Antibiotic Resistance and the Placebo Effect

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Caroline Anderson

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Advisor

Bryn E. Seabrook, Department of Engineering and Society

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Introduction

According to the National Foundation for Infectious Disease, 1 out of every 4 antibiotics prescribed in outpatient settings in the United States is unnecessary (*What Is Antibiotic Resistance?*, n.d.). Antibiotics are exclusively effective against specific bacterial infections, yet are frequently prescribed for conditions for which they are neither necessary nor helpful, such as for viral infections. Overuse of antibiotics accelerates the development of antibiotic resistance, wherein bacteria evolve to evade treatment, an issue that the Center for Disease Control and Prevention has declared as "one of the world's most urgent public health problems" (*About Antibiotic Resistance*, 2019). Despite decades of efforts to reduce antibiotic overuse through education on antibiotic resistance and proper antibiotic usage, prescription rates have shown no substantial decrease over the last five years (*Outpatient Antibiotic Prescriptions*, 2021).

Consistent overprescription of antibiotics despite knowledge of the correct usage and risks of misuse suggests the existence of a perceived benefit derived from consuming antibiotics. The placebo effect describes a phenomenon in which a health outcome becomes associated with a medical intervention, despite the intervention being unable to produce that outcome (*Placebo Effect*, 2021). Inappropriate antibiotic usage can thus be considered a placebo. To investigate the origin and pervasiveness of the antibiotic placebo effect, it is necessary to evaluate the two primary actors in antibiotic usage: the patient and the prescriber. This report aims to use the framework of the Social Construction of Technology (SCOT) to aid in elucidating how the placebo effect impacts antibiotic overprescription in the United States.

Research Question and Methods

The research question guiding this report is as follows: in the context of antibiotic resistance, how does the placebo effect impact antibiotic overprescription in the United States? This paper first explores the historical environment in which antibiotics were developed, including initial patient and prescriber attitudes. The analysis then employs the principle elements of the SCOT framework: interpretive flexibility, relevant social groups, closure, stabilization, and wider context. Wider context, which plays "a minor role in Pinch and Bijker's original conception of SCOT" is included to address critiques that SCOT overlooks the impact of larger social structures (Klein & Kleinman, 2002a). Each element is explored in depth to investigate how the social shaping of antibiotics over time is related to present day overprescription.

Documentary resources and discourse analysis are the primary methodologies this report utilizes. Individual sources are identified using the search engines Web of Science and PubMed. Keywords for search engine queries include: "prescribing trends," "prescriber pressures," "overprescription," "patient requests," "attitudes towards antibiotics," "patient prescriber relations," and "patient action bias". These keywords aim to yield sources that gain an insight into both the perspective of the public and the physicians prescribing the antibiotics.

Overview of the History of Antibiotic Usage

Alexander Fleming is credited with discovering the first antibiotic, penicillin, in 1928 (*The History of Antibiotics*, 2023). World War II served as the impetus for the first wide scale production of penicillin, as the US government encouraged companies to ramp up production in anticipation of D Day. Penicillin became colloquially known as the "miracle drug," likely due to its revolutionary ability to cure infections which previously would have been considered fatal.

Initially, penicillin was available almost exclusively to military personnel, but word soon got to the public as companies leveraged the "miraculous" abilities of penicillin to boost morale and productivity in factory workers. A 1943 article in the *New York Herald Tribune* gives insight into the public's initial attitudes towards the drug: "Many laymen- husbands, wives, parents, brothers, sisters, friends- beg Dr. Keefer for penicillin" (*Discovery and Development of Penicillin*, n.d.). Thus even before penicillin was commercially available, public perception was exceedingly positive.

Post World War II, production of penicillin continued to soar, and the price per dose dropped from $20 to $0.55 in the span of a few years (*Discovery and Development of Penicillin*, n.d.). In 1945, Fleming received the Nobel Prize in Medicine alongside two other scientists who were instrumental in the manufacturing of penicillin (*The History of Antibiotics*, 2023). This same year, Fleming expressed concerns over the potential for the emergence of antibiotic resistance. The commercialization of penicillin sparked the discovery and production of a multitude of antibiotic strains, the last of which was discovered in 1987.

The remnants of the mentality of antibiotics as a "miracle drug" is still found today. One study of American patients found that in a cohort of patients with viral colds, 27% felt they would heal faster if given an antibiotic, and 48% expected that the physician would write them a prescription for antibiotics (Hulscher et al., 2010). In addition, a study on family physicians in the UK found the physicians were more likely to prescribe antibiotics when the patient expressed a desire for a prescription (Sirota et al., 2017). Coupled together, patient desire for a curative treatment may directly affect prescription rates.

Introduction to the Social Construction of Technology (SCOT)

Developed by Wiebe Bijker and Trevor Pinch, the Social Construction of Technology (SCOT) is a theoretical framework which focuses on how relevant social groups, defined as having members who "share the same set of meanings, attached to a specific artifact", participate in the processes of stabilization and closure of the meaning of an artifact (Klein & Kleinman, 2002b). Each relevant social group is considered to contribute equally to the process of closure and stabilization of the technology as an artifact. As Klein & Kleinmann point out, one critique of this approach is that it "overlook[s]… asymmetries of power" (Klein & Kleinman, 2002b). Some social groups may have more members, a greater ability to organize, superior funding, or other attributes that allow them to exert a stronger influence on the shaping of the technology. In order to avoid ignoring the complexity of power dynamics, the influence the social groups have over each other as well as their access to resources will be included in the analysis.

Literature provides numerous examples of contexts in which SCOT has been implemented. One relevant previous usage of SCOT is to explain the normalization of an attitude or activity. Santana used SCOT to show how working overtime became an expectation for employees in the gaming industry (Santana, 2020). A separate study on public perceptions of wind energy used SCOT to explore the origins of common misconceptions about wind energy (Morrow, 2022).

Although many different fields have utilized SCOT over the years, the medical field, with its distinct social groups, long history, and deeply entrenched cultural norms, is particularly well suited to analysis with SCOT. For example, Lin used SCOT to analyze how previous medical trials, particularly the Tuskegee Syphilis Experiment, contributes to distrust in experimental health studies, and how this directly plays into modern day underrepresentation of minorities in

clinical trials (Lin, 2020). A second example of the usage of SCOT in a medically derived context is how Stiglitz used SCOT to analyze how obstacles in the regulatory pathway inhibit innovation and implementation of novel technologies for pediatric patients, and how stakeholders can leverage their influence to alter the process (Stiglitz, 2022).

In the context of antibiotic resistance and overprescription, the two primary social groups are patients and prescribers. Patients possess less clinical knowledge, and may be influenced by action bias to prefer intervention based treatment, but hold the power to alter a physician's reputation. Prescribers possess greater medical expertise, and may be influenced by the desires to please the patient, maintain a positive reputation, and work in an efficient manner. Similar to the examples of SCOT usage presented above, this paper will aim to establish how the historical development of antibiotics impact patient and prescriber perceptions, and finally how these attitudes influence modern day antibiotic usage.

SCOT and the Overprescription of Antibiotics

In order to understand how the placebo effect operates as a modern social phenomenon in antibiotic use, it is necessary to assess how historical factors have shaped previous perceptions of antibiotics. The following analysis is structured according to the principle elements of the SCOT framework: interpretive flexibility, relevant social groups, closure, and stabilization. Interpretive flexibility provides the lens through which the history of antibiotic discovery, production, and use is evaluated. This section follows an approximately chronological timeline, beginning with 1928 and ending with modern day. The remaining sections build upon historical analysis to capture the dynamic interactions between medical practices, patients, and prescribers that have led to a period of simultaneous stabilization and destabilization, and an apparent lack of closure.

Interpretive Flexibility

One of the core elements of SCOT as a framework is interpretive flexibility, which is the concept that the design of a technology can "produce different outcomes depending on the social circumstances of development" (Klein & Kleinman, 2002a). The delayed integration of antibiotics is an illustration of the impact of the social environment on technological development. As covered previously, the first antibiotic, penicillin, was discovered in 1928. Large scale production of penicillin, however, would not occur for well over a decade. The lag time is explained by the evolving social environment during the time period. When Fleming's paper was published, scientists viewed the primary application of penicillin to be in "isolating penicillin-insensitive bacteria from penicillin-sensitive bacteria in a mixed culture" (*Discovery and Development of Penicillin*, n.d.). Efforts to purify and grow penicillin for clinical use began a decade later, the same year that World War II began.

With the start of World War II, penicillin was transformed into no longer just a laboratory tool, but a weapon which when employed could make soldiers healthy again. The Allied Forces saw the potential of the antibiotic to strengthen the army and increase the probability of victory. By 1941, the US Office of Scientific Research and Development was convening meetings with big name pharmaceutical companies such as Merck, Squibb, Lilly, and Pfizer to see what could be done to lower development barriers and increase penicillin yields as quickly as possible (*Discovery and Development of Penicillin*, n.d.). Along with ensuring participating companies were allocated sufficient amounts of materials needed for production, the US War Production Board instructed the heads of these companies to "create enthusiasm for the job, down to the lowest worker" by hanging posters, passing out notices, and telling factory workers that the penicillin they produced would be "saving the life of someone in a few days"

(*Discovery and Development of Penicillin*, n.d.). Such appeals to emotion were wildly successful. The sudden arrival of a treatment that could help bring their loved ones home safely by curing previously deadly diseases naturally lent itself to an air of mystery and magic, and soon the antibiotic was colloquially known as the "miracle drug".

The stark contrast of the public reception of antibiotics pre and post World War II illustrates the profound impact of the social environment on the meaning and usage of the antibiotic as a technology. Had the start of World War II not coincided with the discovery of penicillin, it is plausible that production would not have increased so quickly, as it would have been lacking fervent governmental support. In addition, without government sponsored emotional appeals to a public desperate for the safe return of their family members from war, the public likely would not have embraced penicillin so readily.

Relevant Social Groups

Patients and prescribers serve as the two primary relevant social groups in the narrative of antibiotic overprescription. According to Kleinmann, members of a social group are the "agents"; their "actions manifest the meanings they impart to artifacts" (Klein & Kleinman, 2002a). The negotiation between such relevant social groups is how the meaning of an artifact achieves stability and closure. It is thus critical to assess the needs, motivations, and perspectives that unify the members within each group in order to contextualize their interactions.

The "patient" group includes any person in the United States seeking professional medical care. A commonality found within members of the patient group is the existence of a health issue that the member feels warrants medical attention. Each member is a recipient of care, and seeks advice from a professional whom it is assumed is more knowledgeable about the

condition. There is an implied level of trust in the medical professional, in that the patient sought care and is ready to adhere to the recommended treatment plan.

The "prescriber" group is composed of medical professionals that are legally permitted to write prescriptions for antibiotics. Although regulations vary slightly state by state, generally prescribers include physicians and nurse practitioners. As a service based profession, healthcare tends to attract individuals with high levels of empathy and a predisposition towards taking action. In the United States, outpatient medical practitioners rely heavily on referrals, online patient reviews, and word of mouth to gain new patients. Maintaining a positive reputation is thus critical for the success of the practice.

In a study conducted through the Cleveland Clinic which analyzed the habits of physicians with high and low antibiotic prescribing rates, it was found that regardless of how often a physician prescribed antibiotics, all participating physicians agreed that "prescribing antibiotics improved patient satisfaction" (Patel et al., 2020). Prescribers perceive that patients want to be prescribed antibiotics, and believe that if they do not give the antibiotics to the patient, the patient will be displeased and it will negatively impact profits. It is possible that perhaps prescribers are also not immune to the action bias; they are inherently sympathetic professionals who strive to help and please, who desire to be useful.

Prescribers also face pressures from management concerning efficiency and patient outcomes. Outpatient medical practices receive compensation according to the number of patients that are seen, and the services provided during the visit. Medical offices are thus incentivized to both keep patient visits short and achieve more in a smaller amount of time, all while maintaining the same high quality level of care. Such conflicting expectations put prescribers in a difficult position, where quick but impactful interventions increase in appeal.

Writing a prescription for antibiotics, particularly for a patient who is already requesting them, becomes a logistically favorable option. As high prescribing physicians in the same Cleveland Clinic study by Patel et al. mentioned above stated, prescribing an antibiotic is frequently "easier and faster" when time is tight (2020).

As stated previously, physicians claim that pressure from patients to prescribe antibiotics are a major factor behind overprescription. Patient requests for antibiotics indicate that patients believe taking antibiotics will confer some benefit to them. One explanation for this occurrence could be that there is some level of misunderstanding of the utility of antibiotics among patients. However, online forum posts suggest that this may not be the case.

Reddit threads in communities such as Mommit, a forum built specifically for parents, contain posts and comments which appear to indicate that users are aware of the correct use cases for antibiotics. In addition, multiple responders acknowledge that in order to avoid escalating antibiotic resistance, antibiotics should be reserved for cases in which symptoms persist. In response to one mother's post in which she expressed concern that her sick child had not received a prescription for antibiotics, one user noted that "the vast majority of ear/sinus infections are actually viral" and that "it is becoming increasingly important to only prescribe antibiotics when absolutely necessary" (morewinepwease, 2023). If requests for antibiotic prescription are not a matter of scientific competence, the question remains why prescribers report these requests occurring in cases in which they are not medically indicated.

It is at this point where the placebo effect becomes salient to the discussion. Within Mommit threads, posts containing pro-antibiotic sentiments came almost exclusively from mothers worried about the health of their children. There is an emotional element; the penetrating question, "is there anything I can do?" is a frequent one. It is difficult to see a loved

one in pain and not be able to actively aid in their convalescence. According to a paper published by the Annals of Internal Medicine, a "prescription signifies that the physician has made a diagnosis and that treatment is possible" (Avron & Solomon, 2000). A prescription provides patients with an avenue of action, and places their healing on a trajectory that is well understood and leads towards recovery. Patients understand that when they have a bacterial infection and take antibiotics, the infection is often gone by the time the round of antibiotics is finished. Reception of antibiotics allows patients to assume a familiar role in which they are agents in their own care and can expect to feel better within a specific time window. In a period of confusion and fear, the action bias of the placebo effect gives patients the semblance of control over their health that they crave.

Closure and Stabilization

Whether or not the meaning of the antibiotic as an artifact ever fully achieved complete closure and stabilization is debatable, and is dependent on the interpretation of what is needed for stabilization and closure. If stabilization is meant to refer to a period of little or no change, then one could argue stabilization was present during what is sometimes referred to as the "antibiotic era". This time period encapsulates the 1950s through the 1970s, and corresponds to a time when the number of antibiotics on the market was rapidly expanding. New classes of antibiotics were being discovered seemingly continuously, and a dichotomy of understanding and perception of antibiotics between patients and prescribers persisted, preventing true closure. Multiple scientists expressed concerns about the potential for antibiotic resistance, but there was no widespread coordinated effort to alter usage. Public reception continued to be enthusiastic and somewhat illformed; as Mary Barber, a British pathologist, stated in 1948: "a precise understanding of just what [antibiotics] will and still more important what [antibiotics] will *not* do is often lacking"

(Podolsky, 2018). Stabilization was present in the sense that the meaning of the antibiotic as an artifact remained nearly the same over a period of twenty years. In short, there was stability in artifact meaning, but there was not consensus.

The brief period of relative stability began to dissipate with increasing concern about antibiotic resistance. The first widespread efforts to reduce antibiotic usage started in the late 1970s and early 1980s, with World Health Organization (WHO) organized meetings, and the foundation of the Alliance for the Prudent Use of Antibiotics (APUA). Over the next several decades, efforts to increase public awareness would be launched, as well as programs to educate prescribers on the risks of overprescription. Thus launched the paradoxical period of widespread acknowledgement coupled with a lack of progress that extends to the present day, wherein antibiotic resistance has become an urgent issue.

Stabilization and closure play a counterintuitive role in modern perception of the antibiotic as a technology. Antibiotic misuse remains high, and antibiotic resistance continues to progress, suggesting a negative form of stability. Yet, there is inherent destabilization in the sense that both relevant social groups perceive antibiotic resistance as an issue. In theory, stabilization and closure should go hand in hand, but modern stabilization has taken the form of a stalemate in which no true closure has ever been achieved. Interestingly, it would seem that both patients and prescribers recognize that antibiotic resistance is a problem, but the problem is perceived as an issue with the performance of the other group.

Wider Context

Placing the development of the antibiotic as a technology within the broader medical system allows for the identification of larger themes and implications. It would be remiss to ignore the role power differentials ingrained within the American healthcare system play in the

closure and stabilization of the meaning of the antibiotic as an artifact. As medical professionals, prescribers have an undeniable upper hand in the patient prescriber interaction. The ability of a prescriber to have the final say in whether a patient is given antibiotics inherently ascribes a greater value to the opinion of the prescriber than to the patient. In addition, prescribers dictate the conditions for which antibiotics are "necessary", based upon scientific understanding of disease etiology. Patients do not and cannot play a role in the stabilization of standard of care protocols, and scientifically speaking, their opinion has no effect on the decision. Patients cannot obtain antibiotics without a prescription, and thus overprescription proves prescriber participation in overprescription.

In the consumer based health system present in the United States, the patient also has indirect power over the prescriber. Generally speaking, patients decide when and where they seek medical care. If multiple options are present, which is the case in many scenarios, patients may use online reviews, referrals from other medical professionals, and recommendations from other patients to decide which medical office to select. As mentioned before briefly, negative reviews have the potential to discourage other patients from choosing a specific office, and thus negatively impact the prescriber's business. Prescribers are aware of their reliance on patient satisfaction, and thus are incentivized to please the patient (Kohut et al., 2020). Patients therefore possess a power over the monetary success of the prescriber's business, making the prescriber more likely to comply with patient requests.

There are limitations to these findings, namely that the analysis was tailored specifically to antibiotic overuse in the United States. However, antibiotic misuse is not just a problem in the United States; it is an issue of global concern, and some studies suggest it is more rampant in low to middle income countries. While parallels certainly exist in the manifestation of antibiotic

overuse internationally, the intricacies of the issue differ significantly from place to place according to variations in the structure of the healthcare system, educational level of the public, incidence of bacterial infections, and types of bacterial infections most common in the region, to name a few. For example, there are some central and south American countries in which antibiotics do not require a prescription. In some of these countries, pharmacists are able to give antibiotics at their discretion (Gartin et al., 2010). As a result, pharmacists are a relevant social group that play a much more pertinent role in antibiotic use than they do in the United States.

Ultimately, the findings of this research project could be applied towards a global goal of investigating the effect of different healthcare infrastructures on patient-prescriber interactions in connection with antibiotic misuse. An intermediate goal, and perhaps an area of future research, could be applying the same research question investigated in this paper to a singular central American country in which pharmacists are allowed to prescribe antibiotics to establish a preliminary comparison.

Conclusion

Decades after initial warning bells were sounded, antibiotic resistance continues to be an issue of serious concern in the modern era. Antibiotic resistance persists in large part due to the overprescription of antibiotics, which itself is a product of decades of discrepancy between patients and prescribers in the meaning each group ascribes to the antibiotic as an artifact. Asymmetries of power, historical precedents, and distinct social pressures all perpetuate this instability, precluding the antibiotic from achieving closure as a technology. In the absence of closure, antibiotics cannot be prescribed in a manner that is universally accepted as appropriate, and thus antibiotic resistance continues to proliferate.

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