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Self-Medication and Antibiotic Resistance in Rio de Janeiro, Brazil

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Self-Medication and Antibiotic Resistance in Rio de Janeiro, Brazil

by

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Thesis Paper 1:

Self-Medication: A Cause of Global Antibiotic Resistance?

A Review of the Literature

Self-medication, or the use of a medicinal product on a patient's own initiative or on the advice of a pharmacist or lay person (1, 2), is the most widespread and least studied form of illness management in both the Third World and the West (3). Because of structural factors impeding efficient health care delivery in developing nation communities, self-medication is often an individual's first option for disease treatment or prevention.

Self-medication is equally widespread in developed country settings for the treatment of common or minor health problems (4, 5). The frequent and often unrestricted usage of antibiotics in developing country settings, however, has prompted many biomedical observers to call attention to self-medication as a major factor contributing to the global emergence of antibiotic resistance (6, 7).

In Brazil, these calls have become louder and more urgent in past years (8). Despite reasonably good access to the modern technologies and antibiotics needed for successful treatment of infectious disease in many areas of the country, Brazil is still confronted with serious problems related to infectious disease control and containment. Doctors and researchers have become increasingly concerned about the prevalence of antibiotic-resistant microbes, but few studies have rigorously addressed patterns of resistance or provided data to inform antibiotic treatment guidelines in local settings.

Self-medication with antibiotics, which can be purchased at neighborhood pharmacies despite laws prohibiting sale without prescription, is widely believed to be a

major factor contributing to increasing resistance levels in Brazil(8). Yet this belief is based largely on anecdotal evidence and has been only loosely substantiated by a limited number of studies carried out during the past three decades. Just how common is self-medication with antibiotics in Brazil? How accurate or anecdotal are assumptions about who is self-medicating and why? Is it justified to assume that self-medication practices are one of the primary factors contributing to antibiotic resistance? This paper will examine existing literature on self-medication with antibiotics in Brazil in the context of structural, social, and cultural issues influencing antibiotic usage in developing countries globally. It will also review existing data from community-level studies in Brazil and elsewhere on the prevalence of self-medication with antibiotics and the factors influencing this practice. Finally, it will examine the ways in which existing literature has attempted to answer these questions in order to direct and inform future studies on this topic.

Antibiotic Resistance: Significance and Consequences

Antibiotics play a critical role in decreasing infectious disease-related morbidity and mortality in developing countries. Bacterial diseases including pneumonia, diarrheal disease, skin and soft tissue infection, enteric fevers, meningitis, and tuberculosis cause a significant percentage of illness and deaths in the developing world (6). Antibiotic treatment, along with improvements in sanitation, housing, nutrition, and immunization programs, has led to a dramatic decrease in these deaths during the last half of the 20th century (7). Widespread reports of the emergence and global spread of antibiotic-resistant bacteria are thus a compelling cause for concern.

Resistance to antibiotics is emerging most rapidly among the bacteria which cause the majority of human disease. Some notable examples include penicillin-resistant *Streptococcus pneumoniae*, vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, multi-drug resistant (MDR) salmonellae, and MDR tuberculosis (MDRTB). Infections caused by resistant microbes fail to respond to treatment with first-line drugs. Patients with these infections remain ill for longer, have an increased risk of mortality, and expose the general population to resistant strains during a longer period of infectivity (7).

When resistance-related treatment failures occur, second- and third-line drugs must be substituted for standard first-line treatments. These drugs are generally much more expensive and often are also increasingly toxic. For example, the medicines needed to treat MDRTB are more than one hundred times more expensive than the standard first-line drugs (7). In many developing countries, the high costs of these replacement drugs is prohibitive.

1) Numerous studies testify to the common and often unrestricted usage of antibiotics in developing countries, where most medicines can be easily purchased in pharmacies without a medical prescription (1, 3, 9-15). A report commissioned by the National Institutes of Health (NIH) (16) claims that more money is spent on antibiotics in these countries than on any other class of therapeutic agent. Numerous studies also claim that antibiotics are frequently employed in self-initiated therapy without health professional oversight, often for non-bacterial infections, and often with incorrect dosing (1, 2, 10, 12, 14, 17-21). This "irrational" antibiotic usage has prompted the World Health Organization (WHO)

to call attention to self-medication as a major factor leading to the worldwide emergence of antibiotic resistance (7).

The WHO (7) also cites a number of concurrent global trends which have accelerated the development of resistant microbes during the past few decades:

1) urbanization, leading to overcrowding and unsanitary living conditions for millions of people in developing countries, facilitates the spread of diseases such as typhoid, tuberculosis, and respiratory infections;
2) pollution, environmental degradation, and changing weather patterns affect the incidence and distribution of infectious diseases, particularly those which are spread by insects and other vectors (eg, malaria);
3) the Acquired Immunodeficiency Syndrome (AIDS) epidemic has significantly increased the number of immunocompromised individuals who are at greater risk of contracting often previously rare infections;
4) diseases like malaria and tuberculosis, although treatable and preventable with inexpensive medications, continue to cause high-level morbidity and mortality in developing country settings;
5) the rapid globalization of trade has increased the speed and facility with which infectious diseases and resistant microbes travel between countries and continents; and,
6) antimicrobial use in animal food sources, as growth promoters or preventive agents, encourages the development of resistant microbes and their transmission from animals to humans.

Community-level antibiotic usage, which involves both prescribing by medical professional and self-prescribing by individuals, is situated amidst these larger global and structural issues.

The Microbiology of Resistance

The process by which microbes become "resistant" to antimicrobials is a natural biological phenomenon which can be accelerated by human practice (7). For any type of bacteria, there exists a "spontaneous frequency of resistance" to a given antimicrobial. This is the number of bacilli which, via mutation, become resistant to that drug before directly encountering it. For example, the spontaneous frequency of resistance of *Mycobacterium tuberculosis* to isoniazid (INH), the most commonly used medicine for the treatment of tuberculosis, is about 1 in 1 million. As a pulmonary tuberculosis cavitary lesion can contain up to 1 billion bacilli, there could theoretically be 1000 INH-resistant bugs before treatment with INH is begun. The use of INH to treat tuberculosis exerts a selective pressure on the mycobacteria: resistant microbes survive and non-resistant microbes die. The microbes which adapt and survive carry genes for resistance, which are passed to successive generations of mycobacteria during replication or conjugation. Resistance to a single drug can spread efficiently through a population of bacteria because of their rapid rate of multiplication.

Multiple drug therapy is thus employed to treat diseases like tuberculosis, where there exists an increased probability of resistance with single-drug therapy. Single-drug therapy with INH, for example, would naturally select for drug-resistant strains. But if two or more drugs are given concurrently, the odds of a single bacillus being resistant to

both medicines would be the square of the original spontaneous frequency of resistance, 1 in 10^{12}, which is several orders of magnitude more than the number of infecting organisms. This illlustrates that the development of multi-drug resistant bacteria is iatrogenic in nature: both health professional practice (eg, prescribing the wrong medications, or prescribing medications that will not be available for the entire course of treatment), and patient practice (eg, failure to take the prescribed medications consistently, with correct timing and dosage), exert the selective pressure for the evolution of multi-drug resistant strains.

The most commonly heard critique surrounding the "misuse" of antibiotics relates to overprescribing. However, underuse, as a result of lack of access to antibiotics, is also a significant factor in creating resistance. This is especially relevant in developing country settings where access to drugs is often sporadic. For example, Farmer (22) notes that half of the national tuberculosis programs surveyed in 1992 reported "drug stock-outs" during the previous years (23). Particularly in treating illnesses like tuberculosis, which require uninterrupted medication courses of six to eight months, courses of intermittent and poorly conceived therapy can create the selective pressure for the emergence of antibiotic-resistant microbes.

What is Self-Medication?

"Self-medication" refers to the use of a medicinal product by a consumer, without the advice or prescription of a health care professional, to treat self-recognized disorders or symptoms (1, 2). The term encompasses a wide range of modalities and practices, including purchase of medicines without a prescription, reuse of old prescriptions, and

sharing medicines with friends or family in the home. In Latin America, among other places, it has been widely documented that self-medication [Portuguese: *auto-medicação*; Spanish: *auto-medicación*] is often a social process, involving relatives, friends, and non-physician health specialists (24).

How common are these different modalities of self-medication? One team of Brazilian researchers (25) in Minas Gerais state found that the acquisition of medications without a prescription was most common. Another Brazilian researcher, Barros (26), found that 74% of self-medication among his participants in São Paulo state, Brazil involved simply refilling old prescriptions. This practice helps individuals save money on often costly physician consults. Reuse of old prescriptions is possible in most developing country settings because prescription hard copies are returned to patients after medication purchase; this is distinct from usual practice in developed country settings where pharmacists retain prescriptions. Sharing medicines with friends or family at home or in the community is also perceived as economically advantageous (19) because of the cost-sharing aspect.

Storing leftover medicines for future use in the home can be a strategy to deal with unforeseen health problems, especially when access to medical care is difficult (11). Although the existence of leftover medications may be a consequence of poor compliance with prior antibiotic therapy (eg, discontinuation of therapy before completion of the course), it may also be influenced by packaging and dispensing (27). In many countries, including Brazil, antibiotics are pre-packaged and sold in quantities not always consistent with the number of pills prescribed by health professionals. This frequently results in leftover medication even after full adherence to a prescribed regimen.

Self-medication can also include use of biomedicines according to ideas different from those which motivated the original prescription. Haak (11), in his study of medication consumption patterns among individuals living in two rural communities in Bahia state, Brazil, reported that the mother of one family proudly showed him her own "domestic pharmacy," including chloramphenicol[1], tetracyclines, and steroid preparations; all had been originally prescribed by a physician but the mother was using them according to distinct ideas of illness causality and treatment.

Concern about inappropriate or inadequate usage of antibiotics by self-medicating patients is common in the literature. Ferguson (18) reports that in El Salvador, the most frequent number of pills prescribed or purchased was four, a number with ritual significance in the community. Justice's research in Nepal (28) demonstrated that non-adherence may reflect a cultural belief that drug use should be stopped when symptoms subside. In northern Nigeria, Michel (29) reports that he met a man with a violent urticarial reaction who had been taking dapsone, an antimicrobial generally used in the treatment of leprosy, because it "made him feel good and increased his sexual potency." These authors all report that antibiotics were readily available at weekly markets and pharmacies, and that purchase without prescription was virtually unrestricted.

Structural Issues Influencing Usage of Antibiotics in Developing Countries

Individual self-medication practice and other general trends in antibiotic usage in developing countries must be examined in light of structural problems with health care

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[1] Chloramphenicol is a broad-spectrum antibiotic that causes a reversible dose-dependent bone marrow hypoplasia and rare, irreversible dose-independent aplastic anemia (1 in 30,000 cases) that is sometimes fatal. In neonates, concentration of chloramphenicol reaches toxic levels more readily and less predictably, sometimes leading to cardiovascular collapse ("grey baby syndrome"); it is therefore only given to babies in life-saving cases (eg., typhoid fever). It is never indicated for minor infections and should only be given systemically when there is no suitable alternative.

delivery. Key issues influencing antibiotic usage include the presence or lack of functioning and adequate health care facilities, the availability and accessibility of medicines (6), and physician prescribing practice.

Malfunctioning Health Care Infrastructure

Evidence suggests that self-medication often serves as a substitute for formal health care when the formal health care sector is viewed as inaccessible, unaffordable, or unsatisfactory (19, 25). Both limited access to health care professionals and frequent medicine shortages in state or public health care facilities stimulate the creation of an informal market for antibiotics and other medications (13, 30). Some studies have shown a clear negative association between self-medication and use of formal sector health care services (19). Others note that in some parts of the developing world, pharmacies and non-allopathic medical systems are the only source of medical care available to the poor (31). Scheper-Hughes, a medical anthropologist who lived in rural northeastern Brazil for many years, maintains that pharmacies are the only accessible and dependable primary health care source for much of Brazil's rural population (32).

Many authors note, however, that even where health facilities are reasonably adequate and easily accessible, the prevalence of self-medication remains high (12, 33). For example, in one study on self-medication in Ghana (15), study participants lived within two kilometers of the mission hospital. This, according to the study's authors, indicates that they are a "medically privileged population." Nevertheless, 60% of the population claimed that they would self-medicate before attempting to seek health care in the formal sector. Likewise, a Brazilian study (25) demonstrated that many interviewees

reported seeking medical care only after self-medication failed to resolve their health concerns. Public hospitals and clinics, even when relatively accessible in terms of location and distance, are often viewed as a "last resort" for health care, used only for illnesses perceived as serious or persistent, or after the failure of self-medication or the advice of pharmacists or traditional healers (28, 34).

The Role of Pharmacies

Public hospitals and clinics are commonly viewed as a "last resort" for treatment even when geographically proximate because pharmacies are felt to have a greater social and geographical proximity to patients. This is particularly true in large urban centers where multiple different pharmacies can often be found on the same street or block (3, 18, 30). Consults with pharmacy attendants take considerably less time than consults with physicians in government clinics and hospitals (18). Pharmacy treatment is also convenient because it saves patients money, the opportunity cost of waiting to be seen by a doctor, and the necessity of undergoing a physical examination as a prerequisite for receiving a prescription. Much evidence also suggests that patients believe that treatment in pharmacies leads to good health outcomes (12, 18, 35).

Studies in several developing countries have documented that pharmacies are not only places where medicines are bought and sold, but also sites where health information and advice on medical problems is solicited, often from untrained attendants or pharmacy assistants playing the role of "physicians" (12, 13, 18, 20, 35, 36). Most developing countries require pharmacies to employ at least one trained, licensed pharmacist, but this person is not necessarily required to be present during business hours. Haak (11), for

example, reports that the daughter of the popular town pharmacist in a village in rural Bahia state, Brazil, was "responsible" for three pharmacies in the area. Her permanent residence, however, was in Vitória, the capital of the neighboring state of Espírito Santo, a distance of over 500 kilometers away. During the course of Haak's field work, inspecting authorities frequently shut down pharmacy operations due to extended absence of the supervising pharmacist. A few days after each visit, however, all pharmacies would open again and resume business as usual.

Multiple studies in Brazil and elsewhere affirm that untrained, often very young, assistant pharmacists, clerks, and family members are primarily responsible for transactions with clients. Retailer knowledge thus varies, as does the quantity and quality of information regarding antibiotic use transmitted to clients (3, 6, 37-39). A National Institutes of Health (NIH)-commissioned task force on antibiotic usage in developing countries (6) claimed that this is chiefly of concern in countries or areas where a large proportion of the population is pre-literate and dependent on health care providers for explanations of medication usage. Particularly worrisome, then, are reports that many multinational pharmaceutical firms remove package inserts containing information about drug indications, contraindications, dosing, and adverse effects when selling prescription drugs sold to local pharmacies (18). Pharmaceutical companies claim that this practice discourages over-the-counter sales of these medications and eliminates packaging expenses to consumers (15); Ferguson (18) affirms that this practice merely increases dependency on the pharmacy representatives, themselves with low levels of medical training, to relay crucial information regarding medication indications and usage.

Promotional Activities of Pharmaceutical Companies

Policymakers and anthropologists express concern about the role of pharmaceutical companies in promoting usage of antibiotics and other medicines in developing countries. The ratio of pharmaceutical representatives to clinicians in the United States is approximately 1:10, whereas Brazil and Guatemala have the lowest ratio worldwide, with one pharmaceutical representative for every three clinicians (6). Ngokwey (40) reports that most medical consultants she observed in Brazil were interrupted by pharmaceutical representatives during patient consults. Van der Geest (13) suggests that western pharmaceuticals are transnational products no different than Coca-Cola® in that they are offered for sale everywhere in the world, usually without professional medical supervision.

An NIH-commissioned task force estimating worldwide antibiotic usage found dramatic variations in availability of antibiotics between countries (16). Tetracyclines were most common in Mozambique, the Philippines, and India; broad-spectrum penicillins dominated the market in Korea, and trimethoprim-sulfamethoxazole (TMP-SMX) was most frequently found in Chile. The authors suggest that antibiotic availability in these countries, largely determined by the activities of pharmaceutical companies, dictates prescribing practice regardless of biomedical indications.

Ferguson (18) found that pharmacists who purchased their stock from pharmaceutical firms instead of wholesale distributors received more expensive medicines and were often given overstocks of certain profitable drugs. He claims that pharmacists' prescribing patterns are thus influenced by drug supplier pressures and economic motives instead of medically sound indications for prescription. Employment

practices within pharmacies can accentuate this problem: pharmacy clerk salaries often correspond to what they are able to sell, which provides further incentive for the sale of medications with lucrative profit margins (11).

The Role of Health Care Professionals

Multiple studies have confirmed that physicians in both developed and developing countries tend to overprescribe antibiotics. Antibiotics are given to patients when they are not indicated (eg, viral infections), and broad-spectrum antibiotics are prescribed when more targeted drugs are indicated. One retrospective study (41) in the United States showed that approximately 2 million of the 6.5 million antibiotic prescriptions given to children in 1992 were written for viral illnesses. Another (42) reported that prescribing behavior related to fluoroquinolones was inappropriate in 81% of cases. Vinson et al (43) also found that when under perceived "pressure" or "expectation" from patients or parents, a large group of American physicians were two times more likely to diagnose a cough as bronchitis and prescribe antibiotics.

In developing countries, it should be emphasized that health care professionals are often working under conditions of extreme poverty, lack of resources, and social and professional isolation. Many of the physicians and others who participate in studies on antibiotic use are "only too aware of the inadequacies of their knowledge and practice" (20). The following section is an attempt to review the existing literature on the ways in which health professionals influence antibiotic usage patterns in developing countries. This information is presented, however, without the intent to make overgeneralized professional and moral judgments on individual practitioners working in these settings.

Many studies in developing countries claim that antibiotic overprescribing by physicians and other health care providers in the absence of appropriate medical indications is a major problem impacting both overall antibiotic usage and patient self-medication behavior. Lack of opportunity for follow-up with patients, diagnostic uncertainty, and fear of litigation are a few of the reasons frequently mentioned in the literature to explain this overprescribing (7, 44, 45). Diverse surveys in developing countries have shown that antibiotics are prescribed in 35-60% of clinical visits, though they are appropriate in less than 20% (46). A comparative analysis of studies of health care professional prescribing practice in twelve developing countries, published by the Lancet in 1993 (47), demonstrated that the prescription of medicines was almost invariably part of a clinical visit. An "unnecessarily high proportion" of patients (from 1/4 to almost 2/3) received antibiotics.

Other researchers have shown that self-medication is both implicitly and explicitly encouraged by health care professionals, who see it as a way to reduce the burden on the formal health care system. In a qualitative study in Brazil, ten participants recounted situations in which physicians recommended that they use medications without supervision (25). The practice of reissuing prescriptions to patients without new questioning or exam may also be interpreted by patients as a tacit approval of self-medication (25).

Overprescribing by health care professionals can lead to erratic purchasing of medications when poor patients are unable to buy all of the medications on a prescription and choose arbitrarily (eg., the first on the list, the cheapest, the one that happens to be in stock). Haak(11), for example, reports that because of lack of funds, a doctor's

prescription for an antibiotic and an antipyretic sometimes resulted in purchase of only the less costly antipyretic or a partial course of the antibiotic.

There is also evidence to suggest that physician prescribing habits strongly influence the prescribing habits of other groups of individuals in the community (13, 48, 49). Hardon's comparative study of prescribing practice in the Philippines (49) showed that physician prescribing practice encouraged the use of expensive, often dangerous therapies among patients who self-medicated with antibiotics for upper respiratory infections and childhood diarrhea. A study in Iran (44) reported that pharmacy attendants imitated physician prescribing patterns when selling antibiotics for a variety of illnesses. Medical students may also observe arbitrary use of antibiotics by their preceptors and mimic this behavior in their own practices (6). Some authors attribute this situation to structural problems with health professional education and raise concerns about the highly variable quality of medical education in developing countries. The NIH-commissioned task force was "distressed by the frequently inadequate preparation of medical students in basic knowledge and skills in bacteriology, diagnosis of infectious diseases, and use of antimicrobial therapy" (6).

Many authors also suggest that non-coherent physician/patient explanatory models of disease, or lack of dialogue about ideas of illness causation and treatment, lead patients to seek alternative sources of health care (50). When differences between medical and community explanatory models are not resolved or even addressed during consultations, patients may be more likely to feel that their expectations have not been met and seek treatment from other sources (25). Particularly in Brazil and other

countries with a dramatically unequal income distribution[2], enormous differences in socioeconomic class often exist between physicians and patients. These differences in cultural and social background may contribute to markedly different notions of disease causation, diagnosis, and treatment (50). Michel (29) states that physicians do not address patient ideas about illness and medications because they are simply unaware that these ideas exist. Nations' data (34) suggest that doctors are aware of patients' explanatory models of illness, but fail to acknowledge them during consults or take them into account when developing treatment plans. Justice (28) claims that physicians inadequately communicate with their patients because they believe that their patients will not be able to comprehend the information they are given.

Pharmacy workers, on the other hand, often have closer social and cultural ties with community members. While it can be difficult for patients to develop meaningful relationships with physicians working in overburdened public or government health facilities, patients may be more easily able to form trusting, long-term relationships with community pharmacists. This increases patient confidence in pharmacist recommendations and leads to a greater willingness on the part of community members to seek advice and care for potentially "shameful" or embarrassing conditions (eg, sexually transmitted diseases) (30). Pharmacists generally explain medications and illness in terms of lay medical concepts in order to reduce communication barriers(18). Many authors also report that relations of friendship between consumers and pharmacists facilitate the purchase of medications without physician prescription (15, 25, 51).

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[2] Brazil consistently ranks at the very bottom of a list of countries ranked in terms of income inequality measured by the Gini coefficient (On the 2003 World Bank World Development Index, Brazil ranked 170 out of 175 countries). Latin America has more income inequality than any other global region, and Brazil consistently ranks below all other countries in that region.

Cultural Beliefs and Preferences Supporting Antibiotic Use

Again, it should first be emphasized that only a handful of well-designed, systematic studies attempting to document people's ideas and practices with regard to use of antibiotics and other Western pharmaceuticals have actually been carried out in developing countries. However, there is no paucity of literature detailing the "dangerous" and "irrational" use of antibiotics by individuals (3) and expounding on the factors which contribute to this practice. This review is therefore presented with a caveat: explanations for the "unhealthy cycle" of overprescription by health workers and excessive consumption by patients are undoubtedly varied and complex, and differ between local settings within and across countries.

Much of the existing literature on this topic is filled with somewhat alarmist and overgeneralized statements regarding the "cultural beliefs" which support antibiotic use, eg: "there is an "almost universal desire and demand for drugs in developing countries" (6); "health, it has been argued, is becoming increasingly pharmaceuticalized and commodified as more and more people conveniently 'reach for the pill' at the first sign of ill health" (12); "antibiotics are viewed as wonder drugs capable of healing a wide variety of illnesses ranging from gastrointestinal disease to headaches" (6); the practice of medicine in many developing country settings is dominated by a "prevailing 'pill culture'" (1). Beyond these frequently heard assertions, there are two primary discussions.

The first centers around the notion that antibiotics and other pills provide a concreteness to the physician-patient encounter, providing patients and health workers

with a tangible way to address health and illness. Prescribing thus becomes a "social act" (13) which tangibly demonstrates the doctor's concern for the patient. One author (3) claims that the prescription of broad-spectrum antibiotics has become the main medical act of many consultations because of uncertainty about diagnosis, particularly in settings where diagnostic technologies or laboratories are limited or non-existent.

Medication, as a powerful symbol for health (25), also becomes a proxy for the more abstract healing that can take place in a meaningful relationship between a health worker and patient. Limited time in the clinical encounter is a preoccupation in both developing and developed countries. Medicines, in this setting, can be seen as an effective device for "parceling out the limited time a physician can allot to a patient" (13) As van der Geest (13) adeptly points out in an article on the anthropology of pharmaceuticals, it is generally easier to satisfy patients with drugs than with words.

The centrality of medication prescriptions in consultations in Brazil is highlighted in a sketch of a popular comedy show on prime-time television (52): One of the actors is sick. His friends rush him to a doctor's office. "What do you have? Do you have a headache?" the doctor asks. "Let us see…a headache…Do I have a headache?" the patient asks his friends. "But how would we know?" one of them questions. "Have I asked you for medicine lately?" the patient replies. Ngokwey (40), citing this sketch in her article on individuals' and doctors' remedies in a large urban center in Bahia state, notes that it underscores both the "social" aspects of self-medication, and the notion that remedies act as a substitute for diagnosis and the more intangible aspects of a healing encounter.

The second prominent discussion in the literature revolves around the idea that there is often an idealization [Portuguese: *super-valorização]* of modern pharmaceuticals in many developing nation settings. In one study in southern Brazil (14), 46.5% of participants stated that modern pharmaceuticals were the only legitimate medical treatment. Another study in northeastern Brazil (40) demonstrated that antibiotics were considered "good for anything" remedies. They were distinguished based on their perceived "strength or weakness" rather than by specificity of action. For example, Tetrex®, a very popular brand name formulation of tetracycline easily purchased in most Brazilian pharmacies, was used for ailments as diverse as colds, headache, cough, and toothache, because it is presumed to be strong, rapid, and safe. Half of Haak's (11) study participants in two rural villages in southern Bahia state reported that their choice of treatment for health problems was "modern medicines only." Approximately two-thirds of village residents believed that sickness could not improve without the use of allopathic medicines. People also commonly believed that there was a positive association between the number of medicines utilized and the speed and quality of a patient's recovery. Some villagers, upon his introduction and explanation of the study, apologized for not using enough modern medicines, stating that they already knew they should be using more. Significantly, Haak reports that infants were treated with drugs, particularly antibiotics, most frequently and intensively of all.

Many authors report that this idealization of medicines is particularly harmful in poor areas, where people may not have enough money to buy food for themselves and their children, but believe that modern pharmaceuticals are a prerequisite for health. Michel(29) reports that many poor families in Nigeria spend as much money purchasing

both traditional and modern medications as food. Scheper-Hughes (32), writing of the severe hunger in rural northeastern Brazil, explains: "In visiting door to door to inquire about medications currently in use, I came to think of my Alto friends as 'eating' and 'drinking' their drugs as daily requirements rather like fuel and food." Haak (11) concurs with these reports; many village participants in his study commented that life there was "not healthy," and that because people do not have the money for good food and hygiene, they are obliged to "make life bearable" through the utilization of modern pharmaceuticals.

As a concluding note, Greenhalgh (20), in her study on self-medication and antibiotic usage in India, notes that many patients have grown to overvalue modern pharmaceuticals partially because many physicians uphold the "placebo effect" as an excuse for prescribing unnecessary drugs. Her argument about the ethical implications of this practice is insightful:

> The patient expects, and has faith in, the pills prescribed (and in injections even more so), therefore the placebo effect is high, therefore it is worth prescribing the drug. In addition, if one does not prescribe, the patient either shops around for a doctor who will, or takes his or her complaint to a quack. There is some truth to the argument for the individual case in the short term, and it is difficult to blame the doctor on the spot for responding to the (perceived) immediate needs of the patient and the community. But one cannot ignore the long term effects (and the ethical implications) of encouraging a poorly educated population to develop blind faith in the infallibility of modern medicine and the magical properties of prescribed pills. Placebo prescribing, even of 'safe' drugs, is controversial even when the patient (or the country's health service) can afford them. In India, people who are too poor to buy rice are being led to believe that they need a cough mixture for every cough, an antibiotic for every sore throat, and a tranquilizer to solve the problems of everyday life." (p. 316)

Global Use of Antibiotics: A Literature Review

The following section is an attempt to compile the information coming out of isolated studies on self-medication and antibiotic utilization in various developing

countries over the last three decades. This review includes only articles written in English and included in the National Library of Medicine's PubMed database. The majority of the articles which appear repeatedly in the existing literature on self-medication and antibiotic utilization are summarized here. The literature is limited, particularly with regard to well-designed community-based studies, and the majority of the frequently cited studies were written two decades ago. The following section will include both data on self-medication with antibiotics as well as information relating to health professional prescribing practice, and prescribing practice in pharmacies.

Latin America

A study coordinated by the WHO and the Universitat Autònoma de Barcelona surveyed 242 pharmacies in 11 study areas of 6 countries (Brazil, Chile, Argentina, Colombia, Costa Rica, Nicaragua) (2). The study authors found that antibiotics were the second most-frequently purchased class of drugs, making up 7.4% of purchases. Only analgesics were more frequently purchased (16.8%). The authors considered these to be worrisome findings. However, there were large variations between countries. Systemic antibiotics represented approximately 15% of all requested medications in Nicaragua and Chile, but only 6% of purchases in Brazil. This was the lowest country-specific rate (2).

Another multi-country study (53) designed to compare the availability of antibiotics in Central America with the 16 antibiotics on the WHO Essential Drugs List[3] found that only 2 of 8 countries (Panama and the Dominican Republic) sold less than 200

[3] In 1977, the WHO published a list of "essential" drugs to provide the basis for rational drug utilization in developing countries. Only 16 antibiotics were included. This list was intended to aid developing countries in choosing a limited number of inexpensive, high quality drugs.

antibiotic drug products; at least a third of these were drug combinations "of questionable value" according to the authors. Medicines were easily obtained without a prescription.

Other studies have reported the unrestricted dispensing of combination antibiotics without physician or health worker consult and a general "overuse and abuse" of antibiotics. One study in Guatemala (36) found that antibiotics and injections of all kinds were given and prescribed freely by both traditional and biomedical practitioners.

Calva (10) investigated the pattern of antibiotic use in a periurban community in Mexico City in 1996, via 1659 household visit interviews and a survey of six local drugstores. The authors found that antibiotics were the majority (29%) of drug sales, and that antibiotics were most commonly purchased to treat acute respiratory tract ailments and gastroenteritis, for which they were not indicated. Self-medication and drug purchases without medical prescription were "common" but the majority of antibiotics were, in fact, prescribed by a physician. However, Calva states that 72% of antibiotics were purchased in insufficient therapeutic quantities, and suggests that these data point to misuse.

A study in Ecuador (24) demonstrated the high prevalence of potentially hazardous antibiotics readily available for purchase in pharmacies, and the frequent use of contraindicated antibiotics in children. For example, the authors found that a common folk formula for treating childhood diarrhea consisted of one capsule of terramycina[4] and herbal tea. Combinations of tetracycline and chloramphenicol were commonly purchased without prescription. Clioquinol[5] was being sold every day at both pharmacies surveyed

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[4] Terramycina is a tetracycline; tetracyclines are contraindicated for children under the age of 8 because of the risk of tooth discoloration.

[5] Clioquinol was withdrawn from the world market after the manufacturer was ordered in court to pay almost 500 million dollars in damages to thousands of people who suffered paralysis or blindness from use.

by the authors, and without any information given about potential adverse effects. Kanamycin[6] was sold to someone once every few hours at one of the two pharmacies, and combinations of tetracycline with dipyrone[7] were also frequently purchased.

South Asia

At least two well-designed studies investigating self-medication and antibiotic utilization have been carried out in India (12, 20). Authors report that while there is no shortage of laws to regulate pharmaceutical sale and consumption, numerous loopholes, lack of enforcement from the legal system, and the persistent promotional activities of pharmaceutical companies create a situation in which prescription medications are freely available for purchase without prescription (12, 20). In urban India, pharmacies are prolific and competition so intense that "agents" are hired to persuade patients discharged from public and private to patronize particular shops (12). One author (12) notes that three-quarters of pharmacies opened over the last decade are located in slums and low-income areas, where relatively low amounts of venture capital are required. Medications including antibiotics and a limited number of scheduled drugs are also available for purchase at roadside stalls (20).

Shopkeepers evade legal pharmacy licensing requirements by employing "signature pharmacists" who sign paperwork but are not physically present during hours of operation. Even when present, pharmacists rarely assist customers; Kamat (12) states that 99% of witnessed transactions were managed by untrained counter assistants. As has been reported in other countries, the authors of these studies affirm that much of these

[6] Kanamycin has been shown to cause rare but serious ototoxicity and nephrotoxicity with long-term use.
[7] Dipyrone is no longer available in the United States because it was shown to cause, rarely, agranulocytosis.

assistants' knowledge comes from discussions with pharmaceutical company salespeople. When queried by the study team, employees claimed extensive knowledge about a variety of drugs, but were unable to provide any information about adverse effects or contraindications (12).

Both Kamat (12) and Greenhalgh (20) report that antibiotics are freely available over-the-counter. Greenhalgh states that customers purchasing antibiotics for self-medication typically present a small scrap of paper with the handwritten name of a medication; she conjectures that this name was copied at some point from a doctor's prescription. This same scrap of paper is often reused daily for years. Antibiotics accounted for approximately 9% of medications purchased in Kamat's study and 13% in Greenhalgh's. Both authors state that pharmacists rarely refused to dispense prescription-only medications without prescriptions.

The purchase of antibiotics in "loose" form (eg., buying 1 or 2 pills, or one small strip) was found to be common practice in both studies. Almost all pharmacists stated that customers commonly request loose medications because antibiotics are expensive and many customers are unable to buy an entire course of antibiotics in a single transaction. Some study participants also stated that they preferred to purchase only part of the prescription in order to test the efficacy of the prescribed antibiotic (12). The most popular antibiotic purchased for self-medication was chloramphenicol and 71% of patients bought less than a day's supply (20).

Socioeconomic status was associated with self-medication behavior in Kamat's study: 60% of participants in the high socioeconomic status group purchased medications without prescription as compared with 27% in the middle socioeconomic status group

and 40% in the low socioeconomic status group. The proportion of customers buying scheduled drugs over-the-counter was much greater in the high-income group, and greater in the middle-income group as compared with the low-income group. Kamat's interviews with clients affirmed that individuals from high socioeconomic strata were more likely to self-diagnose, self-prescribe, and self-medicate than those in the lower and middle socioeconomic groups.

Studies in India in the 1970s and 1980s showed that antibiotic resistance was already becoming a significant problem. A 1978 study in Mumbai (54) found strains of multi-drug resistant *Escherichia coli (E. coli)* in 28% of healthy subjects and noted that emerging resistance to gentamicin had also been documented. In a mid-1980s dysentery epidemic in West Bengal, in which over 3500 people died, the responsible bacterial strains were resistant to streptomycin, tetracycline, chloramphenicol, neomycin, kanamycin, and ampicillin (55).

Elsewhere in South Asia, data on self-medication from Sri Lanka suggests that literate individuals self-medicated much more frequently than those who were not literate. This was not specific to treatment with antibiotics (33). Many physicians in one study (45) prescribed antibiotics even after clearly stating that a disease was of viral origin. In this study, tetracycline was given to one-third of patients for illnesses ranging from chronic asthma and bronchiectasis to acute and chronic bronchitis, lung infections, pharyngitis, viral fever, and infected wounds. Reports of tetracycline-resistance among most of the common pathogenic bacteria at the outpatient center of a major hospital (56) imply that this drug should not generally be used for first-line antimicrobial treatment.

Nevertheless, practitioners interviewed ranked it as one of the two most useful antibiotics (45).

Middle East

One study (44) in Iran surveyed 24 pharmacies in Shiraz and showed that 18 regularly prescribed antibiotics for "sore throat," while 6 prescribed lozenges. 20 of 24 prescribed antiamoebics or antibiotics for diarrhea.

Beckerleg et al. (57) claim that health workers in the Gaza Strip have become increasingly concerned about antibiotic resistance as a result of physician overprescribing and "incorrect use" among poorer members of the community, who reportedly self-medicate after seeking advice from pharmacy staff. The authors also state, as was seen in India, that many people buy only partial courses of antibiotics due to financial constraints. 25% of clients purchasing antibiotics from a pharmacy in the Jabalia refugee camp (situated opposite the United Nations Relief and Works Agency (UNRWA)) did not buy a full course of antibiotics.

Southeast Asia

One study from the Philippines (49) reports numerous similarities between physician prescribing practice and patient self-medication practice, and notes that many common antibiotic utilization practices were "harmful." Anti-diarrheal agents containing antibiotics were utilized as first-line treatment by physicians treating simple childhood diarrhea, and likewise, by mothers treating their children without health professional advice. These agents are generally considered unnecessary. Alarmingly, all therapies

used were considered unsuitable for common childhood illness. The most commonly utilized agents contained combinations of streptomycin[8], chloramphenicol, polymyxin[9], furazolidone[10], and neomycin[11] with other medications. Single compound antibiotics were third-choice therapy among both physicians and those choosing to self-medicate, after oral rehydration solution (ORS).

Africa

One study in Nigeria (35) found that the most frequent treatment given by health care providers for any health problem was injection or oral antibiotics. 35% of all treatment included an antibiotic. Michel (29), a researcher in a Nigerian rural health program, commented that African patients whose concerns have resolved after antibiotic use commonly ask for more of the same medicine to ensure a continuing state of good health. He states that these patients "will not readily accept the advice that good food or some other action will be more beneficial at much lower cost," and that traditional healers or private practitioners are generally willing to comply with these requests.

In Ghana, only 32% of pharmacists in a study (15) knew the correct indications for the antibiotics they were prescribing. Chloramphenicol was a commonly prescribed drug, and was often utilized by opening the capsule and sprinkling the medicine onto open wounds. Ampicillin was consistently recommended for menstrual cramps. The authors speculate this may result from community beliefs that blood should be

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[8] Streptomycin is only indicated for serious infections such as tuberculosis and endocarditis because of the risk of adverse effects, and because it has been demonstrated that resistance emerges rapidly.
[9] Oral administration of polymyxin is known to lead to adverse effects including diarrhea and vomiting.
[10] Furazolidone is known to cause intestinal problems, fever, and skin disorders, and is only indicated in serious infections such as typhoid fever and dysentery. It is contraindicated for children under the age of three.
[11] Neomycin in oral administration formulation had been banned for more than five years in the Philippines when this study was carried out, but the drug was still available in pharmacies and commonly utilized in self-medication.

replenished with red medications during menstruation; in this area, ampicillin was commonly sold in capsules with red and black casing.

Multiple trends can be observed from the results of these studies. In all studies, antibiotics were easily purchased without a medical prescription, and were frequently purchased in insufficient therapeutic quantities. Many drug combinations being sold were of questionable medical value, and the sale of hazardous antibiotics was common. Possibly most troubling is the fact that in many cases, these medications were bought to treat infants and children for illnesses in which antibiotics are generally not indicated. In most regions, there was evidence that physicians or pharmacies prescribed antibiotics when they were not indicated. Finally, in South Asia, studies showed that there was a positive correlation between socioeconomic status and likelihood of self-diagnosis, self-prescription, and self-treatment.

A recent global meta-analysis (27) on antibiotic compliance and leftover antibiotic use by geographical region demonstrated that at least one-third of patients did not complete prescribed courses of antibiotics (it is worth noting that the lowest compliance rates were 57.4% in North America and 54.3% in Latin America). Additionally, between 17% (North America) and 31% (Europe) of patients retained antibiotics for future use. These results, according to the authors of the study, indicate a "widespread pattern of poor antibiotic-taking behavior" worldwide.

Antibiotic Utilization in Brazil: Self-Medication and Prescribing Practice

A number of local studies on self-medication have been carried out in Brazil during the last two decades. They generally include limited information about self-medication with antibiotics, are often published only in Portuguese, and may not appear in the PubMed database. Other databases utilized for this portion of the literature review included Scientific Electronic Library Online (SciELO), and Latin American and Caribbean Health Sciences (LILACS). Before reviewing the results from these studies, it is helpful to examine some country- and region-specific structural issues and other social factors influencing antibiotic utilization.

As noted in earlier sections of this paper, a malfunctioning public health care system often acts as an impetus for individuals to seek health care in other forms, including self-medication. Approximately 75% of Brazil's 160 million residents have very limited or no access to the formal health care sector(31, 58), despite Brazil's "universal" health care system, the SUS (*Sistema Único de Saúde*). Accessing health care outside the country's major urban centers is often virtually impossible due to a severe scarcity of facilities. Brazil's rural health insurance fund, FUNRURAL (*Fundo de Assistência ao Trabalhador Rural*), requires rural workers to obtain signed certificates from their employers in order to access free health care at government-operated hospitals. But because of high unemployment rates or the unwillingness of farmers to sign labor declarations, the majority of the population does not have the requisite papers needed to qualify for insurance. A single hospital consult can cost the equivalent of four days wages, and meeting the cost of prescribed medications generally requires an additional

four to five days' wages. In light of these expenses, a hospital visit is generally regarded as a last resort for treatment (11).

Apart from hospitals, health centers [*Centro de Saúde* or *posto de saúde*] with part-time physician staffing should provide free health care and medications via CEME [*Central de Medicamentos*], a government agency started in 1971 to coordinate national production and distribution of pharmaceuticals among the poor. Most statistics and accounts suggest that these objectives have not been effectively achieved by CEME during the last decades. Haak (59) reports that the local health center was virtually non-functional for the duration of his study. Ngokwey (40) adds that the plainly packaged generics being distributed by CEME are often refused by communities, whose residents worry that they are guinea pigs for "untested" medications which are perceived as being universally "weaker" than the comparable brand names.

Even individuals living in relative geographical proximity to government health care facilities are hesitant to access services because of excessive bureaucracy, extremely long waits, and unsympathetic practitioners. An interviewee in Filho's mixed methods study on self-medication in rural Minas Gerais (25) explained that many Brazilians view the public health system as "basically useless," explaining that government doctors often tell patients to seek care with their "own physician." The expense associated with this option makes utilization of the private health care system impractical for most Brazilians.

The quality of care in government facilities is extremely varied. A young dentist working at a rural government health clinic in northeastern Pernambuco state told Scheper-Hughes, "This health post is a scandal, a danger really. People are worse off coming here than treating themselves" (32). Filho (19) reports that many patients agree

with that sentiment. Participants in his qualitative study expressed disillusionment with the physicians working for the public health services in Brazil: "At the social security or public health care system, you get poor treatment. They just run you right through like you're on a conveyor belt. It's almost like they couldn't care less" (25). Numerous patients explained that these feelings of distrust act as a disincentive for physician consults and make self-medication a more "practical" option. Other Brazilian authors (30) confirm that dissatisfaction is expressed most frequently in relation to the government health services, where doctors hardly speak to patients, do not explain recommended treatment plans, and do not give patients the opportunity to ask questions.

Pharmacies, on the other hand, are ubiquitous in urban centers, relatively prevalent in many rural areas, and viewed as socially and logistically accessible. Brazil, in fact, has more pharmacies than any other country, with a total of 50,000, or 1 for every 3,000 residents (60). The number of pharmacies selling allopathic medications in São Paulo city alone exceeds 12,000(9). Resolution 138 of the Brazilian National Agency of Sanitary Surveillance (ANVISA) regulates the sale and advertising of medications, and specifies that antibiotics are to be sold only with a medical prescription. This law, however, is not generally enforced by either local or national governments (8). According to an editorial on self-medication in a Brazilian medical journal (31), the government does not consider regulation of medication sales to be a critical issue.

Many authors (11, 31, 48) assert that media propaganda encouraging the purchase and use of medications is a constant presence on Brazilian television, radio, and the internet. One Catholic radio station, *Radio Aparecida*, operates from southwest Sao Paulo state but is transmitted all over the northeast of the country. Haak (11) reports that this

station "pours out a never-diminishing stream of pharmaceutical commercials" and enjoys great popularity among Brazil's predominantly Catholic population. Public health education or campaigns on the dangers of unsupervised medication use are practically non-existent (31).

Brazil: Data on Self-Medication with Antibiotics

A handful of population-based studies examining the prevalence of self-medication and associated factors have been carried out in Brazil. Very limited research has been done specifically examining self-medication with antibiotics, although use and "misuse" of antibiotics is considered by most authors to be significantly more problematic than use of most other over-the-counter medications (2). One author (31) notes that statistical results in the existing literature are inconsistent, and asserts that the extent of self-medication is not known with any precision. Vilarino (14) suggests that there are two distinct lines of thought presented in existing literature: one which claims that antibiotics are the most commonly used drugs in self-medication, and one that reports that analgesic use is significantly more prevalent. The studies which will be briefly reviewed here all primarily examined the broader topic of self-medication; each included limited information about antibiotic usage and purchase. About half of these studies were published only in Portuguese.

The WHO-coordinated multicenter study of self-medication in Latin America (2, 48), cited in an earlier section of this paper, collected data from three large cities in Brazil. Antibiotics accounted for 5.6% of the medications purchased in pharmacies for self-medication. However, this figure may be an underestimate, as anyone asking advice

from pharmacists before purchase was excluded from the study. In 58% of cases, antibiotics were purchased to treat "acute respiratory infections," including cough and upper respiratory tract infection.

One recent study (61) used a questionnaire to quantify and qualify outpatient antibiotic consumption habits among 6000 households, a "representative sample of the Brazilian population." The average number of treatments with antibiotics over the period of a year was 3.7, and amoxicillin was the most frequently used antibiotic, regardless of socioeconomic status. Notably, most treatments were recommended through medical prescription.

Two studies examined the prevalence of self-medication and associated factors in rural areas. Haak (11, 59) reports that in one rural village in southern Bahia state (Santa Rita), antibiotics were the most commonly used class of medications. In the other village, Salomão, vitamins and analgesics were more commonly used. In this village, every family worked on average one day a week to meet the costs of the family's purchase of modern medicines. Filho's study (19) in rural Minas Gerais state found that antibiotics and chemotherapy drugs together accounted for 6.2% of drugs used in self-medication.

Another two studies looked at self-medication in urban areas. Ngokwey (40) found that 13% of remedies stored in households in one fairly large northeastern city were antibiotics. Vilarino (14) found that antibiotics (along with antifungals and antiparasitics) accounted for 4.7% of the medications bought and consumed by study participants in a city in southern Brazil. Another study (30) in an urban slum [*favela*] in the large northeastern city of Fortaleza followed a cohort of 105 children over a 16-week

period. The authors found that 65 children took 137 courses of antibiotics during this period, and considered this to be "very common" and "often inappropriate" antibiotic use.

Most authors examined demographic data to investigate associations between self-medication and other variables like gender, socioeconomic status, and education status. No convincing trends were found. Moreover, none of the following data are specific to self-treatment with antibiotics.

One study (19) showed that women tend to self-medicate less; two studies assert that women are more likely to self-medicate, though not significantly more (14, 25). Three studies (11, 14, 19) demonstrated that more highly-educated people were more likely to self-medicate (though one did not adjust for confounders); one of the three also found a positive association with income. Schorling's study (30), on the other hand, found that parents from lower socioeconomic status groups were more likely to buy medications at pharmacies without physician prescription. He admits, however, that the confidence limits around this estimate were wide.

The data examining sources of treatment recommendations is equally varied. First, the role of pharmacy attendants in recommending medications is unclear. Haak (59) claims that 44% of medications bought for self-medication were recommended by pharmacy workers. Vilarino (14) and Schorling (30), however, assert that the role of pharmacy attendants is not as prominent as anecdotal reports often suggest; their studies found that only 6% and 7%, respectively, of medication recommendations were attributable to pharmacy worker advice. Advice from "laypeople," or family, friends, and neighbors, accounted for about half of all medication recommendations in the WHO's multicenter study (2, 48) (46% transnationally; 51% within Brazil), but only 12% in

Vilarino's study in a southern Brazilian city (14). Filho (25) heard "several" reports of layperson recommendations during his qualitative interviews in rural Minas Gerais state. Vilarino (14) found that "own choice" accounted for approximately 50% of treatment recommendations, and another 25% of study participants reused old physician prescriptions.

Data on Pharmacy Prescribing Practice

As noted above, data examining the role of pharmacy workers in advising community members about treatment options is inconsistent. The idea that pharmacies in Brazil engage in unrestricted sales of antibiotics is also corroborated by limited, often anecdotal evidence. Only five studies examining pharmacy willingness to sell "prescription-only" medications without prescriptions have been carried out during the last 25 years in Brazil; two of these, from 1980 (14, 38, 39) and recently, one from 2005 (62), specifically looked at antibiotic prescribing. The other two, one from 1986 (17) and the other from 1996 (9), examined prescribing of other "prescription-only" medications. Three of the five studies were published only in Portuguese. Although some of the study results sound alarming, it is important to note that the majority of this data comes from more than 25 years ago.

Bestane (38, 39) utilized groups of female and male medical students to carry out "pseudo-consults" in pharmacies in São Paulo state. The females did 200 "consults" in 5 areas of São Paulo city, complaining of cystitis symptoms (dysuria and polyuria). The study team found that all pharmacists recommended at least one medication, 65% of which contained an antibiotic base. None of these recommendations, Bestane reports

pessimistically, satisfied the minimum requirements (eg., duration of treatment course, dosage, proper choice of drug) for treatment of urinary tract infection with antibiotics. Moreover, only two pharmacists in a sample of 200 inquired about possibility of pregnancy[12].

The male medical students visited 94 drugstores in Santos, a large city in São Paulo state, complaining of infection with gonorrhea [*"de ter apanhado uma gonorreia"*], without further explanations or symptom descriptors. Bestane reports that only 53% of prescribed treatments would have effectively cured a patient with gonorrhea, and recommendations were on average 270% more expensive than the usual cost of gonorrhea treatment. He also reports that all pharmacists prescribed a treatment, and without any further questioning in 60% of the cases. Given the results of his previous study (63), which showed that 90% of men self-diagnosing with gonorrhea seek treatment first at pharmacies, Bestane considered these results disappointing. His previous study also found that 54% of pharmacists, on self-report, claimed they would ask about sexual partners before treating gonorrhea, and that 30% would wait for the result of an antibiogram. Only 3% of pharmacists in this study actually inquired about sexual contacts, and all prescribed without inquiring about prior physician consults or antibiograms.

More recently, Volpato et al (62) used a similar method to determine the percentage of pharmacies selling antibiotics without medical prescription in a medium-sized city in southern Brazil. Medical student "actresses" visited 107 of the city's 136 registered pharmacies, and simulated having a sister with symptoms of non-complicated

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[12] The two classes of antibiotics used most commonly to treat urinary tract infection, trimethoprim-sulfa drugs and fluroquinolones, are contraindicated in pregnancy.

rhino-sinusitis (the "sister" was not present on consultation). Antibiotics were offered in 58% of the pharmacies, and when the actresses insisted on having them, 74% of the pharmacies were willing to comply. In the 26% of pharmacies denying the request, the most frequent reason for denial was not absence of prescription (7.5%) but that the pharmacy attendant deemed antibiotics medically unnecessary based on the illness history (47%).

Carlini also utilized medical students to do "pseudo-consults" in approximately 100 pharmacies in São Paulo city. The students requested medications for a variety of conditions: anxiety ["*estar muito nervoso*"], tiredness ["*estar com muito sono*"], wanting to lose weight ["*querer emagrecer*"] and concern about an alcoholic relative ["*alcoolismo em pessoa da familia*"]. In 98 of 101 visits, the first person to attend to the student prescribed a medication, 75% of which should only have been sold with presentation of a medical prescription. 79% of the medications sold for complaints of anxiety and insomnia were benzodiazepines. Amphetamine-like drugs were freely sold to students complaining of tiredness or wanting to lose weight. Products containing disulfiram were sold to 71% of the students with an "alcoholic relative." Only 17 of the 98 "customers" were given information on side effects, and the advice was frequently incomplete or incorrect.

Bosi Ferraz (9) reports slightly more promising results from a recent study on the ease of acquiring medications for arthritis. His study team requested various classes of medications from pharmacists, including common analgesics, corticosteroids, and sedatives. 13% of pharmacists refused to sell medications without a prescription and advised patients to see a doctor. 68% of requested non-steroidal anti-inflammatory drugs

(NSAIDs) and 65% of the requested corticosteroids were sold, but only 20% of study team members requesting sedatives were obliged. Though these results appear to be more promising than data from older studies, Bosi-Ferraz expresses much pessimism about the current state of prescribing practice in Brazilian pharmacies.

Problems with the Literature

This review of the existing literature on antibiotic utilization, particularly with regard to self-medication practice, exposes some problems and voids. The availability of antibiotics and their role in medication in developing countries has been documented, but often in a non-systematic way (45). Generalizations and vague statements about developing country antibiotic use and idealization are nevertheless pervasive, despite this lack of documentation and data which is inconsistent, outdated, and often anecdotal (3).

As mentioned briefly in an earlier section of this paper, alarmist phrases loudly proclaim the "extensive misuse of drugs," "gross over-prescribing," and the "pill culture" which is "spreading to the Third World" (46). An editorial (31) in a Brazilian medical journal asserts that Brazilians have an "impulsive" tendency to use popular and medications for non-serious health concerns. One American anthropologist (46) asserts that "myths and half-truths about modern medicine are sold along with drugs" and that the "ubiquitous distribution, powerful marketing, benevolent image, and poor control [of antibiotics and other modern pharmaceuticals] mean that they are used and misused for a wide range of afflictions". Another author (49) claims that "lay people in these countries are flooded with expensive, often inessential, and even potentially dangerous drugs." This literature review has revealed that there is some truth to these statements. However,

discussions on pharmaceuticals in developing countries which engage concepts like the "political economic framework" of drug utilization and "dependency theory" (24) often appear far removed from the local scene, and more informed by anecdotal and generalized assumptions than by systematic data. Van der Geest (3) summarizes:

> Western-based critics of present pharmaceutical practice [including] distribution and…use of medications in developing countries…repeatedly mention lack of quality control, inaccessibility of physician-prescription, free availability of prescription-only drugs, predominance of self-medication, lack of information on drug use, and general poverty. Clearly, such commentary is impressionistic, expressed in sweeping generalizations, and usually based on extremely lean evidence….Although the "lamentable" position of drug users in developing countries is the concern of all these deliberations…the victims of "irrational" or "unhealthy" drug use in the Third World still remain largely unidentified. We have only vague notions about their "plight" and how they perceive it. (p. 273)

This situation is in part a result of the dearth of recent studies; authors writing anthropology essays and policy reports on antibiotic utilization in developing countries tend to repeatedly cite the same dozen studies carried out in geographically disparate regions two decades ago.

However, one of the more insidious issues in these discussions is not transparently acknowledged by most authors: a central notion in the documentation of "irrational" use of antibiotics in developing countries is often "ignorance" or "illiteracy" (45) on the part of patients. As such, the perspective from which most articles on this topic are written tends to oversimplistically blame antibiotic misuse on consumers, particularly those who are poor, less-educated, or illiterate. Many examples of this can be found in the literature reviewed herein [italics added for emphasis]: Arrais (48), a Brazilian researcher, writes that the risk of *misusing* self-prescribed medications is generally correlated with the education level, and that less-educated people are more likely to self-medicate because they have limited access to the medical system; Tomson

(1) asserts that "with the prevailing 'pill culture,' it is not surprising that an *uninformed or uncritical person* will resort to drugs, for both trivial and self-limiting and potentially serious illnesses; the WHO (7), even when purportedly writing about the role of health care providers in creating antibiotic resistance, attributes most factors to the behavior of patients instead of providers; eg., *patient "demand"* for antibiotics; Bosi Ferraz (9), although he did not collect any data to inform this statement, emphasizes with the results of his Sao Paulo pharmacy study that "self-medication provides a lower-cost alternative for *poorer people*, who cannot afford to pay for medical practitioners."

An extended example of this tendency to attribute antibiotic misuse to less-educated individuals is revealed on a close reading of an article published in a Brazilian medical journal by Vilarino (14). First, in describing self-medication practices of the study participants *with limited education*, he uses the mutually exclusive categories of "correct use" and "self-treated," asserting that self-medication implies incorrect use of medications. However, when writing about the practice of all other groups he simply uses the terms "self-medicated" and "did not self-medicate" without further value judgments. Their results show, in fact, a positive association between self-medication and higher education level, and no evidence to suggest that "less-informed" or "less-educated" people are more likely to self-medicate. Despite these results, they continually assert in their discussion section that self-medication is generally a phenomenon common among lower classes, and cite a study from Peru to corroborate this assertion. They finally admit that although the existing literature tends to claim that those of lower socioeconomic status are more likely to self-medicate, their results did not support this hypothesis. Other studies cited previously, from Brazil (11, 14, 19), India (12) and Sri

Lanka (33), confirmed that low income or education level is not correlated with a tendency to self-medicate.

This situation points to the need for an expansion of the literature on self-medication with antibiotics in developing country communities. This literature review points to at least three major topics which would benefit from investigation in future studies:

1) How and why are antibiotics used locally? Additional information is needed to better define the epidemiology of antibiotic use at the community level (3, 30). This information should include investigation into the associations between demographic data, eg., gender, socioeconomic status, education level, and use of antibiotics in self-medication. No existing studies have specifically examined these associations.
2) Diverse sources of antibiotic supply have been identified (eg., public sector government hospitals and clinics, private sector commercial pharmacies, traditional healers). To what extent do people utilize each of these systems, and how consistent is current prescribing practice in each setting with usual assumptions about "unrestricted" supply or sale?
3) A better understanding of the factors influencing decision-making around self-medication with antibiotics is needed to inform the largely non-existent discussion on community-level interventions around antibiotic use. How is the cycle of antibiotic overprescription by providers and self-medication by consumers shaped by social, cultural, and economic factors in specific local settings?

Some Background Information for Future Investigations

One way to examine the intersection of self-medication and prescribing practice in community-based settings, especially in light of local concerns about specific patterns of antibiotic resistance, is to investigate these issues in the context of a particular illness. Because this paper's author will have the opportunity to work with a local team of scientists and doctors investigating urinary tract infections and antibiotic resistance in Rio de Janeiro, Brazil, some background literature on that topic will be briefly reviewed here.

Community-acquired urinary tract infections (UTIs) are among the most common bacterial infections in both inpatient and outpatient settings. They are particularly common among women, with 50 to 60 percent of adult women reporting that they have had a UTI at some time during their life (64). The global incidence of UTI is estimated at over 250 million cases (65). The cost of antibiotic treatment, alone, in treating UTI was estimated at $1.6 billion per year in the US (66).

Few detailed studies on UTI morbidity in well-defined populations have been undertaken and published, and relatively little is known about the epidemiology and natural history of UTI in developing countries. Limited available data shows that UTI frequency is higher among women of low socioeconomic status (67).

It has been largely assumed that patients with uncomplicated community-acquired UTI can generally be treated empirically (without urine culture or laboratory investigation) because of the illness's fairly predictable microbiological and clinical profile. First, the causative organisms and their antimicrobial susceptibility profiles are generally known (68). *Escherichia coli*, particularly extraintestinal pathogenic *E. coli* (ExPEC) is the most typically implicated pathogen in UTI, causing between 80-95% of

all infections (69, 70). *Staphylococcus saprophyticus* is responsible for most other episodes, and *Proteus mirabilis*, *Klebsiella* species, enterococci, or other uropathogens are isolated from a small proportion of patients. Second, the clinical criteria for UTI diagnosis are also fairly predictable. A systematic review (71) demonstrated that presentation with both dysuria and urinary frequency, without vaginal discharge or irritation, raises the probability of UTI in a woman to more than 90%.

Despite this fairly predictable etiologic profile and standard clinical presentation, increasing antibiotic resistance among UTI-causing pathogens has complicated therapy. Although empiric treatment with trimethoprim-sulfamethoxazole (TMP-SMX) or fluroquinolones is usually begun before the results of a urine culture are known, resistance levels above 10-20% suggest the need for reevaluation of current empiric treatment. Studies in the Western United States show that resistance rates of ExPEC to TMP/SMX are likely higher than 20% (72). In developing countries, resistance is thought to be much more prevalent, though few comprehensive studies have been undertaken to determine rates and characterize patterns of resistance. The limited and scattered data coming out of hospitals in Brazil has shown that resistance rates of ExPEC to TMP/SMX and ciprofloxacin are very high: 46.3% and 22.5%, respectively (73). This suggests that empiric treatment with either of these two drugs may already be inappropriate.

Brazil's unique development history and an infectious disease profile characteristic of both developed and developing countries make it an ideal setting for a study on antimicrobial resistance and infectious disease. Modern technology in health care and research settings is reasonably accessible, but despite access to the equipment

and antibiotics needed for successful treatment of infectious disease, Brazil is still confronted with serious problems related to infectious disease control and containment. Additionally, Rio de Janeiro's pronounced income inequality provides a particularly appropriate setting for studying a disease which appears to have a heavier burden among lower socioeconomic classes.

Moreover, UTI is a particularly relevant illness for studying the intersection between self-treatment and antibiotic resistance for a number of reasons. First, there is a distinction between health problems for which people do and do not self-medicate. In general, people view "transitory, non-serious problems" as candidates for self-treatment. Familiarity with a problem is also a factor; unknown or worrisome problems (eg., bleeding, fever) prompt people to seek care with physicians. Persistence of a problem also acts as an impetus for presentation at formal health care facilities (25).

UTI's are extremely common and are generally perceived as relatively "non-serious." They are not associated in increases with either long-term renal dysfunction or mortality, so their primary significance to patients is discomfort from symptoms caused by infection. This makes them a good candidate for community self-treatment. Presentation with UTI at a formal health facility (at least in settings where antibiotic treatment can be acquired without prescription) often implies that the infection is more complicated; perhaps the more alarming symptoms (eg., hematuria, fever) are present, or maybe treatment has failed because of resistance.

Second, there is some evidence that young and middle-aged women are more likely to self-medicate. The WHO (2) reports that women between the ages of 16 and 45

are, in fact, the primary group practicing self-treatment. Females in this age range also constitute the majority of patients with UTI.

Finally, medical professionals in developed country settings authorize some self-medication among women with recurrent UTIs. Three studies (74-76) have shown that UTI can be accurately self-diagnosed by women over 85-95% of the time, and that short-course antibiotic therapy is highly effective in curing the infections. These studies also demonstrated that women allowed to self-diagnose and self-treat infections have more symptomatic UTIs than women on continuous or post-coital prophylaxis, but their symptoms resolved quickly and the overall quantity of antimicrobials used was less.

For these reasons, a study examining antibiotic self-prescription among those who present with symptoms of community-acquired UTI in Rio de Janeiro, Brazil, is likely to yield insights into the interplay between self-medication behaviors and the evolution of microbial antibiotic resistance. The planned study will provide information to 1) better define the epidemiology of antibiotic self-prescription at the community level, and 2) situate self-medication within a context shaped both by individual decision-making behaviors as well as social and structural issues pertaining to antibiotic supply and availability in the community sphere.

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Thesis Paper 2:

Self-Medication and Antibiotic Resistance in Rio de Janeiro, Brazil

Urinary tract infection (UTI) is an extremely common illness which is becoming more difficult to treat: uropathogenic *E. coli*, the bacteria which most often causes UTI, is rapidly becoming resistant to standard treatment in Brazil and elsewhere. Yet reports of treatment failures have not prompted studies in Brazil to quantify resistance and provide better guidelines for treatment options. Limited surveillance data from national hospitals in 2001 (1) showed extremely high resistance rates to two antibiotics commonly used for treatment, trimethroprim-sulfamethoxazole (TMP-SMX) (46.3%) and ciprofloxacin (22.5%). These rates suggest that empiric treatment of community-acquired UTI with either of these antibiotics may no longer be appropriate.

In response to this problem, local clinicians approached scientists at the Microbiology Institute of the Federal University of Rio de Janeiro (*Instituto de Microbiologia, Universidade Federal do Rio de Janeiro*, UFRJ) and commissioned a study to provide guidance for the development of more appropriate empiric treatment. The request resulted in a collaboration between Dr. Beatriz Moreira, MD, PhD, Professor of Microbiology at the Institute, and the Riley Lab at the University of California, Berkeley (UCB), School of Public Health. The binational study team will carry out a study to characterize the epidemiology of microbial resistance among patients with community-acquired UTI in Rio de Janeiro, and identify risk factors for presentation with antibiotic-resistant infections.

The existing literature on antibiotic utilization in developing countries asserts that detecting the emergence of resistant microbes, delaying their spread, and assisting health

care providers to select the most effective and affordable treatment agents requires a sustained effort on the part of organizations which can carry out community surveillance and perform capable laboratory analysis (2). This project is an example of a local-level study which has been informed and motivated by these aims.

In the United States and other developed countries, antibiotics may be purchaseed only with medical prescription. But in the majority of the developing world, antibiotics may often be obtained without prescription at local pharmacies and other commercial establishments. The proposal for this study (3) suggests that community use of non-prescription antibiotics is likely to play a significant role in creating high prevalence of resistance. This paper will discuss the results from a sub-study which collected quantitative and qualitative data to examine the validity of this assertion.

Three assumptions are frequently made in the discourse about antibiotic resistance: first, that individuals in the community are treating themselves with antibiotics without the advice or supervision of physicians; second, that pharmacies sell antibiotics to patients without a legally required medical prescription; and, third, that those who self-medicate are often poor, illiterate, or uneducated. The previous literature review cast doubt on the validity of some of these assumptions and highlighted a need for local-level studies to help communities assess the extent of these problems and understand the local "social context" of antibiotic resistance. This study will examine these assumptions in the context of self-medication, pharmacy, and physician prescribing practices for the treatment of urinary tract infection in Rio de Janeiro, Brazil.

Methods

A. Quantifying Self-Medication Behaviors

Study Site: To capture a diverse sample of adults seeking outpatient medical care for UTI and accurately represent the spectrum of access to health care in Rio, we chose three study sites: 1) a public teaching hospital (Hospital Municipal Miguel Couto), which serves a lower socioeconomic status population without health insurance; 2) a private hospital (Hospital São Lucas) which serves individuals across a broad range of socioeconomic status; and, 3) the university hospital (Hospital Universitário Clementino Fraga Filho). Results reported here, however, do not include data from the university hospital because these UTIs were not strictly community-acquired and care was provided on an inpatient basis.

Study Subjects: Physicians at the study sites, including those from the urgent care/ambulatory department, the pre-natal department, and the emergency department, were asked to refer all patients presenting with symptoms of UTI, both those who would have been empirically treated and those who would have been sent for urine culture, to the study coordinators. All willing individuals over the age of 13 were enrolled after being given a verbal explanation of the study and a written information sheet. Both verbal and written informed consent were obtained. Human Subjects Research approval was obtained from both UFRJ and UCB. Confidentiality was maintained at all times.

Study design: This is a cohort study of individuals presenting with symptoms of UTI to the study sites above, carried out to quantitatively assess the extent of self-reported self-medication behavior, examine demographic trends among those who choose to self-medicate, collect information on sources of treatment recommendations and sites where antibiotics are obtained, and determine whether self-medication may influence the risk of presentation with an antibiotic-resistant infection. Study participants were asked a series

of questions to capture information about demographics, UTI symptoms and history, other medical history, self-medication behavior, and risk factors for complicated UTI and for antibiotic resistant infections. All information was verbally self-reported by the patients. The results reported herein refer to data collected between March and June 2005. The pilot study continued through September 2005.

Laboratory Studies: A urine sample was collected for microbiological analysis of bacterial type and resistance profile. Laboratory analysis for urine culture, bacterial identification, susceptibility testing and initial typing by PCR were performed at UFRJ's Microbiology Institute. A positive culture was defined as one with $\geq 10^3$ colonies per ml of urine of one or two significant pathogens. This definition from the Infectious Disease Society of America (IDSA) assures 80% sensitivity for diagnosis of UTI and 90% specificity.

Antimicrobial susceptibility testing was performed on all isolates by the disk diffusion method according to the National Committee for Clinical Laboratory Standards (NCCLS) recommendations. For the purposes of this study, a "resistant infection" refers to one in which the infecting organism was resistant to any of the major antibiotics commonly used to treat UTI: TMP-SMX, fluoroquinolones (ciprofloxacin or norfloxacin) or nitrofurantoin.

Data were analyzed using EpiInfo, a free program for quantitative analysis of epidemiologic data developed by the Centers for Disease Control and Prevention (CDC).

B. Pharmacy Prescribing Practice

The purpose of this part of the sub-study was to assess the willingness of pharmacists to diagnose, prescribe, and sell antibiotics without prescription, in response to a common

health problem (UTI) which is typically treated with antibiotics. Forty pharmacies were chosen in 14 neighborhoods located in the vicinity of subway stops on Rio de Janeiro's primary subway line. During May/June 2005, approximately 3 pharmacies in each neighborhood were visited; most pharmacies were within a 10-block radius of the subway station. An attempt was made to frequent both small (non-chain) and large (chain) pharmacies. 30 of the 40 pharmacies in the sample (75%) were "large" pharmacies, or belonging to a popular chain found commonly in Rio; 10 of the 40 were small, non-chain stores (25%). These 40 pharmacies were a convenience sample selected based on easy accessibility and safety.

The author presented with a fictitious concern of dysuria, or burning with urination [*"tá ardendo quando faço xixi"*] to the first person encountered behind the pharmacy counter. A diagnosis, treatment recommendation, and dosage instructions were then requested. The action taken and advice given by pharmacy attendants, along with a descriptor of the pharmacy's size and its location, was recorded after exiting. The "script" (Figure 1) was devised by the author and revised with the help of Dr. Moreira and a Brazilian medical student working on the study at a public hospital. A similar method has been utilized in a limited number of published studies(4-9), including five in Brazil.

1. *"Tá ardendo quando faço xixi, o que é que você acha que deve ser isso?"* ["It's burning when I pee, what do you think this could be?"]
2. *"Você recomenda algum remédio para eu usar?"* ["Can you recommend a medicine for me to take?"]
3. *"Como é que eu tomo?"* ["How do I take it?"]

Figure 1. Script employed in pharmacy interviews.

Results:

A. Quantifying Self-Medication Behaviors

Population demographics are summarized in Table 1. The sample was comprised of 111 participants, 90 (81.1%) women and 21 (18.9%) men, with an average age of 35.1 years. A wide variety of races were reported by participants. Sixty-four (57.7%) had finished primary school (8 years), 37 (33.3%) had finished secondary school (11 years), and 104 (93.7%) were literate. Of the 90 women, 11 (12.2%) were pregnant. The study cohort was relatively low-income because the majority (85%) were enrolled at the public hospital during these first three months of the study pilot. Forty-six (41.4%) earned less than 700 reais (approximately USD 250) per month, and 84 (75.6%) earned less than 1500 reais (approximately USD 600) per month [monthly minimum wage in Brazil is 260 reais, or approximately USD 100].

The responses to questions about self-medication behavior, including sources of treatment recommendations and places where individuals obtain antibiotics, are summarized in Table 2. Of 111 study subjects, 39 (35.1%) had a history of self-medication with antibiotics, and 32 (84.2%) of those subjects did not have health insurance at the time of self-medication.

Twenty-seven percent of patients had treated their current infection before presentation at the hospital. Sources of treatment recommendations included physicians (65%), own choice (21%), and pharmacy attendants (10%). Of patients who had treated past UTIs, 100% claimed to have received the recommendation or prescription for treatment from a physician. Pharmacies (90% current infection; 93% past infection) were overwhelmingly the most common place where people obtained antibiotics. It is

important to note that patients seeking care from health care professionals at public hospitals are entitled to free medications from the hospital pharmacy. There was no distinction made on the questionnaire between private pharmacies and public/hospital pharmacies. Self-report on treatment for both current and past infections revealed five instances of self-medication with a medication leftover from a past UTI or other illness.

Of the 111 study subjects, 54 (49%) were determined to have a laboratory-diagnosed UTI at the time of presentation. *E. coli* was the etiologic agent in 34 cases. Of the 67 patients with negative cultures, 18 had already treated the infection with antibiotics (all reported they had done so at the recommendation of another doctor) before hospital presentation.

Among the 54 patients with a laboratory diagnosis of UTI, 32 (nearly 60%) were found to have resistant infections. Among the 34 patients with E. coli UTIs, 21 (62%) had resistant infections. Drug susceptibility testing was performed for all subjects with resistant infections.

Of the 54 subjects with resistant infections, 13 (42%) had self-medicated at some point in the past. The history of self-medication was not significantly associated with acquisition of resistant UTI (OR=1.81, 95% CI 0.48-7.01), nor specifically with acquisition of resistant *E. coli* UTI (OR=1.06, 95% CI 0.21-5.30). This information is summarized in Tables 3 and 4.

None of the demographic characteristics was significantly associated with self-medication. The results are presented in Table 4 and some trends are discussed below.

B. Pharmacy Prescribing Practice

Of 40 pharmacies, 34 (85%) gave a diagnosis of urinary tract infection/cystitis (Figure 2) and 28 (82%) of these made a follow-up treatment recommendation. Of these, 24 (86%) recommended an antibiotic. Of the antibiotics recommended (Figure 3), 19 (79%) of 24 were recommended with correct dosage instructions, and 5 (21%) of 24 with incorrect dosage instructions.

The most common treatment recommended (16 times) was Norfloxacin 400 mg, twice daily, for five to seven days. This would be adequate to treat a urinary tract infection (in the absence of resistance). In Rio, there is considerably less resistance to the fluoroquinolones (including Norfloxacin) than to TMP-SMX, the prior standard for empiric treatment. Other antibiotics recommended included TMP-SMX, "Uropac" (a brand-name combination medication with a double-antibiotic base consisting of a sulfa drug and nitrofurantoin, to which there is very little resistance), Ciprofloxacin, and Azithromycin. Two pharmacies stated that taking two antibiotics (Uropac and Norfloxacin) together would give better results (in this case, because Uropac contains two antibiotics, this prescription would actually be for three antibiotics).

Non-antibiotic treatments offered included phenazopyridine (a urinary tract analgesic), "Cystex" (a brand-name combination treatment composed of a variety of herbal medications), and Nystatin (typically used to treat *Candida* but not to treat urinary tract infection).

Nearly one third of the pharmacies (13 of 40) would not recommend or sell antibiotics without a prescription (Figure 4), as per the law, and recommended that the author consult a physician.

Pricing on medications was relatively consistent across the sample of pharmacies. There was no notable difference between prices charged in large and small pharmacies, and the most commonly recommended treatment regimen with Norfloxacin cost between $17-23 reais, with an average price of $19.43 reais, more than twice the daily minimum wage.

Discussion

A. Quantifying Self-Medication Behaviors

Thirty-five percent of patients self-reported a history of self-medication. This figure seems to be an accurate representation of the prevalence of self-medication among this sample because it is consistent with the cumulative number of patients who relied on "own choice," "pharmacy attendant," or "other" as the source of their treatment recommendation when treating their current UTI before hospital presentation (34.4%). All of the patients who treated a past UTI with antibiotics professed to having done so at the recommendation of a physician, but this figure may be an overestimate influenced by the desire of participants to please interviewers, or affected by recall bias.

The results of this analysis, although no variable was found to be statistically significant, reveal that a history of self-medication may have increased the risk of developing an antibiotic resistant UTI (OR=1.81; OR=1.06 for *E. coli* UTI). The relatively small sample size may have contributed to the lack of significant association.

Data on other associations between demographic variables and self-medication were not statistically significant. As noted in the literature review for this study, associations between demographic variables and self-medication from past studies in Brazil were similarly inconclusive. One study (10) showed that women tended to self-

medicate less; two studies asserted that women are more likely to self-medicate, though not significantly more (11, 12). Three studies (10, 12, 13) demonstrated that more highly-educated people were more likely to self-medicate (though one did not adjust for confounders); one of the three also found a positive association with income. Schorling's study (14), on the other hand, found that parents from lower socioeconomic status groups were more likely to buy medications at pharmacies without physician prescription. It is important to acknowledge as well that none of these data were specific to self-treatment with antibiotics; rather, they investigated general self-medication practices.

Although no statistically significant association was seen in the overall analysis on race and self-medication in this study, it is possibly of note that participants who identified as "other" race were much more likely to self-medicate (OR=4.95). This was, in fact, the only sub-analysis which reached statistical significance (p=0.02). The implications of this result are unclear, and the number of participants identifying as "other" race was relatively small (n=13). It would be interesting to see if this trend would continue with a larger number of participants. Unfortunately, due to problems with data entry and the database, the data on education level and history of self-medication could not be analyzed.

The percentage of pregnant women with a history of self-medication (18.2%) was considerably lower than the baseline figure (35%). Further investigation would be needed to determine if this suggests anything about a woman's confidence level with regard to self-medication when the health of her baby might also be affected.

These data show that pharmacy attendants and friends and family members did not play a large role as sources of treatment recommendations. Despite common

assertions about the "social" aspects of self-medication in Latin America (15) and anecdotal reports about the role of pharmacy attendants in helping individuals choose medications, data on this issue from past studies in Brazil has been very inconsistent (10-14, 16).

There were numerous sample-related limitations on these data. First, it is difficult to assess whether or not patients presenting at a public hospital with UTI symptoms might be representative of the population at large with respect to self-medication behavior. Moreover, although the number of patients enrolled at each of the three study sites was expected to be somewhat more equal at the outset of the study, problems with logistics and start-up issues resulted in a gross imbalance of patients being enrolled at the public hospital site. This meant that they were relatively homogeneous with regard to income, which made it difficult to find trends in the data on self-medication and income. A course of antibiotic treatment for UTI at a pharmacy is relatively expensive, and medications are free if patients are willing to wait for physician consults at the public hospital. This suggests that poorer patients may be more likely to seek care at a public hospital instead of self-medicating. On the other hand, patients of higher socioeconomic status are more likely to have private health insurance, which may entitle them to quicker care with private physicians, decreasing incentive to self-medicate. It would be informative to reanalyze the data after the completion of the six-month pilot study, when more patients have been enrolled at the other two study sites.

It is unclear whether self-medication among 35% of a sample is a relatively large or small figure. Past studies in Brazil have never collected self-report data on the extent of self-medication with antibiotics, so there is no existing literature with which to

compare this figure. Finally, while 111 patients is a decent sample size, the analyses on self-medication and antibiotic resistance were done with the much smaller number of patients who had a laboratory diagnosed UTI (n=52). It is possible that a larger sample would have yielded clearer associations.

B. Pharmacy Prescribing Practice

Although the number of pharmacies willing to diagnose and recommend treatment was relatively high (60%), the results of this study are nonetheless encouraging in comparison with results from past studies on pharmacy prescribing practice in Brazil. For example, in this study, a third of pharmacies were not willing to prescribe or sell antibiotics. Results from past studies in Brazilian pharmacies (5-8) demonstrated that nearly all pharmacists did not hesitate to diagnose or prescribe medications including antibiotics. This suggests that pharmacies have become more compliant with laws prohibiting the sale of antibiotics without prescription during the last two to three decades.

Furthermore, 80% of the pharmacies recommending and selling antibiotics (19 of 24) recommended treatment that would have effectively treated a urinary tract infection. Past studies had documented much lower rates of treatment effectiveness: two studies carried out by Bestane (5, 6) in 1978 and 1980 showed that 0% and 53% of prescribed treatments would have been clinically effective in treating cystitis and gonorrhea, respectively.

Nevertheless, the results of this study do point to some issues needing improvement. First, there were distinct differences between the practices of large/chain and small/non-chain pharmacies. Of the 13 pharmacies which refused to prescribe or sell antibiotics without prescription, 12 were large pharmacies, and only 1 was a small non-

chain pharmacy. Therefore, while 40% of large pharmacies refuse to prescribe and sell antibiotics without prescription, only 10% of small pharmacies were seen to do the same. In addition, there seemed to be a tendency among small pharmacies to sell brand-name combination medications, such as "Uropac" and "Cystex." Moreover, there was some confusion among pharmacists when queried as to whether or not "Uropac" contained an antibiotic base (it, in fact, contains two antibiotics). In one small pharmacy, an insufficient amount of "Uropac" (five pills only; a full treatment course consists of 12) in loose form was recommended and sold. Finally, the one wrong diagnosis and prescription choice (Nystatin for *Candida*) came from a small pharmacy. This suggests that smaller pharmacies may be less compliant with laws and less medically informed.

None of the attendants in the 40 pharmacies inquired as to whether the researcher were pregnant. In the case of urinary tract infection, this knowledge significantly affects the treatment prescribed; fluoroquinolones including Norfloxacin, the most frequently prescribed treatment, are generally contraindicated in pregnancy. This result was disappointing and consistent with the results from Bestane's study of pharmacy prescribing practice for cystitis in 1980 (6).

Interest in profit seemed to clearly motivate a treatment recommendation in only five of the 40 pharmacies. In one pharmacy, Azithromycin, a broad-spectrum antibiotic which costs twice as much as Norfloxacin and is not considered appropriate first-line treatment for UTI, was recommended. In two pharmacies, "Uropac" and Norfloxacin were prescribed together though this is of questionable biomedical benefit. One pharmacy attendant admitted that he could not sell antibiotics without a prescription, but tried to convince the author that her infection would resolve with phenazopyridine, an

analgesic with no antimicrobial effect. Finally, one pharmacy tried to sell brand-name Norfloxacin for $30 reais and admitted to stocking the less expensive, generic version of the medication only when queried. Nevertheless, in light of the fact that pharmacies are commercial establishments which must rely on profit-making for economic survival, it is encouraging that an interest in profit seemed to influence treatment in only a very small number of sampled stores.

There appeared to be a relatively high degree of consistency in prescribing or refusal to prescribe among pharmacies within same chain. This information could help local regulatory bodies to focus their efforts if they chose to enforce laws prohibiting the sale of antibiotics without prescription.

Limitations of this part of the study include the fact that the author is foreign (although fluent in Portuguese), which could have aroused suspicion about her intent and decreased the likelihood that an antibiotic would be recommended or sold. In nearly all pharmacies, however, this fact did not seem to perceptibly affect interactions, advice given, or treatment prescribed. Second, the pharmacies in this study were chosen based on easy and safe accessibility, and with a few notable exceptions, were located in middle- or higher-income residential or commercial areas of the city. Finally, the decision to ask for a diagnosis and treatment recommendation may have lowered the probability of antibiotic sale without prescription. Two pharmacies informed the author that she would have been allowed to purchase an antibiotic without a prescription if she had known the name of the antibiotic instead of asking for a recommendation.

Other Structural Factors Influencing Antibiotic Resistance

The quantitative and survey data presented above does not lend itself easily to concrete or objective conclusions. How much self-medication is "too much"? What is reasonable to expect of pharmacy practice in a setting where there is no enforcement of current prescription laws? Is the extent of self-medication and poor pharmacy prescribing practice anecdotally exaggerated in the minds of biomedical and public health observers? And is community and individual agency in creating antibiotic resistance exaggerated by researchers and physicians because it is an "easy" explanation, one which does not prompt a more in-depth critique of structural issues creating a setting which is conducive to the development of resistance? The following is a brief summary of qualitative data and field notes which suggest that self-medication is but one of a number of factors contributing to antibiotic resistance in Rio de Janeiro.

Physician Prescribing Practice

As detailed in the previous literature review, one of the key structural issues influencing antibiotic usage is physician prescribing practice. During the course of collecting quantitative and qualitative data in the public hospital, the author interacted with or received study participant referrals from at least 8 physicians in the emergency, pre-natal, and urgent care/ambulatory departments. Physicians typically wrote prescriptions for UTI treatment before a patient was referred for study participation; the study team thus had access to information on the current prescribing practices of doctors in the hospital. Although TMP-SMX remained the recommended empiric treatment for UTI at this hospital, physicians regularly prescribed at least four other antibiotics including ampicillin, ciprofloxacin, norfloxacin, and cephalexin. Cephalexin was

routinely prescribed for pregnant women. Nitrofurantoin, to which resistance is thought to be extremely low, was not prescribed because it is not included on the hospital formulary; accordingly, patients would not be able to receive this medication for free at the hospital pharmacy. For an uncomplicated UTI, different physicians commonly prescribed the same medication with different dosing regimens; for example, one doctor routinely prescribed Norfloxacin for three days, another for five, and yet another for seven. This wide variability in physician prescribing practice is likely to play a role in the creation of antibiotic resistance, not only because of the inconsistent and poorly conceived treatment regimens, but also because physician prescribing habits are likely to influence the prescribing habits of other groups in the community (pharmacy attendants, individuals, medical students) (2, 17-20).

As noted in the previous paper, hasty prescribing habits of health care professionals can lead to erratic purchasing of medications when poor patients are unable to buy all of the medications on a prescription and choose arbitrarily (eg, the first on the list, the cheapest, the one that happens to be in stock) (13). Examples of this phenomenon were documented in Brazil during this study. For example, one study participant had been given a prescription for ciprofloxacin and a common analgesic by the physician who attended her at the hospital. After one week, she returned for follow-up with the study team and reported that her symptoms had not resolved. Discussion revealed that she had obtained the analgesic for free at the hospital pharmacy, but the ciprofloxacin had been unavailable. The hospital pharmacy clerk had suggested that the woman try to buy the ciprofloxacin at a local commercial pharmacy. As this antibiotic

costs approximately 75 reais, more than one week's minimum wage, she had been taking only the analgesic for the past week.

The inconsistency between antibiotic packaging and physician-prescribed dosing regimens also led to confusion and antibiotic misuse. For example, one study participant, a 57-year old man, had been prescribed 10 days of ciprofloxacin by his physician. He informed us that the first box of this antibiotic had been insufficient for ten days of treatment, so he bought another two boxes and took the medication for 22 days.

Delaying Care: Why Do Individuals Choose to Self-Medicate?

As documented in the previous paper, structural problems with the health care infrastructure in Brazil are also likely to influence the likelihood that individuals will choose to self-medicate instead of seeking care in the formal sector (11, 21). Schorling, the author of a study on antibiotic utilization among children in a *favela* in northeastern Brazil, writes that "understanding why people buy medications especially antibiotics on their own when they were available for free is a critical issue in instituting a rational drug policy in developing areas" (14). To investigate the rationale for self-medication instead of physician consult, study participants who answered that they had self-medicated in the past were asked two follow-up questions: 1) Why did you choose to self-medicate instead of seeking care? and 2) Why did you choose to seek care today, for your current infection? The first question was presented with a number of possible answer choices as well as the option of "other." The second question was open-ended. Responses from the "other' category of the first question, and all responses to the second question were qualitatively analyzed to identify the most common categories of response, and then

coded and grouped based on these themes or categories. Results from these two questions are summarized below, respectively, in Tables 5 and 6.

The responses to these questions were consistent with many of the themes seen in the existing literature on self-medication: antibiotics are more easily obtained at pharmacies, long wait times at public hospital facilities provide a disincentive to seeking care, seeking treatment at a pharmacy is seen as a faster alternative to beginning care for an illness causing significant discomfort. The most commonly heard response was that past experience with these symptoms or illness made individuals confident that they could self-medicate without seeking a physician's advice or recommendation. While this may be more problematic with illnesses which are more difficult to diagnose, it has been shown in multiple studies (22-24) that UTI can be accurately self-diagnosed over 85-95% of the time.

As explained in the previous paper, the hospital or public health service is often considered a "last resort" treatment for when self-medication has failed, or discomfort or pain has increased to a level at which another solution must be sought. This data is consistent with that notion: the three most common explanations patients gave for seeking care at the time of consult were related to symptom/illness recurrence or exacerbation. Three patients also noted that they wanted to undergo a "correct" treatment on this occasion. These answers indicate that patients seeking care with physicians may be more receptive to discussions about antibiotic utilization and self-medication, and more likely to understand that past treatment with antibiotics might influence current treatment failure. Consults, then, could be a potential forum for discussions on the possible role of self-medication with antibiotics in creating antibiotic resistance.

Summary of Findings

The following is a summary of some of the key points presented in this paper, from quantitative, qualitative, survey, and field note data:

1. Thirty-five percent of this study's participants had a history of self-medication.
2. No clear associations were seen between demographic variables (including gender, race, literacy, and age) and a history of self-medication.
3. Of the study participants found to have a laboratory-confirmed UTI, an extremely high percentage (60.8%) had resistant infections.
4. A history of self-medication may have increased the risk of developing an antibiotic resistant UTI (OR=1.81; OR=1.06 for *E. coli* UTI). The relatively small sample size may have contributed to the lack of significant association.
5. Pharmacies, both commercial and hospital, were by far the most common source for obtaining antibiotics.
6. Pharmacy prescribing practice has improved over the last 25 years in Brazil: one third of the pharmacies in this sample refused to recommend or sell antibiotics without a prescription, as per the law. Of the sites which did recommend antibiotics, the majority of treatments recommended (80%) would have effectively treated the "diagnosed" illness. Nevertheless, questionable prescribing practices (multiple antibiotics, insufficient treatment course, incorrect diagnosis or prescription) were still seen, more so in small pharmacies than larger, chain stores.

7. Physician antibiotic prescribing practice for the same illness is often widely variable and inconsistent (eg, antibiotic choice, length of course).
8. Other structural factors, such as the packaging of antibiotics in quantities not consistent with common treatment regimens, may influence the misuse of these medications.

Most public health research collects data that is used to inform policy or individual behavior interventions. In this case, large-scale policy interventions seem less realistic, in light of the fact that existing policies on medication sales in Brazil are not enforced. One author (13) notes that inappropriate use of pharmaceuticals, historically, has never been improved with interventions targeted at the pharmaceutical industry. A more effective approach might be, then, to focus on the two groups who are with patients at "teachable" moments, when information imparted and discussed is of most impact, and whose own prescribing practice is likely to have a tremendous impact on antibiotic utilization: pharmacy attendants and physicians.

Kamat (25) reports that most pharmacy attendants, when asked, were eager to learn more about the drugs they sold and enthusiastic about opportunities for training. The author suggests, however, that with some exceptions, this was likely due to the perception that more knowledge and training would lead to a better-paying job, and had little to do with a desire to better serve the public. He also questions the feasibility and sustainability of pharmacy training programs for attendants given demands on their time and profit motives inherent in their business. Nevertheless, many successful small-scale programs for training pharmacy attendants have been carried out in multiple countries, including Nepal (26) and Uganda (27).

One interesting result from the pharmacy survey section of this study was that prescribing practice seemed to be relatively, though not always, consistent across pharmacies of a common chain. Although study investigators expressed some doubt that the dissemination of results from the larger study on resistance and proper empiric treatment could impact the prescribing practices within pharmacies, this result suggests that dissemination of this information to pharmacies and not only physicians may have some effect.

The negative attitude of many physicians toward self-medication makes many patients less likely to disclose information about this behavior to their physicians. Studies consistently show that doctors are often unaware of the many medications their patients are taking (28). As detailed in the previous paper, patients are also more likely to seek care elsewhere, or self-medicate, if there is a lack of coherence between their ideas of illness etiology and those of their physicians, or if these issues are not addressed (29-32). Physicians often avoid broaching these topics because of fear that patients will not understand explanations or that the discussions will take too long.

Haak (13) maintains that the Brazilian patients in his study were extremely interested in discussions about proper use of medications, and suggests that "perhaps in this keen interest [is] a potential solution to problems of over-medication and the irrational use of pharmaceuticals in the Third World". Moreover, past studies in Brazil have asserted that despite practice, patients generally viewed self-medication negatively. Filho (11) reports that participants who self-medicated saw themselves as "complacent, sloppy, and uninformed" and that participants who did not self-medicate viewed those who did as "ignorant and irresponsible." Field notes taken during patient interviews,

along with qualitative response data [Table 6] affirmed that many patients realize that self-medication may not be the best option for treatment. Instead of turning a blind eye to the behavior of their patients, physicians need to figure out the best way to meet patients on a level where discussions on these issues can be participatory and useful.

During the course of data collection, one open-ended question was asked of participants at the end of each interview to explore community explanatory models of illness, or health beliefs, regarding urinary tract infection: "What do you think caused your current UTI?" Patients correctly identified many factors that could have contributed to their UTIs, such as frequent sex, poor hygiene, and limited water intake. They also expressed some beliefs about UTI etiology that do not fit into the allopathic medical model, e.g., contact with rain, theories of hot/cold, and ideas about food intake [refer to Appendix 1 for a listing of coded answers]. Perhaps even more fascinating and provocative than the content of the responses themselves was the way in which this simple question consistently opened up conversation about health concerns, and gave patients and providers (study investigators) a forum for discussion and inquiry. Participants seemed pleased, and often surprised, to have the space to talk with the study investigators about these issues, and were interested to hear what the study team thought had caused their infections. Many explained that providers in the public health facilities rarely take the time to ask them questions, to explain what causes illness, and to elicit patient opinions and explanations.

These short "interviews" usually added less than one minute of time to each consult and prompted many patients to ask intelligent questions about disease etiology and correct methods of treatment. If discussions about somewhat complicated issues like

antibiotic resistance and self-medication behavior are to take place during physician-patient consults, perhaps a simple question like this one could be a fitting prelude to these conversations. Understanding individuals' beliefs about illness causality enables health providers to establish trust, reinforce accurate beliefs, and correct misunderstandings to both improve the effectiveness of treatment and prevent future infections.

Conclusions

Issues of antibiotic utilization and resistance have become universal concerns in global communities, despite often dramatically different social, economic, and political circumstances. Although the results obtained in this study may not be applicable or generalizable to self-medication and pharmacy prescribing behaviors in other settings, the structure of this study provides a useful model for others wishing to gather more relevant and specific information about antibiotic use and self-medication in local community settings. Replicating these types of inquiry in other settings will yield quantitative and qualitative data to inform analogous though geographically disparate discussions of the multiple social contexts of antibiotic resistance.

Confronting the problem of antibiotic resistance in community-level settings requires creative interventions targeted at multiple levels, from individual/behavioral to structural/policy. The object of investigating who and what contributes to the development of antibiotic resistance should be not to place blame on certain groups of individuals, but to better understand where and how to focus resources, time, and energy. The discussion on self-medication and antibiotics, both in current and future literature, and among biomedical researchers, scientists, and health professionals, needs to be better

informed by the complexities of the situation. This paper has presented one model by which this can be accomplished, in local settings globally, in the future.

TABLE 1: DEMOGRAPHICS (N=111)	
Variable	*Frequency (%)*
Gender	
Male	21 (18.9%)
Female	90 (81.1%)
Age	Mean=35.1
Male	Mean=39.4
Female	Mean=34.0
Race	
White ("Branco/a")	41 (36.9%)
Asian ("Amarelo/a")	1 (0.9%)
Black ("Preto/a")	21 (18.9%)
Mixed Race ("Pardo/a")	35 (31.5%)
Other	13 (11.7%)
Education – Highest Level Completed	
Less than Primary School	47 (42.3%)
Primary School (through 8th grade)	22 (19.8%)
9th grade	2 (1.8%)
10th grade	3 (2.7%)
Secondary School (through 11th grade)	26 (23.4%)
Some Higher Education	11 (9.9%)
Literacy	104 (93.7%)
Monthly Income	
R$0-350	12 (10.8%)
R$351-700	34 (30.6%)
R$701-1500	38 (34.2%)
R$1501-3000	10 (9.0%)
>R$3000	5 (4.5%)
No response given	12 (10.8%)
Pregnant (women only; N=90)	
Yes	11 (12.2%)
No	76 (84.4%)
Not Sure	3 (3.3%)

TABLE 2: SELF-MEDICATION (N=111)	
Variable	*Frequency (%)*
Past History of Self-Medication	**39 (35.1%)**
Had health insurance at time of self-medication	6 (15.8%)
No health insurance at time of self-medication	32 (84.2%)
No Past History of Self-Medication	**70 (63.1%)**
Not sure	2 (1.8%)

CURRENT ILLNESS	
Already treated with antibiotics at time of presentation	29 (26.1%)
Sources of treatment recommendations	
Physician	19 (65.5%)
Own Choice	6 (20.7%)
Pharmacy Attendant	3 (10.3%)
Other	1 (3.4%)
Place where antibiotics obtained	
Friend	0 (0%)
Family member	0 (0%)
Health professional free sample	0 (0%)
Hospital/commercial pharmacy	26 (89.7%)
Leftover from past UTI treatment	1 (3.4%)
Leftover from other past treatment	2 (6.9%)
PAST UTI	
Treated with antibiotics	44 (39.6%)
Sources of treatment recommendations	
Physician	44 (100%)
Own Choice	0 (0%)
Pharmacy Attendant	0 (0%)
Other	0 (0%)
Place Where Antibiotics Obtained	
Friend	0 (0%)
Family Member	0 (0%)
Health professional free sample	1 (2.3%)
Hospital/Commercial Pharmacy	41 (93.2%)
Leftover from past UTI treatment	1 (2.3%)
Leftover from other past treatment	1 (2.3%)

TABLE 3: ANTIBIOTIC RESISTANCE (laboratory-diagnosed UTI, n=54)

Variable	*Frequency (%)*
Microbial Pathogen	
E. coli	32 (59.3%)
Staphylococcus saprophyticus	8 (14.8%)
Polymicrobial	4 (7.4%)
Others (Enterobacteria other than *E. coli*; *Enterococcus)*	10 (18.5%)
Resistant infection	**32 (59.3%)**
E. coli	19 (59.4%)
Staphylococcus saprophyticus	1 (12.5%)
Polymicrobial	4 (100%)
Others	8 (80%)

TABLE 4: DEMOGRAPHICS AND SELF-MEDICATION (n=109)[a]

Variable	*Freq (%) with history of self-medication*	*Freq (%) with no history of self-medication*	*OR (95% CI)*	*P value (Yates)*
Gender				0.76
Male	7 (33.3%)	14 (66.7%)	0.88 (0.28-2.64)	0.99
Female	32 (35.6%)	56 (62.2%)	1.14 (0.38-3.52)	0.99
Race				0.34
White	13 (31.7%)	27 (65.9%)	0.80 (0.32-1.95)	0.74
Asian	0 (0%)	1 (100%)	0	0.77
Black	6 (28.6%)	15 (71.4%)	0.67 (0.21-2.08)	0.61
Mixed Race	11 (31.4%)	23 (65.7%)	0.80 (0.31-2.05)	0.77
"Other"	9 (69.2%)	4 (30.8%)	4.95 (1.25-21)	0.02*
Education[b]				
Literacy				0.77
Yes	37 (35.6%)	66 (63.5%)	0.84 (0.11-7.59)	0.77
No	2 (33.3%)	3 (50%)	1.19 (0.13-9.32)	0.77
Not Sure	0 (0%)	1 (100%)	…	…
Monthly Income				0.99
R$0-350	4 (33.3%)	8 (66.7%)	0.92 (0.21-3.76)	0.85
R$351-700	12 (35.3%)	21 (61.8%)	1.09 (0.41-2.86)	0.98
R$701-1500	13 (34.7%)	24 (63.2%)	0.68 (0.28-1.68)	0.48
R$1500-3000	3 (30%)	7 (70%)	0.77 (0.15-3.68)	0.99
>R$3000	2 (40%)	3 (60%)	1.25 (0.14-9.89)	0.81
Pregnant (n=88)[a]				0.42
Yes	2 (18.2%)	9 (81.8%)	0.33 (0.05-1.80)	0.27
No	30 (38.1%)	44 (59.8%)	3.07 (0.55-22.22)	0.27
Not Sure	0 (0%)	3 (100%)	…	…
Age	Mean=37.7	Mean=34.0	…	…
Laboratory-Diagnosed UTI (n=52)				
Resistant Infection (n=31)	13 (41.9%)	18 (58.1%)	1.81 (0.48-7.01)	0.49
Non-Resistant Infection (n=21)	6 (28.6%)	15 (71.4%)	0.55 (0.14-2.10)	0.49
E. coli UTI[c] *(n=34)*				
Resistant Infection (n=21)	10 (47.6%)	11 (52.4%)	1.06 (0.21, 5.30)	0.79
Non-Resistant Infection (n=13)	6 (46.1%)	7 (53.8%)	0.94 (0.19, 4.69)	0.79

[a]2 participants included in Table 3 figures were unsure of whether or not they had self-medicated, and were excluded from this analysis.
[b]the education analysis could not be performed, for reasons explained in the discussion.
[c]for the purposes of this analysis, polymicrobial infections with an *E. coli* component were included as *E. coli* infections.

Table 5:
PATIENT RESPONSES: WHY DID YOU DELAY SEEKING PHYSICIAN CARE, CHOOSING INSTEAD TO SELF-MEDICATE? (n=39)
(in cases where more than one answer was given, all answers are included in tabulations below)

"I already knew the symptoms."	30
"It was easier to take an antibiotic without a consult."	17
"It would have taken too long to get medical attention."	14
"My symptoms were really bad and I needed to start treatment right away."	13
"I had a problem with transport to the clinic or hospital/the clinic or hospital wasn't easily accessible."	5
"I would have had to pay for the consult and I didn't have enough money."	3
"I didn't trust the available physician or clinic/hospital."	3
Other: "A friend or family member recommended that I self-medicate."	4
Other: "I had time constraints due to work."	1

Table 6:
PATIENT RESPONSES: WHY DID YOU CHOOSE TO SEEK CARE TODAY FOR YOUR CURRENT INFECTION?

Treatment failure/recurrence of infection	9
Worsening symptoms, new symptoms	7
Increasing pain	4
Recommendation or pressure from friends/family/spouse	4
Facilitating factors: proximity to hospital, faster medical care at this hospital	3
Desire to "correctly" treat the infection	3
Abnormal/altered laboratory test results	2

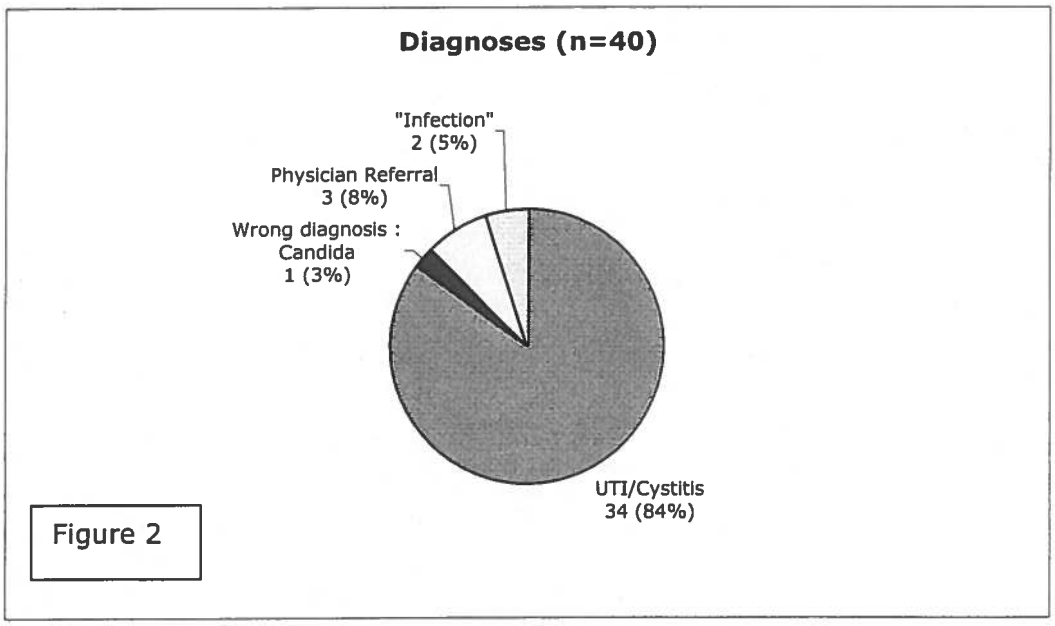

Figure 2

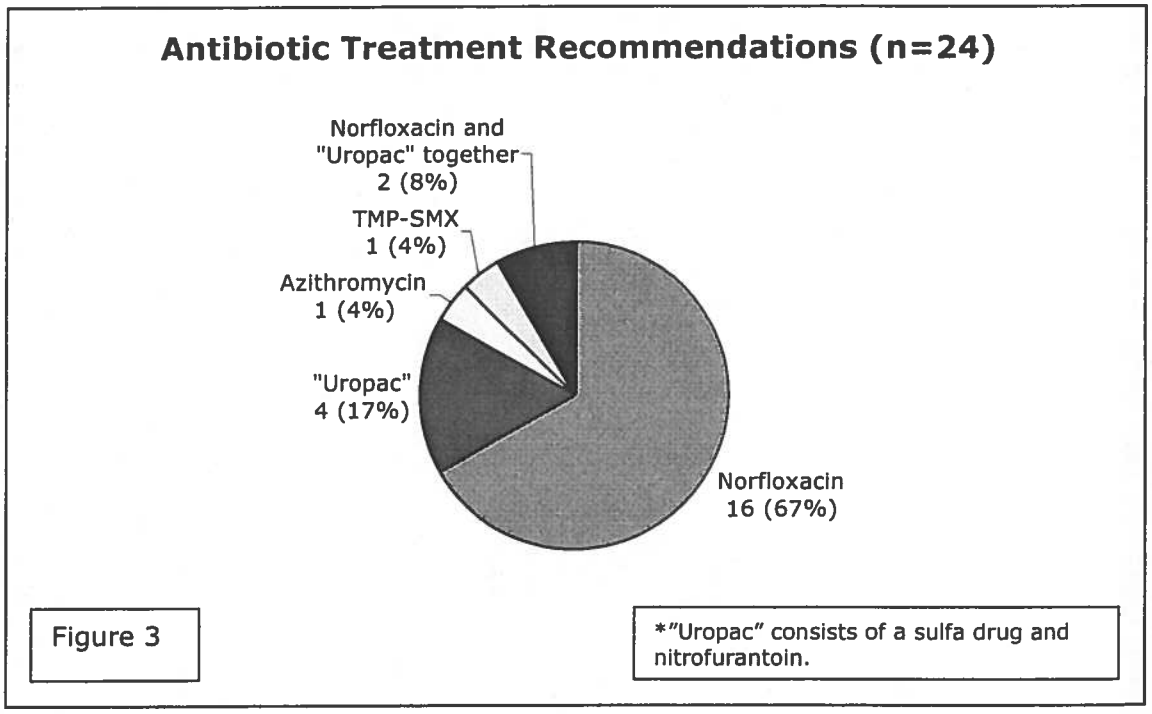

Figure 3

*"Uropac" consists of a sulfa drug and nitrofurantoin.

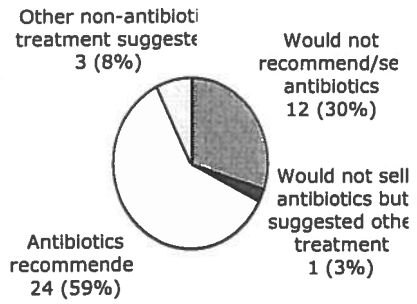
Prescribing Practice (n=4
Other non-antibioti
treatment suggeste
3 (8%)
Would not
recommend/se
antibiotics
12 (30%)
Would not sell
antibiotics but
suggested othe
treatment
1 (3%)
Antibiotics
recommende
24 (59%)

Figure 4

Appendix 1:

Patient Responses to Open-Ended Question – "What do you think could have caused your UTI?"

(n=111; when more than one answer given, each was counted equally in tabulations below)

Other Health Conditions/Medical Problems – 21 (2 participants mentioned more than 1 of the following categories in their answer)

medications – 3

OB/gyn – 7

back pain – 3

other/physiological disposition – 5 (answers were worms, arthritis, increased uric acid or cholesterol, obesity, small stature)

factors recognized by the biomedical community as related to the risk of (complicated) UTI – 5 (answers were diabetes, kidney stones, bladder pathology, pregnancy)

Sex – 16

specifically, without a condom/unprotected – 4 (of the 16)

Hygiene (including contact with public restrooms or other "dirty things" like the ground and street drugs) – 13

Limited Water/Liquid Intake – 10

Stress/Busy Lifestyle – 8

Related to Food/Drink Intake – 6

specifically, too much coffee or soda – 3 (of the 6)

Contact with Water (dirty, salty, rainwater) – 5

Clothing (sharing with others, not washing properly, not ironing) – 5

"Prender" a urina (delaying urination) – 4

Contact with Pets/Animals – 3

Age – 3

Environmental (moon, sun, hot weather) – 3

Menstruation/Menopause – 2

Delaying medical care – 2

Hot/Cold Imbalance – 1

Bacteria – 1

No Cause – 1

Don't Know – 15

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