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Predictors of UTI Antibiotic Resistance for Female Medicaid Recipients in U.S. Ambulatory Care Settings

Wendy Denise Wieseuegel
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Walden University

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Wendy Wieseuegel

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Walden University
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Abstract

Predictors of UTI Antibiotic Resistance for Female Medicaid Recipients in U.S.

Ambulatory Care Settings

by

Wendy D. Wiesehuegel

MS, Walden University, 2009

BSN, Norfolk State University, 1994

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

2017

Abstract

Urinary tract infections are diagnosed in female populations primarily in ambulatory care settings in the United States. Yet, published evidence documents that many of the antibiotics prescribed in these settings are unnecessary, erroneous, or, inappropriately prescribed. Improper management of uncomplicated urinary tract infections in nonpregnant women has resulted in higher morbidity rates due to antibiotic resistance. The purpose of this retrospective observational cohort study was to explore a current national database for associations between nonpregnant American female patients who were exposed to poverty and at risk for urinary tract infection antibiotic resistance in an ambulatory care setting. Krieger's ecosocial theory was utilized as the study's theoretical foundation to complement current public health social change priorities. Data from the National Ambulatory Medical Care Survey were analyzed to explore potential associations with urinary tract infections and antibiotic resistance. The sample consisted of ambulatory patients with urinary tract infection symptoms ($n=45$). The independent variables selected were antibiotics prescribed initially in 3 months or less after the onset of urinary tract infection symptoms, the continuation of antibiotics prescribed in 12 months or less after recurrence, and three classes of antibiotics prescribed for urinary tract infection symptoms known as broad-spectrum, narrow-spectrum, and combined broad- and narrow-spectrum antibiotics, while the dependent variable was urinary tract infection antibiotic resistance. Relationships between the variables were analyzed using binary logistic regression, however, there were no statistically significant outcomes. Promoting antibiotic stewardship programs in all health care settings in the U.S. can effect positive social changes that will prevent further antibiotic resistance.

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Dedication

This is dedicated to my husband Paul, my late son Oliver, my late grandparents, and, all my family, friends, and coworkers who have been very understanding during the countless times that I have passed up parties, birthdays, luncheons, after-work gatherings, graduations, and multiple travel events because “I have to study.” My father may finally be able to say what his daughter does for her career instead of replying “perpetual student.” I may be a retired naval officer; however, my entire career was focused on increasing my education to grow in military rank, and life in general. I will never cease to learn. Those that have stood by and cheered me on during this very difficult doctoral degree program, saw what it was to sacrifice “life.” Knowledge, education, and the drive to change things in the world for the better, even one molecule at a time, as they know, are at the heart of my existence.

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Chapter 1: Introduction to the Study

In the first half of the 20th century, the invention and application of antibiotics astonished us to treat infections (Davies & Davies, 2010; Landecker, 2015).

Astonishment has shifted to concern about uncomplicated urinary tract infections (UTIs), which medical experts have classified as the primary cause of morbidity in females in the United States. (Ciani, Grassi, & Terricone, 2013; Soto, 2014). Disparities in low-income female populations demonstrate substandard quality in health care recommendations and treatment for uncomplicated UTI infections (Kaiser Family Foundation, 2016).

Antibiotic-resistance complications in UTIs are now considered a global public health crisis (Lee, Cho, Jeong, & Lee, 2013).

The incidence and prevalence of antibiotic-resistant UTIs in ambulatory care settings, which include those settings that are specific to outpatient versus inpatient care, have been well-studied across all populations in developing and developed countries outside of the United States (August & DeRosa, 2012). Research in ambulatory care settings for uncomplicated UTIs in the United States have focused on comparing prescribing patterns in pediatric, older adult, and pregnant populations (May, Mullins, & Pines, 2014; Matuszkiewicz-Rowynska, Malyszko, & Wieliczko, 2015). Researchers have not examined the impact of social determinants such as economic status in the prescribing of antibiotics for UTIs in these settings, according to Kobayashi, Shapiro, Hersh, Sanchez, and Hicks (2016).

In 2015, the U.S. Department of Health and Human Services (HHS; 2015) re-established goals after noting that between 2001-2014, health care disparities had made

little progress. Federal initiatives for health care research, policy makers have requested that vulnerable community populations such as low-income women be prioritized in studies (Agency for Healthcare Research and Quality [AHRQ], 2016). An opportunity currently exists to examine the impact of antibiotic resistance and the methods used to prescribe antibiotics for uncomplicated UTIs in nonpregnant, low-income women in U.S. ambulatory care settings. This study may promote positive social change by helping health care practitioners and organizations to reduce barriers in low-income, nonpregnant women's access to quality care in the management of UTIs in ambulatory care settings.

In Chapter 1, I provide descriptive, clinically-related details about antibiotic resistance and UTIs. In support of this study's direction, I also illustrate the complexities of antibiotic resistance patterns related to biomedical implications, epidemiology, economic burden, and the global impact of antibiotic resistance in ambulatory care settings. Additionally, UTI pathogenicity, clinical significance, epidemiology, economic burden, and the relevant impacts of antibiotic prescribing for these infections are examined.

Background

Urinary Tract Microbiology and Pathogenesis

The urinary tract system in and out of the human body consists of normal flora. Normal flora are also known as common commensals; they present *on* (exogenous) or *in* (endogenous) humans as gram positive or negative, or fungal organisms (Findley & Grice, 2014). Common commensals may become altered in a human host environment due to antibiotic influence, coexisting disease, income, genetics, diet, stress, age, or,

environmental factors (Grice & Segre, 2011; Marrie, Swantee, & Hartlen, 1980). Human UTIs are the most common type of infection caused by bacteria (Nienhouse et al., 2014). UTIs may be caused by voiding urine, when the entryway to the genitourinary tract opens (August & De Rosa, 2012). Researchers once thought the inside of the urinary tract to be a sterile environment, yet they recently found that bacteria live in the human host (2012; Flores-Mireles, Walker, Caparon, & Hultgren, 2015; Hilt et al., 2014; Santiago-Rodriguez, Ly, Bonilla, & Pride, 2015). Bacteria normally living in the urinary tract may cause infections but do not normally lead to death (Nicolle, 2014).

Urinary Tract Infection Clinical Significance

Urinary tract infections are clinically significant because urinary tract lab findings produce positive results which usually lead to a diagnosis of UTI and subsequent antibiotic treatment (Grabe et al., 2014). Researchers conducting global studies have found that 50-60% of females under the age of 50 with a low-income status appear to be at considerable risk for UTIs (Al-Badir, & Al-Shaikh, 2013; Minardi, d'Anzeo, Cantoro, Conti, & Muzzonigro, 2011). Anatomical issues (specifically, the urethral location in females) and behavior issues (e.g., noncompliance with medications) appear to correlate with poor clinical outcomes related to antimicrobial resistance (Barber, Norton, Spivak, & Mulvey, 2013; Minardi, d'Anzeo, Cantoro, Conti, & Muzzonigro, 2011; Mohsin & Siddiqui, 2010;). Recurrent UTIs are described as involved in 19% of younger, sexually active female populations that have a diagnosis of cystitis, which is a type of lower UTI (Soto et al., 2006). When initial treatment fails, recurrent UTIs may develop antimicrobial resistance (Ejrnaes, 2010; Bodro, 2015). Clinically-significant management

of UTIs, according to Mohsin and Siddique (2010), involves use of evidence-based guidelines for the clinical management of infections and is dependent on resources, clinical experience, and training.

Urinary Tract Infection Epidemiology

Bacterial UTIs are one of the most common infections treated in ambulatory care settings (Lema, 2015). Bruschi and Bronze (2015) stated that one in five women will be diagnosed with a UTI in their lifetime. Data from AHRQ (2014), a U.S. federal health care agency, revealed that the incidence of UTIs in ambulatory care settings was highest in female patients as evidenced by 13 infections per 10,000 in the broader U.S. population. In the hospital setting, it was noted that there were 4 infections per 10,000 in the U.S. population, (AHRQ, 2014). Current research data indicate that females with complaints of UTI symptoms account for 85% of the 3 million appointments made in ambulatory care settings in the United States (Thoureen, Scott, & Best, 2015). In nonpregnant females who evidence cystitis for the first time, recurrence occurs at least 30-44% of the time (Gupta & Trautner, 2013).

Females of all ages are at risk for UTIs (Lema, 2015). However, women who are age 30-60 have a greater incidence of acute UTIs with the mean incidence peak between 15 to 39 years of age (AHRQ, 2014; Centers for Disease Control & Prevention [CDC], 2014, 2015). Adult women account for around 10% of all symptomatic UTIs annually, and 1 in 3 of these will need antibiotic treatment (Lawal, 2012). Uncomplicated UTIs

have been studied without consideration for social determinants in female populations (Brusch & Bronze, 2015; Hawker et al., 2014). Researchers have documented that hospitalized, pregnant female patients currently have the highest incidence rates of complicated UTIs (AHRQ, 2014; Czaja, Scholes, Hooton, & Stamm, 2007).

Urinary Tract Infection Economic Burden

Over 9 million ambulatory care visits are made annually in the United States for UTIs diagnosed as cystitis (Wagenlehner & Naber, n.d.). Annually, the estimated cost of antibiotic agents prescribed for the treatment of symptomatic or asymptomatic UTIs are over 1 billion dollars, which accounts for 15% of the total money spent by the public on these drugs (Wagenlehner & Naber, n.d.). Poverty, access to care, or inappropriate disease management may lead to prolonged or complex care that becomes a significant drain on insurance policies carried by groups or individuals (Thorpe, Wisniewski, & Lindsay, 2009).

The overall economic burden to patients is high for any disease treatment that involves multiple tests and medications. However, the costs associated with antibiotic-resistant UTIs are much higher and account for at least a 35% to 47% increase in total patient costs (Roley & Truscott, 2013). Nonpregnant low-income female populations in the United States, in particular, face a considerable financial burden (Shartzler, Long, & Benatar, 2015). Medicaid, a source of payment for health care coverage, represents low income as a social determinant (Blumberg, 2012). Patients who receive care in ambulatory care settings may manifest UTI antibiotic resistance patterns related to having Medicaid as their insurance (Alsan et al., 2015). However, studies indicate that even with

the Affordable Care Act in place, disparities continue to exist for low-income women (Alsan, et al, 2015).

Antibiotic Resistance Economic Burden

According to Gandra, Barter, and Laxminarayan (2014), the economic impacts of antibiotic resistance in the United States, and the frequency by which the costs directly concern the public, health care administration, patients, doctors, and pharmaceutical companies, appears to have been poorly documented until recently. Lack of attention to these issues has continued to be a concern, Gandra, Bater, and Laxminarayan asserted. In the United States, researchers have estimated the economic burden of health care cost for infections that are antibiotic-resistant to be approximately \$20 billion, with over \$34 billion attributed to a loss in workforce productivity (Bartlett, Gilberg, & Spellberg, 2013; CDC, 2011a, 2011b, 2015b; Taylor et al., 2014; Song et al., 2015).

Antibiotic Resistance Biomedical Implications

Antibiotic drugs are a class of chemical substances that are formed as medicine to treat bacterial infections by slowing down or destroying bacterial growth (Fair & Tor, 2014). McGowan (2008) noted that antibiotic resistance has a significant impact on incidence outcomes in community UTIs, for example, resistance to current antibiotic agents has increased due to the inappropriate use of these drugs (Nathan & Cars, 2014).

Antibiotic Resistance Epidemiology

Antibiotic resistance strain incidence and prevalence rates continue to climb without the development of new antibiotics (Hawkey & Jones, 2009). Surveillance efforts to generalize and understand the increase in incidence rates of antibiotic-resistant

pathogens is confined to the acute care hospital environment (Sydnor & Perl, 2011). Limited syndromic surveillance in the community is controlled primarily by the strength of funding provided for agricultural and human population studies (Phalkey, Yamamoto, Awate, & Marx, 2013). Ongoing efforts to establish campaigns to promote judicious use of all antibiotics continue in the United States (Purcell, 2012). However, as awareness grows, the pace for the creation of new antibiotics has slowed (Boucher et al., 2009; Sundqvist, 2014). Failure to provide a solution for antibiotic-resistant infections has led to the escalation of human, human-to-animal, and animal-to-human pathogenic transmission (Hawkey & Jones, 2009).

Problem Statement

The current public health-antibiotic-resistance crisis is due to inappropriate infection management as evidenced by many factors. Low-income populations are at a higher risk for antibiotic resistance due to the inappropriate medical management of infectious diseases (Shartz et al., 2015). Inappropriate antibiotic prescribing has also been reported with over 47 million (more than 30%) antibiotics prescribed annually in the United States. (Shapiro, Hicks, Pavia, & Hersh, 2013; Ventola, 2015). Urinary tract infection diagnosis in U.S. female populations comprises more than 84% of the 3 million patients who report to ambulatory care facilities with UTI symptoms (Thoureen, Scott, & Best, 2015). The CDC (2013a) reported that 50% of the antibiotics that are prescribed in ambulatory care settings are unnecessary or suboptimal and, also, empirically prescribed without laboratory confirmation of an infection. Health-care providers are challenged to provide low-cost, generic substitutions when dictated by insurance plans; many

antibiotics may not have a generic substitution (Garau, Nicolau, & Bassetti, 2014; Pronovost, 2013).

The rate of uncomplicated UTIs in women between the ages of 18-49 in the United States who are managed in the ambulatory care setting and receive antibiotic treatment is 28.2% for every 10,000 females (Lawal, 2012). Pregnant, pediatric, or older adult females with a lower economic status in developed countries such as the United States are often reported in the literature as having a high risk for antibiotic-resistant infections such as UTIs (Lawal, 2012). Research reports since the 1980's provide evidence that inappropriate patient infection management by providers is the primary problem leading to antibiotic resistance in UTIs (Vasudevan, 2014).

A gap in the literature exists because U.S. researchers have not examined income distribution in nonpregnant females with UTI complaints in ambulatory care settings (Kobayashi, 2016; May et al., 2014). An opportunity existed to study nonpregnant females, with Medicaid recipient status representing low-income status. This research gap has contributed to antibiotic-resistant UTIs in a population already known to be high-risk (Ciani et al., 2013). Social change can occur by studying the exposures and risks related to ambulatory care antibiotic management for UTIs. This social change concept to study UTI antibiotic management suggested further that there is logic to seeking an increase in funding for future research. For example, research could

include case-control studies aimed at improving care management of all health care problems in low-income populations in ambulatory care settings.

Purpose of the Study

The purpose of this quantitative study was to examine nonpregnant American female patients who were exposed to poverty, as evidenced by the reported payment type of Medicaid, as the reported payment type, and at risk for antibiotic resistance when seeking care for UTIs in ambulatory care settings. Low-income indicators such as insurance type may negatively impact outcomes of antibiotic resistance reduction efforts (Laxminarayan et al., 2013). The significance of this study contributed to the increase in awareness of risks of antibiotic resistance related to poor outcomes in uncomplicated infections such as UTIs. This study was designed to predict outcomes that are associated with risks related to antibiotic resistance in low-income nonpregnant female populations on Medicaid.

Research Questions and Hypotheses

Three research questions governed this study. The outcome (or, dependent) variable of interest was UTI antibiotic resistance (UAR). The independent variables were initial antibiotics, continued antibiotics, and broad-spectrum, narrow-spectrum, and a combination of broad- and narrow-spectrum antibiotics prescribed. The research questions were grounded by the ecosocial theory. This study's research questions incorporated proximal and distal associations with disease process and outcomes. Krieger, the founder of ecosocial theory (2008), stated that proximal associations can only be changed by a patient or his or her provider; however, society must work to

change distal associations such as payment amounts for provider services (p. 223). Social patterns constantly change due to pathways, power, and levels that are proximally and distally associated (2008).

Research Question 1: Are initial antibiotics prescribed for UTIs associated with UTI antibiotic resistance?

H_01 : There is no statistically significant association between antibiotic resistance in UTIs and initial antibiotics prescribed.

H_{a1} : There is a statistically significant association between antibiotic resistance in UTIs and initial antibiotics prescribed.

Research Question 2: Are continued antibiotics prescribed for UTIs associated with UTI antibiotic resistance?

H_02 : There is no statistically significant association between antibiotic resistance in UTIs and continued antibiotics prescribed.

H_{a2} : There is a statistically significant association between antibiotic resistance in UTIs and continued antibiotics prescribed.

Research Question 3: Is the class of antibiotic prescribed for UTIs associated with UTI antibiotic resistance?

H_03 : There is no statistically significant association between UTI antibiotic resistance and class of antibiotic prescribed.

H_{a3} : There is a statistically significant association between UTI antibiotic resistance and class of antibiotic prescribed.

Theoretical Foundation

The theoretical framework for this research study was grounded in Krieger's (2001) ecosocial theory. Chapter 2 will contain a more detailed discussion about this theory. This theory speaks to the criticality of social change and population disease patterns (Krieger, 2001, p. 668). The importance lies in both the biological and societal components of change specific to the epidemiology of the responsibility of social inequality (p. 670). Krieger (2001) produced 4 constructs that are central to Ecosocial Theory and relate to this dissertation project: "accountability and agency, embodiment, the cumulative interplay of exposure, susceptibility and resistance, and pathways of embodiment" (Krieger, 2008). The ecosocial theory (2001) approach works well with the structural levels of populations and those disease outcomes that can be associated with multiple population types.

Nature of the Study

A retrospective, observational cohort design methodology was used to describe the relationship between the incidence of the dependent variable, antimicrobial resistant UTIs, and the role of the independent variables of initial antibiotics, continued antibiotics, broad-spectrum antibiotics, narrow-spectrum antibiotics, a combination of both broad- and narrow-spectrum antibiotics. The variables were utilized to study nonpregnant American women who were between the ages of 25-44, on Medicaid, and sought care for UTI symptoms in ambulatory care clinics. The data was abstracted from a public, national database source known as the National Ambulatory Medical Care Survey (NAMCS). The database was composed of U.S. national ambulatory setting

demographic, payment, pharmaceutical, diagnostic, and laboratory, data needed for this study. The patient data collected in NAMCS was queried for the selection of variables that met criteria of less than 3 months (initial antibiotics prescribed), and 12 months or less (for those antibiotics that were continued). After review of baseline data abstracted, the dependent variable, antibiotic-resistant UTI was queried. Additional independent variables of broad-spectrum, narrow-spectrum, and broad- and narrow-spectrum combined antibiotics were queried. Multiple logistic regression was utilized to analyze patient criteria data.

Definitions

Following are definitions for important terms related to the variables and ideas discussed in this study:

Aerobic organisms: Organisms that need oxygen to survive (Maier, Anderson, & Roy, 2015; Murphy & Frick, 2012).

Anaerobic organisms: Organisms that live in direct proximity to the genitourinary tract and that do not require oxygen to live (Maier, Anderson, & Roy, 2015; Murphy & Frick, 2012).

Antibiotic resistance: A situation that occurs when the efficacy of a drug used in the treatment of infections is compromised (Smith et al., 2014; Zur Wiesch, Kouyos, Engelstadter, Regoes, & Bonhoeffer, 2011).

Antibiotic susceptibility tests: Used to determine what the pathogen will respond to for antibiotic treatment. Utilized by providers in the treatment of infections. Reported out as a “MIC” or “minimum inhibitory concentration” (Street & Staros, 2014).

Broad-spectrum antibiotics: Antibiotics used for empiric therapy when the microorganism is unknown (Pallett & Hand, 2010).

Clinical classifications: Infections involving a variety of tracts in the human body (Brede & Shoskes, 2011).

Common commensals: Nonpathogenic microorganisms which have a primary duty to keep humans healthy (Todar, n.d.).

Narrow-spectrum antibiotic: Antibiotic that can target a specific microorganism (Pallett & Hand, 2010).

Recurrent UTI: Recurrence with UTIs is typically defined as three or more UTIs within 12 months, or two or more occurrences within six months (Arnold, Hehn, & Klein, 2016).

Voiding: The human act of urinating. Takes place in the genitourinary tract with the byproduct being urine (Whiteside et al., 2015; Wolfe & Brubaker, 2015).

Assumptions

In this research, I assumed that the risks for UTI antibiotic resistance in nonpregnant females, ages 25-44, on Medicaid, and symptomatic with an uncomplicated UTI regardless of economic status, were not statistically significant among U.S. ambulatory care settings. According to Garau, Nicolau, Wullt, & Bassetti (2014) antibiotic consumption and antibiotic resistance directly correlate with one another; resistance in UTIs after receiving broad-spectrum antibiotics occurs in 55.3 per 100,000 (women) due to inappropriate antibiotic prescribing.

An additional assumption that was that all diagnoses were made per laboratory standards, and, licensed health-care providers assessed clinical signs and symptoms. Laboratory tests are assumed to be governed by the FDA and standard laboratory testing regulations. Assumptions related to regression analytics that were deployed were that the DV was dichotomous; the factor level “1” represented the desired outcome. It was additionally assumed that there would be more than one IV, and that they would be categorical. It was also assumed that because regression was utilized that a linear relationship would not be necessary, residuals did not need to be normally distributed, and homoscedasticity was not needed for each level of IV. Although I did not collect the data in the national database that I used, a review of the original data collection method was reviewed and it was assumed that the accuracy of the data was solid.

Scope and Delimitations

Inappropriate management practice for UTIs that includes antibiotic prescribing practices, accounts for greater than 150 million ambulatory care visits per year. Of the number of visits per year, more than 13% of all ambulatory care visits provide around 47 million unnecessary prescriptions (The Pew Charitable Trusts, 2016). Clinical guidelines may not be followed for lower socioeconomic status patients in the treatment of urinary tract infections. Less costly generic antibiotics, even when known to go against treatment guidelines, are often prescribed for lower income populations (Denes, Prouzergue, Ducroix-Roubertou, Aupetit, & Weinbreck, 2012). In addition to antibiotic prescribing, there may be multiple other factors placing low-economic populations at risk for antibiotic resistance in the United States. The study focus was to abstract a cohort sample

of ambulatory care data (physician-patient encounter/visit) from U.S. regions. I had identified a national survey database to use, the National Ambulatory Medical Care Survey (NAMCS) (2008- 2012). This database was utilized in the review for risks with UTI antibiotic management in low-income populations as identified by the independent variable, Medicaid.

Ambulatory clinic sampling included only non-federally funded offices and did not include ambulatory visits via phone, house calls, pediatric-specific, or those ambulatory care offices within an acute care health care facility. Population sampling for this study included nonpregnant females between the ages of 25-44 on Medicaid with indicators (diagnosis, medication, reasons for visit, symptoms) that were positive for urinary tract infection. The CDC and only one other study in 2006 reported that women between the ages of 25-44 were most likely to become resistant to antibiotic medications (Butler, Hillier, Roberts, & Dunstan, 2006; CDC, 2011a). Low-income female populations were represented by using Medicaid payment data available in the national data sets that indicated insurance type. The categories of females utilized by regional U.S. studies may not accurately represent all counties within those U.S. regions, therefore, the delimitations may not represent boundaries that I would have clearly made had I originally produced the datasets.

Limitations

The data utilized from the national database was intended to be utilized for this research study. The study data may have been flawed, due to the choice of a retrospective design. I used a large, national, and public database set that originated in

the United States. Additionally, though the database used was large, there was no guarantee that enough subjects would be available with the outcome being investigated. A prospective approach with a cohort study may be a better choice, however the time and expense of such a study was not feasible.

Significance

Researchers have indicated that there is a potential relationship between infection management outcomes and risks for UTI antibiotic resistance related to multiple factors, including prescribing practices in the inpatient acute setting (i.e., hospital) (Shapiro et al., 2013). Research published, however, has not adequately supported the critical need for social change that is focused on UTI clinical management of impoverished nonpregnant females, such as those on Medicaid, in U.S. ambulatory care settings (Kodner & Gupton, 2010). Urinary tract infections and antibiotic resistance prevention progress have been confined to pediatric, elderly female, pregnant female populations, or hospital-related data sources. The literature has not produced quantitative values that can be clinically correlated and can be applied to prevention effort applications in nonpregnant low-income female populations in ambulatory care settings. Furthermore, access to the reliable patient, prescriber, pharmaceutical, laboratory testing and payment data had not been simultaneously available in ambulatory care.

Factors significant for social change patterns are currently evident. Relevant epidemiology studies about antibiotic-resistant UTIs and the economic impacts on specific populations with a high incidence of disease burden related to inappropriate

treatment greatly impacts federal and state funding. Federal regulators such as the Centers for Medicare and Medicaid Services (CMS) have already mandated antibiotic stewardship (ABS) programs in hospitals as part of their conditions of participation (Centers for Medicare and Medicaid Services [CMS], 2012). CMS states that unless all efforts to reduce healthcare-acquired infections (HAIs) has been made, including the implementation of an ABS program, they will not reimburse hospitals for infections after patients are admitted and in their care. Recommendations to introduce the same ABS programs in long-term care facilities has additionally been proposed (CMS, 2015). It would be likely that ambulatory care would be a future target for ABS with CMS.

UTIs and antimicrobial resistance are predominant global health problems that are associated with all ambulatory care patients (Frieden, 2010). Antibiotic treatment choices in ambulatory care can greatly impact morbidity and mortality due to antibiotic resistance (Yang et al., 2013). Community populations are not only associated with antibiotic resistance in UTIs, but the exposures to inappropriate antibiotic treatment may go unnoticed. To what extent this damage is causing may not yet be quantifiable. Databases produced via retrospective collection by health care facilities, universities, state and federal antibiotic-resistance research are becoming available for trend investigation. Local hospital infection control or state syndromic surveillance data programs are in place. These programs apply real-time (active surveillance) data collection techniques to prevent harm to patients (CMS, 2016).

Summary

Urinary tract infection epidemiology and the economic burden have changed over the last few decades. The current climate of antibiotic resistance has become an emergency. Urinary tract infections rely on the appropriate treatment with antibiotics. Nonpregnant, low-income female populations, ages 25-44, with UTI symptoms, and seeking care in ambulatory settings, has been a population in the United States lacking research studies. Many unknowns have existed that include access to care issues, patient behaviors, and provider prescribing habits. Those patients who become mismanaged with antibiotics greatly contribute to the morbidity and mortality of the UTI rate increase found in community ambulatory care populations.

A review of the literature will be discussed and evaluated in Chapter 2. The relationship between UTIs and antibiotic resistance and antibiotic management will be additionally characterized. The literature review will seek to inform readers about the antibiotic resistance gap in U.S. ambulatory care settings, and nonpregnant, low-income women with UTIs. Variables such as broad-spectrum and narrow-spectrum antibiotics were chosen to better understand the utilization and outcome relationships of these drugs prescribed for UTIs. An evaluation of those gaps in the literature related to antibiotic resistance patterns in ambulatory care, low-income populations, will be discussed. The methodology will be revealed in Chapter 3, which will represent my intentions of how the research will be accomplished. Chapter 3 will report out how this study answered the questions that I had proposed. Additionally, I will illustrate how the study variables, ethics, and data will be managed. Finally, the outline of the study results, findings, and

implications for social change will be covered in Chapters 4 and 5. The final pages of the dissertation document will include the references and appendices.

Chapter 2: Literature Review

Introduction

This literature review was conducted to understand historical and current research related to UTI antibiotic resistance and how this research is related to antibiotic treatment in nonpregnant low socioeconomic status females in ambulatory care settings. Chapter 2 includes an overview of historical and contemporary beliefs about UTI antibiotic resistance and how those models have been applied to low-income populations. I searched various databases and then reduced my results to include only those studies and articles that were the most germane to this study.

The chapter will begin with a discussion about ecosocial theory (Krieger, 2008), which I used to ground this study. The fundamental epidemiological history of UTIs and the microbiology of antibiotic-resistant UTIs will also be discussed. In the literature review, I will additionally include data that support an issue of volatility with antibiotic prescribing for UTIs in ambulatory care settings in low-income female populations in developing countries, and comparatively, in the United States. Furthermore, this discussion will include antibiotic stewardship with research-based evidence about antibiotic utilization and how it can be negatively associated with antibiotic resistance in UTIs. In the closing segment, I will examine the variables and related literature that I used in my investigation. I developed my research methodology based on my review of the literature.

Literature Search Strategy

I conducted a comprehensive, computerized literature search to obtain abstracts and published documents relevant via PUBMED, PLoS, Cochrane Database of Systematic Reviews, Walden University ProQuest Dissertations database, CORE, CDC database and web pages, The Centers for Medicare and Medicaid database and web pages, the World Health Organization website, PubMed Central, BioMed Central Hopkins Medicine website, Pacific Group of e-Journals, Wiley Online Library, American Society of Microbiology library web site, Agency for Research and Quality database and website, Whitehouse.gov website, Journal Storage online library, Wisconsin Public Library system.

The 194 documents chosen were based on the most relevant and recent mainly between the years' 2011-2017, except for documents containing historical perspectives, last-known published findings about my topic, or those years that establish the theory which I used. A variety of keywords were utilized independently and in combination with one another in exploring the literature. These included *urinary tract infection, Medicaid, U.S., antibiotic resistance, antibiotic use, low-income female, antibiotic stewardship, antibiotic prescribing, primary health care, and ambulatory care.*

Theoretical Foundation

Krieger (2001) described social change and population health patterns as critical elements (p. 668) of change that is specific to the responsibility of social inequality in epidemiology. Within the health care community, the spotlight is on population health, disease distribution of pathogenic organisms, environmental triggers causing disease, and

social inequalities which could advance human infectious disease states (Gulis & Fujino, 2015). These focal points are evident in key ecosocial theory (Krieger, 2008). Principal areas identified by Krieger (2008) are levels, pathways, and power: accountability and agency, embodiment, the cumulative interplay of exposure, susceptibility and resistance, and pathways of the embodiment (p. 224). According to Krieger social patterns exist in all populations and constantly change, however they do not appear to be economic and political priorities, which result in disparities in unsupported health care endeavors.

Krieger (1994) was the original founder of ecosocial theory (see Figure 1.). This prototype demonstrates that a change in any of the pathways will alter the life course of human health. In any population analysis of disease changes, researchers should take into consideration the causal pathways operating on many diverse levels and spatiotemporal systems (p. 224) as well as examine historical events to describe the burden in disease population distribution and inequality patterns as populations have changed over time (Krieger, 2008).

Krieger (2008) stated that the ecosocial model exposes how proximal and distal factors change socially (p.233). Proximal factors include those that can be controlled by a person or by a medical health professional, and distal factors include those factors that society will have to change (Krieger, 2012). She explained that her theory is an amplification of the concepts of the gene-environment interaction framework which posits that individual variations in genetic makeup are extrinsically related to a composite of disease that has occurred in the human host (Krieger, 1994, 2008; see, also, CDC,

2016; National Human Genome Research Institute [NHGRI], 2014). Pharmaceutical interventions that could halt the expression of those genes and which may be biologically susceptible to disease have been the focus of this type of gene-environment research (Krieger, 2008). Exposures to cumulative pathogenic, behavioral, environmental, and physical processes (promote gene expression) are what Krieger (2008) refers to as the proximal associations that cause disease (p. 233).

The value of the ecosocial theory for this study is to augment the principle foundations of UTI, antibiotic resistance, and those roles and influential characteristics of prescribing antibiotics in a non-pregnant, low-income female population. Social inequality as described by Krieger (2008), was utilized by the authors, Green and Labonte as a blueprint for their book written about public health policy and pathogenic economic justice in developing countries and the United States. At the center of the ecosocial theory are the pathways of population distribution operating within multiple phases of the infection evolution of UTI. Penders, Stobberingh, Savelkoul, & Wolfs (2013) investigated how the influence of cultures, geography, and population density may determine antibiotic susceptibility. Penders et al. (2013) provided evidence indicating a pathogenic resistance of various organisms that cause UTIs in humans. This study demonstrates the population distribution relationship posited by Krieger on emerging antibiotic resistance and how important culture-based studies continue to be even in an era focused on genetic research.

Pathways of Ecosocial Theory

Antibiotic resistance can be attributed to the inadequate prescribing of antibiotics, the innocent patient, or a health-care provider type discrepancy due to lack of availability in the geographical area of care a patient (Sahoo, Tamhankar, Johansson, & Lundborg, 2010). Population distribution influences the levels segment as well health-care provider prescribing competency (2013). Additionally, there may be population factors of a prescription response relationship between low-income female populations and the buildup of resistance that is even due to minimal antibiotic exposure (2013). Social constructs that include individual, household, or regional groups may manipulate the choices found in the pursuit of health treatment. Antibiotic resistance with UTIs may occur if the “power” and exposure to internal or external forces (i.e., access to quality care within a hospital or out in the community) is negatively supported by a remote geographical region or political environment (McDonnell Norms Group, 2008; Bruschi & Bronze, 2015).

Power of Ecosocial Theory

Krieger (2008) used the diagram to describe conservation ecology of forests and disease to describe population disease distribution. The diagram was used to detail the complexity of temporal (old or young forests) and spatial (big or small forests) metrics seen in ecology (2008). Temporal studies have been conducted on antibiotic-resistant UTIs encountered in developing countries (Guyomard-Rabinirina et al., 2016). Antibiotic resistance and UTIs have been found to be like that of a U.S. forest when portrayed as “a level,” either on an individual or group level, which is central to Krieger’s ecosocial

theory (p. 224). The impact on spatial issues arise in forests the same as UTIs in humans, when zoonotic disease such as those that are tickborne (i.e., Babesiosis or Rocky Mountain Spotted Fever) (LymeDisease.org, 2015) increase in incidence because the size and location of a forest changes due to excessive commercial logging operations within a given area (2008). Similarly, UTIs increase in incidence in geographical regions due to excessive overutilization of antibiotics (Rowe & Manisha, 2013). The distribution of forest species may also shift negatively in two ways: increase in those species that are destructive and transmit a dangerous disease to humans and other woodland creatures, or, forest species whose purpose is to keep other harmful species from emerging or overpopulation Martins da Costa, Loureiro, & Matos. (2013). Comparatively the same can be described with antibiotic use and emerging resistance patterns of transmission of antibiotic resistance in humans as studied by Mamuye, Metaferia, Birhanu, Desta, and Fantaw (2015) that portray Krieger's theories as they relate to UTI resistance today.

Levels of Ecosocial Theory

Krieger notes that a population can become quickly eroded because of community epidemics (2008). She used the example of measles as an argument of how perceptions of those experiences in a population are rapidly threatened: if measles appeared endemic within a community (level) the population must exceed a specified number of people (scale), to identify and understand the cause of the problem as an epidemic before it becomes endemic (p. 225). When one is considered and not the other (i.e., a level) the events going on within the population can cripple the community residents if they are not

recognized (2008). These factors interact to increase the rate of infectious disease and may lead to community disintegration (p. 224).

Krieger additionally mapped out a hierarchy of distance that is described by public health as “distal to proximal” as an explanation for epidemic disease (2008, p. 222). Krieger attempted to delete this terminology and replace with “levels, pathways, and power” (p. 228). Krieger’s use of a map (p. 224) was equal to a hands-on approach, and supported the arguments she made for how biological and societal disease patterns originate based on affordability and political agendas. Living standards are associated with race and social class as she explained which has a tremendous impact on outcomes with patient and the prescribing of antibiotics due to these agencies regulate who (class of patient), what (approve types of drugs for use), and how (public health funded or private) our communities are cared for (2008). For example, if the economic trend in public health is to cut funding for syphilis surveillance in young female pregnant populations whose incidence has been rising (CDC, 2015e), initial antibiotic prescribing can impact community prevalence and the spread of this disease. In chapter 2 of this paper, a description of the ecological forces and relationships involved in pathogenic responses related to antibiotic prescribing and ambulatory care patient interactions with health care that has led to antibiotic resistance is illustrated by Krieger’s’ ecosocial theory.

Literature Review Related to Key Variables and/or Concepts

Antibiotic resistance patterns appear to be progressing in intensity and worldwide distribution as mankind perseveres in the war on resistant microorganisms (World Health

Organization [WHO], 2014). It is well understood that antibiotic resistance is purely guided by utilization (Lee et al., 2014). Daniel et al. (2014) report that in the United States over 200 million prescriptions are provided to outpatient populations for the treatment of viral infections alone.

Current State of Antibiotic Resistance

New antibiotic drugs to treat infections need to be developed to keep pace with resistance (Boucher et al., 2009). One early research initiative to reduce inappropriate antibiotic utilization analyzed 39 Cochrane studies (Cochrane.org; 2005) and learned that viral illness will improve on their own if patients are provided with prescriptions and then asked to delay filling prescriptions for two to three days. By not filling a prescription, the percent chance of antibiotic resistance is reduced to zero (Bartlett, Gilberg, & Spellberg, 2013). Regardless of how perfectly this is understood, inappropriate utilization continues.

In the United States, health-care providers make poor choices in the prescribing of antibiotics 50% of the time (CDC, 2013a). Over the last century, it had been possible to control antibiotic prescribing for infections and observe susceptibility without the conferral of antimicrobial resistance (Davies & Davies, 2010). Today, antibiotic resistance patterns have accelerated (Hawkey, 2008). The treatment of infections without resistance is no longer under our human control (President's Council of Advisors on Science and Technology [PCAST], 2014). The effects now span to all classes of antibiotics with many pathogenic isolates, at local, national, and global levels (2010). Efforts to protect those classes of antibiotics that produce rare resistance has become a worldwide priority (Carlet et al., 2012; 2014).

Epidemiology of Antibiotic Resistance

Annually, antibiotic resistance distribution rates associated with morbidity and mortality are published in the United States, the CDC (Centers for Disease Control & Prevention [CDC], 2013b) shows that approximately 23 million deaths occur annually as a direct result of infections that are resistant to one or more classes of antibiotics.

Children in the 1-5-year-old age range have been identified in the United States as one population with antibiotic resistance increasing, however the variability in geographic area, methods of surveillance and data collection, and the identification of risk factors as well as prevalence will need to be researched further (Rush University Medical Center [RUMC], 2014; Bryce et al., 2016).

Current UTI prevalence. The prevalence of antibiotic-resistant UTIs in pregnant women, the most common complication in pregnancy, is also increasing. Rizvi et al. (2011) studied 4,290 urine samples from pregnant females and identified prevalence rates of 78% for asymptomatic bacteriuria (n=3210) and 25.2% (n=1080) with symptomatic UTIs. Pregnant females, unlike nonpregnant females in the United States, regardless of socioeconomic status, are managed with antibiotic medications for both asymptomatic bacteriuria and symptomatic due to the known high morbidity caused by untreated UTIs (2011). The prevalence rate of UTIs in the United States in nonpregnant females who seek care in ambulatory care settings has not been published other than to mention that 85% of UTIs occur in both the pregnant and nonpregnant female populations. Prevalence rates in ambulatory care settings for nonpregnant females who are dependent on assistance with insurance, such as Medicaid, for UTIs, to date, has not been published.

Pregnant females, unlike nonpregnant females, have had regular infusions of unrestricted grant funding for studies to support protocols and further research studies related to antibiotic resistance (Martinez de Tejada, 2014). Nearly 2 million people in the adult U.S. population (p. 11) have died or will have died of serious complications because of antibiotic resistance and were treated by drugs that were designed specifically to eliminate harmful pathogens (Food & Drug Administration [FDA], 2011; Fair & Tor, 2014). The declining effectiveness of antibiotics due to negative outcomes such as mortality, raise concern over the costs that produce widespread economic burden (Gandra, Barter & Laxminarayan, 2014).

Economic Burden of Antibiotic Resistance

The annual economic burden estimated at over 60 billion dollars indicates that of this amount, 35 billion dollars in productivity costs are lost that are directly attributable to antibiotic resistance in the United States (Centers for Disease Control & Prevention [CDC], 2013b; Network for Excellence in Health Innovations [NEHI], 2013). Although it is a challenge to measure the economic burden of antibiotic resistance it is projected that by the year 2050 over 100 trillion dollars and 10 million deaths will contribute to economic loss associated with this problem (O'Neill, 2014). A macroeconomic approach must be carried out in any future studies per Gandra et al. (2014) to quantify the true economic influences of antibiotic resistance. Currently, in the United States there are substantial financial and clinical burdens related to several pathogens causing dangerous levels of resistance (Centers for Disease Control & Prevention [CDC], 2015c).

Antibiotic Utilization

Multiple factors today impair antibiotic treatment and lead to antibiotic resistance, (CDC, 2013a, p. 11). In ambulatory care, the most common antibiotics used are those prescribed for seasonal viral medical conditions caused by pathogens that do not require antibiotic treatment (Shapiro et al., 2013). Examples of medical conditions that do not need antibiotics are cold and Flu viruses (Centers for Disease Control & Prevention [CDC], 2015d). There are times when these viruses cause an illness that exacerbates another underlying medical disease process already in progress (Singanayagam, Joshi, Mallia, & Johnston, 2012). The lowered resistance due to viruses combined with chronic disease processes can trigger or further promote bacterial growth in an organ's location of chronic disease (Kurai, Saraya, Ishii, & Takizawa, 2013; Yamaya, 2012). For example, an individual with Chronic Obstructive Pulmonary Disease (COPD), a chronic respiratory disease, acquires Influenza (a respiratory illness) and may be more susceptible to bacterial pneumonia (a different respiratory illness).

Broad-spectrum antibiotics. Antibiotics that cover many different pathogens utilized by ambulatory care providers are known as Broad-Spectrum antibiotics (Shapiro et al., 2013). Two classes of broad-spectrum antibiotics, macrolides, and fluoroquinolones, are used the most. Studies to understand our current state of antibiotic resistance related to the misuse in antibiotic selection type is needed (Shapiro, Pavia, & Shah, 2011; Walker, 2013).

Epidemiologically Significant Pathogen Emergence

The CDC has compiled a list of hazardous antibiotic-resistant pathogens that often accompany inappropriate prescribing of antibiotics; these pathogens represent an “urgent, serious, or concerning” threat and are quickly progressing antibiotic resistance patterns (Golkar, Bagasra, & Pace, 2014; CDC, 2015c).

Threat levels defined. An “urgent” threat is the most serious due to that there is a high risk for widespread antibiotic resistance to occur. A “serious” threat describes behaviors in pathogens identified that may worsen if they are not closely monitored. Finally, a “concerning” threat may be stated as a low-risk because the choices for antibiotics are still many, however, severe illness can also still occur. These threats were defined by a level of harm thought to be caused by the pathogens identified and intended to be utilized for prevention purposes with epidemiology surveillance programs (CDC, 2015c).

Urgent threats. Larger urban populations produce antibiotic-resistant pathogens that would be considered “urgent” on the CDC threat list. Since the year 2000, key “urgent” pathogens known as Carbapenem-resistant Enterobacteriaceae (CRE) or Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) have increased from less than 1% to greater than 12% in larger urban regions (Satlin, Jenkins, & Walsh, 2014). It is not unusual to find a 50% mortality rate (p. 1) of infection in major medical centers in large urban areas where complicated procedures such as solid organ transplant (SOT) are performed. Facilities that provide SOT have been reporting CRKP infection incidence rates at or greater than 10% (Satlin et al., 2014, p. 2).

In a metanalysis of liver transplant patients, the mortality incidence was five-fold higher in those patients with CRKP infections identified postoperatively in a hospital setting (Kalpoe et al., 2012). In contrast, a different study discussed that healthcare personnel working in an ambulatory setting of one western U.S. region took a model approach to carbapenem-resistance prevention to prove that these resistant pathogens could be decreased (Lee et al., 2016). The authors applied the principles provided in the CDC carbapenem resistance toolkit to simulate a decrease in carbapenem-resistant pathogens. The health care workers conducting the study had identified that by the year 2025 carbapenem-resistant pathogens would grow to endemic proportions, however by utilizing this toolkit, they were able to prove a 50% reduction in incidence rates in the population (Lee et al., 2016).

Serious threats. Other important antibiotic-resistant pathogens in addition to carbapenem-resistant pathogens have indicated a slow upward trend developing in community-acquired antibiotic resistance in various regions in the U.S. pathogens include Vancomycin-resistant *Enterococcus* (VRE), multidrug-resistant *Pseudomonas aeruginosa* (MDR-PA), Imipenem-resistant *Acinetobacter baumannii* (CR-Ab), and resistant *Escherichia coli* and *Klebsiella pneumonia*, both of which are known as “Extended Spectrum Beta Lactamase” (ESBLs) due to that they are resistant to third generation cephalosporins (aka, Beta Lactam antibiotics) (Lee et al., 2013). VRE is often found in immunocompromised patients if it is a true infection, however, there is a high prevalence of carriage in the community (Byappanahalli, Nevers, Korajkic, Staley, & Harwood, 2012). Methicillin-resistant *Staphylococcus aureus* (MRSA) was said to have

been increasing in incidence and prevalence in the community over the last decade (Mekviwattanawong, Srifuengfung, Chokepaibulkit, Lohsiriwat, Thamlikitkul, 2006). In 2010, however, a newer study by the CDC was released that indicated a decrease in community MRSA (Kallen et al., 2010).

Concerning threats. In many geographic regions in the United States, MRSA is now considered endemic (David & Daum, 2010). Endemicity does not lessen the virulence of this pathogen, however. Many of those pathogens previously discussed are carried on a person's body as normal flora (Borchert et al., 2008). Lowering of the immune status may predispose a person to illness as healthy humans are able to coexist with their normal flora, even pathogens (Harvard Health Publications, 2015). Pathogens, however, rapidly learn and adapt faster than antibiotics are produced (Childress, 2013). Strategic deployment of effective and sustainable activities with antibiotic stewardship using education as a multidisciplinary tool, are necessary (Azevedo, Capela, Baltazar, 2013)

Antibiotic Stewardship

According to the Association for Professionals in Infection Control and Epidemiology (APIC, 2012) antimicrobial stewardship is “a coordinated program that promotes the appropriate use of antimicrobials (including antibiotics), improves patient outcomes, reduces microbial resistance, and decreases in the spread of infections caused by multidrug-resistant organisms.” The consequential warnings of future inappropriate utilization of antibiotics were hinted at in 1945 by Sir Alexander Fleming during his Nobel Prize acceptance speech (Fleming, 1945). The Center for Disease Dynamics,

Economics & Policy (CDDEP, 2014) released global data for the third millennium that substantiates Dr. Fleming's long-ago warning indicating that there has indeed been more than a 35% increase in antibiotic utilization between 2000 and 2010.

Antibiotic stewardship priorities in the United States. The two leading concerns that present a challenge for healthcare-providers today as noted by Bjorkman, Berg, Viberg, and Lundborg (2013) are antibiotic resistance and UTIs. The United States is the third largest consumer of antibiotic prescriptions as evidenced by an unprecedented utilization increase. Hicks et al (2015) reported that 182.7 million prescriptions were provided to adult patients, or 789 prescriptions per 1000 adults according to U.S. ambulatory data from 2011 (p. 1311). Narrow-spectrum antibiotics (macrolides and penicillin's) were prescribed for 41%, and broad-spectrum antibiotics prescribed for 31%, of females, >20 years of age, in ambulatory care settings (p. 1313). This represented a rate in antibiotic prescribing in females >20, of 1102.2 (prescriptions per 1000 persons) with an adjusted odds ratio (OR) of 2.4 (confidence interval (CI) 1.9-2.9) (Hicks et al., 2015, p. 1313). By 2013, broad-spectrum antibiotic prescribing in adults increased from 24% to 48% (Lee et al., 2014). Social determinants (2015, p. 1314) were recommended for future research.

The U.S. female population literature gap. The management of urinary tract infections (UTIs) caused by antibiotic resistance in female populations is a challenging responsibility for any healthcare-provider (Pronovost, 2013). The influence on health care management in female populations begins before health problems occur (DeMillo & Nakashian, 2016). U.S. studies to date related to UTIs and antibiotic utilization have only

focused on pregnant female populations and the management of UTIs. This has been primarily due to the elevated risk of harm to the unborn child. Influential studies in the U.S. on social determinants such as income and gender and the role that these play in antibiotic resistance are absent.

Studies conducted in the United States with antibiotic prescribing have determined that females are a high risk for resistant UTIs (Lawal, 2012; Vasudevan, 2014). This evidence is directly related to ambulatory care visits for UTI symptoms and higher antibiotic utilization rates with both narrow and broad-spectrum antibiotics. Females comprise 84.5% of the 3 million patients in the United States with UTI symptoms as their primary complaint and are a high risk for UTIs (Thoureen, Scott, & Best, 2015). The rate of uncomplicated UTIs in females between the ages of 18-49 in the United States who receive antibiotic treatment is 28.2 percent for every 10,000 females (Lawal, 2012). The current gap in the literature is to understand how two classes of antibiotics (narrow and broad-spectrum) are prescribed to nonpregnant females with UTI symptoms in ambulatory care settings and the role in antibiotic-resistant UTIs. Without research studies conducted at home in the United States, barriers will remain unknown and funding cannot be substantiated. Unfortunately, economic study evidence outside of the U.S. is not comparable.

UTI-specific antibiotic stewardship. Antibiotic stewardship in UTIs has become increasingly important. *E. coli* bacteria is the cause of 80% of every 7 million human UTIs diagnosed in the ambulatory care setting (Yadav, Singh, Kumar, Katewa, & Kumari, 2014; *E. coli* 131, a highly resistant strain of *E. coli* bacteria, is said to be

causing a “stealth pandemic” (Brusch, 2016). Recurrence in UTIs is usually related to the same pathogen that caused the initial infection. Antibiotic resistance and the overuse of broad-spectrum antibiotics have been noted as primary contributors in the escalation of antibiotic resistance and recurrence of UTIs outside of the United States (Zowawi et al., 2015). Mazulli (2012) documented that a relapse in a UTI will occur in 25% of women within 6 months of treatment, therefore working towards a cure while limiting unintended consequences such as infection recurrence is the primary goal of antibiotic stewardship (Abbo & Hooten, 2014).

Bacterial strain resistance according to Abbo and Hooten (2014) that have been due to *E. coli* bacteria, prompted researchers to begin really studying antibiotic resistance and stewardship in ambulatory care settings just after the turn of the 21st century. It has been well documented that resistant endemic strains of bacteria and viruses are carried into the hospital setting from the community (Sydnor & Perl, 2011); the community-acquired resistant strain of *Staphylococcus aureus* known as “CA-MRSA” is now present in hospital infections (p. 148). In 2015, a report to the President of the United States was provided to the White House that provided evidence of dire outcomes if antibiotic stewardship was not made a priority (President’s Council of Advisors on Science and Technology [PCAST], 2015). Ambulatory care has made great strides in the stewardship of appropriate prescribing practices as evidenced by studies published recently in the literature (Hicks et al., 2015). It is of great importance as antibiotic stewardship practices advance in ambulatory settings, especially with UTI treatment, that prescribing practices are continually re-evaluated at regular intervals (Abbo & Hooten, 2014).

Health-care providers utilize laboratory tests in the diagnosis, treatment, and continuing management of any illness. According to Bhavsar (2015), clinical significance is not often found among the many urinary cultures that a laboratory receives for testing. This is usually because of contamination that occurs during collection or other factors related to storage and transportation of urine specimens (Bekeris, Jones, Walsh, & Wagar, 2008). It is for these reasons that signs and symptoms must be considered and prescribing choices will need to be based solely on these details (Pallett & Hand, 2010). Unfortunately, this leads to prescribing antibiotics in a blind fashion, or “empirically.”

Prescribing antibiotics empirically is a delicate act of balance that the healthcare-provider must go through to decide on the best course of treatment for their patient; this must be carried out rationally and thoughtfully. Choosing an antibiotic will need to be individualized for the patient and the geographic prescribing region. Consideration taken in advance for known epidemiologically significant pathogens in the area, especially those on the urgent or serious list of resistances (CDC, 2015c) may be the difference between curing illness and increasing the likelihood of recurrence. (Ventola, 2015). Patient factors to consider would be related to allergies, compliance with medications (if known), and costs that may be associated with treatment.

Patients having a lower income status may not have the financial means to pay for more than basic testing or generic medications (Farfan-Portet, Van de Voorde, Vijens, & Stichele, 2012). Recurrent infections may be costlier due to that they may need longer

treatment or medications that are not available on a generic formulary list. Patients with a lower income may also add to the already-present antibiotic stewardship challenges that a healthcare-provider has in treating UTIs that are not associated with monetary costs. Current infection status, for example, may be unknown. The health-care provider may not get an accurate history and unable to discern whether the patient had already been treated for an infection. Poverty is also a known driving factor in medication sharing, hoarding of medications, and resorting to self-directed treatment (Planta, 2007). In today's world, the internet is a place that can be unregulated when it comes to medications, which comes with its own challenges for antibiotic stewardship. Anyone can order almost any medication online and get it shipped directly to them, often without a prescription (Orizio, Merla, Schulz, & Gelatti, 2011). Computers may not even be necessary if you have a smartphone with an internet connection. If you do not have a phone with this technology, the public library has computers that are free for community residents to use (Gates Foundation, 2005). The public may be naïve about the lack of quality control with these medications available through the internet (World Health Organization [WHO], 2011).

Other avenues to gain prescriptions that are not regulated are also available and are not difficult to come by if you have a passport and like to travel. In contrast, before the last two decades, internet services were not available and travel outside of the United States was not commonplace for the everyday resident. Cheap air travel today has afforded many the opportunity to travel to countries outside of the United States which have pharmacies that carry all types of medications including many antibiotics that do

not require prescriptions signed by a provider (Lior & Cots, 2009). The real issue, however, lies in the absence of quality control measures. Medications that have not been checked for quality may pose further health and safety risks (WHO, 2011). According to a Princeton University (1995) publication, in using unregulated antibiotics, old antibiotics, or someone else's antibiotics, a person will be compounding the already difficult task that any licensed healthcare-provider has in trying to cure an often-uncomplicated illness like a UTI.

Past and Present Dynamics with UTI Epidemiology

The historical literature reviewed indicates that prior to 1980, UTI antibiotic resistance was being seen in almost every antibiotic (Bartlett et al., 2011). Resistance patterns vary from region to region. Surveillance data that is normally performed at the local level (Masterton, 2008), to include state syndromic surveillance data captured via emergency departments, is often relied upon to determine antibiotic susceptibility in the community since there can be a large variance seen from region to region. Broad-spectrum antibiotics are known to be the most corrupt out of all the antibiotics; their utilization is greater, therefore, resistant pathogens are also increased (Garau et al., 2014). Of the broad-spectrum antibiotic choices available today, several disturb normal flora, creating an environment for disease and resistant pathogens to flourish (Odonkor & Addo, 2011) and are known to have a higher risk for resistance such as sulfonamides, fluoroquinolones, and cephalosporins (Fair & Tor, 2014). The pathogen most likely to be the cause of up to 90% of UTIs in females are *Escherichia coli* (Gupta, Hooton, & Stamm, 2001; Ulleryd, 2003). Empiric selection of antibiotics has become more

important in recent times due to the increase in antibiotic resistance in *E. coli*. (2001). While previous surveillance studies may have identified significant differences in the frequency of susceptibility to common urinary anti-infectives between isolates collected from male and female patients, currently this has not been consistently observed (Lagace-Wiens et al., 2011). This quantitative study's aim was to investigate the temporal progression of antibiotic resistance incidence in UTIs and consider essential data details like the differences in economic status.

Summary and Conclusions

This chapter provided a literature review of historical, epidemiological, and fundamental knowledge concerning UTIs and antibiotic resistance. Empiric prescribing of broad-spectrum/narrow-spectrum antibiotics were also described which included those elements for antibiotic decision-making by the healthcare-provider. Clearly visible in the literature was the obvious contributory role of antibiotic exposure to urinary tract infection resistance. Additionally, the sample population attributes, independent and dependent variables, and suspected link of an increase in recurrent UTIs was exposed by the literature review. Unfortunately, studies that could be utilized to statistically investigate and reinforce an association between antibiotic resistance and urinary tract infections due to those risks such as health care coverage type, in nonpregnant low-income female populations in U.S. ambulatory care settings, came up short without appropriate comparison of literature, or, did not exist at all. However, those documents in the literature reviewed could support the hypotheses and analysis of the dependent and independent variables. I will include a simplified description of data details, including

variables, to be assembled. The method and design proposed for this research study will be examined in Chapter 3.

Chapter 3: Research Method

Researchers with the NAMCS began data collection in 1973, and, since 1989, have been collecting survey data annually in ambulatory physician clinics in the United States. I analyzed these survey data to evaluate risk factors for antibiotic resistance, with a specific focus on exposures to health care insurance coverage in low-income nonpregnant female populations with UTI symptoms who seek care in the ambulatory setting. Study subjects were drawn from 112 primary sampling units (PSUs) from 50 states in the United States and the District of Columbia. I retrospectively reviewed the survey data to identify U.S. nonpregnant female populations who had sought care for UTI symptoms in ambulatory clinics and had health care coverage with Medicaid. In Chapter 3, I describe the research methodology I used. I provide an overview of my research design, population, and sampling procedures; a description of study variables and my plan for data analysis; and discussion of threats to validity and ethical concerns.

Research Design and Rationale

In this study, I retrospectively illustrated and analyzed NAMCS observational data for a cohort of ambulatory care clinic visits by U.S. women. The design facilitated discovery of important variables that were confounding factors whose relationships to the exposures were in question.

Study Design Selection

The design of a retrospective observational cohort study design was used to estimate antibiotic resistance in UTIs at the group level; ecological bias issues were

considered. I chose a retrospective approach based on the availability of variables during the original survey period chosen when antibiotic resistance is thought to occur (Al-Badir & Al-Shaikh, 2013). The NAMCS survey data available for public use were chosen from the years 2008-2012. The source population appropriate for this design was a cohort from U.S. ambulatory care nonpregnant female patient visits whose risk for UTI antibiotic resistance was due to exposure to poverty. Medicaid, a type of health care coverage was used to identify those with a lower income status. Risk adjustments were based on the NAMCS data collected from 2008-2012. The study design considered time, dose, and nature in the assignment of risks associated with UTI antibiotic resistance in the cohort chosen. The pursuit of a retrospective observational study seemed like a logical way to conduct this study investigation.

Design advantages. The advantage to using a retrospective observational cohort study is that observer bias is lessened and multiple relationships to a single exposure can be investigated (Mann, 2003). Original survey data had already been procured by NAMCS, therefore, this design appeared to be the most efficient, least time-consuming, and most accurate analysis (see Euser, Zoccali, Jager, & Dekker, 2009; Huston & Naylor, 1996). UTIs do not appear to be rare in the population of interest, low-income females. The observational design of this study allowed for access to health care survey information without having to conduct interviews; exposure association assumptions were made without direct observation (Carlson & Morrison, 2009). The data collection methodology for this study was completed using a standard method which allowed for

comparison over time and generalization using multiple regions of the United States for analysis (see Mann, 2003).

Study design disadvantages. Although bias is lessened with this study design, disadvantages in using this type of design are that causal relationships may be difficult to establish with more than one factor in use. Bias and confounding are difficult to control for (University of Portsmouth, 2012). The data I used were not designed specifically for my study which could have put me at a disadvantage. However, the survey data provided by NAMCS contained enough details for analysis. correctly for my examination. For example, it could have been difficult to identify a group to compare for exposure without specific age groups identified by NAMCS. However, this was not the case.

Methodology

Population and Sampling

A secondary database source was utilized for my study which included information on the research design. I used the NAMCS database, a national sampling survey. The survey was designed and managed by the Ambulatory and Hospital Care Statistics branch of the CDC (2011). The sampling frame for 2008-2012 was composed of all nonfederal ambulatory care clinic visits to physician offices (excluding radiologists, pathologists, and anesthesiologists) whose provider data were maintained within the American Medical Association and American Osteopathic Association master file databases. The U.S. Census Bureau staff acted on behalf of the CDC in the collection of clinic visit data for the national ambulatory survey (Hall, Schwartzman, Zhang, & Liu, 2017).

Sampling procedures. Sample visit data collected for NAMCS included physician and patient statistics, as well as patient visit characteristics. A three-stage process of sampling was conducted. Primary sampling units, or, “PSU’s,” were selected by NAMCS surveyors which consisted of first, 112 U.S. geographical regions, second, the selection of physician ambulatory clinics, and third, the selection of patient visits (CDC, 2011). Data processing and medical coding were performed by SRA International, Inc., Durham, North Carolina. Quality assurance and control procedures were performed with 10 percent of patient records used as a sample and were entered and coded individually (2011). Sample data formed standard errors and national estimates after estimated visit samples were weighted (2011). The CDC describes their calculations for each visit as complicated and had many stages designed for weight computations which reduced bias by inflating survey data or weighted national estimates (2001). A four-part activity was undergone for visit weighting that included “inflation by reciprocals of selection probabilities, adjustment for nonresponse, population ratio adjustments, and weight smoothing” (CDC, 2011). The complexity of their design was further explained by their use of Taylor approximations in SUDAAN to estimate the variability in sampling (2001).

Study Population Sample

The target source population for this research project consisted of National Ambulatory Medical Care Survey (NAMCS) patient visits occurring between 2008 and 2012. Female patients, that visited U.S. ambulatory care clinics comprised 57% of the total patient visits in the NAMCS studies between years’ 2008-2012 ($N=199,456$). The

patient visit sample population that met inclusion criteria as high risk for developing antibiotic-resistant UTIs per the literature, were nonpregnant females, age 25-44, reporting to ambulatory care clinics for UTI symptoms, and on Medicaid ($N=51$).

Sample methodology. All demographic and clinical patient visit data were reviewed for potential proximal and distal risk factors for exposure to potential negative outcomes. Proximal factors as explained by Krieger (2008) are those behavioral, biological, psychological, and physical processes that perform on or near the body and are controlled at an individual level. Distal risk factors, or those factors shaping a person's exposure, may be stated as social determinants.

Proximal risk factors for exposure and study inclusions. First, risk factors for proximal exposure were identified from the secondary sample frame population visit data that included the following variables ($N=51$): pregnancy status (nonpregnant), as evidenced by the NAMCS 2012 code "Pregnant" (2012) or ICD9 code classifications referent to a state of pregnancy for years' 2008-2011; sex (female) as evidenced by "female;" age (25-44) as evidenced by "age 25-44;" "Diag1, 2, or 3" with ICD9 diagnosis codes of "5990" (urinary tract infection site not specified), or "5950" (acute cystitis), or "59080" (Pyelonephritis) (NAMCS, 2008; NAMCS, 2009, NAMCS, 2010, NAMCS, 2011, NAMCS, 2012). Antibiotic prescribing methods by the provider, as a proximal factor for exposure, was identified at three levels (broad-spectrum antibiotics, narrow-spectrum antibiotics, and the broad/narrow-spectrum combination of antibiotics). United States population identification for the purposes of this study may include "American" as a surrogate for U.S. nationality.

Distal risk factors for exposure and study inclusion. Distal factors structure a person's exposure and in health care social determinants are influential, according to Krieger (2008). This study reviewed the secondary study data for exposure risk and found that a social determinant was available to include as an indicator of income status: Medicaid ($N=51$). Additionally, risk exposure related to evidence-based antibiotic treatment guidelines for uncomplicated and complicated UTIs in nonpregnant populations (National Institute for Health Care and Excellence [NICE], 2016) recommend a three-day course of antibiotics for uncomplicated UTIs and greater than three days if the UTI is complicated (recurrence, pyelonephritis). Antibiotic treatment status as a risk factor was available at two levels: initial, or continued.

Sample exclusions. Those patient care visits and populations excluded in this study were phone visits, house calls, emergency department visits, federal facility visits, elderly adult, males, pregnant females, females under the age of 25 or over 44, pediatric, and hospitalized patient populations. Patient comorbidities were also not considered for risk now due to too many overall possibilities that would increase study length of time requirements and may have had an overall effect on the design choice. Those patients who were uninsured were additionally not included due to that the reason for not having insurance could not be ascertained. The NAMCS code for type of problem (new, chronic, post-op, etc...), "MAJOR," was also not utilized due to that the "reason for visit" (NAMCS, 2012) (RSV) had several choices, which did not correspond well with the type of problem.

Pregnant female-visit exclusion rationale. In chapter two it was noted that pregnant female UTI incidence was only slightly higher than non-pregnant female UTI incidence with variations between 2% and 13% (Lumbiganon, Laopaiboon, & Thinkhamrop, 2010; Matuszkiewicz-Rowynska, Malyszko, & Wieliczko, 2015). For this study, pregnant female patient visits were not included in the cohort age range selected because pregnant women are a much higher risk for complications due to their state of carrying an unborn child, and unlike nonpregnant females in the general population, pregnant females are screened for bacteriuria because of the high risk of pyelonephritis as a complication (August & DeRosa, 2012; Prakash & Saxena, 2013). All UTIs in pregnancy are considered complicated and normally only treated by a specialty health-care provider. (Johnson & Kim, 2015).

Cohort sample size. Logistic regression tables for sample size were reviewed to estimate the minimum sample size required to confidently accept the results of the analysis (Hsieh, 1989). The literature indicated that the probability of an antibiotic-resistant UTI diagnosis within 6 months was 2, and one year after treatment was 3 (Al-Badir & Al-Shaikh, 2013; Dason, Dason, & Kapoor, 2010). Countries other than the United States have begun publishing overall antibiotic resistance rates for various regions. Historically, the United States had not published overall antibiotic resistance rates, though they have reported individual pathogen resistance rates. In 2011, this changed, and results produced from a survey conducted by the Infectious Disease Society of America Emerging Infections Network indicated that around “60% of participants had seen a pan-resistant, untreatable bacterial infection within the prior year” (Hersh,

Beekmann, Polgreen, Zaoutis, & Newland, 2009). For this study, which was based on a very large national survey, comprised of office visits, and from this, predominant factors already available as variables in the NAMCS data set were utilized to identify the sample frame that included exposures and non-exposures. These variables included “SEX” (1=Female); “PAYMCAID” (1= Medicaid as payment type); “PREGNANT” (2= Nonpregnant) (available only in 2012); “DIAG 1, 2, 3” (ICD 9 Codes indicating an upper or lower urinary tract infection), and, “AGE” (ages 25-44) (National Bureau of Economic Research [NBER], n.d.). From this overall exposure/non-exposure data, a simple random sample was calculated electronically for an appropriate sample size (National Statistical Service, n.d.). To find an odds ratio of 2.0 for a patient exhibiting UTI symptoms and having a positive UTI diagnosis, a one-tailed test was used with one standard deviation above the mean, a significance level of $\alpha= 0.05$, confidence level of 95%, confidence interval of 0.05 (upper 0.55, lower 0.45), standard error of 0.03, relative standard error of 5.10, and a power of 80%, indicating that a minimum of 42 cases were needed; 45 cases were randomly included for the final study sample.

Variable Descriptions

Variables collected for measurement purposes resulted from each ambulatory care visit captured by the national NAMCS survey data set between 2008 and 2012. Each visit was analyzed for possible associations related to the variables chosen for this study. The dependent and independent variable definitions and measurements are stated in Tables 1-3, after the descriptions of all study variables.

Dependent variable. The primary dependent variable (DV) identified was UTI antibiotic resistance (see Table 1). The variable was defined by ICD9 Diagnosis codes that included “5990 (UTI), 59780 (URETHRITIS), 5999 (URINARY DISORDER NOS), 59080 (PYLONEPHRITIS), 5950 (ACUTE CYSTITIS), 5959 (CYSTITIS). Additionally, the variable was defined by utilizing the already present NAMCS codebooks available; “RFV” (reason for visit), included signs and symptoms of a UTI (NBER, n.d.). UTI signs and symptoms may be one of the following codes per NAMCS codebook (NBER, n.d.), “Reason for Visit Tabular Classification:” 1675 (urinary tract infection), 1660 (urinary dysfunction), 1650 (painful urination), 1910.1 (low back pain), 1905 (back symptoms), 1545 (abdominal pain), 2705 (UTI pyelonephritis), 1665.1 & 1665.2 (bladder pain and infection), 1645.0 (urinary urgency and frequency), 1545.2 (low abdominal or quadrant/inguinal pain), 1775 (pelvic pain), 10552 (flank pain) (2012), (AND) at LEAST ONE Antibiotic was Prescribed: “ABXRX: 1=Yes, 0=No, (AND) at LEAST ONE antibiotic must be new or continued.

Measurement of the DV. The dependent variable in question was measured by whether it met definition criteria (1=UTI Resistance Criteria Met, and, (0=UTI Resistance Criteria Not Met).

Table 1

Summary of Dependent Variable

Variable type	Variable	Variable definition	Coded value	Measure	Measure
Dependent	UTI Antibiotic Resistance	1. An ICD9 Diagnosis code of "5990, 59780, 5999, 59080, 5939,5950, 5959."	UAR	"1" = UTI Resistance Criteria Met	"0" = UTI Resistance Criteria Not Met
<i>and/or</i>					
		2. RFV (reason for visit) includes signs and symptoms of a UTI. UTI signs and symptoms may be one of the codes per NAMCS codebook: "Reason for Visit Tabular Classification." See Table 2 for NAMCS codes			

Table 2

NAMCS Codes: Reason for Tabular Classification

Code	Code description
1545	Abdominal pain
1545.2	Lower abdominal or quadrant/inguinal pain
1645.0	Urinary urgency and frequency
1650	Painful urination
1660	Urinary dysfunction
1665.1 & 1665.2	Bladder pain and infection
1675	Urinary tract infection
1775	Pelvic pain
1905	Back symptoms
1910.1	Low back pain
2705	UTI pyelonephritis

Note. The NAMCS codes, reasons for tabular classification, have been extracted from the NAMCS microdata file documentation for NAMCS survey years' 2008-2012.

Independent variables. The independent variables (IV) chosen were relevant to the study questions and hypotheses stated.

IV initial antibiotics prescribed. The first IV, "initial antibiotics prescribed," was coded as "INABXRX." This variable was defined as a new patient visit related to UTI signs/symptoms with onset less than 3 months, (AND) one or more initial antibiotics prescribed. See Table 2.

Measurement of INABXRX. INABXRX was measured by “1=Initial Antibiotics Prescribed, and, 0=Initial Antibiotics Not Prescribed.”

IV continued antibiotics prescribed. The second IV, “continued antibiotics prescribed,” coded as “CONABXRX.” CONABXRX was defined as a recurrent visit, by a referral or previously seen by a primary provider related to UTI signs/symptoms with onset less than 12 months, (AND) one or more antibiotics prescribed are continued. See Table 3.

Measurement of CONABXRX. CONABXRX was measured as “1=Continued Antibiotics Prescribed, and, 0=Continued Antibiotics Not Prescribed.

IV broad-spectrum antibiotics. The third IV, and first antibiotic class of IV’s of “broad-spectrum antibiotics,” coded as “BS,” was defined as a class of antibiotics that covers a variety of different pathogens in the treatment of an infection. Antibiotics selected for this study, including NAMCS codes (NBER, n.d.) were Sulfamethoxazole (29840), Metronidazole (19233), Levofloxacin/Levaquin (97163, 97045), Tindamycin/Tindazole (7212), Ciprofloxacin (92111/6839), Besifloxacin (11096), Ceftriaxone/Rocephin (91069), Azithromycin (93214), Keflex/Cephalexin (16475), Ampicillin (1685), Cefpodoxime (93166/d0095), Fluoroquinolones (8574), Doxycycline (10355), Augmentin/Amoxicillin-Clavulanate (60115), and Ceftizoxime (d00010) (NAMCS, 2012). See Table 3.

Measurement of BS. BS was measured “1=Broad-Spectrum Antibiotics Prescribed, and, 0=Broad-Spectrum Antibiotics Not Prescribed.”

IV narrow-spectrum antibiotics. The fourth IV and second antibiotic class of IV's of "narrow-spectrum antibiotics" was coded as "NS." NS was defined as antibiotics that target specific pathogens. Antibiotics selected for this study, including NAMCS codes (n.d.) were Clindamycin/Cleocin (6920/6905), Macrobid/Nitrofurantoin/Macrochantin (93090/18130), and Trimethoprim (32438). See Table 3.

Measurement of NS. NS was measured as "1=Narrow-Spectrum Antibiotics Prescribed, and, 0=Narrow-Spectrum Antibiotics Not Prescribed."

IV broad- and narrow-spectrum antibiotics. The final antibiotic class of IV's of "broad- and narrow-spectrum antibiotics" was coded as "BSNS." BSNS was defined as either having both broad- and narrow-spectrum antibiotics prescribed during one visit, or, one medication that has a combined chemical combination of a broad-spectrum and a narrow-spectrum antibiotic. Antibiotics selected for this study, including their relevance NAMCS codes (n.d.) were Bactrim/Trimethoprim-Sulfamethoxazole (32423/3430/1017/29843). See Table 3.

Measurement of BSNS. BSNS was measured as "1=Broad- and Narrow-spectrum Antibiotics Prescribed, and, 0=Broad- and Narrow-spectrum Antibiotics Not Prescribed."

Table 3

Summary of Independent Variables and Antibiotic Classes Prescribed

Variable type	Variable	Variable description	Coded value	Measure	Measure
Independent	Initial Antibiotics Prescribed	1. A new patient visit related to UTI signs/symptoms with onset less than 3 months	INABXRX	“1” = Initial Antibiotic Prescribed Meets Defined Criteria	“0” = Initial Antibiotic Prescribed Does Not Meet Defined Criteria
		<i>And</i>			
		2. One or More initial antibiotics were prescribed			
Independent	Continued Antibiotics Prescribed	1. Recurrent visit via referral or previously seen by primary provider related to UTI with onset less than 12 months	CONABXRX	“1” = Continued Antibiotics Prescribed Meets Defined Criteria	“0” = Continued Antibiotics Prescribed Does Not Meet Defined Criteria
		<i>And</i>			
		2. One or more antibiotics prescribed are continued			
Independent	Narrow-Spectrum Antibiotics	Class of Antibiotics that targets specific pathogens in the treatment of an infection	NS	“1” = Narrow-Spectrum Antibiotic Prescribed Meets Defined Criteria	“0” = Narrow-Spectrum Antibiotic Prescribed Does Not Meet Defined Criteria
Independent	Combined Broad & Narrow-Spectrum Antibiotics	1. Prescribed Both Broad & Narrow-Spectrum Antibiotics at the same visit	BSNS	“1” = Broad & Narrow-Spectrum Antibiotics Prescribed Meets Defined Criteria	“0” = Broad & Narrow-Spectrum Antibiotics Prescribed Does Not Meet Defined Criteria

Antibiotic class relevance. The relevance of these two classes of antibiotics is that they include most all classes of antibiotics that are currently used in the U.S. to treat infections (Ventola, 2015), and implicated in the progression of antibiotic-resistant UTIs (Pallett & Hand, 2010; Bartlett, 2011). This study had included all broad- and narrow-spectrum antibiotics available in the study data. Studies indicate that providers have been prescribing both broad-spectrum and other antibiotic classes simultaneously for the initial treatment of UTIs (Leekha, Terrell, & Edson, 2011). This method has been questioned as it is deemed an inappropriate way to practice prescribing antibiotics (Karam, Chastre, Wilcox, & Vincent, 2016) and has negative consequences documented with epidemiologically important gram-negative pathogens in UTIs (Nienhouse, 2014).

Gram-positive bacteria such as *Methicillin-resistant Staphylococcus aureus* (MRSA), is also of epidemiological importance, however, gram-negative pathogens are tougher to treat (Soto, 2014). The literature has evidenced that most complaints about “UTIs” are that the cultures do not grow substantial amounts of bacteria and yet antibiotics are prescribed without an appropriate indication (2010). A cost-effective alternative to antibiotics has been documented in the literature as a simple urinalysis test, or “UA” (Brusch & Bronze, 2015). To demonstrate the impact, Al-Badir & Shaikh (2013) discussed that asymptomatic bacteriuria accounts for about 8% of health care visits where more than 25% of antibiotics are prescribed but rarely ever indicated (Shapiro, 2013). Shapiro et al. (2013) noted that 61% of antibiotics prescribed during ambulatory care visits broad-spectrum antibiotics and of these, macrolides, quinolones, and aminopenicillins accounted for between 12 and 25% of all antibiotics prescribed.

IV Ages. The IV of ages were coded as “AGES.” AGES were defined as those visits whose ages were between 25-44. See Table 4.

Measurement of AGES. AGES were measured as “1 = 25-29, 2 = 30-34, 3 = 35-39, and 4 = 40-44.”

IV Region. The IV of region was codes as “REGION.” REGIONS were defined as those regions of the United States that were included in the NAMCS surveys.

Measurement of REGION. REGION was measured as “1 = Northeast, 2 = Midwest, 3 = South, and 4 = West.” See Table 4.

Table 4

Summary of Independent Variables of Region and Ages

Variable type	Variable	Variable description	Coded value	Measure
Independent	Ages	Includes ages 25-44	AGES	1 = 25-29 2 = 30-34 3 = 35-39 4 = 40-44
Independent	Regions	Includes the four major regions that NAMCS collected data from in the United States: Northwest, Midwest, South, and West	REGION	1 = Northeast 2 = Midwest 3 = South 4 = West

Data Analysis Plan

Data Selection

Data selected for analysis were abstracted from NAMCS datasets and summary tables from the CDC website for the survey (2014). The analysis included my study period of 2008-2012; years' 2013-2015 were not utilized due to that the data was not publicly available when my study was designed (CDC, 2015a). The dependent and independent variable data abstracted from the national data set included for analysis was first done with Excel via a comma separated value (CSV) file that was already prepared for use on the NAMCS website. NAMCS data sets utilized are public, secure, and web-based with Centers for Disease Control & Prevention (CDC) ownership and management of this data (CDC, 2014). The CSV file was scrubbed and recoded to include only relevant data elements for this study. SPSS, version 23, was utilized for the cohort analysis measures of exposures and outcomes. Many of the original code labels in the CSV file were changed for this study so that they were easily identifiable.

The NAMCS public database did not include patient identifiers, therefore it was not necessary to replace patient identity with coding. The independent and dependent variables were either pre-assigned data codes, or I had assigned data codes for analysis. Variances can be produced according to NCHS (2015) by using a generalized variance curve which is discussed in the public-use file literature (2015).

Statistical Testing

Testing for logistic regression was carried out in SPSS to examine whether the independent variables of initial antibiotics prescribed, continued antibiotics prescribed, or broad, narrow, and broad- and narrow-spectrum-combined antibiotics predicted the DV, UTI antibiotic resistance. To assess variability on the dependent variable, the independent variables as predictors utilized the Nagelkerke R². Cross tabs were executed to examine the association between DV and IV's, along with Fisher's Exact Test; Fisher's will be utilized for analysis due to the small sample. Binary Logistic regression was executed for initial and continuous antibiotic prescribing, and also the classes of antibiotics included (broad, narrow, and combined broad- and narrow-spectrum) to illustrate the overall relationships of the IV's significance for logistic regression.

To assess individual predictors and the model fit, Hosmer-Lemeshow and Wald were applied to test the null hypothesis. Classification utilized for the variables and evidenced with a contingency table were: "Expected" (Exp), for the null, which is also written as the number of cases predicted (indicated by 0 or 1) divided by "Observed" (OBS), or the number counted. The odds ratio, or in binary regression known as Exp(B), was analyzed to determine event occurrence probability predictions. Significance was analyzed by using .05, and was identified as significant, >1 will; a 95% CI was additionally included for analysis. The greater the significance of each independent variable over 1.0, the more likely there will be for a risk with UTI antibiotic resistance. Omnibus testing was conducted to test the intercept-only with the fitted model using Chi-square; p-values were interpreted.

Many of the restrictions placed on assumptions with linear regression are not an issue with logistic regression testing (Woltman, Feldstain, MacKay, & Rocci, 2012). A good example of this is that there were no assumptions made for equal variances, normality, or linearity as well as normal distribution was never assumed with an error term variance. The outcome (DV) was dichotomous and separate. With logistic regression, a large sample would have been optimal to use to achieve maximum likely outcomes, however, the sample size was ultimately small and was utilized to conduct analysis. I chose a public data file with a national sample that was very large and was hopeful that this would complement my use of discrete variables so that there was enough data to analyze each variable chosen.

Research Question 1: Are initial antibiotics prescribed for UTIs associated with UTI antibiotic resistance?

H₀1: There is no statistically significant association between antibiotic resistance in UTIs and initial antibiotics prescribed.

H_a1: There is a statistically significant association between antibiotic resistance in UTIs related and initial antibiotics prescribed.

Logistic regression was carried out to test the first hypothesis that there is no statistically significant relationship between continued antibiotics prescribed and UTI antibiotic resistance in nonpregnant females, age 25-44, on Medicaid, in U.S. ambulatory care settings. To test the hypothesis, the statistical significance used was a p-value of 0.05. A p-value of <0.05 indicated rejection of the null hypothesis and failure to reject the alternative hypothesis. Prevalence rate will additionally be calculated.

Research Question 2: Are continued antibiotics prescribed for UTIs associated with UTI antibiotic resistance?

H_{o2}: There is no statistically significant association between antibiotic resistance in UTIs and continued antibiotics prescribed.

H_{a2}: There is a statistically significant association between antibiotic resistance in UTIs and continued antibiotics prescribed.

Logistic regression was carried out to test the second hypothesis that there is no statistically significant relationship between continued antibiotics prescribed and UTI antibiotic resistance in nonpregnant females, age 25-44, on Medicaid, in U.S. ambulatory care settings. To test the hypothesis, the statistical significance used was a p-value of 0.05. A p-value of <0.05 indicated rejection of the null hypothesis and failure to reject the alternative hypothesis. Prevalence rate will additionally be calculated.

Research Question 3: Is the class of antibiotic prescribed for UTIs associated with UTI antibiotic resistance?

H_{o3}: There is no statistically significant association between UTI antibiotic resistance and class of antibiotic prescribed.

H_{a3}: There is a statistically significant association between UTI antibiotic resistance and class of antibiotic prescribed.

Logistic regression was carried out to test the third hypothesis that there is no statistically significant difference in antibiotic resistance in UTIs in low-income nonpregnant females age 25-44 related and initial antibiotics prescribed. The dependent

variable was UTI antibiotic resistance. To test the hypothesis, the statistical significance used was a *p*-value of 0.05. A *p*-value of <0.05 indicated rejection of the null hypothesis and failure to reject the alternative hypothesis. Prevalence rate will additionally be calculated.

Threats to Validity

Data quality procedures for this study looked at those internal and external threats to validity that could occur and directly impact reliability and validity (Dyck, Culp, & Cacchione, 2007). Internal validity may likely be threatened from within the sample selected. The study sample chosen may not be representative of all females on Medicaid because disease likelihood would be related to racial and ethnic genetic traits; only black, white, and Hispanic or Latino, and “others” were utilized in the NAMCS study (2011; 2012). Access to a more detailed account of patient characteristics was not available in the NAMCS public data sets.

To increase the probability of patient characteristics, random selection will be utilized (Creswell, 2009). External validity threats occur when study results are applied to other populations (Steckler & McLeroy, 2008). The threat potentially lies with the fact that the primary study population was not federally-based ambulatory care facilities, and not inclusive of veterans, military ambulatory care, and outpatient public health clinics, emergency departments or acute care (emergency) department. Ambulatory care clinics that are federally funded, would be considered special populations a special and would not be generalizable. To manage this threat, study results would need to restrict those

patients who, in addition to receiving health care at non-federal ambulatory care facilities, including those ambulatory care clinics within a hospital facility, also receive health care at federal ambulatory care facilities such as the VA, military clinic, or public health clinic.

Ethical Procedures

This study was performed using a national, public secondary database, available on the internet via the CDC study website for the National Ambulatory Medical Center Survey (NAMCS). All patient data had been de-identified by the original surveyors prior to posting to the internet. The design variables according to the National Center for Health Statistics (NCHS), are confidential and have never been released to the public. Variances can be produced according to NCHS (2015) by using a generalized variance curve which is discussed in the public-use file literature (2015).

According to NCHS (2015), the NAMCS is governed by Title 42, United States Code, and Section 242K, which permits data collection for health research. Title 42, United States Code, Section 242m (d) provides data confidentiality. The statistical purpose is the only reason that the survey data may be collected. “No information that could identify a person or establishment can be released to anyone, including the President, Congress, or any court, without the consent of the provider” (2015). The data must be protected according to many laws such as but not limited to the Privacy Act, and the Public Health Service Act; Census Bureau staff must sign a declaration of facts (2015). Healthcare-providers and patients can be confident that The NCHS and Census Bureau are protecting everyone’s privacy, as evidenced by a perfect record of privacy

protection (2015). The Walden University Internal Review Board (IRB) governs the handling of all study data; this study followed these procedures for collection and handling of the data.

Summary

For this study, an observational cohort, the retrospective approach was utilized to characterize the relationship between the dependent variable of UTI antibiotic-resistance incidence and the related independent variables of initial, continued, broad-spectrum, narrow-spectrum, and broad/narrow-spectrum antibiotics prescribed, to nonpregnant females, ages 25-44, on Medicaid who were seeking care for UTI symptoms in an ambulatory setting. The study purpose was to examine nonpregnant American female patients who were exposed to poverty and at risk for antibiotic resistance when seeking care for UTIs in ambulatory care settings. This was accomplished using secondary data from a cohort of U.S. ambulatory care facilities from large national surveys that are conducted annually in the United States by NAMCS, a branch of the Centers for Disease Control and Prevention (CDC) (NAMCS, 2008; 2009; 2010; 2011; 2012).

Statistically significant relationship testing between the independent variables to understand why female low-income populations in ambulatory care are at risk for UTI antibiotic resistance was the basis for the data collection and analysis. Statistical analysis via binary logistic regression for the three hypotheses was completed. The next chapter, chapter 4, will detail the results of the analysis activities.

Chapter 4: Results

The purpose of this study was to examine nonpregnant U.S. female patients who were exposed to poverty and at risk for UTI antibiotic resistance. The cohort was secondary data selected from a publicly-available data repository in the United States. This study investigated three key research questions. Research Question 1 (Are initial antibiotics prescribed for UTIs associated with UTI antibiotic resistance?) was designed to investigate whether the very first round of antibiotics prescribed for uncomplicated UTIs in nonpregnant females who had sought care in ambulatory settings might be contributing to antibiotic resistance.

Very few studies in the United States about prescribing patterns of ambulatory care providers have been completed (Costelloe, Metcalfe, Lovering, Mant, & Hay, 2010; Wong et al., 2017). The first round of antibiotics is often prescribed empirically without a culture to prove what antibiotic is necessary to cure a UTI infection (Gibson & Toscano, 2012). The duration and timing of antibiotic therapy has also been in question (Grigoryan, Zoorob, Wang, & Trautner, 2015). Research Question 2 (Are continued antibiotics prescribed for UTIs associated with UTI antibiotic resistance?) proposed that, when patients returned for care because of UTI symptoms that were not going away, the same or different antibiotics prescribed were contributing factors for antibiotic resistance. Research Question 3 (Is the class of antibiotics prescribed for UTIs associated with UTI antibiotic resistance?) was planned to capture the class of antibiotic that may have been contributing to initial or continued antibiotic prescribing and that may have been related to antibiotic resistance. It has been demonstrated that antibiotic guidelines and the actual

class of antibiotics used for UTIs in ambulatory care settings are disparate (Grigoryan et al., 2015).

Data Collection

Data sets, or, more specifically, CSV data file sets for the years 2008-2012) were downloaded from the National Bureau of Economic Research's (NBER) website. This website is a national storage site for this type of data that contains research files in various formats as well as codebooks (National Bureau of Economic Research [NBER], n.d.). Data sets available on the NAMCS website did not include CSV-type files. However, SPSS-ready files were available. CSV-type data were selected for initial data abstraction and the scrub process. SPSS data files were also downloaded directly from the NAMCS webpages and compared to the NBER files for quality assurance.

After the CSV files for Microsoft Excel from NBER were validated for completeness of data, each year's worth of data was scrubbed to meet the ambulatory patient population criteria for my sample frame. These criteria included being female, between the ages of 25-44, and being a recipient of Medicaid. Criteria also included diagnoses variables. The sample frame also included nonpregnant women. Only the 2012 data set included a new variable developed by NAMCS labeled "PREGNANT," which identified a pregnant patient. Therefore, for years 2008-2011, NAMCS codes indicating a current pregnancy state, such as reason for visit (RSV), medications (MED), and ICD9 codes for diagnosis (DIAG), were reviewed and scrubbed. Those cases that were identified as meeting criteria per codes for a positive current pregnancy status were deleted from the cohort sample. The data were further sorted to delete the multiple

extraneous variables that were present and would not be utilized by this study; this made the data more manageable. A separate Excel file was created in CSV format, and each year's worth of scrubbed data was cut and pasted into this file to form one complete file for years' 2008-2012.

Case-Finding

Initially, to ensure research standards with data were met, I reviewed all NAMCS and HAI definitions, then performed any necessary variable remodeling. NAMCS survey years 2008-2012 were reviewed. Regions used in the parent study (Northeast [1], Midwest [2], South [3], and West [4]), were noted as well as Ages 25-44. The first step involved using NAMCS' study's definitions and inserting dummy variables that would better serve the analysis. All variables were identified by the dependent variable (DV) definition were located: (diagnosis) "DIAG1, DIAG2, DIAG3," (reason for visit) "RFV1, RFV2, RFV3," (medication) "MED1-MED8," and (new medication/continued medication) "NUMED, CONTMED." The independent variables of NUMED and CONTMED represented both initial and continuous prescribing as well as prescribing in 12 months or less.

A new variable column labeled "UAR," depicting dichotomous DV UTI resistance, was then inserted into the CSV data file used for this study. To properly have a defined DV (UAR), it was critical that all diagnoses, reasons for visit, and medications were reviewed with each year's code book. Each case that met criteria was entered into the variable UAR as "1," and, each case that did not meet criteria was entered in as "0." All codes in each of these categories that were related to an acute urinary tract infection

(upper or lower) were reviewed and logged for UTI exposure relevance: the sample (n=45) met criteria for UTI exposure out of the sample frame (total nonpregnant female, ages 25-44, on Medicaid, and with a positive diagnosis/symptom of UTI (N=51). Subsequently, the Excel file with all case variables were exported and uploaded into SPSS for analysis.

SPSS Variable View

Once the data were uploaded to SPSS, in “Variable View” (SPSS), each variable header was reconfigured to represent the variable type (numerical) to conduct analysis appropriately. Changes made in variable view: labels were entered; values reflecting the outcome were input; missing data was reviewed and corrected if necessary; measure (ordinal/nominal/scale) was indicated.

Sample Size

As discussed in Chapter 3, simple random sampling calculation conducted electronically was executed by utilizing the total sample frame ($N=51$), a confidence level of 95%, a confidence interval of 0.05 (upper 0.55, lower 0.45), standard error of 0.03 relative standard error of 5.10, and power of 80%. The results had indicated that a minimum sample size of 45 was necessary to perform this study. SPSS was utilized to perform random sampling; $N=51$ was input as criteria for the random sample. Probability sampling was utilized because it has been shown to provide better assurance that the sample is representative of the population (Omair, 2014).

Results

The sample frame ($N=51$) was downloaded into SPSS version 23 from Microsoft Excel and a final sample of $n=45$ was produced. Descriptive statistics was utilized to summarize the demographic sample and antibiotics prescribed.

Assumption Errors and Inquiry

Before the investigation of this study's research questions could begin, frequency distribution, errors, and assumptions were investigated in SPSS. To describe the interactions between two categorical IVs, crosstabs was utilized to create contingency tables. Frequency tables were also created for single categorical variables such as demographics (See Table 5), timing of antibiotics prescribed (initial or continued), and each class of antibiotics (broad-spectrum, narrow-spectrum, and combined broad- and narrow-spectrum (see Table 6).

Table 5

Frequencies and Percentages for Sampled Population Age, Region, Visit Year, Visit Month, and Visit Day of the Week with Symptomatic UTI

	<i>N</i>	Percent (%)
Age frequency and percentage with UTI symptoms		
25-29	15	33.2
30-34	12	26.7
35-39	9	20.0
40-44	9	20.0
Region frequency and percentage with UTI symptoms		
Northeast	10	22.2
Midwest	7	15.6
South	12	26.7
West	11	24.4
Year visit frequency and percentage with UTI symptoms		
January	3	6.7
February	5	11.1
March	6	13.3
April	2	4.4
May	3	6.7
June	2	4.4
July	2	4.4
August	3	6.7
September	5	11.1
October	8	17.8
November	4	8.9
December		
Day of the week visit frequency and percentage with UTI symptoms		
Monday	12	26.7
Tuesday	11	24.4
Wednesday	9	20.0
Thursday	7	15.6
Friday	5	11.1

Table 6

Frequency Distribution of Timing and Antibiotic Class Prescribing for UTI Symptoms

	Frequency	Percent
BS Antibiotics Not Prescribed	21	46.7
BS Antibiotics Prescribed	24	53.3
<i>Total</i>	45	100.0
NS Antibiotics Not Prescribed	29	64.4
NS Antibiotics Prescribed	16	35.6
<i>Total</i>	45	100.0
BSNS Antibiotics Not Prescribed	38	84.4
BSNS Antibiotics Prescribed	7	15.6
<i>Total</i>	45	100.0

Summary Population Frequency Distribution

Of the 45 patients in the sample between the ages of 25-44, the average age of nonpregnant females on Medicaid was 33. The age in this sample who visited ambulatory care the most were 25-29-year-olds (33.2%). The region that reported the most visits by nonpregnant ambulatory care patients were from the Southern region of the U.S (26.7%). Data concluded that nonpregnant females, ages 25-44, and on Medicaid, were also more likely to visit ambulatory care on a Monday (26.7%) during the month of November (17.8%). During the years utilized for this study, 2008-2012,

2009 received the most visits (40%) by the sample population in ambulatory care settings.

Summary Antibiotic Timing and Class Frequency Distribution

Next, frequency distributions of prescribing antibiotics were run on initial antibiotics prescribed (INABXRX) in 3 months or less for a symptomatic UTI (Figure 1), and, continuous antibiotics prescribed (CONTABXRX) (Figures 2) in 12 months or less for a symptomatic UTI. Additionally, frequency tables were provided for those classes of antibiotics included in this study that were prescribed for a symptomatic UTI: broad-spectrum antibiotics prescribed (BS), narrow-spectrum antibiotics prescribed (NS), and combined broad & narrow-spectrum antibiotics prescribed (BSNS) (see Table 3 and Figures 3, 4, 5). There appears to be a higher frequency (36%) of utilization with initial antibiotics prescribed than continued prescribing.

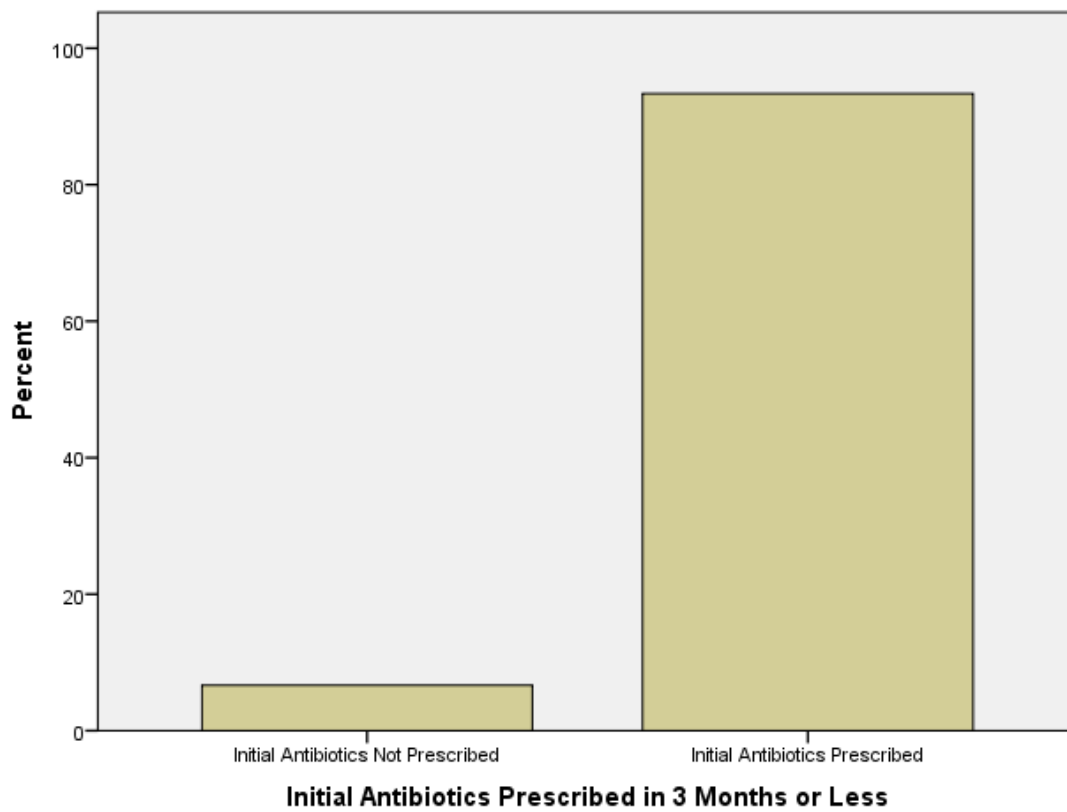


Figure 1. Bar chart of Frequency of Initial Antibiotics Prescribed in 3 Months or Less.

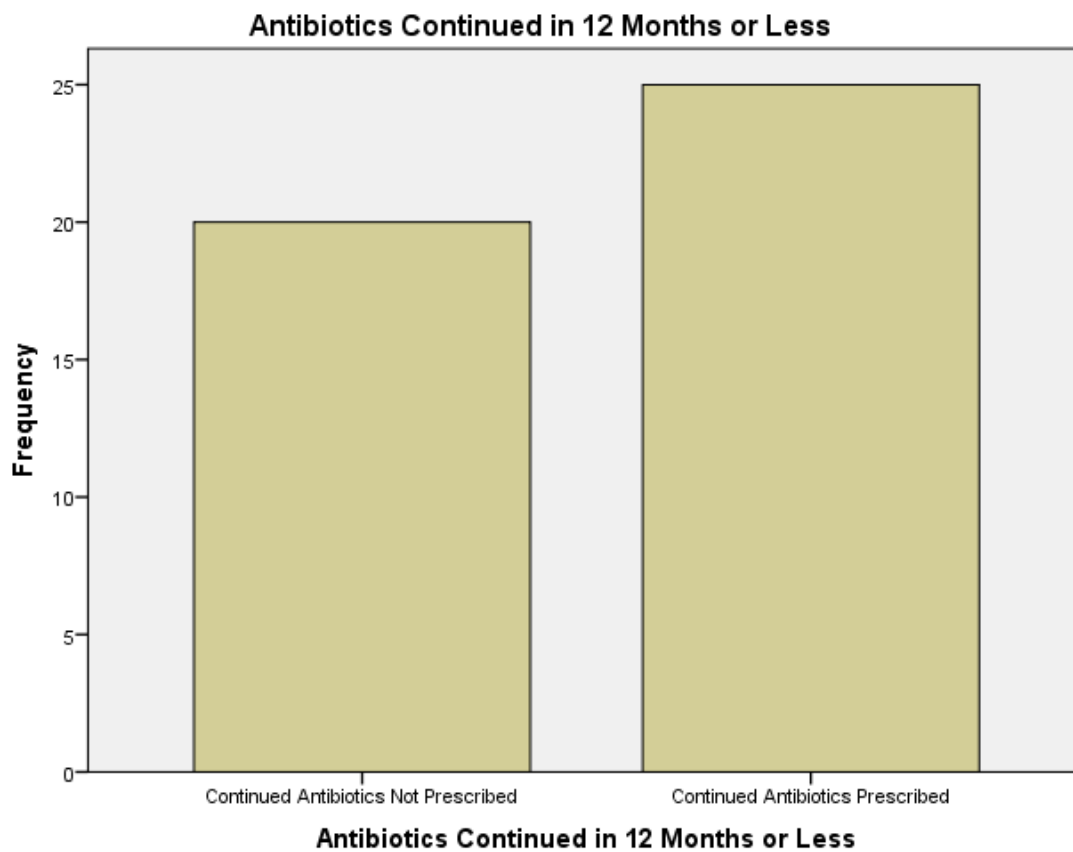


Figure 2. Bar Chart of Frequency of Continued Antibiotics Prescribed in 12 Months or Less

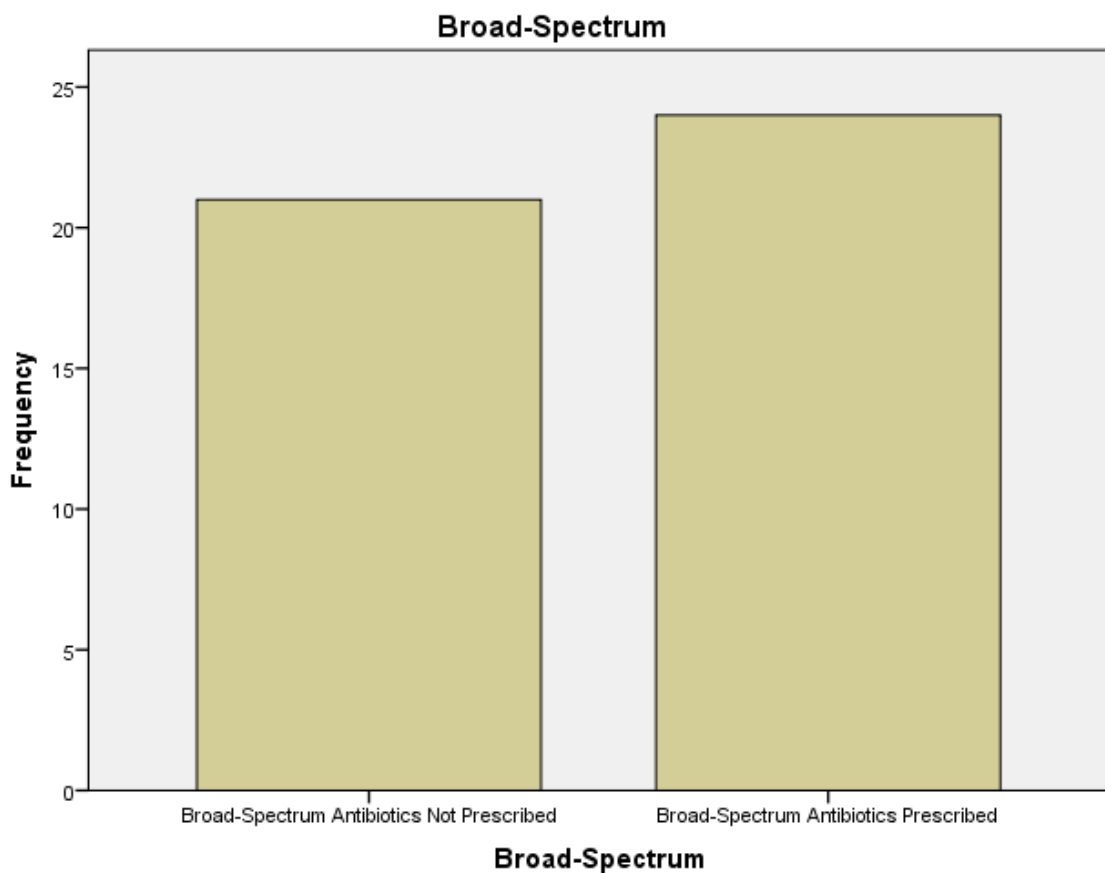


Figure 3. Bar Chart of Frequency of Broad-Spectrum Antibiotics Prescribed

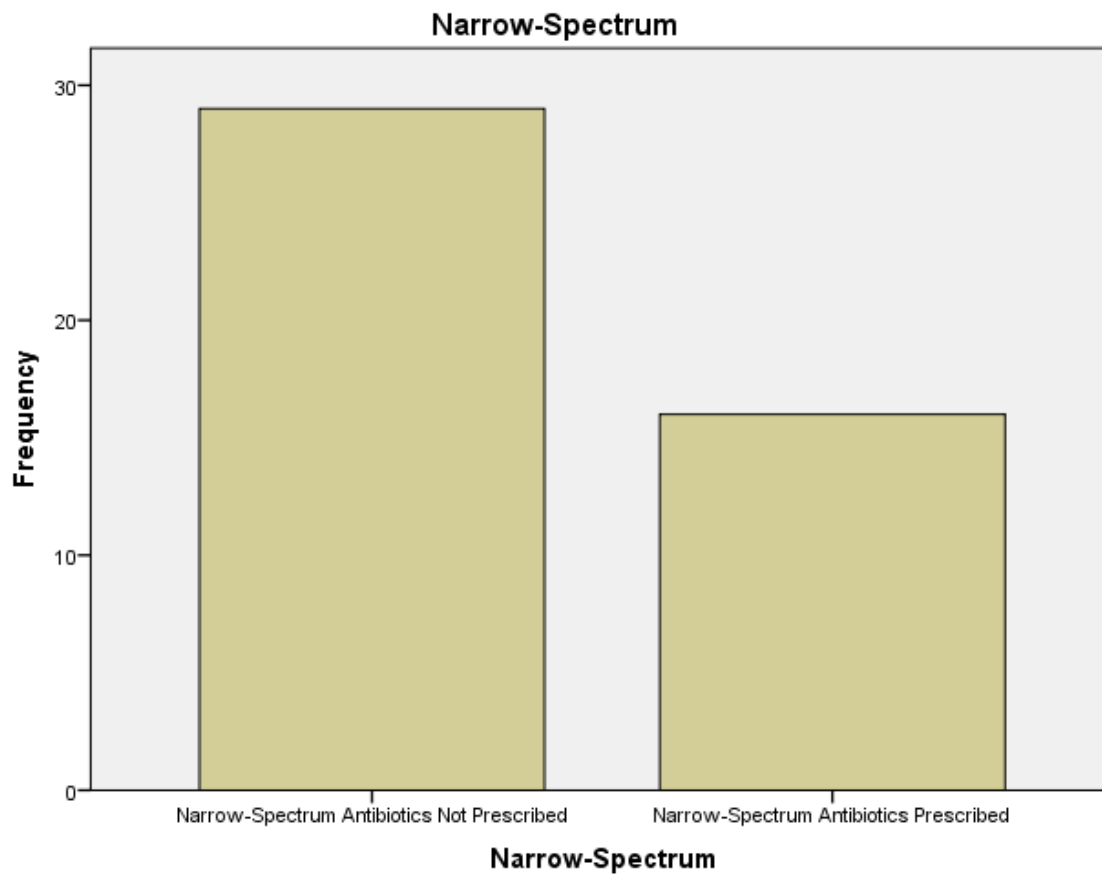


Figure 4. Bar Chart of Frequency of Narrow-Spectrum Antibiotics Prescribed

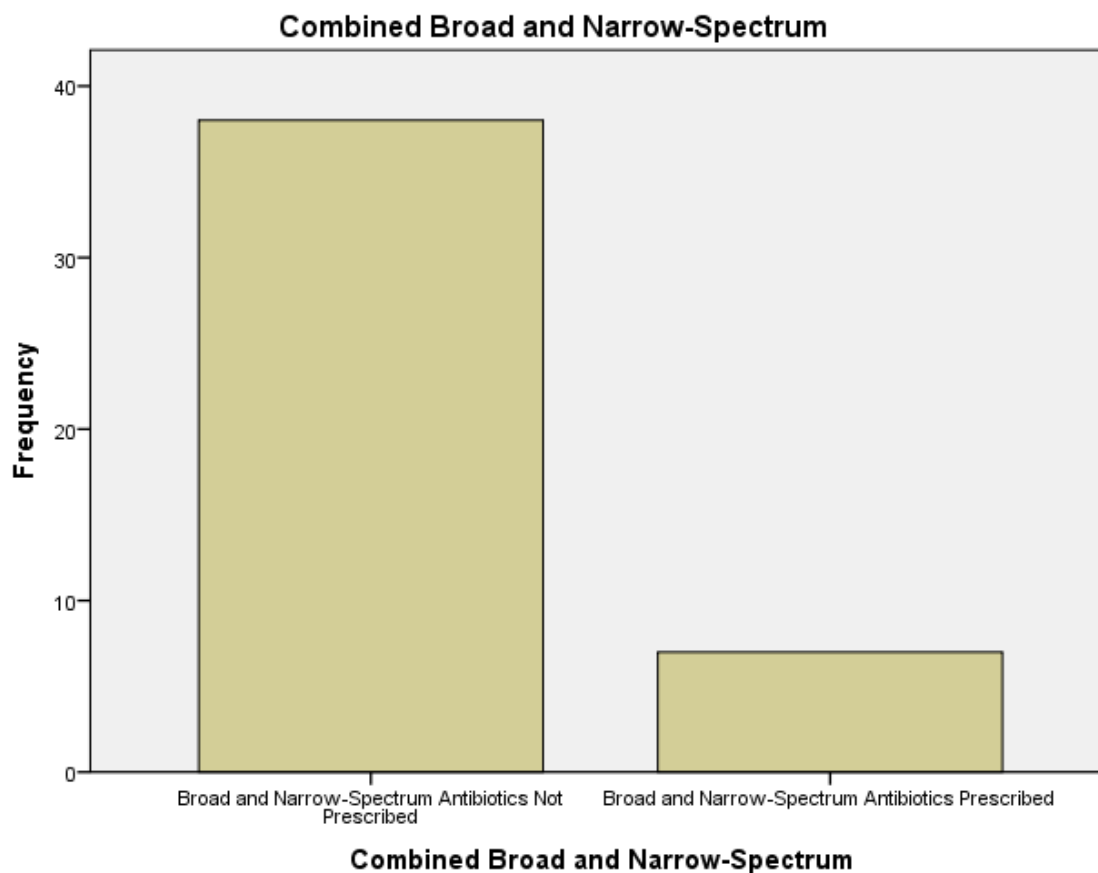


Figure 5. Bar Chart of Frequency of Combined Broad- and Narrow-Spectrum Antibiotics Prescribed

Summary of Antibiotic Prescribing Frequency Distribution

Outcome evidence with antibiotic prescribing after frequency distributions were executed indicated that of the sample ($n=45$), nonpregnant females, ages 25-44, and on Medicaid($n=42$), were likely to be prescribed initial antibiotics within 3 months 91% of the time. Those patients who returned to ambulatory care with recurrent symptoms ($n=12$), were only likely to have antibiotics continued 55.6% of the time. Patients ($n=24$) were more likely (53%) to be prescribed broad-spectrum antibiotics when seeking care in ambulatory clinics for UTIs compared to narrow-spectrum antibiotics, prescribed 18%

less frequently than broad-spectrum, and combined broad- and narrow-spectrum antibiotics, prescribed 38% less frequently than broad-spectrum antibiotics. Narrow-spectrum antibiotics ($n=16$) were only prescribed 36% of the time, and combined broad- and narrow-spectrum antibiotics ($n=7$) were only prescribed 16% of the time.

Research Question 1

Research Question 1: Are initial antibiotics prescribed for UTIs associated with UTI antibiotic resistance?

H₀1: There is no statistically significant association between antibiotic resistance in UTIs and initial antibiotics prescribed.

H_a1: There is a statistically significant association between antibiotic resistance in UTIs and initial antibiotics prescribed.

To analyze research question 1, testing for an association, followed by binary regression and a review of predictor characteristics was executed.

Association.

To test for association between initial antibiotics prescribed (IV), and UTI antibiotic resistance (DV) crosstabulation was executed and analyzed. A contingency table was produced (see Table 7) to display variable counts and percentages. Due to the small sample size and violation of assumptions for Chi-Square testing, Fisher's Exact test was reported. The proportion of those patients who were prescribed initial antibiotics in 3 months or less that developed UTI antibiotic resistance (UAR) was 51.2%, or, 21 out of 41 cases.

Table 7

Initial Antibiotics Prescribed in 3 Months or Less and UTI Antibiotic Resistance

	UTI Resistance Criteria Not Met	UTI Resistance Criteria Met	Total
% Initial Antibiotics Not Prescribed in 3 Months or Less	25%	75%	100%
% Initial Antibiotics Prescribed in 3 Months or Less	48.8%	51.2%	100%

Table 7 Contingency Table

It was noted that the results of Fisher's Exact test (see Table 8) indicated that there was no statistically significant relationship observed between the exposure to initial antibiotics prescribed in 3 months or less and UTI antibiotic resistance in nonpregnant female patients, ages 25-44, on Medicaid, who presented to an ambulatory care clinic with UTI symptoms; the p-value was $>.05$ ($p=.611$) therefore I failed to reject the null hypothesis (see Table 8).

Table 8

Summary of Fisher's Exact Test and Initial Antibiotics Prescribed

	<i>N</i>	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Fisher's Exact Test	45	.611	.357

Binary logistic regression. Binary logistic regression was executed to analyze the risk of antibiotic resistance in UTIs in those patients who were prescribed antibiotics initially for UTI symptoms while controlling for AGES and REGION. The results indicated that initial prescribing of antibiotics was not a statistically significant predictor of UTI antibiotic resistance within 3 months or less after the onset of UTI symptoms ($p > .05$). There was a large improvement with the inclusion of predictor variables and the model fit ($\chi^2=5.502(8)$, $p=.703$, Nagelkerke $R^2=.153$). The final model, however indicated that AGES and REGION had very little effect on initial antibiotics prescribed ($p = >.05$). No further predictions were made thus I failed to reject the null hypothesis. The results of binary regression with initial antibiotics prescribed predicting UTI antibiotic resistance in 3 months or less can be reviewed in Table 9.

Table 9

Summary of Binary Logistic Regression and Initial Antibiotics

Variables	<i>B</i>	Sig.	β
INABAXRX	1.34	.301	3.82
AGES (1)	-1.086	.258	.338
AGES (2)	.248	.813	1.28
AGES (3)	-.216	.839	.806
REGION (1)	.077	.950	1.080
REGION (2)	.570	.558	1.77
REGION (3)	-.229	.831	.795
REGION (4)	.783	.380	2.19

Notes. $R^2 = .153$ ($p > .05$)

To examine the first binary logistic regression model, the Hosmer and Lemeshow test was processed along with a classification table to check for the model fit. Hosmer and Lemeshow indicated that there was a significant improvement between the observed data in block 0 and the final regression model, therefore this model appeared to be a good fit ($>.05$) for the data at an acceptable level ($X^2=2.594(7)$, $p=.920$). The results of the model summary concluded that between 11% and 15% of the variation in UTI antibiotic resistance was explained by the final model. The correct classification rate increased by 13% (51.1 to 64.4.).

A review of the variables in the equation were analyzed. The variable, initial antibiotics prescribed (INABXRX), did not appear to contribute to the model; initial antibiotics prescribed are not statistically significant ($>.05$, $p= .301$). The positive coefficient B indicated that the target group had more cases coded as “1” (initial antibiotics prescribed) than “0” (initial antibiotics not prescribed). Negative coefficients (B) for AGES (1) (25-29-year-olds), AGES (3) (35-39-year-olds), and REGION (3) (Southern United States) indicated that these groups had less cases coded as “1.” Age (AGES) and Region (REGION) overall were not significant. The coefficient (B) for initial antibiotics prescribed revealed that the odds of UTI antibiotic resistance was 1.340 more likely for those prescribed initial antibiotics. The Sig. (.301) concluded that the chi square test for UTI antibiotic resistance versus initial antibiotics prescribed were not statistically significant, therefore I failed to reject the null hypothesis; data remains inconclusive because there is insufficient evidence at the alpha level of significance to reject the claim that initial antibiotics prescribed are related to UTI antibiotic resistance.

The odds for those patients who were prescribed initial antibiotics for symptomatic UTIs were 3.821 (95% CI .302 to 48.364) times more likely to have UTI antibiotic resistance in an ambulatory care setting when prescribed antibiotics initially for a UTI. Since the CI (confidence interval) spans 1.0, the increased odds (3.821) of UTI antibiotic resistance among nonpregnant females, ages 25-44, and on Medicaid, who were prescribed antibiotics initially for UTIs at baseline, does not reach statistical significance.

Predictor characteristics. Predictor characteristics based on descriptive measures of prevalence and incidence, were calculated for initial antibiotics and UTI antibiotic resistance (see Table 10). The prevalence of UTI antibiotic resistance in the total number of sample cases with UTI antibiotic resistance ($n=45$) was 9% when prescribed initial antibiotics. The incidence rate (new cases of antibiotic resistant UTIs) for those at risk in 3 months or less was 7%.

Table 10

Predictor Characteristics of Initial Antibiotics Prescribed

	Prevalence	Incidence
Initial Antibiotics Prescribed	9%	7%

Research Question 2

Research Question 2: Are continued antibiotics prescribed for UTIs associated with UTI antibiotic resistance?

H₀2: There is no statistically significant association between antibiotic resistance in UTIs and continued antibiotics prescribed.

H_{a2} : There is a statistically significant association between antibiotic resistance in UTIs and continued antibiotics prescribed.

To analyze research question 2, testing for an association, followed by binary regression and a review of predictor characteristics was executed.

Association.

To test for association between continued antibiotics prescribed (IV), and UTI antibiotic resistance (DV) crosstabulation was executed and analyzed. A contingency table was produced (see Table 11) to display variable counts and percentages. Due to the small sample size and violation of assumptions for Chi-Square testing, Fisher's Exact test was reported. The proportion of those patients who were prescribed continued antibiotics for recurrent UTIs in 12 months or less who developed UAR was 84.6%, or, 22 out of 26 cases (see table 11).

Table 11

Continued Antibiotics Prescribed in 12 Months or Less and UTI Antibiotic Resistance

	UTI Resistance Criteria Not Met	UTI Resistance Criteria Met	Total
% Continued Antibiotics Not Prescribed in 12 Months or Less	94.7%	5.3%	100%
% Continued Antibiotics Prescribed in 12 Months or Less	15.4%	84.6%	100%

Table 11 Contingency Table

Fisher's Exact test (see Table 12) evidenced a statistically significant relationship observed between the exposure to continued antibiotics prescribed in 12 months or less and UTI antibiotic resistance in nonpregnant female patients, ages 25-44, on Medicaid, who presented to an ambulatory care clinic with UTI symptoms; the p-value was $<.05$ ($p=.000$) therefore the null hypothesis was rejected (see Table 12).

Table 12

Summary of Fisher's Exact Test and Continued Antibiotics Prescribed

	<i>n</i>	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Fisher's Exact Test		.000	.000
	45		

Binary logistic regression. Binary logistic regression was executed to analyze the risk of antibiotic resistance in UTIs in those patients whose antibiotics were continued for UTI symptoms while controlling for AGES and REGION. The results indicated that continued prescribing of antibiotics was not a statistically significant predictor of UTI antibiotic resistance within 12 months or less after the onset of UTI symptoms ($p>.05$). There was an improvement for fit with the inclusion of the variables ($X^2=42.098$, $p=.000$, Nagelkerke $R^2= .810$). The final model, however, indicated that the inclusions of AGES and REGION had very little associated with continued antibiotics prescribed. No further predictions were made, thus I failed to reject the null hypothesis. The results of binary regression with continued antibiotics prescribed predicting UTI antibiotic resistance in 12 months or less can be reviewed in Table 13.

Table 13

Summary of Binary Logistic Regression and Continued Antibiotics

Variables	<i>B</i>	Sig.	β
CONABAXRX	-55.26	.997	.000
AGES (1)	-18.73	.998	.000
AGES (2)	-17.39	.998	.000
AGES (3)	34.67	.997	1.138E+15
REGION (1)	-1.03	.579	.358
REGION (2)	-.231	.899	.794
REGION (3)	17.26	.998	31465879.291
REGION (4)	-.427	.780	.653

Notes. $R^2 = .810$ ($p > .05$)

To examine the second binary logistic regression model, the Hosmer and Lemeshow test was processed along with a classification table to check for the model fit. Hosmer and Lemeshow indicated that there was a significant improvement between the observed data in block 0 and the final regression model, therefore this model appeared to be a good fit ($>.05$) for the data at an acceptable level ($X^2=1.201(6)$, $p=.977$). The results of the model summary concluded that between 60% and 80% of the variation in UTI antibiotic resistance was explained by the final model. The correct classification rate increased by 38% (51.1 to 88.9%).

A review of the variables in the equation were analyzed. The variable, continued antibiotics prescribed (CONABXRX), did not appear to contribute to the model; continued antibiotics prescribed were not statistically significant ($>.05$, $p= .997$). The negative coefficient B indicated that the target group had less cases coded as “1” (continued antibiotics prescribed) than “0” (continued antibiotics not prescribed), and was not significant after controlling for the other variables. Age (AGES) and Region (REGION) did not contribute to the model and were not significant. The coefficient (B) revealed that the odds of UTI antibiotic resistance was .000 more likely for those prescribed continued antibiotics. The Sig. (.997) concluded that continued antibiotics prescribed were not statistically significant, therefore I failed to reject the null hypothesis; data remains inconclusive because there is insufficient evidence at the alpha level of significance to reject the claim that the continuation of antibiotics prescribed are related to UTI antibiotic resistance. The odds for those patients who were prescribed continued antibiotics for symptomatic UTIs were .000 (95% CI .000 to .000) neither more or less

likely to have UTI antibiotic resistance in an ambulatory care setting when prescribed antibiotics initially for a UTI. Since the CI (confidence interval) was 0, the increased odds (.000) of UTI antibiotic resistance among nonpregnant females, ages 25-44, and on Medicaid, who were continued on antibiotics prescribed for UTIs at baseline, did not explain any statistical significance.

Predictor characteristics of continued antibiotics. Predictor characteristics based on descriptive measures of incidence and prevalence were calculated for continued antibiotics and UTI antibiotic resistance (see Table 14). The prevalence of UTI antibiotic resistance in the total number of sample cases with UTI antibiotic resistance ($n=45$) was 51% when antibiotics prescribed were continued for recurrent UTIs. The incidence rate (new cases of antibiotic resistant UTIs) for those at risk in 12 months or less was 49%

Table 14

Predictor Characteristics of Continued Antibiotics Prescribed

	Prevalence	Incidence
Continued Antibiotics Prescribed	51%	49%

Research Question 3

Research Question 3: Is the class of antibiotic prescribed for UTIs associated with UTI antibiotic resistance?

H_{o3}: There is no statistically significant association between UTI antibiotic resistance and class of antibiotic prescribed.

H_{a3}: There is a statistically significant association between UTI antibiotic resistance and class of antibiotic prescribed.

Association.

To test for association between the various classes of antibiotics prescribed (IVs), and UTI antibiotic resistance (DV) crosstabulation was executed and analyzed, and predictor characteristics were discussed. A contingency table was produced (see Table 15) to display variable counts and percentages. Due to the small sample size and violation of assumptions for Chi-Square testing, Fisher's Exact test was reported. The proportion of those patients who were prescribed broad-spectrum antibiotics for symptomatic UTIs in 12 months or less and developed UAR was 79.2% (19 out of 24 patients); narrow-spectrum antibiotic exposure associated with UTI antibiotic resistance was 31.3% (5 out of 16 patients); and an exposure to a combination of broad- and narrow-spectrum antibiotics was 57.1% (4 out of 7 patients) (see table 15).

Table 15

Classes of Antibiotics Prescribed in 12 Months or Less and UTI Antibiotic Resistance

Class of Antibiotics	UTI Resistance Criteria Not Met	UTI Resistance Criteria Met	Total
% Broad-Spectrum Antibiotics Not Prescribed	81.0%	19.0%	100%
% Broad-spectrum Antibiotics Prescribed	20.8%	79.2%	100%
% Narrow-Spectrum Antibiotics Not Prescribed	37.9%	62.1%	100%
% Narrow-Spectrum Antibiotics Prescribed	68.8%	31.3%	100%
% Combined Broad & Narrow-Spectrum Antibiotics Not Prescribed	50%	50%	100%
% Combined Broad & Narrow-Spectrum Antibiotics Prescribed	42.9%	57.1%	100%

Table 15 Contingency Table

The results of Fisher's Exact test (see Table 16) did not indicate a statistically significant relationship ($<.05$) observed between an exposure with the broad-spectrum (.000) class of antibiotics prescribed in 12 months or less and UTI antibiotic resistance in nonpregnant female patients, ages 25-44, on Medicaid, who presented to an ambulatory care clinic with UTI symptoms. Thus, the null hypothesis was rejected for broad-spectrum antibiotic prescribing. There were, however, statistically significant relationships observed in both narrow-spectrum and combined broad- and narrow-spectrum antibiotics prescribed ($p>.05$): .065 (NS); 1.00 (BSNS). Thus, I failed to reject the null hypotheses for narrow-spectrum and combined broad- and narrow-spectrum antibiotics (see Table 16).

Table 16

Summary of Fisher's Exact Test and Classes of Antibiotics Prescribed

	<i>n</i>	Exact Sig. (2-Sided)	Exact Sig. (1-Sided)
Fisher's Exact Test			
BSABX	45	.000	.000
NSABX	45	.065	.047
BSNSABX	45	1.00	.526

Binary logistic regression. Binary logistic regression was executed to analyze the risk of antibiotic resistance in UTIs in those patients exposed to three distinct classes of antibiotics (broad-spectrum, narrow-spectrum, and combined broad- and narrow-spectrum), while controlling for ages (AGES, (1)25-29, (2)30-34, (3)35-39, (4)40-44),

region (REGIONS, (1) Northeast, (2) Midwest, (3) South, and (4) West), initial antibiotics prescribed (INABXRX), and continued antibiotics prescribed (CONABXRX). Coding of the variables BS, NS, and BSNS was indicated by “0=Broad/ Narrow/ Combined Broad- and narrow-spectrum antibiotics not prescribed,” and “1=Broad/ Narrow/ Combined Broad- and narrow-spectrum antibiotics prescribed.

Broad-spectrum antibiotics and binary logistic regression. The results of Broad-spectrum antibiotics as a predictor of UTI antibiotic resistance indicated that this was not a statistically significant predictor after the onset of UTI symptoms ($p > .05$). AGES, REGION, INITIAL, and CONTINUED were controlled for ($R^2 .923$ (10), $p = 52.997$). Thus, I failed to reject the null hypothesis. The results of binary regression with broad-spectrum antibiotics prescribed predicting UTI antibiotic resistance in 12 months or less can be reviewed in Table 17.

Table 17

Summary of Binary Logistic Regression and Broad-Spectrum Antibiotics

Variables	<i>B</i>	Sig.	β
BS	-70.11	.995	.000
AGES (1)	-71.36	.997	.000
AGES (2)	-51.49	.999	.000
AGES (3)	52.40	.998	5.694E+22
REGION (1)	-18.28	.996	.000
REGION (2)	14.15	1.00	1390232.41
REGION (3)	15.43	1.00	5024326.69
REGION (4)	17.59	.997	.000
INABXRX	-35.15	.995	.000
CONABXRX	-71.93	.995	.000

Notes. $R^2 = .923$ ($p > .05$)

To examine the third binary logistic regression model, the Hosmer and Lemeshow test was processed along with a classification table to check for the model fit. Hosmer and Lemeshow indicated that there was neither significant or insignificant improvement between the observed data in block 0 and the final regression model, therefore this model did not appear to be of a good fit ($<.05$) without an acceptable level ($X^2=.000(5)$, $p=1.000$). The results of the model summary concluded that between 69% (Cox & Snell R^2) and 92% (Nagelkerke R^2) of the variation in UTI antibiotic resistance could be explained by the final model. The correct classification rate had increased by 42% (51.1 to 93.3.).

A review of the variables in the equation were analyzed. The variable, broad-spectrum antibiotics prescribed (BS), did not appear to contribute to the model; broad-spectrum antibiotics prescribed was not statistically significant ($p>.05$, $p= .995$). The negative coefficient B (-70.105) indicated that the target group had less cases coded as “1” (broad-spectrum antibiotics prescribed) than “0” (broad-spectrum antibiotics not prescribed), and was not significant after controlling for the other variables. Age (AGES), Region (REGION), initial antibiotics prescribed (INABXRX), and continued antibiotics prescribed (CONABXRX) did not contribute to the model and were not significant ($p>.05$). The coefficient (B) revealed that the odds of UTI antibiotic resistance was .000 more likely for those prescribed broad-spectrum antibiotics. The Sig. ($p>.05$, .995) concluded that broad-spectrum antibiotics prescribed were not statistically significant, therefore I failed to reject the null hypothesis and data remains inconclusive because there is insufficient evidence at the alpha level of significance to reject the claim that

broad-spectrum antibiotics prescribed are related to UTI antibiotic resistance. The odds for those patients who were prescribed broad-spectrum antibiotics for symptomatic UTIs were .000 (95%CI .000 to .000) neither more nor less likely to have UTI antibiotic resistance in an ambulatory care setting when prescribed antibiotics initially for a UTI. Since the CI (confidence interval) was 0, the increased odds (.000) of UTI antibiotic resistance among nonpregnant females, ages 25-44, and on Medicaid, who were prescribed broad-spectrum antibiotics for UTIs at baseline, did not explain any statistical significance either way.

Predictor characteristics and broad-spectrum antibiotics Predictor

characteristics based on descriptive measures of incidence and prevalence were calculated for broad-spectrum antibiotics and UTI antibiotic resistance (see Table 18). The prevalence of UTI antibiotic resistance in the total number of sample cases with UTI antibiotic resistance ($n=45$) was 60% when prescribed broad-spectrum antibiotics. The incidence rate (new cases of antibiotic resistant UTIs) for those at risk in 12 months or less was 47%.

Table 18

Predictor Characteristics of Broad-Spectrum Antibiotics Prescribed

	Prevalence	Incidence
Broad-Spectrum Antibiotics Prescribed	60%	47%

Narrow-spectrum antibiotics and binary logistic regression. The results of narrow-spectrum antibiotics as a predictor of UTI antibiotic resistance indicated that this was not a statistically significant predictor (R^2 .841(10), $p= 44.837$). AGES, REGION, INABXRX, and CONABXRX were controlled for. Thus, I failed to reject the null hypothesis ($p>.05$). The results of binary regression with narrow-spectrum antibiotics prescribed predicting UTI antibiotic resistance in 12 months or less can be reviewed in Table 19.

Table 19

Summary of Binary Logistic Regression and Narrow-Spectrum Antibiotics

Variables	<i>B</i>	Sig.	β
NS	-19.73	.998	.000
AGES (1)	-17.55	.998	.000
AGES (2)	-15.93	.998	.000
AGES (3)	36.47	.997	6.875E+15
REGION (1)	-.242	.924	.785
REGION (2)	.382	.845	1.47
REGION (3)	18.06	.998	69985861.09
REGION (4)	.574	.805	1.78
INABXRX	-1.244	.537	.288
CONABXRX	-73.98	.996	.000

Notes. $R^2 = .841$ ($p > .05$)

To examine the fourth binary logistic regression model, the Hosmer and Lemeshow test was processed along with a classification table to check for the model fit. Hosmer and Lemeshow indicated that there was neither significant or insignificant improvement between the observed data in block 0 and the final regression model, therefore this model did not appear to be of a good fit ($<.05$) without an acceptable level ($X^2=.217(6)$, $p=1.000$). The results of the model summary concluded that between 63% (Cox & Snell R^2) and 84% (Nagelkerke R^2) of the variation in UTI antibiotic resistance could be explained by the final model. The correct classification rate had increased by 49% (51.1 to 91.1).

A review of the variables in the equation were analyzed. The variable, narrow-spectrum antibiotics prescribed (NS), did not appear to contribute to the model; narrow-spectrum antibiotics prescribed was not statistically significant ($p>.05$, $p= .998$). The negative coefficient B (-19.726) indicated that the target group had less cases coded as “1” (narrow-spectrum antibiotics prescribed) than “0” (narrow-spectrum antibiotics not prescribed), and was not significant after controlling for the other variables. Age (AGES), Region (REGION), initial antibiotics prescribed (INABXRX), and continued antibiotics prescribed (CONABXRX) did not contribute to the model and were not significant ($p>.05$). The coefficient (B) revealed that the odds of UTI antibiotic resistance was .000 more likely for those prescribed narrow-spectrum antibiotics. The Sig. ($p>.05$, .998) concluded that narrow-spectrum antibiotics prescribed were not statistically significant, therefore I failed to reject the null hypothesis; the data remains inconclusive because there is insufficient evidence at the alpha level of significance to reject the claim that

narrow-spectrum antibiotics prescribed are related to UTI antibiotic resistance. The odds for those patients who were prescribed narrow-spectrum antibiotics for symptomatic UTIs were .000 (95%CI .000 to .000) neither more nor less likely to have UTI antibiotic resistance in an ambulatory care setting when prescribed antibiotics initially for a UTI. Since the CI (confidence interval) was 0, the increased odds (.000) of UTI antibiotic resistance among nonpregnant females, ages 25-44, and on Medicaid, who were prescribed narrow-spectrum antibiotics for UTIs at baseline, did not explain any statistical significance either way.

Predictor characteristics and narrow-spectrum antibiotics Predictor

characteristics based on descriptive measures of incidence and prevalence were calculated for narrow-spectrum antibiotics and UTI antibiotic resistance (see Table 17). The prevalence of UTI antibiotic resistance in the total number of sample cases with UTI antibiotic resistance ($n=45$) was 49% when prescribed narrow-spectrum antibiotics. The incidence rate (new cases of antibiotic resistant UTIs) for those at risk in 12 months or less was 31%.

Table 20

Predictor Characteristics of Narrow-Spectrum Antibiotics Prescribed

	Prevalence	Incidence
Narrow-Spectrum Antibiotics Prescribed	49%	31%

Combined broad- and narrow-spectrum antibiotics and binary logistic

regression. Combined broad- and narrow-spectrum antibiotics were not statistically significant as a predictor of UTI antibiotic resistance within 12 months or less after the onset of UTI symptoms (R^2 .873(10), $p= 47.818$). Thus, I failed to reject the null hypothesis. The results of binary regression with combined broad- and narrow-spectrum antibiotics prescribed predicting UTI antibiotic resistance in 12 months or less (see Table 21).

Table 21

Summary of Binary Logistic Regression and Combined Broad- and Narrow-Spectrum Antibiotics

Variables	<i>B</i>	Sig.	β
BSNS	51.61	.995	2.592E+22
AGES (1)	-43.23	1.00	.000
AGES (2)	-43.23	1.00	.000
AGES (3)	61.17	.999	3.695E+26
REGION (1)	-18.57	.996	.000
REGION (2)	34.14	.996	6.685E+26
REGION (3)	37.71	.999	2.392E+16
REGION (4)	-17.47	.996	.000
INABXRX	-35.40	.995	.000
CONABXRX	-122.97	.994	.000

Notes. $R^2 = .873$ ($p > .05$)

To examine the fifth binary logistic regression model, the Hosmer and Lemeshow test was processed along with a classification table to check for the model fit. Hosmer and Lemeshow indicated that there was neither significant or insignificant improvement between the observed data in block 0 and the final regression model, therefore this model did not appear to be of a good fit ($p < .05$) without an acceptable level ($X^2 = .000(6)$, $p = 1.000$). The results of the model summary concluded that between 65% (Cox & Snell R^2) and 87% (Nagelkerke R^2) of the variation in UTI antibiotic resistance could be explained by the final model. The correct classification rate had increased by 40% (51.1 to 91.1.).

A review of the variables in the equation were analyzed. The variable, combined broad and narrow antibiotics prescribed (BSNS), did not appear to contribute to the model; combined broad- and narrow-spectrum antibiotics prescribed was not statistically significant ($p > .05$, $p = .995$). The positive coefficient B (51.609) indicated that the target group had more cases coded as “1” (combined broad- and narrow-spectrum antibiotics prescribed) than “0” (combined broad- and narrow-spectrum antibiotics not prescribed), and was not significant after controlling for the other variables. Age (AGES), Region (REGION), initial antibiotics prescribed (INABXRX), and continued antibiotics prescribed (CONABXRX) did not contribute to the model and were not significant ($p > .05$). The coefficient (B) revealed that the odds of UTI antibiotic resistance was .000 more likely for those prescribed combined broad- and narrow-spectrum antibiotics. The Sig. ($p > .05$, .995) concluded that combined broad- and narrow-spectrum antibiotics prescribed were not statistically significant, therefore I failed to reject the null hypothesis;

there was insufficient evidence at the alpha level to reject the claim that combined broad- and narrow-spectrum antibiotics prescribed is related to UTI antibiotic resistance. The odds for those patients who were prescribed combined broad- and narrow-spectrum antibiotics for symptomatic UTIs were 2.592E+22 (95%CI .000 to .000) more likely to have UTI antibiotic resistance in an ambulatory care setting when prescribed antibiotics for a UTI. Since the CI (confidence interval) was 0, the increased odds (2.592E+22) of UTI antibiotic resistance among nonpregnant females, ages 25-44, and on Medicaid, who were prescribed combined broad- and narrow-spectrum antibiotics for UTIs at baseline, were not statistically significant and therefore I failed to reject the null hypothesis.

Predictor characteristics and combined broad- and narrow-spectrum

antibiotics. Predictor characteristics based on descriptive measures of incidence and prevalence were calculated for combined broad- and narrow-spectrum antibiotics and UTI antibiotic resistance (see Table 22). The prevalence of UTI antibiotic resistance in the total number of sample cases with UTI antibiotic resistance ($n=45$) was 49% when prescribed combined broad- and narrow-spectrum antibiotics. The incidence rate (new cases of antibiotic resistant UTIs) for those at risk in 12 months or less was 31%.

Table 22

Predictor Characteristics of Combined Broad- and Narrow-Spectrum Antibiotics Prescribed

	Prevalence	Incidence
Combined Broad and Narrow-Spectrum Antibiotics Prescribed	49%	31%

Summary

Three research questions, inclusive of five binary logistic regressions were conducted with the statistical program, SPSS, to examine possible relationships between the timing of antibiotic prescribing, either initial antibiotics prescribed within three months or less, or, antibiotics continued in 12 months or less, and, those classes of antibiotics prescribed for UTIs (broad-spectrum, narrow-spectrum, and combined broad & narrow-spectrum), and antibiotic resistance in urinary tract infections in nonpregnant females, ages 25-44, on Medicaid who sought care in an ambulatory setting. The first research question explored whether antibiotics prescribed at the onset of a UTI was associated with antibiotic resistance. The results of the first binary regression indicated that there was no impact on UTI antibiotics resistance within 3 months or less and initial antibiotics prescribed. Additionally, there was no impact with initial antibiotics prescribed and the age of the patient or the region where the visit took place. The second research question explored whether antibiotics that were continued for recurrent UTIs that had been initially treated previously in an ambulatory care setting, were associated with antibiotic resistance. Results of the second binary regression indicated that there was no impact on UTI antibiotics resistance within 12 months or less and continued antibiotics prescribed. Additionally, neither age or region was impacted by continued antibiotic prescribing. The third question explored whether the class of antibiotics prescribed for UTIs impacted antibiotic resistance. Results of the third binary regression indicated that there was no impact on UTI antibiotics resistance and broad-spectrum, narrow-spectrum, or combined broad- and narrow-spectrum antibiotics prescribed.

Additionally, there was no impact found with the age of the patient, or the region where the visit took place.

The study findings will be investigated and explained further in Chapter 5. Chapter 5 will compare the findings with the literature review and background of the theoretical framework. Chapter 5 will additionally provide recommendations based on this study's limitations, as well as examine the potential for social change while providing recommendations for future antibiotic prescribing practice in health care.

Chapter 5: Discussion, Conclusions, and Recommendations

The purpose of this quantitative study was to examine nonpregnant U.S. female patients who were exposed to poverty, as evidenced by Medicaid, the reported payment type, and, at risk for antibiotic resistance when seeking care for UTIs in ambulatory care settings. The exploration of those relationship potentials with UTI antibiotic resistance and prescription timing laid the groundwork for larger cause-effect studies that should be conducted in the future. This study's sample was small; however, findings indicate that the broad-spectrum class of antibiotics continue to be overutilized. Additionally, the prescribing of combined classes of antibiotics, broad- and narrow-spectrum, may be an increasing concern to consider and not simply an artifact results related to a small study.

The significance of this research study is to distribute education associated with negative outcomes related to the inappropriate prescribing and utilization of antibiotics in the treatment of UTIs in an ambulatory clinic setting. Specific classes of antibiotics were selected to find out if these had an impact on UTI antibiotic resistance. Relationships that may occur between the timing of when antibiotics are prescribed and UTI antibiotic resistance were also examined. To my knowledge, this is the first study of its kind to utilize the NAMCS data to examine the relationships among antibiotic prescribing and UTI antibiotic resistance in low-income women in an ambulatory clinic setting.

Five binary logistic regressions were executed with the three research questions posed utilizing a statistical program, SPSS 23. Binary logistic regression analyzed relationships between the timing of antibiotic prescribing and UTI antibiotic resistance. Before regression was carried out, descriptive statistics were executed; frequencies, cross

tabs, and prevalence were calculated and reviewed. I found that 91% of nonpregnant women between the ages of 25-44 and on Medicaid and who followed up at an ambulatory care clinic were more likely to be prescribed broad-spectrum antibiotics initially and, also, when continued on antibiotics for a UTI. Women who required follow-up for recurrent UTIs were continued on antibiotics 85% of the time; of those, 73% were antibiotic resistant to broad-spectrum antibiotics.

Interpretation of the Findings

The diagnosis and treatment of UTIs and their association with antibiotic resistance have significant implications for patient health and costs associated with health care (Magliano et al., 2012). According to Langdon, Crook, and Dantas (2016), research-based studies in the United States are valuable for the identification of factors that may negatively alter resistance rates in underserved populations, such as nonpregnant women on Medicaid. However, *pregnant* female Medicaid populations have been the focus of UTI antibiotic research because of potential teratogenic effects on the fetus (Minardi et al., 2011). Efforts should be made to increase the prediction of antibiotic-related UTIs for the women on Medicaid and supported by financial, pharmaceutical, demographic data. Efforts should also be made to increase the research grants issued in this area.

In the United States, the rate of UTIs are greater than 13,000 per 100,000 adult women per year (Kattan & Gordon, 2013). UTI prevalence studies appear to evidence wide fluctuations in reporting depending on the population being studied. Both pregnant and nonpregnant females have been reported to have the same prevalence rates with community-acquired UTIs, however, pregnant females have been the focus research

studies in the United States (Salem & El-Azab, 2011; Anozie, Lawani, Esike, Mamah, & Ajah, 2016).

Literature reviewed for this study combined the most current study outcomes and research history related to community-acquired UTIs nonpregnant women in low-income populations in the United States. Females between the ages of 25-44 were found to be the most likely group to become resistant to antibiotics according to one of the earliest studies on UTIs and antibiotic resistance in an ambulatory setting (Butler, Hillier, Roberts, & Dunstan, 2006). In one large multi-year study between 2002-2008, over 35% of female patients on both Medicare and Medicaid were found to have uncomplicated UTIs, however, all study participants were over the age of 18, therefore age as a confounder was not controlled for and antibiotic utilization and resistance were not discussed.

The mean age for nonpregnant women in my study population who developed antibiotic resistance in uncomplicated UTIs was 33 years of age (age range 25-44). This was consistent with the uncomplicated study element and findings by Kobayashi et al (2016) indicating that women in the age range of 30-49 had a higher percentage of uncomplicated UTI occurrences in ambulatory care settings (35%). Kobayashi et al, however, did not incorporate antibiotic utilization and resistance factors into their study. Geographically, my study evidenced a higher occurrence with uncomplicated UTIs in low-income women in the Southern region of the United States than other states. The Southern U.S. regional data reported by Kobayashi et al. was consistent with my study finding that the Southern United States had the highest rates of occurrence (27%) in

uncomplicated UTIs. My study however, produced a small reduction in occurrence outcomes with uncomplicated UTIs in low income females from the South (44%) compared to the Western United States (24%). However, both the South and the Western regions of the United States had a higher percentage of UTI occurrences than the Northeastern (22%) or Midwestern (16%) United States. As I could not find similar studies conducted to date in the United States related to uncomplicated UTIs in low-income female populations, I used references of results identified in global studies.

Broad-spectrum antibiotics are the most appropriate class of antibiotics in the empiric treatment of UTIs (Merli et al., 2016). They are normally prescribed for just a few days of treatment after the initial diagnosis, however it is becoming more common to find UTIs that need prolonged treatment (Mazzulli, 2012; Lamb, 2016). Antibiotic resistance may occur when a provider fails to order a timely urine culture, or, the laboratory does not reflex a urine test when the urinalysis meets a specific threshold (Eliopoulos, Cosgrove, & Carmeli, 2003; Wolf, 2016); as a result, inappropriate antibiotics are prescribed (Humphries & Dien Bard, 2016). This type of care can increase resistance patterns either already present, or provides an environment for resistance to occur (Lee, Cho, Jeong, & Lee, 2013).

This study indicated that 91% of nonpregnant females on Medicaid were prescribed antibiotics initially for symptomatic UTIs. Of these patients, 84% were continued on antibiotics in 12 months or less. This means that only 7.2% of the Medicaid nonpregnant female population who were initially prescribed antibiotics may not have been treated adequately or appropriately and had to return for further UTI antibiotic

treatment. Of those patients (initial and continued combined) who were prescribed antibiotics and became resistant, 79% were prescribed broad-spectrum antibiotics, 31% were prescribed narrow-spectrum antibiotics, and 57% were prescribed a combination of broad- and narrow-spectrum antibiotics. This study's sample outcomes appeared to be consistent with current treatment guidelines indicating that the administration of broad-spectrum antibiotics should be *reduced* for suspected UTIs (Goodman et al, 2016); providers appear to be overprescribing broad-spectrum antibiotics. Although not included in the analysis, this study's initial case review anecdotally noted that fluoroquinolones were the primary broad-spectrum category of antibiotics prescribed initially for UTIs.

Most of the nonpregnant female Medicaid cases in the sample population ($n=45$) had evidence of UTI signs and symptoms per the NAMCS codebook; 89% of the sample was recorded as having a UTI signs and symptom. Those patient cases that did not have signs and symptoms evident, had a UTI diagnosis code present per ICD-9 coding (5990). Access to a complete medical chart was not available to review the rationale for those sample cases that did not meet UTI signs and symptoms study criteria (11%, or, 5 cases) but were coded as a UTI (5990). Several cases in the sample additionally did not meet for UTI resistance criteria, but were noted to have been prescribed initial or continued antibiotics. The initial or continued antibiotics coded in relation to UTI resistance was documented with an ICD-9 diagnosis code for a medical condition other than UTI, even in the presence of an ICD-9-documented UTI code, therefore these cases did not meet criteria for UTI antibiotic resistance. Since each of the patients in the sample had laboratory evidence of a urinalysis and had an ICD-9 code of "5990" documented, initial

or continued antibiotics should have been prescribed according to practice recommendations (IDSA, 2011).

Ecosocial Theory and Interpretation of Findings

In Chapter 2, I described an ecosocial interactive method of analysis framework for disease inequalities, distribution, and a population's health (Krieger, 2008). As a result, the study increased the understanding for one social determinant, poverty, as evidenced by Medicaid, and the roles/influential characteristics that prescribing any class of antibiotic at any stage of a UTI, has on the nonpregnant female population. Population health distribution (health outcomes) includes antibiotic susceptibility (Penders, Stobberingh, Savelkoul, & Wolffs, 2013) as well as other tangible and psychological care for a UTI, all of which are at the heart of population distribution. Pathways from health distribution leads to the process of UTI treatment. Inequalities of class, race, ethnicity, and gender surround population health distribution as these pathways are traveled. Healthcare-provider competency weighs heavily on antibiotic exposure outcomes, and these prescribing decisions are often not based on hard evidence (lab test results, for example), but based on the interactions between the patient and provider (Meropol, Mercalio, & Metlay, 2013).

Studying a social determinant was pertinent in the analysis of poverty and antibiotic resistance. The ecosocial theory approach anticipates large and small scale-level effects on a social determinant such as poverty and health outcomes (Krieger, 2005). Additionally, individual beliefs are determinants on a patient's health outcome which can affect every aspect of a patient visit (Krieger, 1994; Krieger, 2001; Krieger,

2008). Every woman that experiences poverty in this study must be able to reference how their care should be when they go to an ambulatory care setting with symptoms of a UTI. They should be able to intrinsically evaluate how decisions for their care are made so that they can deter future risks of occurrence or recurrence. Group-level knowledge is also important, especially today with social media (Krieger, 2008; Krieger, 2012). An individual can connect with others on the internet and find out about experiences, or, access how providers are “graded” (Woods et al., 2013). Each patient, no matter what language they speak or what social class they are from should be able to understand what constitutes treatment with dignity by the provider and other health care staff (Dickert & Kass, 2009); those with disabilities will have to rely on their caregiver for this, which may or may not be a bias (Seibert, Stridh-Igo, & Zimmerman, 2002) on the pathway to care.

Disadvantaged groups have been known to have barriers with access to care, and, those processes that affect appropriate management (Artiga, 2016). A Harvard staff writer stated, “You don’t have to travel all the way to Malawi, you can go to any rural house in America” (Powell, 2016, p.1) (regarding where to find overlooked health inequalities). Inequalities are representative of the structural inequalities found in society that include economic, political, and social (Krieger, 2012). Determinants can influence UTI antibiotic management and access to the right provider, laboratory, diagnostic, or pharmacy services. The distribution of nonpregnant females on Medicaid that encounter symptoms of a UTI may will go one of two ways: the UTI goes away after initial

antibiotics are prescribed, or, the UTI is recurrent and antibiotics must be continued.

Either way the Medicaid patient must be treated the same as any other patient.

The complexity with both initial antibiotic prescribing and continued antibiotic prescribing for UTIs can further influence the ecosocial diagram. These aspects of care by medical providers will significantly impact a patient's health outcome and future outcomes. Unfortunately, when a symptomatic patient presented for care in my study, due to not having access to a complete medical chart that could have documented other signs and symptoms of UTI, the review of the provider's choice of antibiotics, and objective, and subjective content, could not be ascertained. Several cases clearly did not have antibiotics issued, although they had positive signs and symptoms of a UTI and had a urinalysis performed. Many Medicaid patients who were prescribed antibiotics at their initial appointment also came back to be re-treated for their UTIs. There was additionally evidence of no treatment, yet Medicaid patients returned to their provider for treatment, therefore, treatment occurred after the initial appointment somewhere. It is unknown without a complete medical record, whether there was a reason noted by the provider about why antibiotics were not prescribed for a positive urinalysis and signs and symptoms of UTI criteria were met and if the patient was referred to an ED for treatment.

My study supported findings that a urinalysis should be conducted and antibiotics prescribed for complaints if UTI symptoms were also present (Bates, 2013). A urinalysis is not recommended for asymptomatic bacteriuria (Abbo & Hooton, 2014). There were no patients in my study with asymptomatic bacteriuria who underwent a urinalysis, and coded with a UTI. Studies in the literature have concluded that in the presence of positive

nitrites and leukocytes found on a urinalysis (Simon, 2012), however, a UTI should always be included in the differential as it is usually indicative of a bacterial UTI; a bacterial UTI in the presence of positive symptoms and patient history should always be treated with an appropriate antibiotic (Mody & Juthani-Mehta, 2014).

An initial review of the data collected for my study before analysis was conducted indicated that 3 out of 45 (7%) patients returned to their primary care provider for a recurrent UTI and was prescribed initial antibiotics elsewhere. Therefore, these Medicaid patients saw their provider, were not treated, went elsewhere for care for their UTIs, were prescribed antibiotics, then returned to the original healthcare-provider that they saw initially because they were still having UTI symptoms. A diagnosis code was created to represent a UTI when the Medicaid patients were initially seen, however, they were not prescribed initial antibiotics. This information is consistent with one study that reported that after an initial diagnosis in primary care was made, an emergency department (ED) visit will occur 68% of the time, or, 180 days from the original diagnosed medical condition (Lash et al., 2017). Without the full medical chart, I was unable to deduce where the initial antibiotics prescribed had come from. It was already known that their primary providers that they saw initially when their UTI symptoms first occurred, were present, as indicated by the data, however they were not prescribed initial antibiotics. I could have hypothesized that these patients consulted with an ED after they did not receive initial UTI treatment from a primary provider. However, again, without the full medical chart, I was unable to confirm this for this study.

Evidence that patients on Medicaid are seeking care for simple medical problems in an ED or urgent care clinic is much costlier for treatment than by a primary provider and not appropriate (Kellermann & Weinick, 2012). Patients on Medicaid should not have to resort to an ED or urgent care clinic for the care of an acute, uncomplicated UTI. According to Kellermann & Weinick (2012), in a study that spanned two decades, involved anonymous callers who phoned primary care clinics posing as Medicaid patients and asked if they accepted Medicaid for minor treatment. When the answer was “no” they did not accept Medicaid, there was a 26% response-rate of being referred to an “ED” for treatment. My study supported findings by Kobayashi et al that initial treatment with antibiotics by a primary care provider for UTIs (2016) should be recommended for those patients on Medicaid and not an ED (2012; Trinh & Klinker, 2015). This was evidenced in my study with 26 out of 45 Medicaid patients (58%) that had to undergo continued treatment (recurrence) of the initial UTI; Medicaid patients should be afforded the same continuity of care as anyone else. Therefore, were those 3 patients possibly told upon discharge from their own primary care provider to follow up at an ED if they had any further problems versus coming back for care again? Siek, Hefner, Wexler, Taylor, & McAlearney (2016) found that cultural and other educational issues may be a barrier to a patient’s perception of their need for an emergency department.

Patient’s truly may not understand why they would be referred for further problems to an ED, if it also was not explained that care for the same problem, that was not an emergency, should bring them back to their primary care provider. Education with the medical staff about how to communicate with patients should always be reviewed by

another competent medical staff supervisor (Gesme, Towel, & Wiseman, 2017). A Medicaid patient who is seen in an ED for an uncomplicated UTI after being diagnosed in a clinic, then re-treated in the ED, is disadvantaged because the provider that they return to after an ED appointment, may not have laboratory results or other diagnostic information to enable them to continue these patients on antibiotics appropriately, whereby, creating an environment for UTI antibiotic resistance.

Interpretation of Statistical Findings

The sample of 45 nonpregnant female patients, ages 25-44, and on Medicaid were all positive for UTI diagnosis, yet 41 (91%) of these patients received initial antibiotics in 3 months or less. Of the 41 patients who were prescribed antibiotics in 3 months or less, 21 (51%) became UTI antibiotic resistant. Of the 41 patients who received initial antibiotics and became UTI antibiotic resistant, 11 (27%) received a broad-spectrum antibiotic, 4 (10%) received a narrow-spectrum antibiotic, and 4 (10%) received a combined broad- and narrow-spectrum antibiotic. Of the sample ($n=45$), 26 patients (58%) were continued on antibiotics within 12 months or less from their initial UTI diagnosis. Of the 26 patients who were continued on antibiotics, 22 (85%) became UTI antibiotic resistant. Of the 22 patients who received continued antibiotics in 12 months or less and became UTI antibiotic resistant, 16 (73%) were prescribed broad-spectrum antibiotics, no patients were prescribed narrow-spectrum antibiotics, and 3 (14%) were prescribed combined broad- and narrow-spectrum antibiotics. Of the sample ($n=45$) who became UTI antibiotic resistant, 3 (7%) were prescribed both broad-spectrum and a combined broad- and narrow-spectrum antibiotic on the initial appointment; patients were

never prescribed combinations of narrow-spectrum or combined broad- and narrow-spectrum at their initial appointment. Therefore, my study findings indicated that over half (51%) of those non-pregnant females, ages 25-44 and on Medicaid, who were prescribed antibiotics during their initial appointment in ambulatory care for UTI symptoms, became UTI antibiotic resistant. The predominant antibiotic prescribed that was associated with UTI antibiotic resistance was broad-spectrum antibiotics.

Additionally, this study indicated that 84% of those nonpregnant females between 25-44 years of age and on Medicaid who followed-up with recurrent UTI symptoms, and were prescribed antibiotics, and had a positive outcome of UTI antibiotic resistance, were predominantly prescribed broad-spectrum antibiotics. These findings concur with Shapiro et al (2013) who conducted the only adult study published in the United States at this time on antibiotic utilization in an ambulatory care setting, that concluded that broad-spectrum antibiotics were prescribed more than any other antibiotic.

Limitations of the Study

There are multiple study limitations that need to be acknowledged. First, this study was limited using secondary data; I neither directed nor supervised the collection of the survey data. The second limitation was the relatively small sample size. Data was assumed to be accurately collected, however, prior to the year 2012 the category code describing gestational status identified as “Pregnant” (NAMCS, 2012) was not available as a variable for analysis. To compensate for the absence of an all-inclusive variable and ensure internal validity of this status prior to 2012, NAMCS code books were used to identify codes related to pregnancy. Possible underreporting of UTI

diagnoses may have been related to erroneous sampling and coding errors in the sample frame as evidenced by the limited number of UTI cases identified for this study. Other research studies that have utilized NAMCS data have also expressed the possibility with potential coding issues (May, Mullins, & Pines, 2014). During data validation of the secondary data source codes for my study, NAMCS secondary codebook codes were substituted for ICD-9 codes at times resulting in errors in the interpretation of a diagnosis, therefore those cases were not included. All codes were reviewed for accuracy during my study's internal validation process.

The final case count after all related codes were abstracted indicating that only 51 cases of UTIs were recorded. I questioned this and made an inquiry to NAMCS. NAMCS responded with a concurrence to my findings, except that they found even less than I had because they did not include both upper and lower UTI codes, only those that were coded specifically as "UTI" (ICD-9 code 5990). A closer review may indicate that there is substantial underreporting with UTIs, or, coding errors are an issue in ambulatory care settings. Global research studies provide data that strongly support the notion that low-income nonpregnant women between the ages of 25-44 who have been treated in ambulatory care clinics for uncomplicated UTIs are a high-risk population that deserves to be further studied.

The sample frame represented all 4 census regions of the United States. Each population variable (nonpregnant, female, and Medicaid) was represented in this national survey. My choice of conducting a retrospective cohort study narrowed the availability of potential confounding factors resulting in selection bias (Euser, Zoccali, Jager, & Dekker,

2009; LaMorte, 2016) however, a prospective study would have been hindered by time and expense (Song & Chung, 2010). Song and Chung (2010) stated that a retrospective study is a refined and efficient way to conduct research studies because of the ability to use historical data. Fisher's exact test was the obvious choice for analysis due to the small number of cases. The smaller sample produced an overestimation in the odds ratios which was due to the use of logistic regression (Nemes, Jonasson, Genell, Steineck, 2009). A larger study sample may have produced more robust results by providing an adjustment with additional confounders, and decreased the potential for a biased odds ratio that may have led to an overestimation of the effect measure.

At this time, there is no gold standard available to measure how to prevent uncomplicated UTI antibiotic resistance in nonpregnant women. There is no way to know the sensitivity and specificity of implied analysis. Confounders such as geographical regions were used because according to the literature search antibiotic susceptibility, because of inappropriate utilization patterns, regional politics, or regional patient behaviors and access to care, are related to antibiotic resistance. A larger study to assess the causal effects of geographical region on antibiotic resistance would be recommended and this study was limited by the choice of study design.

Generalizability was lacking in my study due to the unexpected small sample size. A more detailed sample frame of data related to regions, age ranges, and specific antibiotics that were prescribed for uncomplicated UTI cases could have been used to substantiate generalizability. Random sampling was conducted because it is not rational to study an entire population (Kukull & Ganguli, 2012), however this did not improve

external validation. Kukull & Ganguli (2012) posit that when a study is comprised of clinic visits, it is less important to focus on generalizability and more important to capture the accuracy in diagnostics. The authors explain that any study's results that are clinic-based can become negatively skewed if the disease in question is not identified properly, and, any misclassification of disease (those that are positively versus negatively diagnosed) may diminish and misconstrue results of a study (Kukull & Ganguli, 2012). Internal validation for my study clearly confirms that the disease was classified properly. The extent to which my study results could be generalized may be a consequence in choice of confounders controlled for. This study explored age and region as confounders because of the associations with antibiotic resistance exposures already documented in UTIs. This introduction was used to attract other researchers and motivate towards the engagement of future research in this area.

The third limitation was that this study did not allow inference for causes and effects, therefore data associations were limited. Underlying medical conditions and detailed antibiotic dosing that could have been associated with UTI symptom management and antibiotic resistance were found to be unreliable for analysis. For example, indicators often used to "define daily dose (DDD)" (p. 5) according to Schechner, Temkin, Harbarth, Carmeli, & Schwaber (2013) in cohort studies were not available. DDD may over-, or, under- generalize results (Schechner et al., 2013). Further analysis of appropriate variables that are time-dependent may be one key to inappropriate antibiotic prescribing for UTIs. This may be accomplished by the interpretations of the relationships between the initial provider appointment activities and future appointments

linking the same patient with continued UTI symptoms. The final limitation was evidenced by the analysis outcomes for initial and continued prescribing of antibiotics and antibiotic resistance. Initial and continued prescribing of antibiotics hypothesized as factors contributing to antibiotic resistance was not found to be statistically significant. The allocation and timing of antibiotics once a patient was discharged could not be determined.

Recommendations

Future research to overcome the limitations found in this study is crucial. Data must be thoughtfully collected and interpreted so that the results can be applied to actual ambulatory care settings. Although the sample size was small and generalizability was difficult to produce, the obvious overutilization of the broad-spectrum class of antibiotics evidenced by this study's outcomes substantiates the notion that these antibiotics are the main cause for antibiotic resistance (CDC, 2013). It is recommended that subsequent studies should attempt to include medical record details from a broad, general, nonpregnant female Medicaid ambulatory care population, between the ages of 25-44, that is a nationally representative sample, and anticipate if antibiotics are clinically indicated for UTIs. This information should be utilized for a cause and effects study that can interpret those barriers with antibiotic prescribing and resistance in this population. This data may then potentially be utilized by a team of companies, private and public, such as pharmacies, laboratories, emergency departments, and ambulatory health clinics, to put their resources together and propose a plan for antibiotic prescribing. Conditions that lead to hospitalizations, known as ambulatory care-sensitive conditions (ACSC)

appear to also be prevalent (Mkanta, Chumbler, Yang, Saigal, & Abdollahi, 2016) with UTIs. Many studies have already shown that there are multiple disconnects and barriers to appropriate prescribing that are dependent on the many levels related to type of care that a patient must receive once they are symptomatic with a UTI (Hossain & Laditka, 2009; Kellermann & Weinick, 2012).

The need to include a larger sample is highly recommended due to the altered relationships that were seen with the distribution and odds ratios with binary logistic regression; the power needs to be increased. Variables that are more robust would serve this study well. The variables of age and region in this study, although categorized appropriately, did not provide enough of a relationship and the outcome was a poor model fit. Statistical significance may have improved, however, possibly age and region may have seen a more generous relationship had the sample size been larger.

Antibiotic class-induced antibiotic resistance has been well documented (Harbarth et al., 2015; Ventola, 2015) while the discrete prescribing of nonpregnant Medicaid females in the development of UTI antibiotic resistance has not (Minardi et al., 2011; Eells, Bharadwa, McKinnell, & Miller, 2014). Studies that could utilize U.S. licensed antibiotic agents of all classes to treat UTIs with nonpregnant female Medicaid populations would augment the knowledge currently published and identified by this literature gap.

Implications

This study's conclusions afforded an improved understanding of UTI antibiotic resistance epidemiology in this distinct, and impoverished UTI-positive population. This study additionally provided significant implications for social change. An improved understanding can be groundbreaking for new areas of inquiry, and lead to necessary future studies. The main goal of antibiotic stewardship in the United States and globally, is to minimize potential harm that may come to patient's due to the inappropriate treatment of antibiotics. UTI incidence of antibiotic resistance before and after implementing antibiotic stewardship programs has been described across the United States, however, this has only been studied in hospitalized patients, pregnant women, or long-term care patients with urinary catheters (May, Mullins, & Pines, 2014; Shapiro et al., 2013; Mkanta et al., 2016).

Antibiotic stewardship is new to ambulatory care clinics; infection control surveillance, other than outpatient surgery, and more recently, outpatient dialysis (CDC, 2011c, p. 1), currently does not have a way to appropriately collect denominator data. Recent government attention though has created grants and other opportunities for study in order to create appropriate surveillance programs for ambulatory care (Magill, Dumyati, Ray, & Fridkin, 2015). This research study revealed that there continues to be inappropriate prescribing with broad-spectrum antibiotics in particular, but additionally, narrow-spectrum and combined broad- and narrow-spectrum. Additionally, follow-up visit communication after the initial antibiotic have been prescribed to nonpregnant females on Medicaid appears to be an issue. Therefore, the need to further study

communication activities upon discharge in outpatient settings with nonpregnant Medicaid when they are prescribed antibiotics could be a crucial step in antibiotic stewardship endeavors. Organizational and local levels in outpatient medicine could be influenced from epidemiology studies produced about nonpregnant female Medicaid patients' timing of antibiotics and discharge communication.

The relationship between antibiotic delivery in ambulatory care settings and the epidemic crisis of antibiotic resistance may benefit health-care providers. This may be related to communication education that has been in the spotlight for informing prescribing decisions that they will have to make. To implement comprehensive evidence-based measures with communication education for health-care providers about impoverished nonpregnant women and UTI antibiotic stewardship, more research studies are greatly needed, however individual state legislation and Medicaid also should be a priority for legislation. Antibiotic stewardship that leads to resistance with UTIs in the population are current health care issues affecting ambulatory care settings where Medicaid patients are often seen for care. Disparities in health care and poverty have been persistent and long-standing because Medicaid has not been expanded in 19 states in the United States; as of 2017, the coverage gap under the Affordable Care Act (ACA) remains uncertain because of the ability for states to opt out (CNBC, 2016; KFF, 2016; Johnson, 2016; Advisory Board, 2017).

Ambulatory care patients on Medicaid need to increase their understanding of how UTIs are contracted to prevent or decrease antibiotic resistance and further complications that could result because of inappropriate treatment that includes antibiotic

prescribing. The key to prevention is active participation regardless of social economic status (Vahadat, Hamzehgardeshi, Hessam, & Hamzehgardeshi, 2014). The internet is free and available to anyone, in locations such as the library, schools, or even public health clinics. Also, in today's modern world, even those on Medicaid may be eligible to have a free cellular telephone, which may come with internet access (Federal Communications Commission, 2017). Individuals who arm themselves with antibiotic knowledge are more likely to take their medications as prescribed, or, discuss the rationale for an antibiotic prescribed before even taking it (Awad & Aboud, 2015).

These proactive interventions are likely to reduce health care visits to ambulatory settings as well as hospitalizations for complications of UTIs. This would unfortunately need to be under tight surveillance; a resource not a priority in the ambulatory care setting. The person(s) providing the surveillance would need to be able to promptly report data to the providers onsite as well as educate them in the moment. Awareness at the time that a decision is made that could have a negative impact (active surveillance required), rather than passive, or, retrospective surveillance, and, education that may be lost to meaning as time moves beyond the problem, is needed. Real-time data that shows a healthcare-provider what their decisions are doing, will impact the patients' future care. Health-care providers usually want to do what is right for any patient. There are providers, however, who have practiced medicine a certain way for such a long time, and may severely resist change, no matter how much data they are shown. These providers may also be reluctant to engage in any educational confrontations and may take offense to someone proposing to do this, even to help them and improve their patients' care

outcomes (Sillito, 2016). Although for our canine brethren, an old dog may learn slower, but they will be able to learn a new trick (Coren, 2016), this does not decrease the necessity for provider responsiveness to antibiotic resistance education. Cross-cultural education may be stated as a “soft science” (Kripalani, Bussey-Jones, Katz, & Genao, 2006, p. 1118), however, a reduction in morbidity and mortality that can be clearly viewed, may be the positive after-effect when communication education is provided to those that prescribe to the underserved population.

Conclusions

The purpose of this retrospective observational cohort study was to investigate nonpregnant American female patients on Medicaid who were at risk for UTI antibiotic resistance. The aim of this study was to understand the relationships between prescription timing and classes of antibiotics that were prescribed for uncomplicated UTIs treated in an ambulatory care setting. The regression analysis for the three research questions did not prove to be significant. However, this small study pointed at the same indications about antibiotic resistance that is currently found in the literature; broad-spectrum antibiotics are overutilized no matter when they are prescribed and are likely the offenders of antibiotic resistance in UTIs.

The descriptive statistics results, proved to be worthy of analysis. This activity provided evidence in support of continued antibiotic research. Rearranging the class of antibiotic accordingly may decrease the number of those returning with recurrent UTIs. Specific antibiotics within the classes was not analyzed in this study. Furthermore, this study had indicated that there was a minuscule trend that may be indicative of poor

discharge communication. This was evidenced by a lack of antibiotic prescribed at the initial appointment, however, the recurrence of UTI symptoms and a return appointment indicated that antibiotics were continued. This was worrisome for both the patient and the provider. The patient, without clear discharge instructions may have misinterpreted being told to go to an emergency room if the problem continued. This could have been remedied by simply saying to return to the provider office if the problem continued, or, state that only in the case of an emergency (and provide parameters that the patient can understand, such as a fever of 104 or greater) they may need to go to an emergency room for care. Consistent messaging is an important piece of a patient care visit no matter what type of patient the care is for, or where they decide to go for care. It is important to remember that the patient has choices and will go where they feel comfortable and cared for.

Future research with antibiotic stewardship should target UTI antibiotic resistance reduction endeavors to decrease UTI resistance frequency by addressing inappropriate prescribing and utilization in the nonpregnant female Medicaid population. This study portrayed the need to focus future research on appropriate antibiotic prescribing and make it a primary goal to include disparate populations, such as those on Medicaid. The ultimate focus, however, should be on decreasing unintentional negative outcomes of antibiotic prescribing practices.

References

- Abbo, L. M., & Hooton, T. M. (2014). Antimicrobial stewardship and urinary tract infections. *Antibiotics*, *3*, 174-192. doi:10.3390/antibiotics3020174
- Advisory Board. (2017). Where the states stand on Medicaid expansion. Retrieved from <https://www.advisory.com/daily-briefing/resources/primers/medicaidmap>
- Agency for Health Care Research & Quality. (2014). Health care cost and utilization project (ACUP). Retrieved from <http://www.ahrq.gov/research/data/hcup/index.html>
- Al-Badir, G., & Al-Shaikh, A. (2013). Recurrent urinary tract infections management in women. *Sultan Qaboos University Medical Journal*, *13*, 359–367. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3749018/>
- Alsan, M., Shoemaker, L., Eggleston, K., Kammili, N., Kolli, P., & Bhattacharya, J. (2015). Out of pocket health expenditures and antimicrobial resistance in low-income and middle-income countries; an economic analysis. *Lancet Infectious Diseases*, *15*, 1203-1210. doi:10.1016/S1473-3099(15)00149-8
- Anozie, O. B., Lawani, O. L., Esike, C. U. O, Mamah, E., & Ajah, L. O. (2016). Prevalence and common microbial isolates of urinary tract infection in pregnancy; A four-year review in a tertiary health institution in Abakaliki, South-East Nigeria. *American Journal of Clinical Medicine Research*, *4*, 25-28. doi:10.12691/ajcmr-4-2-2

- Arnold, J. J., Hehn, L. E., & Klein, D. A. (2016). Common questions about recurrent urinary tract infections in women. *American Family Physician, 93*, 560-569. Retrieved from <http://www.aafp.org/afp/2016/0401/p560.html>
- Artiga, S. (2016). Disparities in health and health care: Five key questions and answers. Retrieved from <http://kff.org/disparities-policy/issue-brief/disparities-in-health-and-health-care-five-key-questions-and-answers/>
- Association of Professionals in Infection Control & Epidemiology. (2012). Antibiotic stewardship. Retrieved from <http://www.apic.org/Professional-Practice/Practice-Resources/Antimicrobial-Stewardship>
- August, S. L., & De Rosa, M. J. (2012). Evolution of the prevalence of urinary tract infection in Panamanian women. *PLoS ONE, 7*, e47752. doi:10.1371/journal.pone.0047752
- Awad, A. I., & Aboud, E. A. (2015). Knowledge, attitude, and practice toward antibiotic use among the public in Kuwait. *PLoS ONE, 10*, e0117910. doi:10.1371/journal.pone.0117910. eCollection 2015
- Azevedo, M. M., Capela, C., Baltazar, F. (2013). *Microbiology, 4*, 1542-1547. Retrieved from <http://www.formatex.info/microbiology4/vol3/1542-1547.pdf>
- Barber, A. E., Norton, P., Spivak, A. M., Mulvey, M.A. (2013). Urinary tract infections: Current and emerging management strategies. *Clinical Infectious Disease, 57*, 719-724. doi:10.1093/cid/cit284
- Bartlett, J. G., Gilbert, D. N., & Spellberg, B. (2013). Seven ways to preserve the miracle of antibiotics. *Clinical Infectious Diseases, 56*, 445-450. doi:10.1093/cid/cit070

- Bates, B. N. (2013). Interpretation of urinalysis and urine culture for treatment of UTI. *Pharmacist*, 38, 65-68. Retrieved from <https://www.uspharmacist.com/article/interpretation-of-urinalysis-and-urine-culture-for-uti-treatment>
- Bekeris, L. G., Jones, B. A., Walsh, M. K., & Wagar, E. A. (2008). Urine culture contamination: a college of American pathologists Q-Probes study of 127 laboratories. *Archives of Pathology and Laboratory Medicine*, 132, 913-917. Retrieved from [http://www.archivesofpathology.org/doi/full/10.1043/1543-2165\(2008\)132%5B913%3AUCCACO%5D2.0.CO%3B2](http://www.archivesofpathology.org/doi/full/10.1043/1543-2165(2008)132%5B913%3AUCCACO%5D2.0.CO%3B2)
- Bhavsar, T. (2015, January 18). Predictability of urinalysis parameters in the diagnosis of urinary tract infection: A case study. *Medical Laboratory Observer-Online*. Retrieved from <http://www.mlo-online.com/predictability-of-urinalysis-parameters-in-the-diagnosis-of-urinary-tract-infection-a-case-study.php>
- Björkman, I., Berg, J., Viberg, N., & Lundborg, C. S. (2013). Awareness of antibiotic resistance and antibiotic prescribing in UTI treatment: A qualitative study among primary care physicians in Sweden. *Scandinavian Journal of Primary Health Care*, 31, 50-55. doi:10.3109/02813432.2012.751695
- Bodro, M., Sanclemente, G., Lipperheide, I., Allali, M., Marco, F., Bosch, J., Cofan, F., ...Cervera, C. (2015). Impact of antibiotic resistance on the development of recurrent and relapsing symptomatic urinary tract infection in kidney recipients. *American Journal of Transplantation*, 15, 1021-1027. doi:10.1111/ajt.13075

- Borchert, D., Sheridan, L., Papastoris, A., Faruqz, Z., Barua, J. M., Junaid, I., Pati, Y.,...Buchholz, N. (2008). Prevention and treatment of urinary tract infection with probiotics: review and research perspective. *Indian Journal of Urology*, 24, 139-144. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2684288/>
- Boucher, H. W., Talbot, G. H., Bradley, J. S., Edwards, J. E., Gilbert, D., Rice, L. B.,...Bartlett, J. (2009). Bad bugs, no drugs: No ESKAPE! An update from the Infectious Disease Society of America. *Clinical Infectious Diseases*, 48, 1-12. doi:10.1086/595011
- Brede, C. M., & Shoskes, D. A. (2011). The etiology and management of acute prostatitis. *National Reviews, Urology*, 8, 207-212. doi:10.1038/nrurol.2011.22
- Brusch, J. L., & Bronze, M. S. (2016). Prevention of urinary tract infections. *Medscape*. Retrieved from <http://emedicine.medscape.com/article/2040239-overview>
- Bryce, A., Hay, A. D., Lane, I. F., Thornton, H. V., Wootton, M., & Costelloe, C. (2016). Global prevalence of antibiotic resistance in pediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: systematic review and meta-analysis. *BMJ*, 2016, 352. doi:10.1136/bmj.i939
- Butler, C. C., Hillier, S., Roberts, Z., & Dunstan, F. (2006). Antibiotic-resistant infections in primary care are symptomatic for longer and increase workload: outcomes for

patients with *E. coli* UTIs. *The British Journal of General Practice*, 56, 686-692.

Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1876635/>

Byappanahalli M. N., Nevers M. B., Korajkic A., Staley Z. R., & Harwood V. J. (2012).

Enterococci in the environment. *Microbiology and Molecular Biology*

Reviews, 76, 685–706. doi:10.1128/MMBR.00023-12

Carlet, J., Jarlier, V., Harbarth, S., Voss, A., Goossens, H., & Pittet, D. (2012). Ready for

a world without antibiotics? The Pensières Antibiotic Resistance Call to Action.

Antibiotic Resistance and Infection Control, 1, 1-13. doi:10.1186/2047-2994-1-11

Carlson, M. D. A., & Morrison, R. S. (2009). Study design, precision, and validity in

observational studies. *Journal of Palliative Medicine*, 12, 77-82.

doi:10.1089/jpm.2008.9690

Centers for Disease Control and Prevention. (2011a). Emerging infectious disease.

Retrieved from http://wwwnc.cdc.gov/eid/article/17/2/70-0286_article

Centers for Disease Control and Prevention. (2011b, April 07). Antimicrobial resistance

posing growing health threat: CDC and partners celebrate World Health Day 2011 to draw attention to the issue.

http://www.cdc.gov/media/releaincome/2011/p0407_antimicrobialresistance.html

Centers for Disease Control & Prevention. (2011c). Denominator simplification project.

NHSN, 6, 1. Retrieved from

https://www.cdc.gov/nhsn/PDFs/Newsletters/NHSN_NL_MAR_2011_final-updated-12-2011.pdf

Centers for Disease Control and Prevention. (2013a). *Antibiotic resistance threats in the United States, 2013*. Retrieved from <http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>

Centers for Disease Control and Prevention. (2013b). Untreatable: report by CDC details today's drug-resistant health threats. Retrieved from <http://www.cdc.gov/media/releaincome/2013/p0916-untreatable.html>

Centers for Disease Control and Prevention. (2014). Infectious Disease: National Ambulatory Medical Care Survey, 2011 and 2012, summary tables, [Data file]. Retrieved from <http://www.cdc.gov/nchs/fastats/infectious-disease.htm>

Centers for Disease Control & Prevention. (2015a). Ambulatory health care data [Data file]. Retrieved from <http://www.cdc.gov/nchs/ahcd.htm>

Centers for Disease Control & Prevention. (2015b). Economic impact of antibiotic resistance. Retrieved from http://wwwnc.cdc.gov/eid/article/7/2/70-0286_article

Centers for Disease Control & Prevention. (2015c). Antimicrobial resistance: biggest threats. Retrieved from http://www.cdc.gov/drugresistance/biggest_threats.html

Centers for Disease Control & Prevention. (2015d). Antibiotics aren't always the answer. Retrieved from <http://www.cdc.gov/features/getsmart/>

Centers for Disease Control & Prevention. (2015e). Syphilis statistics. Retrieved from <http://www.cdc.gov/std/syphilis/stats.htm>

Centers for Disease Control & Prevention. (2016). State genomics programs. Retrieved from <http://www.cdc.gov/genomics/translation/states/index.htm>

- Center for Disease Dynamics, Economics & Policy. (2014). Antibiotic resistance. Retrieved from <http://www.cddep.org/research-area/antibiotic-resistance#sthash.n6b3IRRP.dpbs>
- Centers for Medicare and Medicaid Services. (2012). Medicare and Medicaid programs: Reform of hospital and critical access hospital conditions of participation Retrieved from <https://www.federalregister.gov/articles/2012/05/16/2012-11548/medicare-and-medicaid-programs-reform-of-hospital-and-critical-access-hospital-conditions-of>
- Centers for Medicare and Medicaid Services. (2015). Medicare and Medicaid programs: Reform of long-term care facilities. Retrieved from <https://www.federalregister.gov/articles/2015/07/16/2015-17207/medicare-and-medicaid-programs-reform-of-requirements-for-long-term-care-facilities>
- Centers for Medicare and Medicaid Services. (2016). Readmissions Reduction program (HRRP). Retrieved from <https://www.cms.gov/medicare/medicare-fee-for-service-payment/acuteinpatientpps/readmissions-reduction-program.html>
- Childress, Sarah. (2013, October 13). Hunting the nightmare bacteria. Dr. Arjun Srinivasan: “We’ve reached the end of antibiotics, period.” *Frontline*. Retrieved from <http://www.pbs.org/wgbh/frontline/article/dr-arjun-srinivasan-weve-reached-the-end-of-antibiotics-period/>
- Ciani, O., Grassi, D., & Terricone, R. (2013). An economic perspective on urinary tract infection: the “costs of regulation.” *Clinical Drug Investigation*, 33, 255-261. doi:10.1007/s40261-013-0069-x

- Clinical Laboratory Standards Institute. (2015). Performance standards for antimicrobial susceptibility testing; twenty-fifth informational supplement (M100-S25)
- CNBC. (2016). Obama's Medicaid expansion leading to health insurance boom in some states. Retrieved from <http://www.cnbc.com/2016/07/20/obamacares-medicaid-expansion-leading-to-health-insurance-boom-in-some-states.html>
- Cochrane.org. (2005). Improving how antibiotics are prescribed by physicians working in the community. Retrieved from http://www.cochrane.org/CD003539/EPOC_improving-how-antibiotics-are-prescribed-by-physicians-working-in-the-community.
- Coren, S. (2016). You can teach an old dog new tricks. *Psychology Today*. Retrieved from <https://www.psychologytoday.com/blog/canine-corner/201602/you-can-teach-old-dog-new-tricks>
- Costelloe, C., Metcalfe, C., Lovering, A., Mant, D., & Hay, A. D. (2010). Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and metanalysis. *British Medical Journal*, 340, c2096. doi:10.1136/bmj.c2096
- Creswell, J. W. (2009). *Research design. Qualitative, quantitative, and mixed-method approaches* (3rd ed.). Los Angeles: CA: SAGE.
- Czaja, C. A., Scholes, D., Hooton, T. M., Stamm, W. E. (2007). Population-based epidemiologic analysis of acute pyelonephritis. *Clinical Infectious Diseases*, 45, 273-280. Retrieved from <http://cid.oxfordjournals.org/content/45/3/273.full.pdf+html>

- Dason, S., Dason, J. T., & Kapoor, A. (2010). Guidelines for the diagnosis and management of recurrent urinary tract infection in women. *Canadian Urological Association Journal*, 5, 316-322. doi:10.5489/cuaj.11214
- David, M. Z., & Daum, R. S. (2010). Community-associated methicillin-resistant *Staphylococcus aureus*: epidemiology and clinical consequences of an emerging epidemic. *Clinical Microbiology Reviews*, 23, 616-687. doi:10.1128/CMR.00081-09
- Davies, J., & Davies, D. (2010). Origins and evolution of antibiotic resistance. *Microbiology and Molecular Biology Reviews*, 74, 417-433. doi:10.1128/MMBR.00016-10
- DeMillo, L., & Nakashian, M. (2016). Using social determinants of health data to improve health care and health: A learning report. Retrieved from <http://www.rwjf.org/en/library/research/2016/04/using-social-determinants-of-health-data-to-improve-health-care-.html>
- Denes, E., Prouzergue, J., Ducroix-Roubertou, S., Aupetit, C., & Weinbreck P. (2012). Antibiotic prescription by general practitioners for urinary tract infections in outpatients. *European Journal of Clinical Microbiology and Infectious Diseases*, 31, 3079-3083. doi:10.1007/s10096-012-1668-9
- Dickert, N.W., & Kass, N. E. (2009). Understanding respect: learning from patients. *Journal of Medical Ethics*, 35, 419-423.

- Dyck, M. J., Culp, K., & Cacchione, P. Z. (2007). Data quality strategies in cohort studies: lessons on a study on delirium in nursing home elders. *Applied Nursing Research, 20*, 39–43. doi:10.1016/j.apnr.2006.01.004
- Eells, S. J., Bharadwa, K., McKinnell, J. A., Miller, L. G. (2014). Recurrent urinary tract infections among women: Comparative effectiveness of 5 prevention and management strategies using a Markov Chain Monte Carlo model. *Clinical Infectious Diseases, 58*, 147-160. doi:10.1093/cid/cit646
- Ejrnaes, K. (2010). Bacterial characteristics of importance for recurrent urinary tract infections caused by *Escherichia coli*. Retrieved from http://www.danmedj.dk/portal/pls/portal/!PORTAL.wwpob_page.show?_docname=9026897.PDF
- Eliopoulos, Cosgrove, & Carmeli, (2003). The impact of antimicrobial resistance on health and economic outcomes. *Clinical Infectious Diseases, 1433-1437*. doi:10.1086/375081
- Euser, A. M., Zoccali, C., Jager, K. J., & Dekker, F. W. (2009). Cohort studies: prospective versus retrospective. *Nephron Clinical Practice, 113*, c214-c217. doi:10.1159/000235241
- Fair, R. J. & Tor, Y. (2014). Antibiotics and bacterial resistance in the 21st century. *Perspectives in Medicinal Chemistry, 6*, 25-64. doi:10.4137/PMC.S14459
- Farfan-Portet, M. I., Van de Voorde, C., Vijens, F., & Stichele, R. V. (2012). Patient socioeconomic determinants of the choice of generic versus brand name drugs in the context of a reference price system: evidence from Belgian prescription data.

The European Journal of Health Economics, 13, 301-313. doi:10.1007/s10198-012-0377-8

Federal Communications Commission. (2017). Lifeline program for low income consumers. Retrieved from <https://www.fcc.gov/general/lifeline-program-low-income-consumers>

Findley, K., & Grice, E. A. (2014). The skin microbiome: A focus on pathogens and their association with skin disease. *PLoS Pathogens*, 10, e1004436. doi: 10.1371/journal.ppat.1004436

Fleming, A. (1945, December 11). Penicillin. *Nobel Lecture*. Retrieved from http://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-lecture.pdf

Flores-Mireles, A. L., Walker, J. N., Caparon, M., & Hultgren, S. J. (2015). Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. *Nature Reviews Microbiology*, 13, 269-284. doi:0.1038/nrmicro3432

Food and Drug Administration. (2011). Battle of the bugs: Fighting antibiotic resistance. Retrieved from <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143568.htm>

Frieden, T. R. (2010). Antibiotic resistance and the threat to public health. Retrieved from <http://www.hhs.gov/asl/testify/2010/04/t20100428b.html>

Gandra, S., Barter, D. M., & Laxminarayan, R. (2014). Economic burden of antibiotic resistance: How much do we really know? *Clinical Microbiology and Infection*, 20, 973-980. doi:<http://dx.doi.org/10.1111/1469-0691.12798>

- Garau, J., Nicolau, D. P., Wullt, B., & Bassetti, M. (2014). Antibiotic stewardship challenges in the management of community-acquired infections for prevention of escalating antibiotic resistance. *Journal of Global Antimicrobial Resistance*, 2, 245-253. doi:10.1016/j.jgar.2014.08.002
- Gates Foundation. (2005). U.S. public libraries provide access to computers, the internet, and technology training. Retrieved from <http://www.gatesfoundation.org/Media-Center/Press-Release/income/2005/06/Support-Needed-for-Library-Technology>
- Gesme, D. H., Towle, E. L., & Wiseman, M. (2017). Essentials of staff development and why you should care. *The Journal of Oncology Practice*, 6, 104-106. Retrieved from <http://ascopubs.org/doi/pdf/10.1200/JOP.091089>
- Gibson, K., & Toscano, J. (2012). Urinary tract infection update. *American Journal of Clinical Medicine*, 9, 82-86. Retrieved from <http://www.aapsus.org/wp-content/uploads/uti82.pdf>
- Golkar, Z., Bagasra, O., & Pace, D., G. (2014). Bacteriophage therapy: A potential solution for the antibiotic resistance crisis. *Journal of Infections in Developing Countries*, 8, 129-36. doi:10.3855/jidc.3573
- Goodman, K. E., Lessler, J., Cosgrove, S. E., Harris, A. D., Lautenbach, E., Han, J. H., Milstone, ... A. M., Massey, C. J. (2016). A clinical decision tree to predict whether a bacteremic patient is infected with an extended beta lactamase-producing organism. *Clinical Infectious Diseases*, 63, 896-903. doi:10.1093/cid/ciw425

- Grabe, M., Bartoletti, R, Bjerklund-Johansen, T. E., Cek, H. M., Pickard, R. S., Tenke, P., Wagenlehner, F.,...Wullt B. (2014). Guidelines on urological infections. *European Association of Urology*, 1-107. Retrieved from http://uroweb.org/wp-content/uploads/19-Urological-infections_LR.pdf
- Greenland, S., & Robbins, J. (1994). Invited commentary: Biases, misconceptions, and counterexamples. *American Journal of Epidemiology*, 139, 747-760. Retrieved from <http://aje.oxfordjournals.org/content/139/8/747>
- Grice, E. A., & Segre, J. A. (2011). The skin microbiome. *National Review of Microbiology*, 9, 244-253. doi:10.1038/nrmicro2537
- Grigoryan, L., Zoorob, R., Wang, H., & Trautner, B. W. (2015). Low concordance with guidelines for treatment of acute cystitis in primary care. *Open Forum Infectious Diseases*, 1-6. doi:10.1093/ofid/ofv159
- Güclü, I. (2015). Cox Proportional Hazards Model in social science. *International Journal of Social Science*, 36, 63-74. doi:10.9761/JASSS2951
- Gulis, G., & Fujino, Y. (2015). Epidemiology, population health, and health impact assessment. *Journal of Epidemiology*, 25, 179-180. doi:10.2188/jea.JE20140212
- Gupta, K., Hooton, T. M., & Stamm, W. E. (2001). Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. *Annals of Internal Medicine*, 135, 41-50. doi:10.7326/0003-4819-135-1-200107030-00012
- Gupta, K., Hooton, T. M., Naber, K. G., Wullt, B., Colgan, R., Miller, L. G., Moran, G. J.,...Soper, D. E. (2011). International clinical practice guidelines for the

treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Disease Society of America and the European Society for Microbiology and Infectious Disease. *Clinical Infectious Diseases*, 52, e103-e120. doi:10.1093/cid/ciq257

Gupta, K., & Trautner, B. W. (2013). Diagnosis and management of recurrent urinary tract infections in non-pregnant women. *British Medical Journal*, 346, 3140. doi:10.1136/bmj.f3140

Guyomard-Rabinirina, S., Malespine, J., Ducat, C., Sadikalay, S., Falord, M., Harrois, D., Richard, V.,...Dozois, C. (2016). Temporal trends and risks factors for antimicrobial resistant Enterobacteriaceae urinary isolates from outpatients in Guadeloupe. *BMC Microbiology*, 16, 121. doi: 10.1186/s12866-016-0749-9

Hall, M. J., Schwartzman, A., Zhang, J., & Liu, X. (2017). Ambulatory surgery data from hospitals and surgery centers: United States: 2010. *National Health Statistics Report*. Retrieved from <https://www.cdc.gov/nchs/data/nhsr/nhsr102.pdf>

Harbarth, S., Balkhy, H. H., Goossens, H., Jarlier, V., Kluytmans, J., Laxminarayanan, R., Saam, ...Pittet, D. (2015). Antimicrobial resistance: One world, one fight! *Antimicrobial Resistance and Infection Control*, 4, 49. doi:10.1186/s13756-015-0091-2

Harvard Health Publications. (2015, August 7). How to boost your immune system: What can you do? Retrieved from <http://www.health.harvard.edu/staying-healthy/how-to-boost-your-immune-system>

- Hawker, J. I., Smith, S., Smith, G. E., Morbey, R., Johnson, A. P., Fleming, D. M., Shallcross, L.,...Hayward, A. C. (2014). Trends in antibiotic prescribing in primary care for clinical syndromes subject to national recommendations to reduce antibiotic resistance, UK 1995–2011: Analysis of a large database of primary care consultations. *Journal of Antimicrobial Chemotherapy, Advance Access*, 1-8. doi:10.1093/jac/dku291
- Hawkey, P. M. & Jones, A. M. (2009). The changing epidemiology of resistance. *Journal of Antibiotic Chemotherapy*, 64, i3-i10. doi:10.1093/jac/dkp256
- Hawkey, P. M. (2008). The growing problem of antibiotic resistance. *Journal of Antibiotic Chemotherapy*, 62, (Suppl. 1), i1-i9. doi:10.1093/jac/dkn241
- Hersh, A. L., Shapiro, D. J., Pavia, A. T., & Shah, S. S. (2011). Antibiotic prescribing in ambulatory pediatrics the United States. *Pediatrics*, 128, 1-11. Retrieved from <http://pediatrics.aappublications.org/content/pediatrics/128/6/1053.full.pdf>
- Hersh, A. L., Beekmann, S. E., Polgreen, P. M., Zaoutis, T. E., & Newland, J. W. (2009). [Poster Presentation]. Prevalence of antimicrobial stewardship programs in pediatrics. Retrieved from http://ein.idsociety.org/media/resources/publications/posters/2012/Poster_Peds_ASP_SHEA_2009.pdf
- Hicks, L. A., Bartoce, M. G., Roberts, R. M., Suda, K. J., Hunkler, R. J., Taylor, T. H., & Schrag, S. J. (2015). U. S. outpatient prescribing variation according to geography, patient population, and provider specialty in 2011. *Clinical Infectious Diseases*, 1-9. doi:10.1093/cid/civ076

- Hilt, E. E., McKinley, K., Pearce, M. M., Rosenfeld, A. B., Zilliox, M. J., Mueller, E. R., Brubaker, L.,...Schreckenberger, P. C. (2014). Urine is not sterile: Use of enhanced urine culture techniques to detect resident bacterial flora in the adult female bladder. *Journal of Clinical Microbiology*, *52*, 871-876. doi: 10.1128/JCM.02876-13
- Hossain, M. M., & Laditka, J. N. (2009). Using hospitalization for ambulatory care conditions to measure access to primary health care: An application of spatial structural equation modeling. *International Journal of Health Geographic's*, *8*, 51. doi: 10.1186/1476-072X-8-51
- Hsieh, F. Y. (1989). Sample size tables for logistic regression. *Statistics in Medicine*, *8*, 795-802. doi:10.1002/sim.4780080704
- Humphries, R. M., & Dien Bard, J. (2016). Point-counter-point: Reflex cultures reduce laboratory workload and improve antimicrobial stewardship in patients suspected of having urinary tract infections. *Journal of Clinical Microbiology*, *54*, 254-258. doi:10.1128/jcm.03021-15
- Huston, P., & Naylor, C. D. (1996). Health services research: reporting on studies using secondary data sources. *Canadian Medical Association Journal*, *155*, 1697-1702. Retrieved from http://www.collectionscanada.gc.ca/eppp-archive/100/201/300/cdn_medical_association/cmaj/vol-155/issue-12/1697.htm
- IMS Institute for Health Informatics. (2011). HSRN data brief: National prescription audit. Retrieved from https://www.imshealth.com/files/web/IMSH%20Institute/NPA_Data_Brief-.pdf

- Infectious Disease Society of America. (2011). Uncomplicated cystitis and pyelonephritis. Guidelines for antimicrobial treatment of acute uncomplicated cystitis and pyelonephritis in women. Retrieved from [http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Infections_by_Organ_System/Genitourinary/Uncomplicated_Cystitis_and_Pyelonephritis_\(UTI\)/](http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Infections_by_Organ_System/Genitourinary/Uncomplicated_Cystitis_and_Pyelonephritis_(UTI)/)
- Johnson, C. Y. (2016). The striking difference between states that expanded Medicaid and the one's that didn't. *Washington Post*. Retrieved from https://www.washingtonpost.com/news/wonk/wp/2016/09/13/the-difference-between-states-that-expanded-medicaid-and-the-ones-that-didnt/?utm_term=.a6b7ae12609b
- Johnson, E. K., & Kim, E. D. (2015, May 06). Urinary tract infections in pregnancy. Retrieved from <http://emedicine.medscape.com/article/452604-overview>
- Kaiser Family Foundation. (2016). Disparities in health and health care: Five key questions and answers. Retrieved from <http://kff.org/disparities-policy/issue-brief/disparities-in-health-and-health-care-five-key-questions-and-answers/>
- Kallen, A. J., Mu, Y., Bulens, S., Reingold, A., Petit, S., Gershman, K., Ray, S. M.,...Fridkin, S. K. (2010). Health care-associated invasive MRSA infections: 2005-2008. *Journal of the American Medical Association*, *304*, 641-648. doi:10.1001/jama.2010.1115
- Kalpoe, J. S., Sonnenberg, E., Factor, S. H., Martin, J., Schiano, T., Patel, G., & Huprikar, S. (2012). Mortality associated with carbapenem-resistant *Klebsiella*

pneumoniae infections in liver transplant recipients. *Liver Transplantation*, 18, 468-474. doi:10.1002/lt.23374

Karam, G., Chastre, J., Wilcox, M. H., & Vincent, J. L. (2016). Antibiotic strategies in the era of multidrug resistance. *Critical Care*, 20, 136. doi:10.1186/s13054-016-1320-7

Kattan, J. N., & Gordon, S. (2013). Acute uncomplicated urinary tract infections.

Retrieved from

<http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/infectious-disease/urinary-tract-infection/>

Kellermann, A. L., & Weinick, R. M. (2012). Emergency departments, Medicaid costs, and access to primary care. Understanding the link. *The New England Journal of Medicine*, 366, 2141-2143. doi:10.1056/NEJMp1303247

Kobayashi, M., Shapiro, D. J., Hersh, A. L., Sanchez, G. V., & Hicks, L. A. (2016).

Outpatient antibiotic prescribing practices for uncomplicated urinary tract infection in women in the United States, 2002-2011. *Oxford University Press*.

Advance online publication. Retrieved from

<http://ofid.oxfordjournals.org/content/early/2016/08/02/ofid.ofw159.full.pdf>

Kodner, C. M., & Gupton, E. K. T. (2010). Recurrent urinary tract infections in women: diagnosis and management. *American Family Physician*, 82, 638-643. Retrieved from <http://www.aafp.org/afp/2010/0915/p638.html>

- Krieger, N. (1994). Epidemiology and the web of causation: Has anyone seen the spider? *Social Science Medicine*, 39, 887-903. Retrieved from <http://www.havenscenter.org/files/krieger1.pdf>
- Krieger, N. (2001). Theories for social epidemiology in the 21st century: an Ecosocial perspective. *International Journal of Epidemiology*, 30, 668-667.
doi:10.1093/ije/30.4.668
- Krieger, N. (2005). *Embodying inequality: epidemic perspectives*. Amityville, New York: Baywood Publishing
- Krieger, N. (2008). Proximal, distal and the politics of causation: What's level got to do with it? *American Journal of Public Health*, 98, 221-230.
doi: 10.2105/AJPH.2007.111278
- Krieger, N. (2012). Methods for the scientific study of discrimination and health: An ecosocial approach. *American Journal of Public Health*, 102, 936-944.
doi: 10.2105/AJPH.2011.300544
- Kripalani, S., Bussey-Jones, J., Katz, M. G., Genao, I. (2006). A prescription for cultural competence in medical education. *Journal of General Internal Medicine*, 21, 1116-1120. doi:10.1111/j.1525-1497.2006.00557.x
- Kukull, W. A., & Ganguli, M. (2012). Generalizability. *Neurology*, 78, 1886-1891. doi: 10.1212/WNL.0b013e318258f812
- Kurai, D., Saraya, T., Ishii, H., & Takizawa, H. (2013). Virus-induced exacerbations in asthma and COPD. *Frontiers in Microbiology*, 4, 293.
doi: 10.3389/fmicb.2013.00293

- Lagace-Wiens, P. R., Simner, P. J., Forward, K. R., Taylor, F., Adam, H. J., Decorby, M., Karlowsky, J.,...Zhanel, G. G. (2011). Analysis of 3789 in-and-outpatient *Escherichia coli* isolates from across Canada: results of the CANWARD 2007–2009 study. *Diagnostic Microbiology of Infectious Disease*, 69, 314-319. doi: 10.1016/j.diagmicrobio.2010.10.027
- Lamb, M. (2016). Urinary tract infections: Causes and treatment update. *Pharmacist*, 41, 18-21 Retrieved from <https://www.uspharmacist.com/article/urinary-tract-infections-causes-and-treatment-update>
- LaMorte, W. W. (2016). Advantages and disadvantages of cohort studies. Retrieved from http://sphweb.bumc.bu.edu/otlt/MPH-Modules/EP/EP713_CohortStudies/EP713_CohortStudies5.html
- Landecker, H. (2015). Antibiotic resistance and the biology of history. *Body & Society*. doi:10.1177/1357034X1456134
- Langdon, A., Crook, N., & Dantas, G. (2016). The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. *Genome Medicine*, 8, 39. doi:10.1186/s13073-016-0294-z
- 13<http://www.mdedge.com/jcso/article/137152/practice-management/emergency-department-use-recently-diagnosed-cancer-patients...>
- Romano, P. S. (2017). Emergency department used by recently diagnosed cancer patients in California. *The Journal of Community Oncology*, 15, 95-102. Retrieved from

- Lawal, K. (2012). Asymptomatic and symptomatic urinary tract infections: Magnitude, special settings, and diagnostic testing. Retrieved from <http://www.americanmedtech.org/Portals/0/PDF/STEP%20Articles/392.pdf>
- Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K., Wertheim, H. F. L., Sumpradit, N., Vlieghe, E.,...Cars, O. (2013). Antibiotic resistance: The need for global solutions. *The Lancet Infectious Diseases*, 13, 1057-1098. doi: [http://dx.doi.org/10.1016/S1473-3099\(13\)70318-9](http://dx.doi.org/10.1016/S1473-3099(13)70318-9)
- Lee, C. R., Cho, I. H., Jeong, B. C., & Lee, S. H. (2013). Strategies to minimize antibiotic resistance. *International Journal of Environmental Research and Public Health*, 10, 4274-4305. doi: 10.3390/ijerph10094274
- Lee, G. C., Reveles, K. R., Attridge, R. T., Lawson, K. A., Mansi, I. A., Lewis, J. S., & Frei, C. R. (2014). Outpatient antibiotic prescribing in the United States: 2000-2010. *BMC Medicine*, 12, 96. doi:10.1186/1741-7015-12-96
- Lee, B. Y., Bartsch, S. M., Wong, K. F., McKinnell, J. A., Slayton, R. B., Miller, L. G., Cao, C.,...Huang, S. S. (2016). The potential trajectory of Carbapenem-resistant Enterobacteriaceae, an emerging threat to health-care facilities, and the impact of the Centers for Disease Control and Prevention Toolkit. *American Journal of Epidemiology*, 183, 471-479. doi:10.1093/aje/kwv299
- Leekha, S., Terrell, C. L., & Edson, R. S. (2011). General principles of antimicrobial therapy. *Mayo Clinic proceedings*, 86, 156-167. doi:10.4065/mcp.2010.0639
- Lema, V. M. (2015). Urinary tract infection in young healthy women following

- heterosexual anal intercourse: Case reports. *African Journal of Reproductive Health*, 19, 133-138. Retrieved from <http://www.bioline.org.br/pdf?rh15029>
- Lior & Cots. (2009). The sale of antibiotics without prescription in pharmacies in Catalonia, Spain. *Clinical Infectious Diseases*, 48, 1345-1349.
doi:10.1086/598183
- Lipsitch, M., & Samore, M. H. (2002). Antimicrobial use and antimicrobial resistance: A population perspective. *Emerging Infectious Diseases*, 8, 347-354.
doi:10.3201/eid0804.010312
- Lumbiganon, P., Laopaiboon, M., & Thinkhamrop, J. (2010). Screening and treating asymptomatic bacteriuria in pregnancy. *Current Opinions in Obstetric Gynecology*, 22, 95–9. Retrieved from
<http://www.ncbi.nlm.nih.gov/pubmed/20139763>
- Lyme Disease.org. (2015). About Lyme disease. Retrieved from
<https://www.lymedisease.org/lyme-basics/lyme-disease/about-lyme/>
- Magill, S. S., Dumyati, G., Ray, S. M., Fridkin, S. K. (2015). Evaluating epidemiology and improving surveillance of infections associated with health care, United States. *Emerging Infectious Diseases*, 21, 1537- 1542. Retrieved from
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4550137/>
- Magliano, E., Grazioli, V., DeFlorio, L., Leuci, A. I., Mattina, R., Romano, P., Cocuzza, C. E. (2012). Gender and age-dependent etiology of community-acquired urinary tract infections. *The Scientific World Journal*, 1-6.

doi:<http://dx.doi.org/10.1100/2012/349597>

- Maier, E., Anderson, R. C., & Roy, N. C. (2015). Understanding how commensal obligate anaerobic bacteria regulate immune functions in the large intestine. *Nutrients*, *7*, 45-73. doi:10.3390/nu7010045
- Mamuye, Y., Metaferia, G., Birhanu, A., Desta, K., & Fantaw, S. (2015). Isolation and antibiotic susceptibility patterns of Shigella and Salmonella among under 5 children with acute Diarrhea: a cross-sectional study at selected public health facilities in Addis Ababa, Ethiopia. *Clinical Microbiology*, *4*, 186. doi:10.4172/2327-5073.1000186
- Mann, C. J. (2003). Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *BMJ*, *20*, 54-60. doi:10.1136/emj.20.1.54
- Marrie, T.J., Swantee, C. J., & Hartlen, M. (1980). Aerobic and Anaerobic urethral flora in healthy females in various physiological age groups and of females with urinary tract infections. *Journal of Clinical Microbiology*, *11*, 654-659. Retrieved from <http://jcm.asm.org/content/11/6/654.full.pdf>
- Martinez de Tejada, B. (2014). Antibiotic use and misuse during pregnancy and delivery: benefits and risks. *International Journal of Environmental Research and Public Health*, *11*, 7093-8099. doi:10.3390/ijerph110807993
- Martins da Costa, P., Loureiro, L., & Matos, A. J. F. (2013). Transfer of multidrug-resistant bacteria between intermingled ecological niches: The interface between humans, animals, and the environment. *International Journal of Environmental Research and Public Health*, *10*, 278-294. doi: 10.3390/ijerph10010278

- Masterton, R. (2008). The importance and future of antimicrobial surveillance studies. *Clinical Infectious Diseases*, 47 (Suppl 1), S21-S31. doi:10.1086/590063
- Matuszkiewicz-Rowińska, J., Malyszko, J., & Wieliczko, M. (2015). Urinary tract infections in pregnancy: Old and new unresolved diagnostic and therapeutic problems. *Archives of Medical Science*, 11, 67-77. doi: 10.5114/aoms.2013.39202
- May, L., Mullins, P., & Pines, J. (2014). Demographic and treatment patterns of infections in ambulatory settings 2006-2010. *Academic Emergency Medicine*, 21, 17-24. doi:10.1111/acem.12287
- Mazulli, T. (2012). Diagnosis and management of simple and complicated urinary tract infections (UTIs). *Canadian Journal of Urology*, 19, 42-48. Retrieved from <http://canjurol.com/html/free-articles/V19I5S1F-07-DrMazulli.pdf>
- McGowan, A. P. (2008). Clinical implications of antibiotic resistance for therapy. *Journal of Antibiotic Therapy*, 62, ii105-ii114. doi:10.1093/jac/dkn357
- McDonnell Norms Group. (2008). Antibiotic overuse: the influence of social norms. *Journal of the American College of Surgeons*, 207, 265-275. doi:<http://dx.doi.org/10.1016/j.jamcollsurg.2008.02.035>
- Mekviwattanawong, S., Srifuengfung, S. S., Chokepaibulkit, K., Lohsiriwat, D. L., & Thamlikitkul, V. T. (2006). Epidemiology of *Staphylococcus aureus* infections and the prevalence of infection caused by community-acquired Methicillin-resistant *Staphylococcus aureus* in hospitalized patients at Siriraj Hospital. *Journal of the Medical Association of Thailand*, 89 (Suppl 5), S106-S117. Retrieved from <http://www.medassocthai.org/journal>

- Meropol, S. B., Localio, A. R., & Metlay, J. P. (2013). Risks and benefits associated with antibiotic use for recurrent respiratory infections: A cohort study. *Annals of Family Medicine, 11*, 165-172. doi:10.1370/afm.1449
- Minardi, D., d'Anzeo, G., Cantoro, D., Conti, A., & Muzzonigro, G. (2011). Urinary tract infections in women: etiology and treatment options. *International Journal of General Medicine, 4*, 333-343. doi:10.2147/IJGM.S11767
- Merli, M., Lucidi, L., Di Gregorio, V., Lattanzi, B., Giannelli, V., Giusto, M., Farcomeni, A.,... Venditti, M. (2016). An empirical broad spectrum antibiotic therapy in health-care-associated infections improves survival in patients with cirrhosis: A randomized trial. *Hepatology, 63*, 1632-1639. Retrieved from <http://onlinelibrary.wiley.com/doi/10.1002/hep.28332/full>
- Mkanta, W. N., Chumbler, N. R., Yang, K., Saigal, R., & Abdollahi, M. (2016). Cost and predictors of hospitalizations for ambulatory care-sensitive conditions among Medicaid enrollees in comprehensive managed care plans. *Health Services Research & Managerial Epidemiology*. Retrieved from <http://journals.sagepub.com/doi/full/10.1177/2333392816670301>
- Mody, L., & Juthani-Mehta, M. (2014) Urinary tract infections in older women. *Journal of the American Medical Association, 311*, 844-854. doi:10.1001/jama.2014.303
- Mohsin, R., & Suddiqui, K. M. (2010). Recurrent urinary tract infections in females. *Journal of Pakistan Medical Association, 60*, 55-59. Retrieved from <http://www.jpma.org.pk/PdfDownload/1903.pdf>

- Murphy, E. C., & Frick, I. M. (2012). Gram positive anaerobic cocci: Commensals and opportunistic pathogens. *Federation of European Microbiological Societies Microbiological Review*, 37, 520-553. Retrieved from <http://onlinelibrary.wiley.com/doi/10.1111/1574-6976.12005/epdf>
- Nathan, C., & Cars, O. (2014). Antibiotic resistance: problems, progress, and prospects. *New England Journal of Medicine*, 371, 1761-1763. doi:10.1056/NEJMp1408040
- National Center for Health Statistics. (n.d.). National Ambulatory Medical Center Survey [NAMCS] scope and sample design. Retrieved from http://www.cdc.gov/nchs/ahcd/ahcd_scope.htm
- National Center for Health Statistics. (2008). National Ambulatory Medical Center Survey [NAMCS] web tables. Retrieved from http://www.cdc.gov/nchs/ahcd/web_tables.htm
- National Center for Health Statistics. (2009). National Ambulatory Medical Center Survey [NAMCS] web tables. Retrieved from http://www.cdc.gov/nchs/ahcd/web_tables.htm
- National Center for Health Statistics. (2010). National Ambulatory Medical Center Survey [NAMCS] web tables. Retrieved from http://www.cdc.gov/nchs/ahcd/web_tables.htm
- National Center for Health Statistics. (2011). National Ambulatory Medical Center Survey [NAMCS] web tables. Retrieved from http://www.cdc.gov/nchs/ahcd/web_tables.htm

National Center for Health Statistics. (2012). National Ambulatory Medical Center

Survey [NAMCS] web tables. Retrieved from

http://www.cdc.gov/nchs/ahcd/web_tables.htm

National Statistical Service. (n.d.). Sample size calculator. Retrieved from

<http://www.nss.gov.au/nss/home.nsf/pages/Sample+size+calculator>

NAMCS. (2008). 2008 NAMCS micro-data file documentation. Retrieved from

ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS

NAMCS. (2009). 2009 NAMCS micro-data file documentation. Retrieved from

ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS

NAMCS. (2010). 2010 NAMCS micro-data file documentation. Retrieved from

ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS

NAMCS. (2011). 2011 NAMCS micro-data file documentation. Retrieved from

ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS

NAMCS. (2012). 2012 NAMCS micro-data file documentation. Retrieved from

ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS

National Bureau of Economic Research (n.d.) National Ambulatory Medical Care Survey

(NAMCS) data. Retrieved from <http://www.nber.org/data/national-ambulatory-medical-care-survey.html>

National Human Genome Research Institute. (2014). The genes, environment, and health

initiative. Retrieved from <https://www.genome.gov/19518663>.

- Nemes, S., Jonasson, J. M., Genell, A., & Steineck, G. (2009). Bias in odds ratios by logistic regression modelling and sample size. *BMC Medical Research Methodology*, 9, 56. doi:10.1186/1471-2288-9-56
- Network for Excellence in Health Innovation (2013). How many more studies will it take? A collection of evidence that our health care system can do better. Retrieved from [http://www.nehinet/writable/publication_files/file/how many more studies will it take introduction.pdf](http://www.nehinet/writable/publication_files/file/how_many_more_studies_will_it_take_introduction.pdf)
- Nicolle, L. E. (2014). Catheter-associated urinary tract infections. *Antibiotic resistance and infection control*, 3, 23. doi:10.1186/2047-2994-3-23
- Nienhouse, V., Gao, X., Dong, Q., Nelson, D. E., Toh, E., McKinley, K., Schreckenberger, P.,...Radek, K. A. (2014). Interplay between bladder microbiota and urinary antibiotic peptides: Mechanisms for human urinary tract infection risk and symptom severity. *PLoS ONE*, 9, e114185. doi:10.1371/journal.pone.0114185
- Odonkor, S. T., & Addo, K. K. (2011). Bacteria resistance to antibiotics: recent trends and challenges. *International Journal of Biological and Medical Research*, 2, 1204-1210. Retrieved from https://www.researchgate.net/publication/256734983_Bacteria_Resistance_to_Antibiotics_Recent_Trends_and_Challenges
- Omar, A. (2014). Sample size estimation and sampling techniques for selecting a representative sample. *Journal of Health Specialties*, 2, 142-147. doi:10.4103/1658-600X.142783

- O'Neill, J. (2014). Antimicrobial resistance: tackling a crisis for the health and wealth of nations. Retrieved from http://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf
- Orizio, G., Merla, A., Schulz, P. J., & Gelatti, U. (2011). Quality of online pharmacies and websites selling prescription drugs: A systematic review. *Journal of Medical Internet Research*, *13*, e74. doi:10.2196/jmir.1795
- Pallett, & Hand, K. (2010). Complicated urinary tract infections: practical solutions for the treatment of multi-resistant Gram-negative bacteria. *Journal of Antimicrobial Chemotherapy*, *65* (Suppl 3), iii25-iii33. doi:10.1093/jac/dkq298
- Penders, J., Stobberingh, E. E., Savelkoul, P. H., & Wolffs, P. F. (2013). The human microbiome as a reservoir for antibiotic resistance. *Frontiers in Microbiology*, *4*, 87. doi:10.3389/fmicb.2013.00087
- Phalkey, R. K., Yamamoto, S., Awate, P., & Marx, M. (2013). Challenges with the implementation of an Integrated Disease Surveillance and Response (IDSR) system: systematic review of the lessons learned. *Health Policy & Planning*, *2*, 1-13. doi:10.1093/heapol/czt097
- Planta, M. B. (2007). The role of poverty in antibiotic resistance. *Journal of the American Board of Family Medicine*, *20*, 533-539. doi:10.3122/jabfm.2007.06.070019v

- Powell, A. (2016). The costs of inequality: money=quality health care=longer life. Retrieved from <http://news.harvard.edu/gazette/story/2016/02/money-quality-health-care-longer-life/>
- Prakash, D., & Saxena, R. S. (2013). Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of Meerut City, India. *International Scholarly Research Notices*, 2013, 1-13. Retrieved from <http://dx.doi.org/10.1155/2013/749629>
- President's Council of Advisors on Science and Technology. (2014). *Report to the President on combating antibiotic resistance*. Retrieved from https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf
- Pronovost, P. J. (2013). Enhancing physician's use of clinical guidelines. *JAMA*, 310, 2501-2502. doi:10.1001/jama.2013.281334
- Purcell, M. L. (2012). The need for consistency: a proposal for a standardized nationwide antibiotic awareness campaign. Retrieved from <http://utdr.utoledo.edu/cgi/viewcontent.cgi?article=1542&context=graduate-projects>
- Rizvi, M., Khan, F., Shukla, I., Malik, A., & Shaheen. (2011). Rising prevalence of antimicrobial resistance in urinary tract infections during pregnancy: necessity for exploring newer treatment options. *Journal of Laboratory Physicians*, 3, 98-103. doi:10.4103/0974-2727.86842

- Roley, L. & Truscott, W. (2013). The costly burden of health care-associated infections. *The Clinical Issue*, 7, 1-4. Retrieved from http://pt.halyardhealth.com/media/128741/h0044_1301_clinicalissue_v7_f.pdf
- Rowe, T. A. & Manisha, J. M. (2013). Urinary tract infection in older adults. *Aging Health*, 9, 1-15. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3878051/pdf/nihms537914.pdf>
- Rush University Medical Center. (2014). Antibiotic-resistant bacteria among children in U.S. on the rise. Retrieved from <https://www.sciencedaily.com/releaincome/2014/03/140320100522.htm>
- Sahoo, K. C., Tamhankar, A. J., Johansson, E., & Lundborg, C. S. (2010). Antibiotic use, resistance development and environmental factors: a qualitative study among health care professionals in Orissa, India. *BMC Health*, 10, 269. doi:10.1186/1471-2458-10-629
- Salem, T. A., & El-Azab, M. H. (2011). Uropathogens causing urinary tract infections in females and their susceptibility to antibiotics. *Uro Today*, 4, 1-7. Retrieved from https://www.urotoday.com/index.php?option=com_dms&view=document&id=185&Itemid=393
- Santiago-Rodriguez, T. M., Ly, M., Bonilla, N., & Pride, D. T. (2015). The human urine virome in association with urinary tract infections. *Frontiers in Microbiology*, 6, 14. doi:10.3389/fmicb.2015.00014
- Satlin, M. J., Jenkins, S. G., & Walsh, T. J. (2014). The global challenge of Carbapenem-resistant Enterobacteriaceae in transplant recipients and patients with hematologic

malignancies. *Clinical Infectious Diseases, Advance Access*, 1-10.

doi:10.1093/cid/ciu052

Schechner, V., Temkin, E., Harbarth, S., Carmeli, Y., & Schwaber M. (2013).

Epidemiological interpretation of studies examining the effect of antibiotic use on resistance. *Clinical Microbiology Reviews*, 26, 289-307.

doi:10.1128/CMR.00001-13

Seibert, P. S., Stridh-Igo, P., & Zimmerman, C. E. (2002). A checklist to facilitate cultural awareness and sensitivity. *Journal of Medical Ethics*, 28, 143-146.

Retrieved from <http://jme.bmj.com/content/medethics/28/3/143.full.pdf>

Shapiro, D. J., Hicks, L. A., Pavia, A. T., & Hersh, A. L. (2013). Antibiotic prescribing for adults in ambulatory care USA, 2007-09. *Journal of Antimicrobial*

Chemotherapy, Advance Access, 1-7. doi:10.1093/jac/dkt301

Shartzner, A., Long, S. K., & Benatar, S. (2015). Health care costs are a barrier to care for many women. Retrieved from <http://hrms.urban.org/briefs/Health-Care-Costs-Are-a-Barrier-to-Care-for-Many-Women.html>

Siek, C. J., Hefner, J. L., Wexler, R., Taylor, C. A., & McAlearney, A. S. (2016). Why do they do that? Looking beyond typical reasons for non-urgent ED use among Medicaid patients. *Patient Experience Journal*, 3, 22-30.

Sillito, V. (2016). Changing prescribing habits is easier said than done. Retrieved from <http://www.pharmaceutical-journal.com/opinion/blogs/changing-prescribing-habits-is-easier-said-than-done/20201297.blog>

- Simon, H. (2012). Urinary tract infection. Retrieved from
<http://www.umm.edu/health/medical/reports/articles/urinary-tract-infection>
- Singanayagam, A., Joshi, P. V., Mallia, P., & Johnston, S. L. (2012). Viruses exacerbating chronic pulmonary disease: the role of immune modulation. *BMC Medicine*, *10*, 27. doi:10.1186/1741-7015-10-27
- Smith, R. A., M'Ikanatha, N. M., & Reed, A. F. (2014). Antibiotic resistance: A primer and a call to action. *Health Communication*, *30*. doi: 10.1080/10410236.2014.943634
- Song, J. W., & Chung, K. C. (2010). Observational studies: Cohort and case-control studies. *Plastic and Reconstructive Surgery*, *126*, 2234-242. doi:10.1097/PRS.0b013e3181f44abc
- Song, X., Quek, R. G. W., Gandra, S. R., Cappell, K. A., Fowler, R., & Cong, Z. (2015). Productivity loss and indirect costs associated with cardiovascular events and related clinical procedures. *BioMed Central Health Services Research*, *15*, 245. doi: 10.1186/s12913-015-0925-x
- Soto, S. M., Smithson, A., Horcajada, J. P., Martinez, J. A., Mensa, J. P., & Vila, J. (2006). Implication of biofilm formation in the persistence of urinary tract infection caused by uropathogenic *Escherichia coli*. *Clinical Microbiology & Infection*, *12*, 1234-1236. Retrieved from
<http://www.clinicalmicrobiologyandinfection.com/article/S1198-743X%2814%2962037-1/pdf>

- SRS Pharmaceuticals, Ltd. (2010). Narrow-spectrum antibiotics: Uses, Advantages, Disadvantages. Retrieved from <http://www.srspharma.com/narrow-spectrum-antibiotics.htm>
- STATA. (n.d.). FAQ. <http://www.stata.com/support/faqs/statistics/compare-levels-of-categorical-variable/>
- Steckler, A., & McLeroy, K. R. (2008). The importance of external validity. *American Journal of Public Health, 98*, 9-10. doi:10.2105/AJPH.2007.126847
- Street, T., & Staros, E. B. (2014). Antimicrobial susceptibility. Retrieved from <http://emedicine.medscape.com/article/2103786-overview>
- Sundqvist, M. (2014). Reversibility of antibiotic resistance. *Upsala Journal of Medical Sciences, 119*, 142-148. doi:10.3109/03009734.2014.903323
- Sydnor, E. R. M., & Perl, T. M. (2011). Hospital epidemiology and infection control in acute-care settings. *Clinical Microbiology Reviews, 24*, 141-173. doi: 10.1128/CMR.00027-10
- Taylor, J., Hafner, M., Yerushalmi, E., Smith, R., Bellasio, J., Vardavas, R., Bienkowska-Gibbs, T.,...Rubin, J. (2014). Estimating the economic costs of antibiotic resistance: Model & results. Retrieved from http://www.rand.org/content/dam/rand/pubs/research_reports/RR900/RR911/RAND_RR911.pdf
- The Pew Charitable Trusts. (2016, May 03). Antibiotic use in outpatient settings: health experts create national targets to reduce unnecessary antibiotic prescriptions. Retrieved from

<http://www.pewtrusts.org/en/research-and-analysis/reports/2016/05/antibiotic-use-in-outpatient-settings>

Thorpe, K. E., Wisniewski, A. C. & Lindsay, G. M. (2009). The burden of chronic disease on business and U.S. competitiveness. Retrieved from

https://www.prevent.org/data/files/News/pfcdalmanac_excerpt.pdf

Thoureen, T., Scott, S., & Best, J. (2015). Urinary tract infection. *Monograph*. Retrieved from <http://www.ahcmedia.com/articles/135127-urinary-tract-infection>

Todar, K. (n.d.). The normal bacterial flora of humans. Retrieved from

http://textbookofbacteriology.net/normalflora_3.html

Trinh, T. D., & Klinker, K. P. (2015). Antimicrobial stewardship in the emergency room.

Infectious Disease Therapy, 4, S39-S50. doi 10.1007/s40121-015-0084-8

Ulleryd, P. (2003). Febrile urinary tract infection in men. *International Journal of*

Antimicrobial Agents, 22 (Suppl), 89-93. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/14527778?dopt=Abstract>

University of Portsmouth. (2012). Advantages and disadvantages of conducting observational research. Retrieved from

[http://compass.port.ac.uk/UoP/file/664e8001-f121-4e5d-aa06-](http://compass.port.ac.uk/UoP/file/664e8001-f121-4e5d-aa06-6c95c797e8af/1/Observations_IMSLRN.zip/page_04.htm)

[6c95c797e8af/1/Observations_IMSLRN.zip/page_04.htm](http://compass.port.ac.uk/UoP/file/664e8001-f121-4e5d-aa06-6c95c797e8af/1/Observations_IMSLRN.zip/page_04.htm)

U.S. Department of Health and Human Services. (2015). HHS action plan to reduce

racial and ethnic health disparities: implementation progress report 2011-2014.

Retrieved from

http://minorityhealth.hhs.gov/assets/pdf/FINAL_HHS_Action_Plan_Progress_Report_11_2_2015.pdf

- Vahadat, S., Hamzehgardeshi, L., Hessam, S., & Hamzehgardeshi, Z. (2014). Patient involvement in health care decision making: A review. *Iranian Red Crescent Medical Journal*, *16*, e12454. doi:10.5812/ircmj.12454
- Vasudevan, R. (2014). Urinary tract infection: An overview of the infection and associated risk factors. *Journal of Microbiology and Experimentation*, *1*, 1-15. doi:10.15406/jmen.2014.01.00008
- Ventola, C. L. (2015). The antibiotic resistance crisis. Part 1: causes and threats. *Pharmacy & Therapeutics*, *40*, 277-283. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/>
- Wagenlehner, F. M. & Naber, K. G. (n.d.). Urinary tract infections: General. Retrieved from <http://www.antimicrobe.org/e4e.asp>
- Walker, T. (2013, August 16). Broader spectrum antibiotics overprescribed in ambulatory settings. [Review of Antibiotic prescribing for adults in ambulatory care in the USA, 2007–09]. *Journal of Antimicrobial Chemotherapy*. Retrieved from <http://drugtopics.modernmedicine.com/drug-topics/content/tags/adam-hersh/broader-spectrum-antibiotics-over-prescribed-ambulatory-settings>
- Whiteside, S. A., Razvi, H., Dave, S., Reid, G., & Burton, J. P. (2015). The microbiome of the urinary tract: A role beyond infection. *Nature Reviews Urology*, *12*, 81-90. doi:10.1038/nrurol.2014.361

- Wilson, M.L., & Gaido, L. (2004). Laboratory diagnosis of urinary tract infections in adult patients. *Clinical Infectious Diseases*, 38, 1150-1158. doi:10.1086/383029
- Wolf, J. (2016). Predicting UTI antibiotic resistance. *American Society for Microbiology*, 16, 30. Retrieved from <https://www.asm.org/index.php/mbiosphere/item/427-predicting-uti-antibiotic-resistance>
- Wolfe, A. J., & Brubaker, L. (2015). "Sterile urine" and the presence of bacteria. *European Urology*, 68, 173-174. Retrieved from <http://www.europeanurology.com/article/S0302-2838%2815%2900206-7/fulltext/sterile-urine-and-the-presence-of-bacteria>
- Woltman, H., Feldstain, A., MacKay, J. C., & Rocci, M. (2012). An introduction to hierarchical linear modeling. *Tutorials in Quantitative Methods in Psychology*, 8, 52-69. doi:10.20982/tqmp.08.1.p052
- Wong, C. K.M., Kung, K., Au-Doung, P. L. W., Ip, M., Lee, N., Fung, A., & Wong, S. Y. S. (2017). Antibiotic resistance rates and physician antibiotic prescription patterns of uncomplicated urinary tract infections in southern Chinese primary care. *PLoS ONE*, 12, e0177266. doi:10.1371/journal.pone.0177266
- Woods, S. S., Schwartz, E., Tuepker, A., Press, N. A., Nazi, K. M., Turvey, C. L., Nichol, W. P. (2013). Patient experiences with full electronic access to health records and clinical notes through the MyHealthVet personal health record pilot: Qualitative study. *Journal of Medical Internet Research*, 15, e65. doi:10.2196/jmir.2356

- World Health Organization. (2011). Safety and Security on the internet: Challenges and advances in member states. Retrieved from http://www.who.int/goe/publications/goe_security_web.pdf
- World Health Organization. (2014). Antibiotic resistance: Global report on surveillance 2014. Retrieved from <http://www.who.int/drugresistance/documents/surveillancereport/en/>
- Yadav, A.K., Singh, S., Kumar, S., Katewa, T., & Kumari, R. (2014). Prevalence and antibiotic resistance pattern of *E. coli* isolated from UTI in tertiary care hospital, Khanpur. *CIBTECH Journal of Microbiology*, 5, 35-39. Retrieved from http://www.cibtech.org/J-Microbiology/PUBLICATIONS/2016/VOL_5_NO_1/06-CJM-008-AMOD-PREVALENCE.pdf
- Yamaya, M. (2012). Virus infection-induced bronchial asthma exacerbation. *Pulmonary Medicine*, 2012, 1-14. doi:10.1155/2012/834826
- Yang, C. J. Chung, Y. C., Chen, T. C., Chang, H. L., Tsai, Y. M., Huang, M. S., Chen, Y. H.,...Lu, P. L. (2013). The impact of inappropriate antibiotics on bacteremia patients in a community hospital in Taiwan: An emphasis on the impact of referral information for cases from a hospital affiliated nursing home. *BMC Infectious Diseases*, 13, 500. doi:10.1186/1471-2334-13-500
- Zowawi, H. M., Harris, P. N. A., Roberts, M. J., Tambyah, P. A., Schembri, M. A., Pezzani, M. D., Williamson, D. A.,...Paterson, D. L. (2015). The emerging threat

of multidrug-resistant gram-negative bacteria in urology. *Nature Reviews*

Urology, 12, 570-584. doi:10.1038/nrurol.2015.199

Zur Wiesch, P. A., Kouyos, R., Engelstadter, J., Regoes, R. R., & Bonhoeffer, S. (2011).

Population biological principles of drug-resistance evolution in infectious disease

income. *The Lancet Infectious Diseases*, 11, 236-247. doi:10.1016/S1473-

3099(10)70264-4