

## **Economic Implications of the Quality of Antimalarials in Dar es Salaam**

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### **Abstract**

*This paper economically analyses the actual quality of antimalarials in Dar es Salaam using drug quality analysis involving identification, uniformity of weight, and an assay of active ingredients. It seeks to determine the actual quality of antimalarials in Dar es Salaam and to determine the impact of this quality on health consumer utility, using the drug quality results to infer on the impact of quality on health consumer utility. Findings reveal all sampled drugs met the necessary condition of good quality drugs by containing amounts of active ingredients that complied with the British Pharmacopoeial (BP) specifications. However, analysis beyond the assay of active ingredients tests revealed some batches of antimalarials manufactured in Tanzania possessed less quality relative to other sampled drugs. This increased the probability of the production of drugs that may be outside the pharmacopoeial specified active ingredients quantities. Some locally manufactured antimalarials are thus less adequate in reducing sick time, and therefore provide less utility to healthcare consumers. Regulation can thus be enhanced increasing focus on drug quality monitoring activities beyond assessing whether drugs comply with pharmacopoeial standards or not, as well as well as increasing emphasis on monitoring drug manufacturers.*

### **1. Introduction**

Healthcare quality is categorized into perceived quality and actual quality. The former involves perception regarding a consumer's assessment of the relative quality of healthcare services, while the latter involves health professionals' objective evaluation of the quality of healthcare based on norms or standards. Perceived healthcare quality mostly drives healthcare utilization choice, while actual healthcare quality largely influences health outcomes.

An individual obtains utility from consumption goods and health goods or services such as antimalarials that impact time spent in illness (sick time). A health good such as antimalarials can be analysed in the context of sick time and utility of Wagstaff's (1986b) version of Grossman's demand for health model, where an individual derives utility from consumption goods and the time spent in illness (sick time). Consumption of antimalarials in response to malaria illness impacts sick time, and thus affects individual utility depending on whether it reduces or increases sick time.

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Consumption goods and sick time impact utility with antimalarials affecting the latter as individuals derive utility from consumption goods and disutility from sick time. Sick time affects an individual's welfare via health stock. An individual inherits health stock after birth, which later evolves following the law of motion of health, that is, the difference between gross health investment and depreciation of health stock.

An illness like malaria leads to health stock depreciation that necessitates health investment through consumption of healthcare inputs such as antimalarials to maintain health stock in an optimal trajectory via improving post-illness health. Investment in health inputs such as antimalarials reduces sick time, and therefore increases an individual's utility if the input has good healthcare quality.

Healthcare quality influence health stock by affecting the productivity of gross investment in health, which in turn impacts the rate of change of health stock. The actual quality of antimalarials consumed in response to malaria illness will thus affect an individual's sick time, and subsequently utility. It is thus necessary to analyse the quality of antimalarials to obtain an idea on the extent to which they impact health stock, and ultimately health consumers' utility. This paper presents an economic analysis of the actual quality of antimalarials in Dar es Salaam, and the extent to which they affect sick time and utility.

## **2. Drugs and Healthcare Choice**

Factors such as human biology, environment, lifestyle, and healthcare determine health (Lalonde, 1974), which is the objective of health systems. Healthcare is the easiest of these factors to manipulate policy-wise. Healthcare is important in improving post-illness health, and is in turn produced using inputs like personnel, equipment, supplies, drugs, buildings, regulations, and codes of conduct.

One of the most prominent health inputs is drugs, which are regarded as being synonymous with healthcare. Drugs are at the core of healthcare because they can visibly enhance health stock and subsequently utility by promptly reducing sick time through elimination or reduction of illness. Drug availability is one of the structure quality components of healthcare that plays a significant role in determining health-seeking behaviour via its perceived or actual ability to improve deteriorated health (Mwabu et al., 1993; Waweru et al., 2003; Shaikh & Hatcher, 2005; Chibwana et al., 2009; Danso-Appiah et al., 2010).

Drug availability can influence healthcare utilisation in one way or another as it is an important health improvement factor. Perception about drug effectiveness in improving health can influence provider choice as consumers perceive drug availability as enhancing healthcare facility quality. Such perceptions can influence consumption of healthcare from formal health facilities rather than informal ones after severe bouts of illness, as most drugs can only be obtained from formal rather than from informal health facilities (Flores et al., 2001; Chibwana et al., 2009; Danso-Appiah et al., 2010). Drug availability can also influence provider

choice by influencing people with access to drugs to alter healthcare utilization behaviour. Waweru et al. (2003) and Mujica Mota et al. (2009) found that most people who could access drugs without attending health facilities utilised health facilities less than those who obtained drugs only after visiting a health facility.

Drug availability is an important motivation for seeking formal healthcare as it leads to significant changes in healthcare utilisation. Shaikh and Hatcher (2005) found health facility utilisation in Pakistan was associated mostly with issues of acceptability, of which drug availability was a key factor. Mondal (1997), on the other hand, found provision of medicine by a healthcare facility or purchase from bazaars affected healthcare utilisation in Rajasthan. Provision of drugs by healthcare facilities thus led to increased utilisation of such facilities, while provision of drugs by bazaars led to decreased utilisation of healthcare facilities.

Several studies have investigated the role drugs play in healthcare utilisation, subsequently revealing the vital role of drugs in healthcare in general. Keeler and Rolph (1983), Lohr et al. (1986), and Smith (1993) investigated the effect of increased healthcare costs on healthcare demand in the United States that increased costs. They found that although increased costs led to decrease in treatment episodes, this was compensated by increased ingredient cost per prescription; implying healthcare consumers regarded drugs as a better and more effective alternative to consultation in the face of reduced access to healthcare. In an analysis of the elasticity of demand for prescription drugs for the elderly in Canada, Grootendorst et al. (1997) found people with poor reported health status as being more likely to increase prescription drug use with first-dollar coverage, implying the importance of drugs as a healthcare input increased with age.

The fact that drugs are a healthcare input intended to improve health implies their use should affect amounts of other health inputs required to produce or improve health if they are effective in achieving their intended objectives. Cecil et al. (2006) and Li et al. (2007) investigated the relationship between drugs and other healthcare inputs, namely physician visits, in the United States and Canada, respectively. They found a relationship between physician office visits and drug use: increase in drug costs led to decreased use of drugs, and increased demand for physician visits; implying reduced access to drugs led to increased use of other healthcare inputs.

### **3. Quality of Drugs**

Drugs are only useful if they improve health by eliminating or reducing illness. Drugs that do not improve health are inefficient health inputs that add no value to health. Drugs may be ineffective in improving health because of poor prescribing, or the existence of counterfeit or sub-standard drugs in the market, with the latter being the most common cause.

Counterfeit drugs are those that are deliberately and fraudulently mislabelled, while sub-standard drugs are genuine drug products that do not meet pharmacopoeial standards (WHO, 2009). Both counterfeit and sub-standard drugs

are ineffective, and therefore termed poor quality drugs. Poor quality drugs are those that are deliberately or inadvertently mislabelled, contaminated during the manufacturing process, or those that may have originally been of good quality but have become sub-standard because of poor storage or exposure to different conditions (ibid.).

Poor drug quality has negative consequences on public health and safety, and the economy in general. Sub-standard drugs are found in both industrialised and developing countries; and make up more than 10-15 percent of the global drug supply with an estimated 25 percent of drug supply in less developed countries, more than 30 percent of the drug supply in Africa and up to 70 percent of drug supply in Nigeria (WHO, 2003; WHO, 2009; Primo-Carpenter, 2009). There has been a significant increase in the presence of sub-standard drugs in previous years, whereby the sub-standard drug market was estimated to be \$39bn in 2005, and estimated to grow 13 percent annually to reach \$75bn in 2010 (Pitts, 2005).

Poor quality drugs are perpetuated by such factors as poor regulatory framework, high prevalence of infectious diseases, inability to afford or obtain access to lifesaving drugs through legitimate channels, laws and levies, lack of adequate civil liability, weak or absence of rule of law, and difficulties signalling quality to consumers (Bale, 2001; Bate, 2008; Harris et. al, 2009; and Fenoff and Wilson, 2009). The fact that these factors are more common in poor countries imply poor quality drugs are more prevalent in such countries.

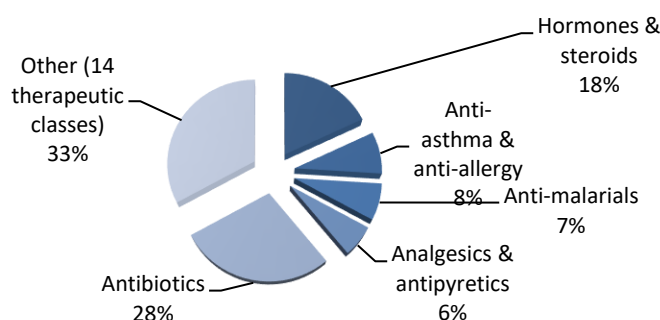
The prevalence of sub-standard drugs represents a significant share of medicines in some least developed countries (LDCs), especially in Africa (Taylor, 2008; Bate et al., 2016; Izevbekhalet al., 2017). Various studies have revealed the problem of sub-standard drugs to be highly prevalent in various African countries because of such issues as fake or insufficient active ingredients (Sow et al., 2002; Amin et al., 2005; WHO, 2006; Bate et al., 2008; Kaur et al., 2016). Several studies in Tanzania have found the prevalence of poor drug quality as there are factors perpetuating such a prevalence of sub-standard drugs existing in the country (Hebron et al., 2005; Minzi et al., 2003; Braun, 2005; Kaur et al., 2008; WHO, 2011).

Poor quality drugs have serious economic and health impacts due to their inadequate levels of active ingredients or wrong quantities of drugs that affect consumers in two ways. First, there is no therapeutic value whatsoever from the use of such drugs, which increases sick time rather than reducing it, leading to lower consumer utility accompanied with waste of resources.

Second, low levels of active ingredients or wrong quantities of drugs increase the risk of drug resistance by creating environments that assist microorganisms to exist and perpetuate diseases in the body. Increased risk of morbidity and mortality by poor quality drugs erode the benefits of health by leading to increased expenditure on health, as well as reduced productivity and investment in human capital such as education due to loss in school days.

The consumption of poor-quality drugs leads to the use of resources with no gain in utility, which is tantamount to misallocation of scarce resources, as less resources could have been better utilised had good quality drugs been used from the onset of an illness (Flores et al., 2001; Alter Hall et al., 2006). Poor quality drugs can harm people who consume them even to the extent of death. According to the INTERPOL (2008), an estimated 200,000 children die each year because of using counterfeit anti-malarial medications. Most of these deaths are due to malaria and tuberculosis, implying the use of sub-standard drugs to treat these illnesses has deadly consequences. Harris et al. (2009) estimate the number of worldwide deaths due to tuberculosis and malaria attributed to counterfeit drugs to be 700,000 annually.

Drugs are manufactured to treat diseases in different therapeutic classes, of which there are several major ones. On the same note, there are also sub-standard drugs by therapeutic class. As such drugs are alleged to deal with diseases in specified therapeutic classes. Fig. 1 shows reported sub-standard drugs by therapeutic their class.



**Figure 1: Sub-Standard Drug by Therapeutic Class**

Source: WHO Impact Report, 2010

Fig. 1 shows 7 percent of antimalarial drugs to be sub-standard. This is of great public health concern because malaria is a major health problem in the world, especially in developing countries in Africa, Asia, and Latin America. Half the world's population was at risk of malaria in 2008, with 247m annual cases, out of which 212m were in Africa. There were about 900,000 deaths from malaria, with over 90 percent of the deaths occurring in Africa. Most of the deaths involved children, with a child dying every 45 seconds, leading malaria to account to 20 percent of all childhood deaths (RBM, 2011).

Malaria has negative economic impacts because it negatively impacts the level of health in a way that diminishes the productivity and incentive effects that emanate from good health. This leads to increased use of resources that could have been used on other fronts that impact economic growth.

Malaria can decrease gross domestic product (GDP) by as much as 1.3 percent in countries with high levels of transmission, which over the long term have resulted in substantial differences in GDP between countries with and without malaria, particularly in Africa (RBM, 2011; WHO, 2011). Apart from economic costs, malaria has specific health costs involving personal and public expenditures on prevention and treatment, whereby it accounts for up to 40 percent of public health expenditures; 30-50 percent of inpatient hospital admissions; and up to 60 percent of outpatient health clinic visits in some high incidence countries (WHO, 2007).

Several studies have assessed the actual quality of antimalarials in Tanzania (Hebron et al., 2005; Minzi et al., 2003; Braun, 2005; Kaur et al., 2008; WHO, 2011). The studies, however, focused on assessing the quality of the first line antimalarial sulphadoxine/pyrimethamine, with less focus on other antimalarials. Furthermore, the studies mainly focused on the examination of the actual quality of antimalarials in terms of amount of active ingredient relative to pharmacopoeial specifications, while ignoring other aspects of quality pertaining to identification and weight.

The reviewed literature is notable in the sense that the reviewed studies evaluated the actual quality of antimalarials in Tanzania and focused on determining whether the antimalarials met pharmacopoeial specifications or not with respect to their levels of active ingredients, but did not examine the extent to which they complied or did not comply with pharmacopoeial specifications in terms of deviation from the specifications.

The reviewed studies thus provided static actual quality results that only described current situations without providing information on future prospects of actual antimalarial quality. Information on the future prospects of actual antimalarial quality can be obtained by dynamic actual quality results that reveal not just whether an antimalarial complies with pharmacopoeial specifications or not, but also the extent to which it does or does not.

This paper addresses the gap in previous studies by examining the actual quality of the three most common antimalarials namely, sulphadoxine/ pyrimethamine (SP), amodiaquine, and quinine by undertaking a drug quality analysis based on identification, uniformity of weight, and assay of active ingredient; as well as analysing them to determine compliance with pharmacopoeial specifications as well as the extent of compliance or deviation. The study has two objectives. First, is to determine the actual quality of antimalarials in Dar es Salaam; and second to determine the impact of quality of antimalarials on health consumer utility. The second objective is met by utilising the drug quality results to infer on the impact of quality on health consumer utility via the impact of quality on sick time.

## **4. Methodology**

### **4.1 The Model**

Drug consumers lack complete information when making decisions on purchasing antimalarials, and thus face some levels of ignorance. This must be considered

when assessing antimalarial quality. Modifying Chawla (2002) to incorporate antimalarials as a health input, an individual's decision to purchase an antimalarial is driven by several factors, of which an individual's self-assessment of the effectiveness (quality) of the drug in treating malaria is the main one.

$$Q^c = \theta Q^a, 0 < \theta \leq 1 \quad (1)$$

where,  $Q^c$ ,  $Q^a$  and  $\theta$  are the individual's perception of the quality of an antimalarial before buying it, actual quality of the antimalarial, and the degree of consumer ignorance, respectively.  $\theta$  depicts the extent to which an individual's assessment of the quality of an antimalarial differs from its actual quality. Determinants of an individual's perception of drug quality are presented as  $Q^c = Q^c(r, i)$ ; where  $r$  and  $i$  are individual's assessment of the effectiveness of a drug and information on the drug, respectively.

Once an individual facing an illness episode decides to buy an antimalarial, he interacts with a drug supplier who also assesses the quality of the antimalarial. A supplier's assessment of drug quality is represented as

$$Q^s = \phi Q^a, 0 \leq \phi \leq 1 \quad (2)$$

where  $Q^s$  is the supplier's assessment of the quality of the drug,  $Q^a$  is actual quality of the drug as previously defined, and  $\phi$  is the degree of supplier ignorance, which depicts the extent to which a supplier's assessment of the quality of an antimalarial differs from its actual quality. Determinants of a supplier's perception of drug quality are presented as  $Q^s = Q^s(c, v, o, Q^c)$  where  $c, v, o, Q^c$  are drug procurement cost, manufacturer's reputation, country in which drug is manufactured and a consumer's assessment of drug quality, respectively.

Variation between an individual and supplier's assessments of antimalarial quality and actual antimalarial quality implies prevalence of poor quality antimalarials in the market, which hinder achievement of optimal health outcome leading to an individual attaining utility  $U^i$  rather than  $U^q$  whereby,

$$U^q = U(h_q, x_q, \varepsilon_q; \varphi_q);$$

$$U^i = U(h_i, x_i, \varepsilon_i; \varphi_i);$$

$$U^i < U^q$$

where  $h$  is health status,  $x$  is non-health consumption,  $\varepsilon$  is a random error term, and  $\varphi$  is a parameter vector. Health status resulting from taking a good quality antimalarial ( $h_q$ ), and health status resulting from taking a poor quality antimalarial ( $h_i$ ) are represented as health production functions, ( $h_q = h(z; \beta_q)$ ) and ( $h_i = h(z; \beta_i)$ ), where  $z$  is a vector of individual, household, socioeconomic and supplier characteristics, and  $\beta$  is a vector coefficient of  $z$ .

Since variation is assessed and actual antimalarial quality leads to sub-optimal health outcomes, information on actual antimalarial quality can reveal the extent to which consumption of an antimalarial leads to sub-optimal health outcomes or increases the risk of sub-optimal health outcomes. Considering this, the study undertakes drug quality analysis of antimalarials in Dar es Salaam to determine the actual quality of antimalarials in Dar es Salaam and subsequently the impact on health outcomes emanating from consumption of antimalarials. The study assesses actual quality based on the country of origin of the drug, implying actual antimalarial quality is a function of country of origin of antimalarials.

$$qd = (spsw, spsa, spt1, spt2, spt3, spk1, spk2, qnc, qnk, amt1, amt2, amk) \quad (3)$$

where,  $qd$  is the quality of antimalarial drugs (good quality and poor quality);  $spsw$  is SP originating from Switzerland;  $spsa$  is SP originating from South Africa;  $spt1$  is the first batch of SP originating from Tanzania;  $spt2$  is the second batch of SP originating from Tanzania;  $spt3$  is the third batch of SP originating from Tanzania;  $spk1$  is the first batch of SP originating from Kenya;  $spk2$  is the second batch of SP originating from Kenya;  $qnc$  is quinine originating from Cyprus;  $qnk$  is quinine originating from Kenya;  $amt1$  is the first batch of amodiaquine originating from Tanzania;  $amt2$  is the second batch of amodiaquine originating from Tanzania; and  $amk$  is amodiaquine originating from Kenya.

#### 4.2 Data

Common antimalarial drugs (amodiaquine, quinine, and sulphadoxine/pyrimethamine) were procured from pharmacies and drug stores in Kinondoni, Ilala, and Temeke districts of Dar es Salaam. The sample consisted of 12 batches of drugs namely, 2 batches of quinine bisulphate from Cyprus and Kenya; 3 batches of amodiaquine, 2 being from Tanzania and 1 from Kenya; and 7 batches of sulphadoxine/pyrimethamine, 3 being from Tanzania, 2 from Kenya, and 1 each from Switzerland and South Africa. Each batch consisted of 100 tablets. Dar es Salaam is sampled as it is the largest metropolitan in the country that has abundant antimalarial consumers.

The sample size was adequate to undertake a drug quality analysis. Once procured, the quality of the drugs was assessed via drug quality analysis by the Chief Chemist Laboratory Agency using identification, uniformity of weight, and assay of active ingredient; as well as analysing to determine compliance with pharmacopoeial specifications.

#### 5. Results and Discussion

All sampled drugs complied with pharmacopoeial specifications for the identification of active ingredients, uniformity of weight, and assay of active ingredients tests. The key focus of the drug analysis tests was on the assay of active ingredients test because it measured the amount of active ingredient of a drug as a percent of the amount prescribed by pharmacopoeial specifications that describes the potency of a drug in attacking an illness.



Results of the assay of active ingredients test are shown below. Table 1 shows results of assay of active ingredients tests for the sampled drugs.

**Table 1: Assay of Active Ingredients Test for Quinine, Amodiaquine, and SP**

<b>Drug</b>	<b>WHO Specifications</b>	<b>Results</b>	<b>Comments</b>
Quinine Sulphate – Cyprus (34069)	95-105	105	Complies
Quinitab – Kenya (090930)	95-105	104.45	Complies
Amodar – Tanzania (9003)	93-107	104.38	Complies
Malaridose – Tanzania (UE 9003)	93-107	104.38	Complies
Amobin - Kenya (081442)	93-107	100.61	Complies
	(90-110)		
Fansidar – Switzerland (28204)	Sulphadoxine	102.4	Complies
	(90-110) Pyrimethamine	100.0	Complies
Fansidar – South Africa (28076)	(90-110) Sulphadoxine	101.7	Complies
	(90-110) Pyrimethamine	103.0	Complies
	(90-110)		
Sulphadar – Tanzania (9001)	Sulphadoxine	91.0	Complies
	(90-110) Pyrimethamine	92.0	Complies
Sulphadar –Tanzania (9006)	(90-110)		
	Sulphadoxine	105.5	Complies
	(90-110) Pyrimethamine	101.0	Complies
Sulphadar – Tanzania (9008)	(90-110) Sulphadoxine	92.0	Complies
	(90-110) Pyrimethamine	93.3	Complies
Orodar –Kenya (9C 109)	(90-110) Sulphadoxine	105.0	Complies
	(90-110) Pyrimethamine	102.0	Complies
Orodar – Kenya (9C 110)	(90-110) Sulphadoxine	106.1	Complies
	(90-110) Pyrimethamine	103.0	Complies

**Source:** Government Chemist Laboratory Agency, Tanzania

Table 1 shows quinine tablets from Cyprus and Kenya have adequate amounts of active ingredients, and thus comply with BP specifications of assay of active ingredients. The sampled quinine tablets have the maximum or near maximum amounts of active ingredients; implying high drug quality, which is crucial for a second-line antimalarial drug like quinine. Furthermore, the sampled amodiaquine tablets comply with BP specifications of assay of active ingredients. Amodiaquine tablets from Tanzania are more potent and thus superior to those from Kenya due to higher quantities of active ingredients.

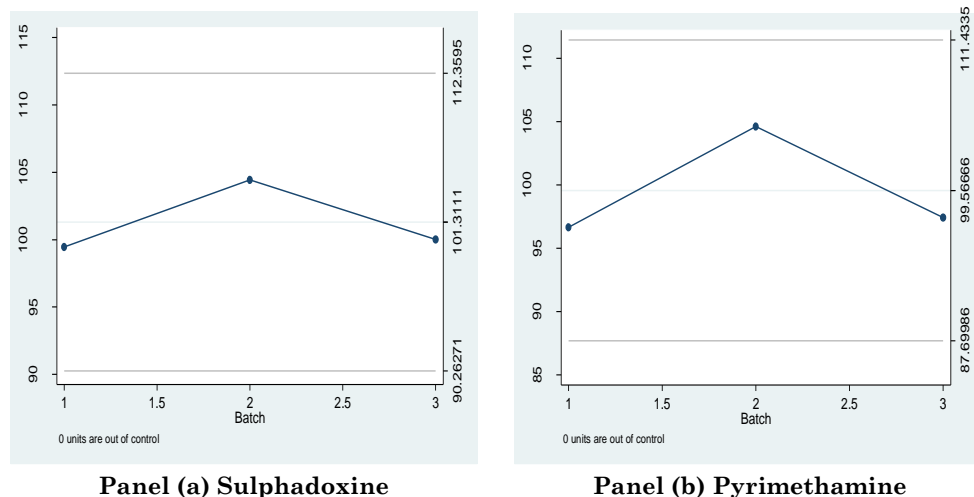
Sampled SP tablets (Swiss and South African Fansidar) comply with BP specifications of assay of active ingredients, and are thus of good quality with amounts of active ingredients being either average or above the average the BP specified amount. SP tablets manufactured in Tanzania (Sulphadar) comply with BP specifications of assay of active ingredients test, although they differ from the other sampled drugs by having wide variation in amounts of sulphadoxine and pyrimethamine contained. SP tablets from Kenya (Orodar) comply with pharmacopoeial specifications of assay of active ingredients test and are thus of good quality. The amount of active ingredients in the tablets is above the average, implying significant potency of the drug as a first-line antimalarial drug.

All the sampled drugs comply with pharmacopoeial specifications for the identification of active ingredients, uniformity of weight, and assay of active ingredients tests. This differs from Hebron et al. (2005) and Kaur et al. (2008), who found some antimalarials to be of poor quality. However, the study further examined the results of the assay of active ingredients test to determine quality parameters that can be obtained beyond pharmacopoeial specifications of the assay of active ingredients test.

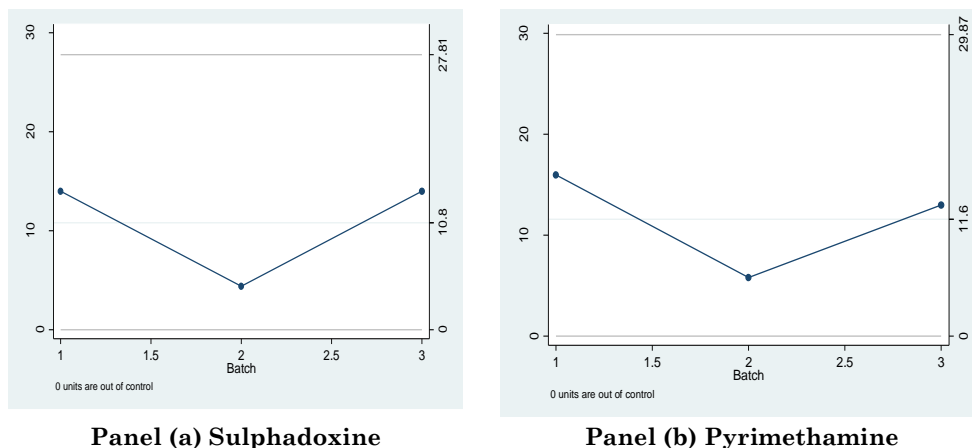
Determination of quality parameters is important, as compliance with pharmacopoeial specifications is a static condition for good quality, which analyses quality at only a given point in time. However, drug quality analysis should also involve a dynamic aspect to take account of the fact that drug quality can change at any time. The dynamic aspect of drug quality analysis provides information that helps in making inference on the quality of a drug eventually.

The key focus of the drug analysis tests was on the assay of active ingredients test as it measures the amount of active ingredient of a drug as a percent of the amount prescribed by pharmacopoeial specifications. This test thus describes the potency of a drug in attacking an illness. However, pharmacopoeial specifications have lower and upper ranges, whereby the nearer to the upper range a drug is, the more potent it is, and the better quality it has and vice-versa.

All batches of the sampled drugs passed the assay of active ingredients test. However, further analysis determined quality by using quality control charts to analyse the deviation of amounts of active ingredients from the central lines of control charts. In such charts, small deviations from pharmacopoeial specifications (central line) imply good quality and vice-versa for large deviations. Figs. 2 and 3 show the variations of sulphadoxine and pyrimethamine in the SP manufactured in Tanzania.



**Fig. 2: Tanzania SP Control Line Chart**



Panel (a) Sulphadoxine

Panel (b) Pyrimethamine

**Fig 3: Tanzania SP Range of Dispersion**

Source: Calculations from Results of Assay of Active Ingredients Tests

Figs. 2 and 3 show control line and range of dispersion charts, respectively. They show that although no batch of Tanzanian SP is out of control, the pattern of amounts of active ingredient is not smooth due to wide variation with each other. One batch (9006) has amounts of sulphadoxine and pyrimethamine that are not dispersed far from the central line, while the other batches (9001 and 9008) contain amounts of sulphadoxine and pyrimethamine dispersed far from the central line with amounts alarmingly near the lower control limit of pharmacopoeial specifications. Thus, Batches 9001 and 9008 have common cause variation and not special cause variation.<sup>1</sup> Such variation may be due to several factors such as poor design, quality control errors, variability in settings, ambiguous standard operating procedures, etc.

Since the occurrence of two batches out of three being on one side of the central line is above the expected probability of such an event happening, there is a likelihood of the manufacturing process drifting out of control in the future. This is likely to lead to the manufacture of poor quality antimalarials with low productivity in terms of being able to reduce sick time. Inability to reduce sick time perpetuates or even increases the disutility resulting from sick time and thus reduces utility even further as well as leading to waste of resources.

Although all three batches of Tanzanian manufactured SP comply with pharmacopoeial specifications in terms of levels of active ingredients, large deviations of the two batches of Tanzanian manufactured SP from the average levels of active ingredients specified by pharmacopoeial standards imply that they have good quality in a static sense. Tanzanian manufactured SP, however, had

<sup>1</sup> Common cause variation is variation in process that is predictable probabilistically while special cause variation is variation in process which probabilistically unpredictable.

poor quality in dynamic terms as inconsistency in adherence to manufacturing standards increases the likelihood of poor quality in the future. This increases the risk of the drugs reducing consumer utility.

The poor quality of Tanzanian manufactured SP relative to SP drugs from other countries in terms of levels of active ingredients may eventually result in lower effectiveness in treating malaria. Reduced effectiveness of Tanzanian manufactured SP negatively impacts the outcome obtained from their use, thus resulting in lower consumer utility relative to the other brands. Since consumers are averse to lower health outcomes, they are likely to respond by reducing their demand for such inputs eventually. This may be a major reason why the Tanzanian manufactured SP (Sulphadar) is the least popular SP drug in the country despite being the cheapest in the market (TFDA, 2009).

Low demand for Tanzanian manufactured SP indicates consumers have preference for quality antimalarials, which increase utility because they are more effective in reducing sick days. Such preference leads to low price sensitivity, as healthcare consumers' desire for greater reduction in sick days outweighs the desire to spend less on antimalarials. Furthermore, the importance of reduction in sick days over paying low prices for antimalarials indicates that consumers learn from past experience and adapt accordingly until perceived quality of antimalarials eventually coincides with actual quality, leading to low demand for Tanzanian manufactured SP despite its low price.

The low demand for Tanzanian manufactured SP despite its low price may be the result of consumers' low sensitivity to antimalarial prices because of their preference for quality of antimalarials overriding the cost concern. Such preferences are optimal in the sense that high quality antimalarials are more effective in reducing sick time, which leads to higher utility and productivity.

## 6. Conclusion

Results of drug quality analysis of malaria drugs sampled antimalarials are generally good as all the tested drug batches complied with pharmacopoeial specifications pertaining to the identification of active ingredients, uniformity of weight, and assay of active ingredients tests. Results of the assay of active ingredients tests for the sampled drugs revealed all sampled drugs met the necessary condition of good quality containing amounts of active ingredients that complied with BP specifications. This finding differs from Minzi et al. (2003), Hebron et al. (2005) and Kaur et al. (2008). This study has, however, gone further by analysing variation in compliance to project future quality.

Further analysis of the assay of active ingredients tests beyond mere examination of whether the active ingredient contents of the drugs were within pharmacopoeial specifications or not, provided more insight to malaria drug quality in Dar es Salaam. The analysis revealed two batches of SP manufactured in Tanzania by the same manufacturer to be of questionable quality despite meeting the active

ingredient content of BP specifications. The sulphadoxine and pyrimethamine amounts of these two SP batches showed significant dispersion downward from the average levels, and barely passed the lower thresholds of the BP specifications. Furthermore, the two poor quality batches of Tanzanian SP differed significantly from a third good quality SP batch produced by the same manufacturer.

The poor quality of Tanzanian manufactured SP relative to SP drugs from other countries results in decreased demand and low popularity, despite being the cheapest drug in the market. This indicates that the Tanzanian SP is considered an inferior good due to relatively poor quality. Furthermore, it seems quality issues with the Tanzanian manufactured SP have persisted for some time, and that the perceived quality of healthcare eventually coincides with actual quality of healthcare. This implies that consumers of antimalarials observe and disseminate information on the quality of antimalarials to each other, consistent with Leonard et al. (2009).

Wide variation of the amount of active ingredient relative to lower and upper thresholds as per pharmacopoeial specifications indicate that the manufacturing of SP in the country lacks stringent adherence to quality standards, thereby leading to inconsistencies in the quality of the final product. This increases the probability of the production of drugs that may be outside the pharmacopoeial specified active ingredients quantities, hence increasing the risk of having poor quality malaria drugs in the market that will not impact sick time and thus fail to improve the utility of healthcare consumers.

The presence of poor quality locally manufactured malaria drugs due to inconsistency of the amounts of active ingredients they contain has two important health and economic implications. First, extreme fluctuations towards the lower limit of pharmacopoeial specifications may lead to failure to effectively treat malaria, resulting in requiring further use of drugs that may increase the probability of developing drug resistance. Second, the inconsistency of the local manufacturer in adhering to uniform or near uniform SP tablet standards increases the future risk of the manufacturer producing drugs that do not comply with pharmacopoeial specifications of active ingredients. Analysis of deviation in amounts of active ingredients from the mean levels specified by pharmacopoeial standards can thus serve as an early drug warning system, which can be used to monitor and control drug quality.

The economic implication of the presence of poor-quality SP drugs in the Tanzanian market results from the fact that the use of poor-quality drugs may result in ineffective malaria treatment, resulting in lower consumer utility. There will thus be a need for consumers of such drugs to seek retreatment because of the initial drugs failing to effectively treat the illness. The use of more than one dose of treatment due to the use of poor-quality drugs implies consumers spend more money than would have been required had they consumed the right high-quality drugs. This is tantamount to a misallocation of resources in terms of directing resources towards ineffective health inputs, as well as unnecessarily directing more resources to health expenditure when effective results could be obtained by use of less resources.

The fact that three batches of SP drugs that were locally manufactured by the same manufacturer showed alarming variations in the amount of their active ingredient content, suggests the need to enhance drug quality monitoring activities beyond assessing whether drugs comply with pharmacopoeial standards or not. The irregular variation shown by the three batches of SP drugs that were locally manufactured by the same manufacturer is a quality monitoring issue, which falls under the domain of the Tanzania Food and Drug Authority (TFDA). The TFDA has various methods of monitoring the quality of drugs. It focuses mostly on the consumption level more than on the manufacturing level, with Post Marketing Surveillance (PMS)<sup>2</sup> being its main method. However, not all samples taken for analysis during PMS are tested, as over a fifth of samples were not tested because of expiring before testing due to lack of equipment, chemicals, and personnel (TFDA, 2009). Furthermore, the TFDA monitors drug manufacturers by paying them visits, but on an infrequent basis.

It is necessary for the drug authority to increase emphasis on monitoring of manufacturers to enhance the analysis of drugs that comply with pharmacopoeial standards, further to complement PMS at the lower level of the value-chain, while also ensuring PMS is done effectively and in a timely fashion.

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<sup>2</sup> This involves the TFDA taking samples of drugs at the marketing level for analysis

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