratory infections. CLINICAL PROBLEM: ATB prescription rate. SETTING: 8 U.S. Veteran and 8 U.S. Non-veteran Hospitals
Interventions	One-hour on-site clinician education session followed by one year of quarterly audit and feedback of prescribing for bacterial and viral ARTIs DESIRED CHANGE: appropriate prescribing for acute viral respiratory infections as well as bacterial infection.
Outcomes	PRESCRIBING: Rate of broad-spectrum ATB for bacterial ARTIs.
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk
Allocation concealment	Low risk
Blinding of participants and personnel	Unclear risk
Blinding of outcome assessment (subjective data)	Low risk
Blinding of outcome assessment (objective data)	Low risk
Incomplete outcome data Other bias	Low risk Low risk
Selective reporting	Low risk
Adequate protection against contamination.	Low risk

Table 9 Mc Ginn 2015

Methods	**Cluster RCT**
Participants	PROVIDERS: Clinicians who worked in selected facilities. Patients treated for acute respiratory infections. CLINICAL PROBLEM: ATB prescription rate. SETTING: 2 large health settings in NYC
Outcomes	Frequency, rate, and types of ATB prescribed
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk
Allocation concealment	Low risk
Blinding of participants and personnel	Low risk
Blinding of outcome assessment (subjective data)	Low risk
Blinding of outcome assessment (objective data)	Low risk
Incomplete outcome data Other bias	Low risk
Selective reporting	High-risk
Similar baseline characteristics	Low risk
Adequate protection against contamination.	Low risk
Other bias	Low risk

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Table 10: Meeker, 2016

Methods	**Cluster RCT**
Participants	PROVIDERS: Emergency physicians, physician-assistants, emergency nurses. Patients treated for acute respiratory infections. CLINICAL PROBLEM: ATB prescription rate. SETTING: 49 primary care practices from 3health systems located in Massachusetts and Los Angeles
Interventions	DESIRED CHANGE: appropriate prescribing for acute viral respiratory infections
Outcomes	Antibiotic prescribing rates for visits with antibiotic-inappropriate diagnoses from18months preintervention to 18month s afterward, adjusting each intervention's effects for co-occurring interventions and preintervention trends, with random effects for practices and clinicians
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk due to c RCT
Allocation concealment	Low risk
Blinding of participants and personnel	Low risk
Blinding of outcome assessment (subjective data)	Unclear risk
Blinding of outcome assessment (objective data)	Unclear risk
Incomplete outcome data	Low risk
Selective reporting	Low risk
Similar baseline characteristics	Low risk
Adequate protection against contamination.	Low risk
Other bias	Low risk

Table 11: Meeker, 2014

Methods	**Cluster RCT**
Participants	PROVIDERS: Emergency physicians, physician-assistants, emergency nurses. Patients treated for acute respiratory infections. CLINICAL PROBLEM: ATB prescription rate. SETTING: 49 primary care practices from 3 health systems
Interventions	Displaying poster-sized commitment letters to avoid inappropriate antibiotic prescribing for ARTIs
Outcomes	PRESCRIBING: Decrease antibiotic prescribing for acute respiratory infections.
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk
Allocation concealment	Low risk
Blinding of participants and personnel	Unclear risk
Blinding of outcome assessment (subjective data)	Unclear risk
Blinding of outcome assessment (objective data)	Unclear risk
Incomplete outcome data Other bias	Unclear risk
Selective reporting	Low risk
Similar baseline characteristics	Low risk
Adequate protection against contamination.	Low risk
Other bias	Low risk

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Table 12: Mainous 2013

Methods	Quasi-experimental
Participants	PROVIDERS: Clinicians who worked in selected facilities. Patients treated for acute respiratory infections. CLINICAL PROBLEM: ATB prescription rate.
Interventions	DESIRED CHANGE: appropriate prescribing for acute viral respiratory infections.
Outcomes	Inappropriate prescribing Broad-spectrum antibiotic use
RISK OF BIAS	AUTHOR JUDGEMENT
Random sequence generation	Low risk
Allocation concealment	Low risk
Blinding of participants and personnel	High risk
Blinding of outcome assessment (subjective data)	High risk It is possible that the volunteers might be more oriented toward controlling antibiotic use
Blinding of outcome assessment (objective data)	Unclear
Incomplete outcome data Other bias	High risk Unclear
Selective reporting	Moderate risk It is possible that the volunteers might be more oriented toward controlling antibiotic use.
Similar baseline characteristics	High risk the two groups were similar at baseline. So any orientation toward controlling antibiotic prescribing in the intervention group was not evident before the intervention.
Adequate protection against contamination.	Low risk

Abbreviation

AR : Antibiotic Resistance
ARTI : Acute Respiratory Tract Infection
ASP : Antimicrobial Stewardship Program
CDC : Center for Disease Control and Prevention
CDS : Computer-assisted Decision System
CDSS : Clinical Decision Support System
CMS : Center for Medicaid and Medicare Services
CPR : Clinical Prediction Rule
c RCT : Cluster Randomized Controlled Trial
ED : Emergency Department
MPH : Master of Public Health
NHE : National Health Expenditure
PDS : Printer-assisted decision support
PICO : Participants, Intervention, Comparison, control, Outcome
PPRNet : Practice Partner Research Network
RCT : Randomized Control Trial
SES : Socioeconomic status
VRI : Viral Respiratory Infection

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