A LIFESAVING PILL: AN ANALYSIS OF THE GLOBAL PHARMACEUTICAL MARKET'S IMPACTS ON SUB-SAHARAN AFRICA

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Bachelor of Science in Chemical Engineering

By

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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.

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In 1909, the lesser-known German physician Paul Ehrlich discovered a chemical which proved effective in the treatment of syphilis. He described his discovery as a “magic bullet”, or a compound that only targeted disease-causing microbes and not host cells. Unknowingly in this compound Ehrlich had discovered what would become the world’s first antibiotic, arsphenamine (Aminov, 2010). Over the coming century, antibiotics would become a staple of healthcare and be used to save millions of lives. As research into antibiotics improved and spread around the world, antibiotics became commonplace in the developed world. However, parts of the world today have been left out of these advancements, causing bacterial diseases such as pneumonia, pertussis, and tuberculosis to run rampant in spite of the existence of effective treatments. The two primary regions affected most by this inequity are southern Asia and sub-Saharan Africa.

Deaths in sub-Saharan Africa due to bacterial diseases is in direct contrast with the decrease in antibiotic cost and the increase of antibiotic production in the developed world. With the development of antibiotic technology, why is there an increase in bacterial related deaths in this part of the world? The STS thesis aims to answer this question through the creation of an Actor Network model in accordance to Actor-Network Theory (ANT). An enhanced understanding of the relationships between various stakeholders in the global pharmaceutical market can allow for an investigation into a proposed course of action to right the wrongs that the industry has created. This analysis is pertinent to any entity attempting to enter the pharmaceutical market in Africa, such as the focus of the technical project.

To reduce the number of deaths caused by bacterial diseases in sub-Saharan Africa, the technical project involves the design of a manufacturing facility for the production of the active pharmaceutical ingredient penicillin V in South Africa. Penicillin V is one of the most prescribed antibiotics in the world, and further processing of it can result in Amoxicillin and Ampicillin

derivatives. It is included on the World Health Organization's model list of essential medicines, a list which details the critical drugs a country should secure supply for in order to satisfy the primary health care needs of their population. Ensuring ample amounts of the drug in the region through its local manufacture can significantly impact availability. The project further aims to use wastepaper as a feedstock, alleviating strain on South Africa's garbage disposal network and limiting the environmental impact of the facility. The technical team aims to reduce drug cost to consumers as much as possible while maintaining profitability of the facility. The technical thesis will be completed along with Justin Harrington, Nathan Ruppert, Shining Wang, and Kingsford Yeboah under the direction of Eric Anderson in the department of chemical engineering.

The technical and STS topics are tightly coupled as the facility designed to manufacture penicillin V could provide the much-needed medication to sub-Saharan Africa, thus alleviating the strain discussed. Additionally, analysis of the network presented can inform the technical group of any possible problems that may arise were the hypothetical facility to be implemented. The introduction of this facility in the region will no doubt produce ripple effects ranging from stimulation of local economy, changes in foreign trade, infrastructure reform, and enhanced government regulation. All of these effects can be traced back through the complicated relationships between entities with vested interest in the cause.

THE CURRENT STATE OF ANTIBIOTICS IN AFRICA

According to the Centers for Disease Control, antibiotics are a class of drugs that fight infections caused by bacteria. Among the most prevalent of these are such conditions as strep throat, whooping cough, and urinary tract infections (CDC, 2021). While in America and much of the developed world these diseases are considered highly treatable and thus non-fatal for the majority of the population, this is not the case in poorer areas of the world where steady access to antibiotics is limited. As shown in Figures 1 and 2, lower respiratory infection, a condition easily treatable by antibiotics, was the fourth leading cause of death globally in 2019, but the second leading cause of death in low-income countries. With over 400,000 deaths per year, the majority of those being children under 5, it begs the question on why these deaths occur.

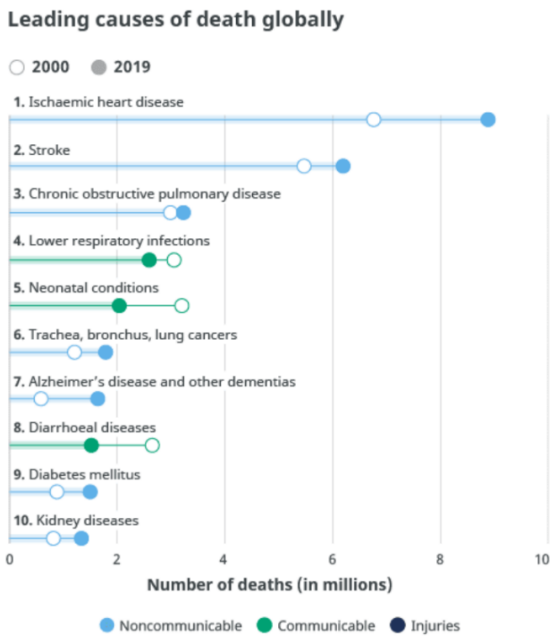

Figure 1: Leading Global Causes of Death. This figure shows the top ten global leading causes of death from 2000 and 2019 (World Health Organization, 2020a).

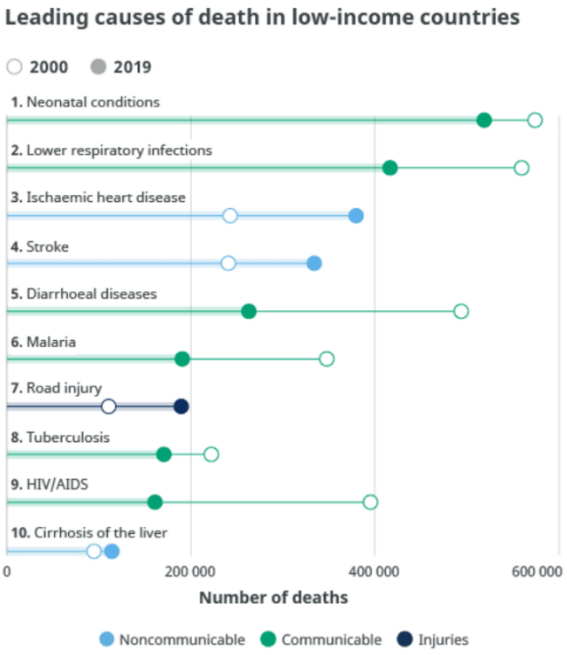

Figure 2: Causes of Death in low-income countries. This figure shows leading causes of death in low-income nations from 2000 and 2019 (World Health Organization, 2020a).

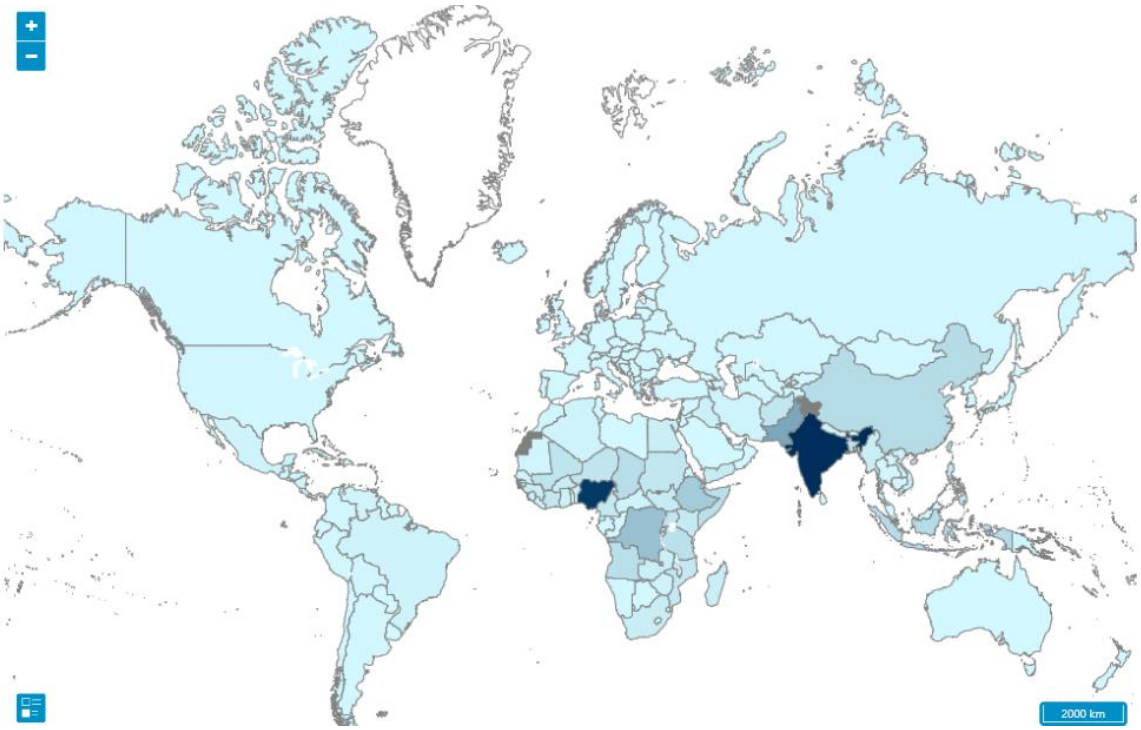

Figure 3: Infant Deaths from Lower Respiratory Infections. This figure shows a heat map of children aged 0-4 deaths due to lower respiratory infections (World Health Organization, 2020b).

Two regions of the world are responsible for the majority of these deaths: Southern Asia and sub-Saharan Africa, as seen in Figure 3. Focusing specifically on sub-Saharan Africa, numerous reasons exist for why antibiotic access remains difficult. Firstly, registration of new drugs is a significant hurtle for drug companies to provide access to new technology. In an article published by the National Institutes of Health, the 54 different National Medicine Regulatory Agencies (NMRAs) in Africa each have unique authority in their respective countries and thus, each have unique regulatory requirements for the registration of new drugs (Ndomondo-Sigonda, 2017). It is unlikely that these agencies will be able to unify under a common authority, such as the African Union, so for now, providing widespread access to the region is difficult and costly. In the timespan of 1999-2014, of the 21 new antibiotics to enter the global market, only 4 were

registered in the majority of countries in sub-Saharan Africa (Madhumita, 2019). The regulatory hoops that pharmaceutical companies must jump through to access the African market far outweigh the potential benefits.

Second, low spending by the government causes most drugs to become unaffordable for most Africans. In a case study conducted in Uganda, an estimated 41% of healthcare spending is out-of-pocket. This equates to 23% of households spending more than 10% of their income on healthcare (Madhumita, 2019). The subsidy designed to alleviate this economic strain, the National Minimum Health Care Package, only ended up being 30% funded in 2011 (Wright, 2015). With this lack of local government support, it is difficult for companies to maintain profitability in the region. For increased access, drug cost must be kept low, but to please stakeholders and investors, price should be moderated to ensure profitability. In cases such as this where some portion of the global market cannot afford full cost drugs, manufacturers will sometimes sell at a discount in these regions. This is the case with Altripla, Gilead Science's HIV medication. In a New York Times article published in 2018, it was reported that the drug was being sold in Africa for $75 for a yearly regiment, while in America the same regimen cost nearly $39,000 (Rosenberg, 2018). Granted, this statistic is likely more representative of the relationship between drug manufacturers and insurance companies in the United States, it still stands that Gilead Science is willing to provide the drug at a loss in Africa and make up profits in more affluent markets.

Third, poor infrastructure leads to supply chain issues that prevent certain drugs from being able to be administered in Africa. Issues with infrastructure range from lack of proper healthcare treatment facilities, such as hospitals and clinics; roads, railroads, airstrips, and other means of transportation; reliable clean water supply; and electricity power grid. As seen in

Figure 4, the majority of sub-Saharan Africa is not electrified, with only 12 countries reporting greater than 50% electrification (Lakmeeharan et al., 2020). When countries do embark in large-scale infrastructure projects, data shows that very few achieve the necessary funding to complete. Less than 10% of proposals achieve adequate funding, with 80% of all projects failing in the feasibility and business-plan stage (Lakmeeharan et al., 2020). With these failed infrastructure projects, getting drugs to caregivers poses significant problems. For drugs that are highly temperature sensitive, timely transportation is critical to ensure drug stability. Without proper cold storage, even if these drugs arrive at their destination intact, it is unlikely that they can be stored effectively and thus may go unused. Furthermore, for vaccines, lack of access to clean syringes due to shipping delays severely compromises patient care. Until infrastructure is updated and modernized, access to quality pharmaceuticals will remain an issue.

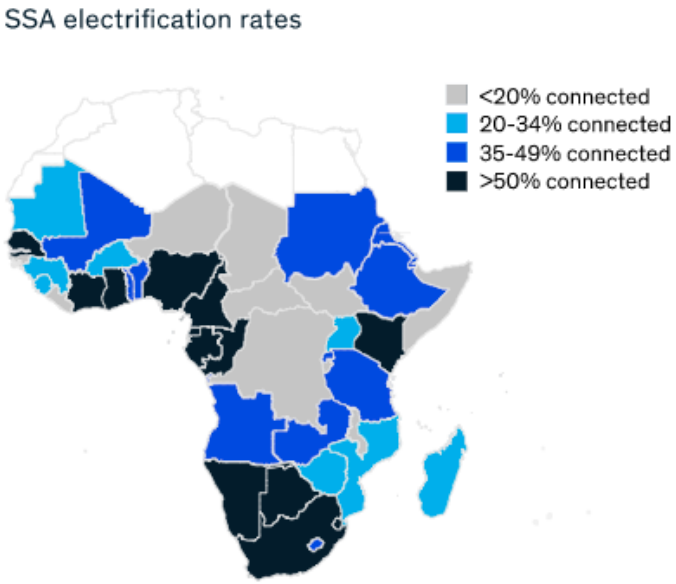

Figure 4: Electrification of Sub-Saharan Africa. This figure shows the electrification rates of each country in Sub-Saharan Africa (Lakmeeharan et al., 2020).

Finally, a widely uninformed public has resulted in the overuse of antibiotics, leading to increased drug resistance across the region. In a 2012 study from the Jomo Kenyatta University of Agriculture and Technology in Kenya, it was found that Pencillase-producing *Neisseria gonorrhoeae* (an antibiotic resistant strain of gonorrhea) increased from being present in 4% of infections to 16%. Strains resistant to tetracycline, a different antibiotic, were detected in 36% of

cases, up from 0% in 2004 (Kimang'a, 2012). This increase in resistance to antibiotics is directly caused by their use. As antibiotics kill off non-resistant bacteria, those that have mutated survive and go on to reproduce. This deadly cycle leads to highly resistant strains of common infections, many of which mean that traditional antibiotic treatments are less effective if still effective at all. This cycle is difficult to reverse, however, securing access to a range of antibiotics is key to fighting resistant infections. As resistance has increased to certain medications, the demand for such medication dies out. If, due to the issues previously discussed, a company's new antibiotic is not adequately stocked, then the disease is allowed to spread unchecked. Even with secured supply of an array of antibiotics, this can sometime not be enough. It is commonplace for doctors to receive incentives from drug manufacturers to prescribe and endorse certain brands. Additionally, prescribers can have financial interest in private pharmacies, prescribing more expensive drugs in return for a kick-back. Corruption causes doctors to not provide the best care, which in tern leads to antibiotic resistance.

The issues presented here in no way encompass the full complexity of this issue, however, these 4 are certainly major influencers. Understanding the interplay between each and the entities most at blame for each can provide the clarity to develop potential solutions.

ANALYSIS OF THE GLOBAL PHARMACEUTICAL DISTRIBUTION NETWORK

Law and Callon's Actor-Network Theory can be used to analyze this distribution network (Law & Callon, 1988). Figure 5, as shown on the following page, shows the connections between many of the relevant actors in the global pharmaceutical market. The actors can be placed into two primary categories: healthcare entities, shown in orange, and non-healthcare entities, shown in blue. The distinction between these two groups is critical as non-healthcare entities are outsiders to the market, in other words, there are not selling or trading goods. Instead,

they act merely as a source of financial capital and regulation. Through the understanding of the various motivations, interactions, and ethics of each actor within this network, the healthcare stakeholders and by extension, the individual patients being affects can potentially generate a solution.

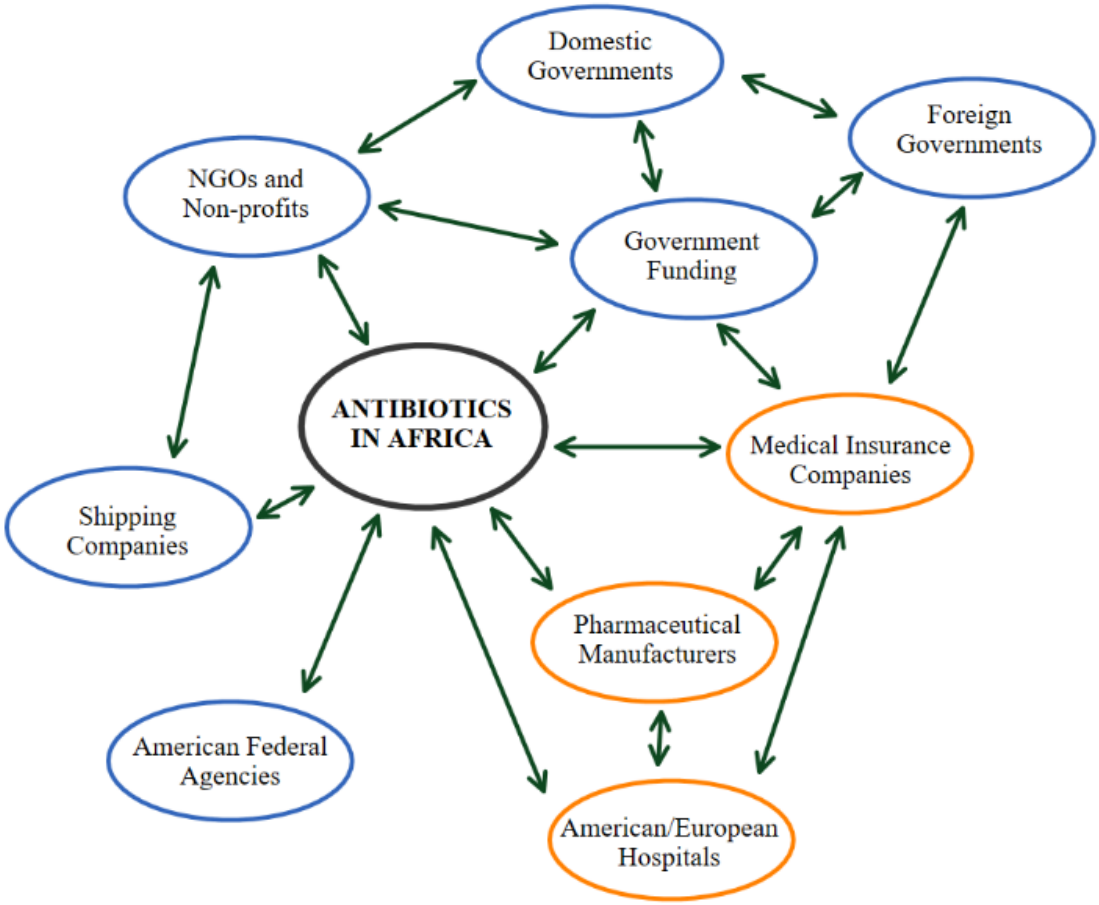

Figure 5: Relevant Actors in the Sub-Saharan Africa antibiotic crisis. This figure is a graphical representation of a proposed network of actors involved in the antibiotic crisis in Africa (Bruns, 2021)

ALEIVIATING INEQUITY IN HEALTHCARE

Ideally, corporations and companies would act out of humanitarian motivation and provide necessary healthcare to sub-Saharan Africa, but on the whole, this is simply not the case. Much of the aid is left up to governments and non-profit organizations that rely on taxpayer

dollars and private donations to fund their aid efforts. This complex network of agents relies inherently on each other, but as discussed, barriers exist that prevent fruitful and mutually beneficial relationships from developing to their fullest potential. To combat these barriers and solve the issue of the antibiotic crisis in Africa, a number of potential solutions have been proposed.

One solution is to provide local manufacturing of pharmaceuticals to address the need at the source. There are numerous benefits to such a plan. Besides the stimulation of the local economy, improved public health, and additional skilled labor positions provided, locally produced drug might end up being more affordable. In an analysis conducted in Ethiopia by McKinsey & Company, the largest management consultancy in the world, a generic over the counter drug could have as much as 12% savings through the use of local manufacturing (Conway et al., 2019). The majority of these savings come from reduced shipping and import costs. This figure however is optimistic at best; with current facilities and resources available in sub-Saharan Africa, the implementation of a drug manufacturing plant would be significantly higher than Indian or Chinese counterparts. Furthermore, as discussed above, the associated cost of patent holders of medications to obtain licenses for African markets often outweighs the financial benefits. In order for it to be feasible and desirable for companies to invest in African manufacturing, government subsidies or private donations will likely need to provide the initial capital. In the same study conducted by McKinsey & Company, further suggestions for local production are provided such as building plants with sufficient production capacity to be profitable and competitive with imports, the creation of regional hubs to include smaller countries where manufacturing is unfeasible, centralize and upgrade current distribution networks, and focusing on securing raw material for production. With all these suggestions, it is

unlikely that the political and economic environment in sub-Saharan will be suited for such investment in the near future, however, alternatives exist.

Ultimately, the most feasible solution is one of government regulation. Many sub-Saharan African nations lack the proper funding to aid themselves, so often rely on international aid packages. While reliance on these packages is proven to be detrimental to local economies, for the time being it appears to be the only solution that the international community can agree to support. Bettering watchdogs to ensure proper spending of aid would be critical to ensuring long term success. Perhaps and attainable goal would be to unify healthcare regulation and drug approval processes for all of Africa, ensuring that drug companies are posed fewer barrier to providing care. Further research should be conducted to determine the feasibility of such changes and the expected outcomes.

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