Tackling the Challenges of Antimalarial Drug Resistance in Nigeria

By

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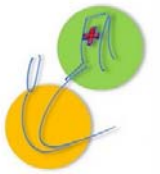

A Community Based Master's Project presented to the faculty of Drexel University School of Public Health in partial fulfillment of the requirement for the Degree of Master of Public Health.

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Table of Contents

ABSTRACT

Tackling the Challenges of Antimalarial Drug Resistance in Nigeria

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This Community Based Master's Project for the Degree of Master of Public Health is a comprehensive work aimed to outline the relationship with antimalarial drug resistance and policies in Nigeria. The purpose of this research is to develop and evaluate the impact of antimalarial drug policies on the social welfare and public health needs of the Nigerian people.

Introduction

Malaria is a preventable and treatable infectious disease that affects hundreds of millions of people primarily in the developing world. It is the most important of the parasitic diseases of humans with 107 countries and territories having areas at risk of transmission, and containing close to 50 percent of the world's population (4). Malaria is endemic in parts of Asia, Africa, Central and South America, Oceania, and certain Caribbean islands. The global scale of the problem is heavily confined to Nigeria, as the health of its community and citizens are threatened by the sustained suffering and death that the disease causes. Antimalarials are agents used in the treatment of malaria. Usually, they are classified on the basis of their action against plasmodia at different stages in their life cycle in the human. Over the past decades, antimalarial drug resistance has developed. Antimalarial drug resistance has been defined as the “ability of a parasite strain to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within tolerance of the subject” (33).

Hypothesis: Increased antimalarial drug resistance is perpetuated by poor surveillance, improper regulation, and ineffective policies.

Specific Aims of Study:

1. To assess the effects of Nigeria's antibiotic-regulation policies on malaria disease burden.
2. To evaluate the efficacy and efficiency of current government regulatory techniques, and physician regulation oversight with respect to antibiotic resistance.
3. To identify gaps and limiting factors in current policy implementation guidelines in current policies.

Research Design and Methods:

Specific aims (1-3) above will be addressed through literature based analyses. These include collecting and analyzing data from peer reviewed articles, textbooks, and journals. We searched journals and public domain literature articles on MEDLINE for policy documents that contained advanced keyword searches on "antibiotic drug resistance," "malaria," "Nigeria," and, "National Drug Policy in Nigeria, the National Agency for Food, Drug Administration & Control (NAFDAC)." Search results were evaluated on their abstract, especially if they included a comprehensive scope of criteria that we specified. Specification parameters to restrict our findings included humans, the literature review in English, and relevant publications in the years between 1998 and 2009. The articles we focused on sought to explore and highlight topics relevant to national antimalarial drug resistance and control in Nigeria. We obtained data about malaria polices and factors such as behavior, cost, supply, pharmaceutical company regulation, physician regulation, and surveillance that influence drug resistance. In addition to the literature review, we also relied on interviews and analyses from agencies and experts with special interest in the policy problem (Emmanuel Anteyi, MD (National Hospital, Abuja):, John Idoko MD (Jos University Teaching Hospital and AIDS Prevention Initiative Nigeria), Dr M. Etiebet, MD MBA (Institute of Human Virology, Abuja; Kenolisa Onwueme MD, PhD Brigham and Women's

Hospital, a teaching affiliate of Harvard Medical School) regarding antibiotic practices in Nigeria. Our interviews were conducted by telephone, email, and in-person. Responses to survey questions were collected by note-taking and then later annotated and grouped into themes pertaining to question, and finally analyzed in comparison with the literature review to derive our conclusion. We used these methods to analyze collected data regarding policy and regulation in Nigeria. Moreover, we hoped to deduce and identify strategies to improve public health needs of antimalarial drugs. These methods were used to obtain the data required to meet the specific aims of this literature based study.

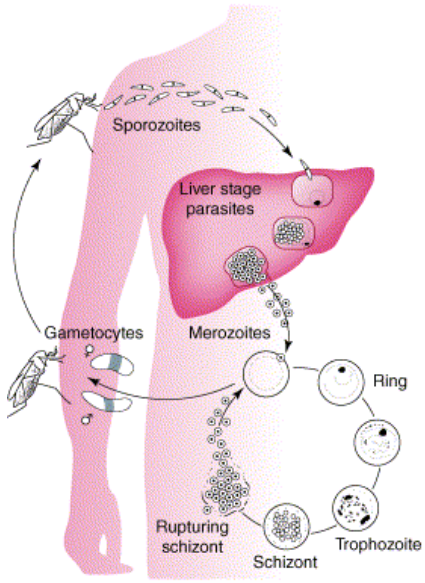

Figure 1. Malaria Cycle. Source: www.fda.gov/CbER/blood/malaria071206sk5.gif

Malaria: **Background and Significance**

As a health problem, malaria continues to persist in many parts of sub-Saharan Africa and South Asia, whereas it has been virtually eliminated in much of the rest of the world. In sub-Saharan Africa, about 300 million people suffer acute cases of malaria each year, with one million dying at least 70% of who are children or pregnant women (5). In Nigeria, malaria has

threatened the current healthcare of its citizens and presents an urgent challenge to the country. Nigeria is a country in Western Africa, bordering between Benin and Cameroon with an estimated population of 146,000,000. See figure 2. Throughout the country, malaria is transmittable 10 months out of the year, from February to December (16). This correlates with lower life expectancy and compounds excess morbidity and mortality. Malaria is caused by parasites from the plasmodium family. Their transmission is mediated by the A*nopheles* mosquito vector of which there are some 32 species. There a four major plasmodium species that account for the majority of diseases in humans: *plasmodium malariae*, *plasmodium falciparum*, *plasmodium ovale*, *plasmodium vivax*, with the main parasite as Plasmodium *falciparum*.

Figure 1 illustrates the different stages of the pathogen's life cycle. During this process malaria parasites destroy red blood cells, interfering with their replenishment, and causing anemia in both the acute and chronic forms. When left untreated, malaria can cause numerous complications: including kidney failure, anemia, coma, and death, along with the serious threat it presents to pregnant women (11).

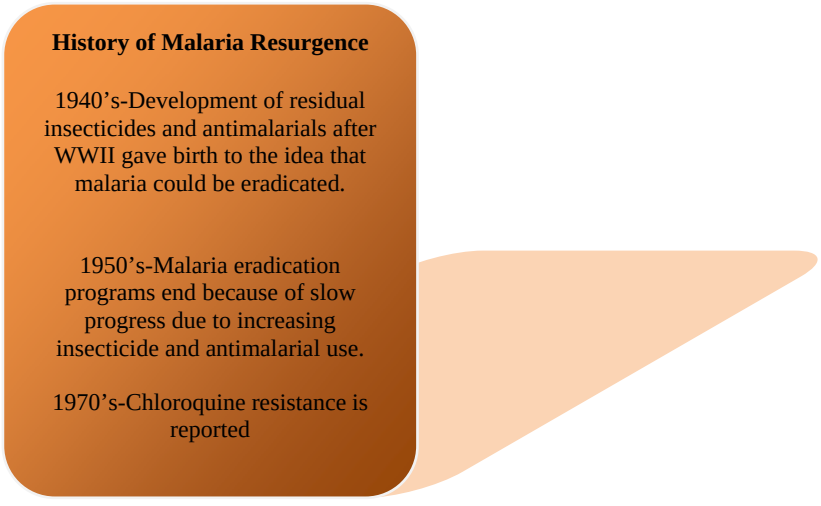

Chart 1. History of Malaria resurgence

The detection of resistance by proliferation of vector borne parasites occurred in the early 1970's (see chart 1), and are attributed to 4 main factors: 1) local environmental conditions (temperature, humidity), 2) abundance of vectors and intermediate or reservoir hosts, 3) prevalence of the disease-causing pathogen suitably adapted to vectors and human or animal host, and 4) resilience behavior and immune status of human populations. However, in recent decades, resistance to certain antimalarials has developed, posing a threat to the immediate society where the endemicity is high, and should sound a global alarm at the threat it poses.

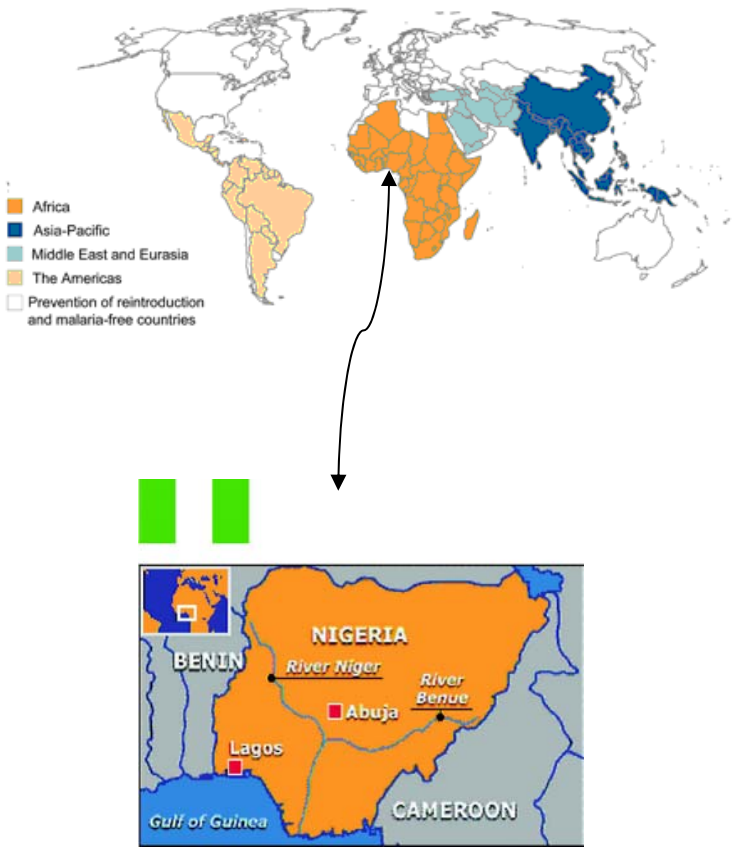

Figure 2. Approximate distribution of Malaria Source: WHO/CSR from http://www.who.int/emc

Nigeria's current antimalarial-regulation policies in their present form are failing to curtail the disease burden.

More importantly, we are continually reminded that the global scale of the problem is not confined to Nigeria, as the health of US travelers and relief workers is threatened, thus widening the humanitarian aid crisis and damaging efforts for life-saving treatments.

The sustained suffering and death of individuals dealing with the ills of malaria cannot be allowed to continue. Peddling of fake drugs, combined with the short shelf-life of many antimalarials on the market, and the lack of trained officials in the supply-chain and distribution pipelines leads to a great deal of improper use, waste, and death. This project initiative will require closer collaboration with key government representatives and agencies with special interest in the policy problem in order to make better use of resources.

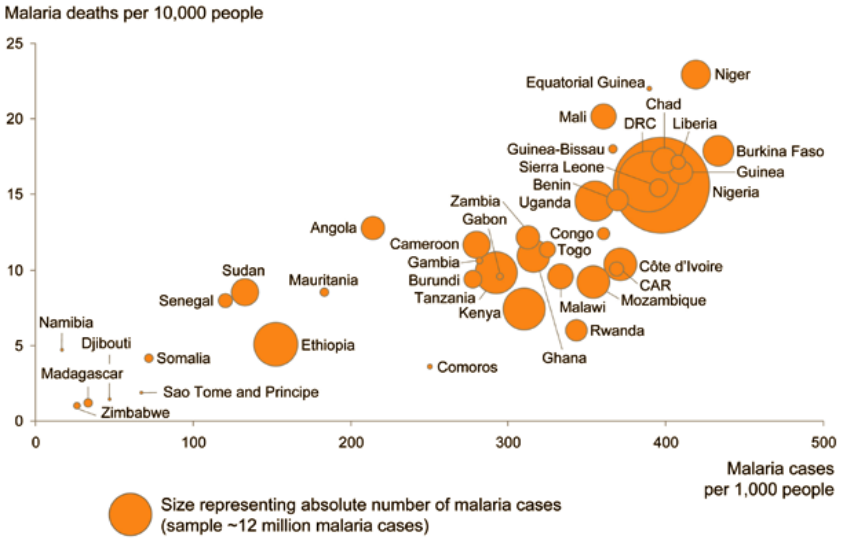

Figure 3. Burden of malaria cases. Source: *World Malaria Report 2008*.

Significance of Problem: **Antimalarial Drug Resistance**

Antimalarial drug policy control in Nigeria is based almost exclusively on chemotherapy using quinines (QUI), the cheapest antimalarial drug, or its close derivatives. The two main derivatives are chloroquine (CQ) and mefloquine (MQ). Often, chloroquine is the first line drug for uncomplicated Malaria, but mefloquine is more widely used due to emerging chloroquine resistance. Sulphadoxine-pyrimethamine (SP, Fansidar), is the second-line of treatment recommended for severe Malaria (16). Between 1978 and 1988 p*lasmodium falciparum* resistance to chloroquine had been reported in all countries of tropical Africa (5). Malaria parasites had developed a genetic mutation preventing chloroquine and quinine absorption, and expelling them from the parasite's body. This defense mechanism does not allow chloroquine and quinine to be effective. In 1972, a crystalline compound was extracted from the qinghaosu plant, known in western countries as "artemisinin" (ACM) to treat malaria, due to the waning efficacy of other low-cost drugs and the emergence of drug resistance in Asia (14). Administered orally, and with no major side effects or severe toxicity reported, artemisinins have been used for the prevention of malaria in pregnancy. The reasons for the development and spread of drug resistance involve the interaction of drug-use patterns, characteristics of the drug itself, human host factors, parasite characteristics, sub-standard or fake drugs, and vector related environmental factors (14). See figure 4. The antimalarial drugs (chloroquine, fansidar, camouqin) have long been thought of as the most effective remedies to treat malaria because of their efficacy, low-cost and availability. Antimalarials drugs are obtainable with or without prescription. In hospitals, all medication is dispensed only by prescription unlike the case in the wider communities where CQ and SP's can be purchased over the counter (OTC). The comparative retail price per dose of these medications was in the order: ACMs > QUI > SP > CQ

(33). Artemisinins cost about 20 times more than chloroquine, and African countries and their citizens cannot afford their higher price tag. Currently, the practice in Nigeria for recommended treatment regimens often do not reflect the current state of antimalarial drug resistance. In theory, recommended treatment regimens should be tailored specifically to a given region based on resistance patterns found in that area. However, considerations such as cost, cost-effectiveness, availability, ease of administration, capabilities of the health care infrastructure (i.e. do health care workers have the equipment and training to safely use parenteral routes of administration?), perceived efficacy, and perceived safety of the drug (acceptability of the drug by the population) must be acknowledged (33).

Factor	Characteristic	Example
Drug	Half-life	Resistance to drugs with a short half-life develop more slowly than dugs with long half-lives
	Dosing	Use of subtherapeutic doses in self-treatment; poor drug compliance; mass drug administration with subtherapeutic doses
	Non-target drug pressure	Presumptive use of antimalarial drugs without laboratory diagnosis or for indication other than malaria
	Pharmacokinetics	Use of drug formulations with reduced bioavailability
Human	Host immunity	A more potent immune response would increase the efficacy of chemotherapy
	Maintenance of resistant parasite reservoir	Non-detection of drug failure
Parasite	Genetic Mutations	Discussed in the article
	Transmission level	Whether low or high transmission has more influence on drug resistance is debatable; prevalence of drug resistance is higher in regions of low transmission
Vector and environment	Vector affinity of parasites	Increased infectivity and productivity of drug resistant parasites in its vector (mosquito)

Figure 4. Factors contributing to antimalarial drug resistance

Surveillance

Where malaria prospers most, human societies have prospered least. The global distribution of per-capita gross domestic product shows a striking correlation between malaria and poverty, but also shows that malaria-endemic countries have lower rates of economic growth (4). Although the last century witnessed many successful programs at country level to eliminate the malaria parasite, the world is now facing a rapidly increasing malaria disease burden (5).

Antimalarial drug resistance has been attributed to several causes including population movements into malaria-endemic regions, changing agricultural practices (e.g. the building of dams and irrigation schemes), deforestation, weakening of public health systems in poor countries, and more speculatively, long-term climate changes such as more pronounced El Niño cycles and global warming. Furthermore, the deterioration of public health infrastructure, agricultural practices, poor surveillance, prevention and control of vector borne-disease contribute to antimalarial resistance.

Literature review: Nigerian National Drug Policies

In Nigeria, it is very clear to all healthcare professionals that a major source of substandard products in Nigeria is the multitude of unregulated drug markets in major cities. These markets have existed since the 60's and have grown in number and complexity over the years. They have survived the efforts of various Nigerian governments to forcefully dismantle them, which never succeeded (28). With previously failed regulation techniques and seemingly uncontrollable distribution channels, the National Agency for Food, Drug, Administration & Control (NAFDC) was created to intervene on present markets, and decide on a new approach. The establishment of NAFDAC by Decree 15 of 1993 regulates and controls the manufacture, importation, exportation, distribution, advertisement, sale and use of food, drugs, cosmetics,

medical devices, chemicals and packaged water (28). The difficulty of policing antimalarial counterfeit production as well as adherence, we must note some factors that are unique to Nigeria, and others that are not. “The ones that are common are just pure resistance to change, and inertia of habit,” said one public health official we interviewed. Those that are unique are the influence of high degree of corruption and lack of accountability. Public officials often have high significance but with divested interest between their private and public enterprise duties versus their public service and public safety. There was significant opposition to NAFDAC, so much so that the head of NAFDAC, Dr.Akunyili had numerous assassination attempts on her life. Following these death threats, there were arson fires at the operational laboratory headquarters of NAFDAC in Lagos, and Kaduna. Nonetheless, Nigeria faces further concerns with misleading advertisements. For example, there might be ten or more varieties of chloroquine on the market, all marketed as malaria therapies under different brand names (28). In reality, many of these drugs are the same thing, but since being advertised as different drugs the general public were left confused. “If they had malaria they would often buy one brand, and then if they didn't improve buy another brand, and so on, without understanding that they were in fact buying the same pharmaceutical substance,” says Dr.Akunyili of NAFDC (24).

As many have pointed out, the health cost of counterfeit drugs on the population of Nigerian citizens has jeopardized the reputation of the public health system; including health care professionals, pharmaceutical industries, hospitals and clinics, and national Drug Regulatory Authorities (DRA’s). Cases of antimalarial drugs containing no active ingredients, or with wrong ingredients or without correct quantities of the active ingredient, prolong the treatment periods, which can lead to the emergence of resistant organisms. It is no wonder then that concerns over trust and safety continue to linger amidst patients who receive genuine

antimalarials, but may fail to respond due to resistance induced from consumption of reduced-dose counterfeit antimalarials.

Literature has also shown overwhelming concerns about adherence to drug regimens by patients, which directly influences antimalarial efficacy that could lead to drug resistance. Underuse through lack of access, inadequate dosing, poor adherence, and substandard anti-microbials may play as important a role as overuse (27). Second tier antimalarial drugs, such as Artensunate, that require an expensive extraction process makes them too costly for developing countries is a problem, because the few patients who can afford them, often have difficulty complying with the course of treatment. Research has also shown that in some cases, a chloroquine injection, administered by ill-qualified patient medicine dealers contributes to antimalarial drug resistance. Two aspects of drug abuse [are] observed here, i.e. the utilization of sub-curative doses of chloroquine and monotherapy are believed to be two of the factors that lead to the several chloroquine treatment failures (32). The importance of public education in rational drug use and proper adherence seems to be a critical aspect in antimalarial drug resistance. .

NAFDAC operational guidelines:

The decree setting up NAFDAC mandated it to regulate and control the importation, exportation, manufacture, advertisement, distribution, sale and use of drugs. Some of its other functions to regulate general antibiotic access are as follows:

- Registration of locally manufactured food, drugs, cosmetics, medical devices, water, detergent and chemicals.

- Registration of imported food, drugs, cosmetics, medical devices, water, detergent and chemicals.
- Exportation of locally manufactured regulated products.
- Importation of regulated products.
- Issuance of Narcotics and Controlled Substances permit.
- Registration of vaccines and biologicals.

To enforce these regulatory practices, the NAFDAC proposed the concept of Zonal Drug Distribution Centers in the six Geo-political zones of Nigeria.

Nigerian Government Antimalarial Drug Regulation

NAFDAC's proposed concept of Zonal Drug Distribution Centers in the six Geo-political zones of the country was meant to centralize drug distribution across the country. This idea is similar to the combination drug market concept of India, Cameroon and the solely government-run retail pharmacy system of Sweden, the Apoteket AB. This is similar to the concept of Zonal Drug Distribution Centers (ZDDC) that was explored in the past but was abandoned due to funding constraints (28, 29). Despite that initial setback, Dr. Akunyili's fight against counterfeit unregulated products has produced rewarding results because of awareness campaigns and enforcement activities embarked upon by NAFDAC. Since their inception, three special zonal offices [that were] established in the high incidence areas of distribution of faking/counterfeiting of regulated products Onitsha, Aba, and Kaduna in addition to Lagos, have assisted NAFDAC in confiscating and destroying fake drugs and other regulated products worth

several billions of Naira (29). These drugs are concealed in men's, women's, and children's clothing, duvets, and shoes (see figure 5). NAFDAC's bid to rid the country of fake, adulterated, substandard drugs lies solely on distinguishing features between their genuine products and fake ones. Workshops held with various stakeholders dwelt on the dangers of fake drugs, resulted in billboards being erected in strategic parts of the country warning against the health hazards of fake drugs and other substandard products have also been produced and circulated nation-wide. The Agency also publishes a Bi-annual NAFDAC News magazine and consumers safety bulletin (29). Identifying these salient gaps is enforced by the directorate for necessary action toward importers and manufacturers of unregistered products spurred by publications to initiate registration of their products due to the negative publicity and reduction in sales they get from the publication (29). NAFDAC also engages in periodic publication of blacklisted companies, both local and international, who do not conform to World Health Organization (WHO) certified Good Manufacturing Practice (GMP) or produces substandard products, to warn importers and consumers so as to shun products from these companies (29). The overall responsibility for enforcing the provisions of this Decree rests on the Federal Task Force on Counterfeit and Fake Drugs, hitherto a unit under the office of the Director – General. Their duties include but are not limited to**:**

1)-Coordinating the state Task Forces by the Federal Task Force as provided by the Law.

2)-Tracking down the increasing perverseness of spurious products fakers and importers.

3)-Coping with increasing sophistication of the criminals involved in faking products.

Lastly, the Director-General also held top level meetings with the managing director of Federal Airport Authority of Nigeria (FAAN) and Airline officials over the airlifting of fake drugs and substandard regulated products by Ethiopian Airline, KLM and other courier companies. A major fall-out of the meeting was the new standing policy that any airline carrying fake regulated products will be prosecuted by NAFDAC apart from having their aircrafts grounded. This is a practical approach towards tackling the latest dimension of using airports as route for importing fake drugs into the country (29). Similar sentiments were felt by drug companies who were fearful that their brands would be rejected if news of fake drugs was broken to the media. Other third world countries like Mali have also experimented with other relevant drug initiatives.

Figure 5: Fake drug concealment. Source: NAFDAC

Bamako Initiative

In 1987 in Bamako, Mali, an initiative was taken and adopted by African health ministers to implement strategies designed to establish realistic national drug policies to increase the availability of essential drugs and other healthcare services for Sub-Saharan Africa. These observations could indicate that the availability of ACMs is probably sustainable on the basis of the Drug Revolving Fund (DRF) scheme, which is a drug supply management strategy to ensure that the majority of service users have access to a sustainable supply of safe, effective, and affordable drugs to meet their health care needs. This scheme was adopted to overcome the inability of public health facilities to meet their drug demands that usually results from limited budgetary allocation from government and high drug prices that involves a competitive tendering process where retail prices are set in such a way as to recover cost with a profit margin of ~5%.

Prices are fixed to make our drugs more competitive than are obtainable at our competitor private pharmacies (33). This observation is [also] intriguing within the context of Nigeria, where the majority of users of public health facilities either belong to the low-or middle-income groups, huge price differentials between ACMs and the older classes of antimalarials plays a factor in mortality and morbidity (33), just as the Obala Foundation initiative or experiment reveals.

Obala Foundation

Obala Foundation is a non-profit organization based in the United States and Nigeria since 2001. The problem, as Obala Foundation perceives it, is an inefficient and sub-optimal use of both monetary and human health care resources to tackle antimalarial drug resistance, which impedes implementation of even the most well thought-out policies. As its mission statement states, "its principal approach is to foster stakeholder partnerships that focus on improving health care access and optimizing use of current resources. Obala Foundation would like to use proven cost-effective technical interventions and techniques that address among other themes: health funding that goes towards drug resistance in the form of surveillance, control of antimalarial drug distribution through integrated health information services, and involving stakeholders in the process to overcome opposition to antimalarial drug policy changes in Nigeria.

Obala's vision to address these thematic problems requires a multi-step process that will allow identification of gaps and limiting factors that impede current policies. Obala's goal is to explore the lack of antimalarial drug regulation on malaria, and whether it would be beneficial to have policies that regulate antimalarial drugs. There are two trains of thought Obala would like to explore. First, is the case that antimalarial drug use should be solely on a prescription basis in order to reduce drug resistance, reduce rate of complication, and reduce the number of fake drugs. In contrast, is the idea that regulating these antibiotics (i.e. antimalarials) solely on a

prescription basis limits access, which the Bamako Initiative sought to prevent. In short, if there was no regulation and things were kept the way they are now, the percentage of people you would be helping by allowing access to OTC drugs is more than the people you would be helping if you had regulation. Simply, because OTC drug access reduces cost barriers such as physician fees. However, drug resistance to antimalarials is being caused by substandard dosing which is related to OTC drug use, when people do not take the medication correctly. Furthermore, distribution of access may also "increase inequity since they will initially reach those who are already better off (11), which means that public good distribution must also be considered. Obala also understands that there are other confounding issues; economics, political unrest, lack of interest groups, staying power, corrupt government, human behavior, climate changes, poverty, access to healthcare, health care providers, and resentment against government interference. Still, they are determined in their efforts to pursue new ideas and bold projects that should enable Nigerian communities to live a better life, free from disease and suffering

Expert Interviews:

Our interview questions (Please refer to Appendix) sought the input of high level experts and officials whom we gathered their input by careful note taking, e-mail, and phone interviews. Based on these finding along with the literature review, we were able to surmise their thoughts and comments to come to our own conclusions. After each interview was conducted, we qualified and grouped each answer by the interviewee into themes. Those interviewees that had similar answers to the same question were then linked and summarized together in our analysis.

Discussion/Results:

Malaria, and the difficulty in controlling antimalarial drug resistance is determined by a variety of factors, each varying in degree of intensity, breadth, and scope as it relates to antimalarial resistance. In all, these factors must and will evolve positively or negatively over the next few years to contribute to lessoning Nigeria's antimalarial drug resistance problem: including, climate, ecology, personal behavior, and compliance with appropriation for safe antimalarial drug use as an eminent dilemma. However, practical steps can be taken to push that day further into the future (13). These practical steps should include bolstering the fragmented relationship of the government to the private sector, the distribution of authority and responsibility within a federal system of government, the relationship between policy formation and implementation, and using incrementalism as the strategy for reform and better public education campaigns as they relate to antimalarial resistance.

The core recommendations from this literature review are built on fundamental principles of a human rights framework that acknowledge a community-patient focus. The framework is based on public health principles and disease management, with a strong emphasis on health promotion, and integration of resource utilization practices that can be incorporated across the continuum of care. A wide range of health-related disciplines must join forces if opportunities to reduce the morbidity and mortality associated with chronic disease are to be realized. Presently, there is an opportunity to establish new guidelines for antimalarial drug resistance prevention. This will involve education at schools, workplaces, community-based clinics, hospitals, and greater prevention efforts from government officials to prevent counterfeit and substandard drugs from flooding the markets. The results and recommendations are summarized below.

Climate & Ecology: The evolution of drug resistance is an inevitable consequence of genetics and natural selection when drugs are used against microbial pathogens, including the protozoan parasites that cause malaria. As effective and robust as the artemisinin drugs are today, it is only a matter of time before genetically resistant strains emerge and spread. There is some hope however with emerging research as reported by Nature that shows promise in an antimalarial drug called acridone derivative, which is being developed by Jane Kelly and colleagues at Portland State University. The drug "targets the way mosquitoes digest hemoglobin in red blood cells, from which they take amino acids as their food… a chemical which prevents the malaria parasite from getting rid of a toxic by-product of feeding on red blood cells. Furthermore, "it also disables a genetic defense that prevents the existing drugs chloroquine and quinine [from] working, useful again by combining those with this new one could help combat the rising tide of drug resistance in this neglected disease." However, it could be nearly 10 years before the drug is available to pharmaceutical markets.

Education & Compliance: Over the years, there has been significant criticism of OTC drug regulation in developing countries as it relates to resistance. As one scientist says, "more education was needed knowing when to use an antibiotic is as important as knowing which antibiotic to choose" (26). Citizens can buy OTC antimalarials, which must contribute significantly to development of resistance. There are arguments in favor of keeping the current policy in place stemming from people who can't afford the fees. As one virologist we interviewed noted, "there are benefits to having people buying OTC drugs. One of those benefits would be, if you consider all the barriers to health care that people face when buying OTC drugs,

you avoid those cost barriers which include doctor's fees visits, administrative costs, transportation expenses." But on the contrary, as a study that was conducted at the University Teaching Hospital in central Nigeria suggested affordability was less of a factor in the acceptability of ACMs as the preferred treatment of malaria. Moreover, "on an individual basis this may makes sense, but on a population-wide basis this is very detrimental because of easy access to irrational drug use, and high resistance. Even when the policies have changed, and we have limited the effectiveness with efficacy in reaction with other drugs, introduce culture of self prescribing and self diagnosis that may lead to misdiagnosis of people or late diagnosis of incorrect symptom, which is the very thing that proponents are trying to avoid."

Cost Containment: Poverty in sub-Saharan Africa, although not the chief factor, stifles the ability of people to purchase artemisinins, which at a dollar or two per course are both inexpensive by U.S. or European standards and highly cost effective by any norm. But neither national governments nor consumers in most malaria-endemic countries can afford them in quantities that remotely approach the world's current consumption of chloroquine, roughly 300-500 million courses of treatment per year. Commitments from international funding agencies are substantially greater than the sums needed for an antimalarial drug subsidy but still modest in terms of their return on investment, which are therefore needed to advance malaria control overall (13). A global subsidy near the top of the distribution chain will stabilize demand and create incentives for ACT production, resulting in lower prices (13). Essentially, this will give the global community leverage to dissuade artemisinin manufacturers who wish to sell through the subsidized system from producing artemisinin monotherapy, minimize administrative costs of applying the subsidy, minimize the incentives for counterfeit ACT production, and minimize

incentives for diversion and smuggling of ACTs (13). The United States Agency for International Development (USAID) is one such agency that realizes "since improved health and education are key determinants of development in Nigeria, previously separate efforts in basic education and health care will be integrated into a new objective for improved social sector service delivery"(USAID). Expanding access to [cost] effective treatment will be essential to gain ground against malaria and drug resistance drugs. Furthermore, at least one million people die each year from malaria, most of who could have been saved by adequate treatment. Merely substituting artemisinin combination therapies (ACTs) for chloroquine is not the whole answer (13). Without funding for effective treatment, malaria mortality could double over the next 10 to 20 years and transmission will intensify (14). Policy-makers [must] increasingly engage in explicit discussions of the links between malaria, poverty, and inequity to adequately reflect, and distribute the same pattern of socio-economic inequity that influences the distribution of infection. (11) Combination therapies like these have been used in treating HIV/AIDS, tuberculosis, as well as malaria.

Policy Implementation & Government Oversight: The primary purpose of any malaria drug policy is to ensure prompt, effective, and safe treatment of malaria (5). What will be required from the government is a distribution of authority and responsibility that regulates the implementation and availability of effective drugs at the local level through better control efforts that previously may have been suppressed by corruption and ineffective drugs (13). Government policy programs should implement interventions that develop a network of checks and balances to safeguard the antimalarial drug distributors, suppliers, and product content. This is not a short term solution, but a steady long term approach that will require an investment toward safety

networks, and sufficient credible processes. To what extent these credible sources can be developed and mobilized for efficiency, will require selective expertise in ideological, political and economic policy. In addition, monitoring and evaluation systems are critical when scaling up to sustain control and monitor pharmacovigilance and quality assurance. An aggressive stance during these challenging times will take greater effort and heavier supervision of pharmaceutical drugs for malaria and their counterfeits. Presumably, enacting a technical approach that has been shown to work in other countries will be required to meet the emerging needs of the population, and special interest agencies. One such approach was the use of procurement and supply chain management systems (PSMs). Effective and timely PSM systems are critical in delivering interventions and providing real-time feedback to NMCPs and district health centers on the flow of interventions. PSM systems need to be optimized to avoid forecasting errors, treatment expiries and intervention stock-outs. Furthermore, effective PSM systems can aid quality assurance and quality control (34). Development and implementation of product access plans to ensure timely and effective delivery of new antimalarial drugs will require personal expertise in relevant areas, including regulatory affairs, marketing, distribution and supply chain logistics epidemiology (IOM). Lastly, constructive engagement of all interested agencies must occur in a regional approach to have an effective policy dealing with the present day challenges.

Antimalarial Treatment: Scientifically, certain aspects of antimalarial drug mechanisms are not yet fully understood. In the absence of vaccines, these two plant-based compounds (Quinine and artemisinin) and their derivatives have been crucial in the control of malaria. The complexity of the parasite mechanism coupled with progressive resistance to malarial drugs presents

researchers with numerous difficulties in the development of both effective vaccines and more powerful pharmaceuticals (14). Biomedically, the artemisinins are the *only* first-line antimalarial drugs appropriate for widespread use that still work against all chloroquine-resistant malaria parasites. A combination of mefloquine and artesunate [derivative of artemisinins] is highly effective even against multi-drug resistant malaria (14). However, if resistance to artemisinins is allowed to develop and spread before replacement drugs are at hand, malaria's toll could rise even higher. The key, therefore, to preserving the artemisinins is to eliminate their routine use as monotherapies and to treat patients with uncomplicated malaria (the vast majority of cases) with artemisinin-based combination therapies (ACTs) instead. See figure 6.

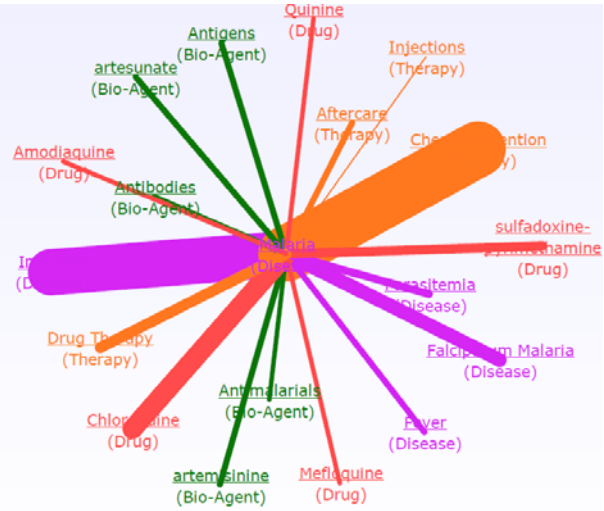

Figure 6: Malaria disease. Edge thickness reflects relative strength of relationship.

Community Health Workers: Increasing the number of NAFDC trained personal, along with general community health workers are preventative techniques that when combined with standard quality antimalarials may prevent disease morbidity statistics, reduce transmission, and prevent overall drug-resistance. However, lack of sufficient human resources to run programs

and factors such as high attrition rates of skilled staff, difficulty filling positions in rural areas, and competing demands with other programs directly influence control measures against antimalarial drug resistance. Better incentives to retain professionals, especially technical experts such as entomologists and public health workers are imperative to successful antimalarial intervention coverage. Other creative approaches to expanding the workforce should be considered, such as using community health workers, volunteer networks or professionals in the private sector (34).

Conclusion

In summary, a great deal of work must be done to have access to a sustainable supply of safe, effective, and affordable drugs to meet the health care needs of an ailing Nigerian population. The fear with the current financial and economic crisis facing the United States, and much of the world, is that it is likely that we will witness a shriveling of already limited humanitarian aid to fight diseases in developing countries. Without such funding, the challenge of arriving at a different conclusion is merely speculative.

Public health policy care and reform in Nigeria will demand much from its champions. They will have to rebuild institutions which have lost the public trust and these champions will have to win support from the communities they hope to serve. What must be expected from the government is to use its complete power to prevent extreme inequality in health - not only by expanding healthcare access, but also by imposing containment costs and prioritizing quality measures that lead to improvements for all. We must act decisively and imaginatively if we are

to be faithful to George B. Shaw's inspiring vision: "You see things; and you say, 'Why?' But I dream things that never were; and I say, "Why not?"

Appendix:

Definition of Terms:

Artemisinin: An antimalarial drug that is a peroxide derivative of sesquiterpene and is obtained from the leaves of a Chinese artemisia (*Artemisia annua*) or made synthetically.

Chloroquine: Drug used in the treatment or prevention of malaria.

Mefloquine: An antimalarial drug similar to quinine that is administered especially for the prevention and treatment of falciparum malaria

Bamako Initiative: In 1987 in Bamako, Mali, a formal statement initiative was taken and adopted by African health ministers to implement strategies designed to increase the availability of essential drugs and other healthcare services for Sub-Saharan Africans.

Drug (Medicine): A pharmaceutical product, used in or on the human body for the prevention (prophylaxis), mitigation, diagnosis and/or treatment of disease, or for the modification of physiological function. This definition includes prescribed medicines, over-the-counter medicines, vaccines, herbal medicines, traditional medicines and biologicals including blood and blood-related products e.g. sera, plasma (28).

Malaria: a human disease that is caused by sporozoan parasites (genus Plasmodium) in the red blood cells, is transmitted by the bite of anopheles mosquitoes, and is characterized by periodic attacks of chills and fever (m-w.com)

Naira: Monetary unit of Nigerian currency.

OTC: Over the counter

Good Manufacturing Practice: Is a term that is recognized worldwide for the control and management of manufacturing and quality control testing of foods, pharmaceutical products, and medical devices

Interview Questions (25)

1. In some other countries that have made radical changes in drug policy, there has been considerable organized opposition, for example from industry and also from professional groups, to the new legislation. Did that happen in Nigeria?
2. May I ask you about the formal linkage between the decree and the national drug policy document that was published? This is a very comprehensive document covering every single aspect of pharmaceutical supply and use, so presumably some of the goals in this document are long term rather than short term?
3. One aspect that is particularly interesting in the policy document is the emphasis on the importance of public education in rational drug use, because this is the vital final link in the chain of drug supply. Even if you succeed in establishing a stable supply of rationally prescribed drugs, if the general public and patients don't understand how to use them, put pressure on health professionals for inappropriate therapies or modes of administration, or go and buy OTC products in a completely irrational way, then all the previous work is for nothing.
4. Could we now turn to the development process of the Nigerian National Drug Policy? In some countries, Malawi is an example, all interested parties involved with the supply and use of drugs: industry, the pharmacists, the medical profession, lawyers, etc, were invited to participate in the development of the national drug policy. Other countries have adopted a somewhat different approach, and policy/legislation has been developed primarily within the government and with more limited participation from other interests, because those countries felt that the pressure of different interests might weaken the eventual legislation. How would you describe the Nigerian approach?
5. We have found that the very process of developing a national drug policy, in many cases, has brought together professional groups who have had very little contact with each other before, and bringing those people together to interact and communicate is a strengthening process in itself. With that, how do you see the future development of Nigeria's pharmaceutical policy and sustainability efforts?

IOM: Institute of Medicine

Sulphadoxine-Pyramthenine (Fansidar): Used for treatment of uncomplicated *Plasmodium falciparum* malaria Synergistic action against susceptible attacks the different development stages of the parasite.

WHO: World Health Organization

Bibliography

1. Obala Foundation from; http://www.obalafoundation.org/

2. Drexel University School of Public Health community based maters thesis project handbook from; http://publichealth.drexel.edu/SiteData/docs/2008-09%20Drexel%20SPH%20CBMP%20Guidebook/905e78b0f842df24ddb6cd31164b77bd/2008-09%20Drexel%20SPH%20CBMP%20Guidebook.pdf

3. Virulence in Malaria: An Evolutionary Viewpoint Author(s): Margaret J. Mackinnon and Andrew F. Read Source: Philosophical Transactions: Biological Sciences, Vol. 359, No. 1446, Reviews (Jun. 29, 2004), pp. 965-986 Published by: The Royal Society Stable URL: http://www.jstor.org/stable/4142210 Accessed: 26/08/2008 14:31

4. Sachs J., Malaney P., The economic and social burden of malaria. Nature| Vol 415| 7 February 2002 | www.nature.com. Center for International Development, John F. Kennedy School of Government, Harvard University, 79 John F. Kennedy St., Cambridge, Massachusetts 02138, USA (e-mail: pia_malaney@harvard.edu) Commission on Macroeconomics and Health, World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland

5. Jean-Franc¸ Ois Trape. The Public Health Impact of Chloroqiuine Resistance in Africa American Journal of Tropical Medicine Hygiene. 64(1, 2) S, 2001, pp. 12–17 Copyright 2001 by The American Society of Tropical Medicine and Hygiene

6. Joel G. Bremen, Anne Mills, Robert W. Snow, Jo-Ann Mulligan, Christian Lengeler, Kamini Mendis, Brian Sharp, Chantal Morel, Paola Marchesini, Nicholas J. White, Richard W. Steketee, and Ogobara K. Doumbo. Disease Control Priorities in Developing Countries: Conquering Malaria

7. Goodman A. C., Coleman G. P., and MILLS J. A., The Cost-Effectiveness Of Antenatal Malaria Prevention in Sub-Saharan Africa. Am. J. Trop. Med. Hyg., 64(1, 2) S, 2001, pp. 45–56

Copyright 2001 by The American Society of Tropical Medicine and Hygiene Health Policy Unit, Department of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, United Kingdom; Disease Control and Vector Biology Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom.

8. Ramanan Laxminarayan, Zulfiqar Bhutta, Adrian Duse, Philip Jenkins, Thomas O'Brien, Iruka N. Okeke, Ariel Pablo-Mendez, and Keith P. Klugman Drug Resistance: Disease Control Priorities in Developing Countries

9. Gallup L. J., and SACHS D. J., The Economic Burden Of Malaria. Am. J. Trop. Med. Hyg., 64(1, 2)S, 2001, pp. 85–96 Copyright 2001 by The American Society of Tropical Medicine and Hygiene Center for International Development, Harvard University, Cambridge, Massachusetts

10. Foster S., Laing R., Melgaard B., and Zaffran M. Ensuring Supplies of Appropriate Drugs and Vaccines. Disease Control Priorities in Developing Countries

11. Brentlinger E. P Health, Human Rights, and Malaria Control: Historical Background and Current Challenges: Health and Human Rights, Vol. 9, No. 2, Rights-Based Approaches to Health (2006), pp. 10-38 Published by: The President and Fellows of Harvard College , on behald of Harvard School of Public Health/François-Xavier Bagnoud Center for Health Stable URL: http://www.jstor.org/stable/4065400

12. Summary and Cross-Cutting Themes, Disease Control Priorities in Developing Countries Summary, Cross-Cutting Themes

13. Burke E., Deasy J., Hasson R., McCormack R., Randhawa V. and Walsh P., Antimalarial Drugs from Nature

14. Kenneth J. Arrow, Claire Panosian, and Hellen Gelband, Editors, Committee on the Economics of Antimalarial Drugs. Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance http://www.nap.edu/catalog/11017.html

15. Medicines for Malaria Venture International Centre Cointrin Entrance G, 3rd floor Route de Pré-Bois 20 PO Box 1826 1215 Geneva 15 Switzerland. April 2006

16. World Health Organization. Malaria Country Profiles: Nigeria

17. Barnes I K. Rolling back malaria in Africa: January 2007, Vol. 97, No. 1 SAMJ

18. Ndyomugyenyi R., Kroege A. Using schoolchildren's reports of bed net use monitored by schoolteachers as a proxy of community coverage in malaria endemic areas of Uganda. Tropical Medicine and International Health

19. Weatherall D., Greenwood B, Chee H.L., and Wasi P. Science and Technology for Disease Control: Past, Present, and Future Disease Control Priorities in Developing Countries

20. Seppa N., Malaria Reversal Science News, Vol. 170, No. 20 (Nov. 11, 2006), pp. 307 Published by: Society for Science & the Public Stable URL: http://www.jstor.org/stable/4017398

21. Preker S.P, McKee M, Mitchell A, and Wilbulpolprasert S., Strategic Management of Clinical Services.

22. Peabody W.J., Taguiwalo M.M. Robalino A.D., and Frenk J. Improving the Quality of Care in Developing Countries. Disease Control Priorities in Developing Countries

23, 24. Ebrahim M. Samba, Director, World Health Organization Regional Office for Africa, Medical School, C Ward, Parirenyatwa Hospital, Mazoe Street, P.O. Box BE 773, Belvedere, Harare, Zimbabwe; Phone: 00263 4 703580, FAX: 00263 4 700742, e-mail: sambae@whoafr.org

25. Ransome O.K. National Drug Policy in Nigeria Journal of Public Health Policy, Vol. 13, No. 3 (Autumn, 1992), pp. 367-373 Published by: Palgrave Macmillan Journals Stable URL: http://www.jstor.org/stable/3342734

26. Gould I. M., Van der Meer W. M. J Antibiotic Policies: Theory and Practice. Kluwer Academic/Plenum Publishers New York

27. WHO | Antimicrobial resistance. http://www.who.int/mediacentre/factsheets/fs194/en/print.html. Revised January 2002

28, 29. Headline News: FDA | Fake Drugs | Drug Testing Copyright © 2002-2007 nafdacnigeria.org from http://www.nafdacnigeria.org/publichealth.html

30. WHO | GMP Question and Answers http://www.who.int/medicines/areas/quality_safety/quality_assurance/gm...

31. Survey report on training courses on malaria and other vector-borne diseases and planning their control. Roll back Malaria Department Operations Support and Capacity Development (MCO)

32. Ezedinachi EN. Ejezie GC. Emeribe AO. Problems of chloroquine-resistant P. falciparum in Nigeria: one antimalarials drugs' utilization in metropolitan Calabar. [Journal Article] Central African Journal of Medicine. 37(1):16-20, 1991 Jan.)

33. Bloland. P. Drug Resistance in Malaria. World Health Organization 2001. Malaria Epidemiology Branch Centers for Disease Control and Prevention, Chamblee, GA, United States of America. From http://www.who.int/emc

34. *World Malaria Report 2005*, Geneva, World Health Organization, 2005; Roll Back Malaria; WHO; UNICEF. http://rollbackmalaria.org/gmap/part3.pdf