Vulnerability of the Malaria Vaccine Implementation Network in Sub-Saharan Africa

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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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Introduction

Malaria incidence in the World Health Organization (WHO) African region plagues over 200 million individuals in sub-Saharan Africa each year, most of the cases occurring in children under the age of five (WHO, 2018). To combat this public health burden, Pharmaceutical Group GlaxoSmithKline (GSK) introduced the world's first malaria vaccine, Mosquirix, in early 2019 to be administered in three African countries (Malawi, Ghana, and Kenya) as part of a pilot programme to gather efficacy and safety data. However, the administration of the malaria vaccine organized by GSK has political, social, and economic barriers that limit its success. Scholars such as Jadhav argue that the role of vaccine manufacturers in immunization revolves only around the pricing of the drug product, but fail to acknowledge their non-technical responsibilities such as providing appropriate training to clinical researchers to respectfully engage local trial communities (Jadhav et al., 2014). By disregarding the full spectrum of functions that GSK has in this pilot program, the network for vaccine administration will remain prone to instability.

I will outline how the responsibilities of GSK transcend technical aspects of production into the organization of the immunization program, and by not recognizing these roles, the network is vulnerable. Specifically, I will describe how actors such as the government, clinical researchers, and donors of the initiative have ill-defined roles that jeopardize the quality and robustness of data that will be collected from the pilot program. The malaria vaccine pilot program can be analyzed using Actor-Network Theory (ANT), which highlights the responsibilities of human and non-human actors associated with a heterogeneous network that is meant to accomplish a common goal (Cressman, 2009). I will employ Michel Callon's concept

of Translation, which consists of a five-step method to form and maintain a network, to illustrate at what point the actor-network that GSK is building became susceptible to instability.

Literature Review

Many scholars have researched the challenges of routine immunization in Africa, however, the majority of the analysis tends to focus on the shortcomings of individual stakeholders. In the cases where authors examine community structure, a great deal of the blame is placed on respective African governments for the paucity of funding and resources for immunization. In other instances, the role of vaccine manufacturers in developing countries revolved solely around their pricing of the product. These viewpoints fail to consider how actors are intertwined and rely on one another's actions to create a successful immunization program.

In Mihigo's article, *Challenges of immunization in the African region*, he faults governments in Africa for the stagnant and inequitable immunization coverage. Mihigo highlights the importance of resource mobility, government transparency, and accessibility to vaccination services, which are not always offered. He attributes rising infant mortality to "funding shortfalls and a sapping of political will" (Mihigo et al., 2017). Additionally, he discusses the need for administrations to establish National Immunization Technical Advisory Groups (NITAG) to offer guidance to vaccine regulators based on local epidemiology rather than to depend on incognizant external policy makers. While Mihigo raises a valid point of the importance of governmental input in vaccine coverage, he does not address whose responsibility it is to encourage the government to allocate time and funding towards necessary immunization resources.

Moreover, Jadhav explores the part vaccine manufacturers play in vaccinations in developing countries. He states that by "supplying… the vaccines at affordable prices, [there could be] more vaccine coverage and universal accessibility of Expanded Program on Immunization (EPI) vaccines" (Jadhav et al., 2014). Jadhav's viewpoint places emphasis on how the manufacturers' sole function in immunization is to provide products at a low cost to the consumers, but it disregards their non-technical responsibilities in establishing a successful vaccine implementation program.

The malaria vaccine pilot program has drawn attention globally for its potential to prevent millions of deaths if endorsed by the WHO. There are various challenges in isolating the effects of the vaccine alone as political, social, and economic factors can intervene in immunization practices. The success of Mosquirix depends on human and non-human actors, and thus the administration of this vaccine in sub-Saharan Africa can be analyzed using Actor-Network Theory (ANT) to address how the network that GSK, the network builder, is currently forming is susceptible to instability.

Conceptual Framework

The science, technology, and society (STS) framework Actor-Network Theory (ANT) considers the roles of both human and non-human actors associated with a heterogeneous network that is designed by a network builder to achieve a common goal (Callon, 1987). In ANT, the same systematic and descriptive framework is used for humans, machines, and technology. It is pertinent to consider the structure of a network, as technological design revolves around social and technical engineering in an environment of diverse components that must collaborate to create a stable entity (Law, 1987).

Actor-network theory focuses on the network builders as primary actors and is used as an interpretive lens to understand the process of network construction through the eyes of network builders. Michel Callon's concept of "Translation" describes the process of network formation and outlines the power dynamics between actors. Translation consists of a five step method for a network builder to develop a stable network: Problemitization, Interessement, Enrolment, Mobilisation, and Black-box. Problemitization describes the act of a network builder identifying a problem that must be addressed and the relevant actors who need to be recruited. Interessement occurs as the network builder enlists human and non-human actors and aligns their interests to serve those of the network. Enrolment takes place as the network builder assigns roles to the actors, which they accept and perform. Mobilization eventuates as the network builder accepts the role of coordinating and representing the other actors. Finally, a network becomes a "black-box" when it functions as a stable whole and the primary actor is able to maintain its integrity amidst challenges (Callon, 1987).

Callon demonstrates how a network can collapse if one or more of the actors do not cooperate or fulfill their respective roles. I will use ANT to illustrate GSK's role in forming a network that is prone to instability. The concept of translation will not only highlight relevant human and non-human actors whose roles remain ill-defined but also unaddressed areas of the malaria vaccine administration that threaten the viability of this network.

Analysis

Formation of GSK's Network

First, it is important to describe why and how GSK built this network for the malaria vaccine implementation program, which can be done by applying the conceptual framework of

Actor-Network theory. The malaria epidemic in sub-Saharan Africa has the potential to become a pandemic disease due to climate change, heightening the urgency of a long-term solution for the disease. After 30 years of development, GSK developed Mosquirix, the vaccine that offers partial protection against malaria for children. The clinical trial results had some success but were not sufficient for the WHO to add Mosquirix to the routine immunization program for children in the specified African region. The position of WHO is subject to change depending on the results obtained from the pilot program in Malawi, Kenya, and Ghana, which will determine the feasibility of the vaccine and its safety in the context of routine immunization. The network builder is thus the manufacturer, GSK, who is responsible for aligning the interests of relevant actors to establish a successful and sustainable network that allows for the evaluation of safety and efficacy of the vaccine. However, an argument can be made that the network GSK is building is currently vulnerable.

As proposed by Michel Callon's concept of translation, problemitization is the first step in forming a network. GSK is the network builder for the malaria vaccine pilot program actor-network. GSK, as the primary actor, recognized that the WHO will not endorse Mosquirix without robust data that accurately reflects the vaccine's potency, thus leading to the formation of the pilot program. With the goal of acquiring meaningful data from the pilot program, GSK identified relevant actors to recruit for its actor-network. Not only was the cooperation of local governments essential for approving the project, GSK needed to arrange for clinical researchers to be on-site to administer the vaccine and collect appropriate data (Cohen et al., 2010). Furthermore, GSK understood that it needed to exceed the WHO standards for vaccine effectiveness to be considered for wide-scale deployment, as well as communicate to various

disease related organizations, such as Bill and Melinda Gates Foundation and PATH, to continue receiving funding for the development of the vaccine (Kelland, 2015).

During interessement, GSK recruited the relevant actors by aligning their interests with the network's overall goal. GSK first recruited the WHO, which dictates the future production of Mosquirix. Because malaria is a public health burden and currently has no preventative method to combat the disease, the WHO has struggled to accomplish the Sustainable Development Goals (SDGs) to reduce disease incidences specifically in sub-Saharan Africa (Schnirring, 2013). With that, GSK was able to align its task of obtaining meaningful vaccine data from the pilot program with the aims of the WHO to diminish malaria morbidity. GSK also had to enlist the respective African governments so the pilot program could take place in Malawi, Kenya, and Ghana. The prevalence of malaria has been pervasively dampening economic growth in many African nations (Gallup & Sachs, 2001). With a fruitful economy in mind, the intentions of each government lined up with the goal of GSK. Finally, GSK recruited clinical researchers for immunization services and data collection, as well as disease control groups for the funding of research.

Through enrolment, GSK defined the roles of the relevant actors in the network, which were then, ideally, adhered to for the formation of a successful pilot program initiative. GSK sought the approval of the authorities, namely the WHO and local governments, to establish the program, and expected only technical outcomes from the clinical researchers and consistent funding from well established organizations. Mobilization occured as GSK maintained correspondence between the actors. By communicating the potential rewards of the pilot program to all actors involved, GSK was able to form a seemingly stable network.

Excluded Relevant Actors

GSK was able to recruit various stakeholders for it's network, but neglected one of the most crucial actors who directly contribute to the robustness of data: the local community members. GSK believed that with the cooperation of actors such as the WHO and respective governments, that it indirectly recruited the trial communities to be vaccinated. Since there is high infant mortality due to malaria in sub-Saharan Africa, GSK was confident that the local communities would actively participate in the immunization program. There was no active effort made in educating parents about the importance of immunization, which has been directly correlated with the uptake of vaccines in developing countries (Jheeta & Newell, 2008). For successful immunization programs, "incorporating community values… are key strategies that address human realities in large scale… pilot implementation" (van den Berg et al., 2019).

Parents in local communities face various obstacles to vaccinate their children. They must be proactive in ensuring their kids receive all four doses of the vaccine in a timely manner to fully benefit from the efficacy of Mosquirix. However, the parents can be discouraged by the opportunity costs, such as lost income and time, incurred by taking their children to clinics, especially given that sub-Saharan Africa has the highest poverty rate globally (Patel, 2018). Furthermore, the vaccine has only thus far been introduced to immunization systems in randomly selected districts within the programme, which means that not all the clinics are conveniently located and so accessibility may be limited (Machingaidze et al., 2013). This issue is aggravated further by the underdeveloped public transportation system in certain African regions.

By not addressing the barriers that parents face to vaccinate their children, it is unlikely that parents will go out of their way to receive the malaria vaccine, diminishing the robustness of data that could be collected through the pilot program.

Ill-defined Roles of Actors

GSK inherently excluded trial communities as relevant actors by assigning ill-defined roles to recruited actors. For example, in Malawi, transportation to the clinics is inaccessible for most trial communities and would thus require support from the local government to update the current infrastructure (Machingaidze et al., 2013). During enrolment, the roles assigned to the governments were minimal, as GSK only sought their approval to initiate the pilot program. It appears that the government needed more of an involved position in this actor-network by not only improving accessibility for local communities, but also by allocating funding towards immunization services and updating health policies (Verweij & Houweling, 2014). As mentioned by Mihigo, to improve vaccine coverage in Africa, the government has an important role of creating demand for immunization and surveying the effects long term (Mihigo et al., 2017). By eluding the complete responsibilities of the respective governments, GSK is excluding vulnerable members of trial communities.

Furthermore, studies have indicated that relational ethics, acknowledgment of community dynamics, and commitment to long-term monitoring of the implementation programme need to be prioritized to foster cooperation between clinical researchers and trial communities for successful data collection (van den Berg et al., 2019). Vaccination practices are complex, and the relationship between vaccinators and parents, as well as their perceived intent and technical

competence, are valuable for encouraging guardians to immunize children. GSK assigned only technical roles to the clinical researchers; although it is critical for workers to adhere by formal research regulations, program feasibility is just as important for making a public health impact (van den Berg et al., 2019).

The engagement of trial communities and shared ownership of research is necessary for a successful vaccine campaign (Romore et al., 2015). Close relations between field workers and parents facilitates cooperation between the two parties, leaving guardians with a sense of collaboration to confront social and political issues. It was found that "even in contexts where parental awareness of the vaccine was low, there remained a keen desire to enroll children in the vaccination programs" due to the kinship-like relationships they developed with researchers (Romore et al., 2015). From previous clinical trials for Mosquirix in Tanzania, various stakeholders emphasized the need for a communication and implementation strategy that is inclusive of local communities and their sociocultural backgrounds (Leung et al., 2004). Thus far in the pilot program, GSK has only focused on the technical responsibilities of clinical researchers and risks losing community involvement in the pilot program, a concern expressed by the researchers from Tanzanian clinical trials (Galactionova et al., 2015).

Ethical conduct by field workers does not only apply to the administration of a vaccine but is also encompassed in research, surveillance, and implementation. The behavior of clinical researchers extends to the long-term monitoring results as well, and is inherently needed for the vaccinators to adhere to the stringent ethical guidelines (van den Berg et al., 2019). The vaccine efficacy of Mosquirix dwindles with age and contracting severe malaria is plausible in children at a later age. Although continued evaluation of research sites is resource exhausting, it is

fundamental in discerning the significance of intervention methods and the evolving disease epidemiology. It is through engagement with the field workers that parents are encouraged to report adverse symptoms observed in vaccinated children, which results in identification of risks that can then be clinically investigated (Leung et al., 2004).

The sustained communication between the researchers and trial communities is particularly important for future vaccine uptake. Since the vaccine is less efficacious in older children, parents who are unaware of this diminishing protection could doubt the effectiveness of Mosquirix, and vaccines, overall if their child eventually contracts malaria. Researchers who have gained trust of and developed a relationship with guardians have the ability to describe the shifting disease prevalence that impacts potency of the vaccine, which avoids the potential uncertainty that parents could feel towards vaccines in general (Romore et al., 2015).

Redefining the role of clinical researchers would ultimately benefit GSK in addressing the original problem that set up the actor-network. Close community engagement is favorable as "communities can provide key insights and facilitate research familiarization with the research setting" (Leung et al., 2004). Through effective planning and site organization, greater efficiency for the pilot program could be obtained, which can result in more robust data and reductions in required funding.

Unpredictability in the Network

The low efficacy of Mosquirix could result in further issues in maintaining the actor-network as the support from various actors, such as the WHO or charities, could wane with time. Sub-Saharan Africa has the highest poverty rate in the world, about 30% above the world

average (Patel, 2018). Mosquirix is administered in four doses to be efficacious, with each dose costing about $5; these high costs make the vaccine inaccessible to impoverished individuals susceptible in endemic regions. Therefore, the pilot program has so far been able to launch due to generous donations by charities. However, the future of this funding may be unpredictable. Based on the modest 40% efficacy of the vaccine, immunized children can still contract malaria. Organizations such as the Bill and Melinda Gates Foundation sponsor research for various diseases. Parents whose children are vaccinated but then contract malaria lose confidence for these highly reputable groups and their intentions (Jheeta & Newell, 2008). Potential distrust of sponsoring organizations makes the support of Mosquirix a reputational risk. Additionally, donor support is likely to wane over time due to reductions in developmental budgets and competing priorities within the health sector (Gavi, 2018). Without open communication and acquisition of robust data, GSK could face losses in financial assistance from donors (Kelland, 2015).

I have illustrated that GSK is the network builder and why it is in GSK's best interest to recruit and define roles for relevant actors, which includes local governments, clinical researchers, financial sponsors, and the WHO. On the other hand, some may argue that supervision of the pilot program is actually the responsibility of the WHO, that the goal of GSK to produce an effective vaccine is secondary to that of the WHO to reduce malaria incidence in sub-Saharan Africa and reach the Sustainable Development Goals (SDGs). The WHO does have more authority, influence, and experience in ensuring data quality for such trials to be a more successful network builder compared to GSK (Schnirring, 2013). However, this viewpoint fails to consider what the WHO has at stake by preemptively supporting the Mosquirix pilot program.

Similar to the situation of donors, the low efficacy of the malaria vaccine means that the WHO risks potential distrust of trial communities if it sponsors the Mosquirix pilot program, which could ultimately damage its credibility when endorsing future products or programs. As outlined in the Vaccine Alliance Risk and Assurance Report, one of the greatest risks for immunization is insufficient demand, which is defined as a "significant drop in vaccine demand due to hesitancy and prioritization" (Gavi, 2018). The government has a role to play in providing access to health care services that are safe and affordable to prioritize vaccines, but attention must be paid to where vaccine "hesitancy" arises– it revolves around improving vaccine confidence and trust, and this ultimately depends on who endorses the drug product. This is important to note as the malaria vaccine pilot program is meant to further evaluate the efficacy of Mosquirix, and is not actually being recommended by an organization. If the WHO, a highly regarded global organization, was to be responsible for introducing a low efficacy vaccine, it could be interpreted as a sign of support. Considering most of the recipients are likely to contract malaria even within the recommended age group, the WHO would damage its credibility and future vaccine consumers would feel mistrust towards products endorsed by the WHO, ultimately sparking vaccine hesitancy (Jheeta & Newell, 2008). Additionally, since the pervasive ventures of the WHO in developing countries transcend immunization programs, lack of trust towards the organization would be catastrophic (Eccles et al., 2007). Thus, the potential risks for the WHOs reputation outweighs the incentive it has to oversee the success of the pilot program, whereas GSK can benefit greatly from developing the world's first malaria vaccine for which a treatment method has been elusive. An unsuccessful vaccine for a manufacturer is not severely

damaging for its reputation since failure is part of research (Eccles et al., 2007). Therefore, GSK has the responsibility to supervise the pilot program to establish a successful network.

Conclusion

Individuals globally are anticipating the results from the malaria vaccine implementation program in sub-Saharan Africa, hoping for a more promising form of preventative care for the devastating disease. GSK's Mosquirix can be approved for wide-scale deployment if it can present robust and meaningful data from the pilot program to the WHO. Using the sociotechnical framework of ANT, it can be outlined how the current actor-network that GSK is building is prone to instability.

Through an analysis of the neglected actors, ill-defined roles of current actors, and unpredictability of future actor participation, it is evident that the network is vulnerable due to GSK's emphasis on only technical aspects of the pilot program. By applying the concept of Translation, the reader can identify the shortcomings of GSK as a primary actor and how this could potentially lead to the failure of the malaria vaccine launch. Additionally, pharmaceutical companies can benefit from this analysis of the malaria vaccine pilot program as it provides insight as to how they can avoid destabilizing a similar network for vaccine implementation.

Word Count: 3452

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