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Stakeholder perspectives on the demand and supply factors driving substandard and falsified blood pressure lowering medications in Nigeria: a qualitative study

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ABSTRACT

Objectives: Although substandard and falsified blood pressure lowering (BP) medications are a global problem, evidence on the factors driving this in Nigeria has not been reported. This study provides information on factors driving demand for and supply of low-quality BP lowering medications in Nigeria and potential strategies to address these factors.

Methods: This was a cross-sectional qualitative study. Between August 2020 and September 2020, we conducted 11 in-depth interviews and 7 focus group discussions with administrators of health facilities, major manufacturers and distributors of BP lowering medications, pharmacists, drug regulators, patients, and primary care physicians purposively sampled from the Federal Capital Territory, Nigeria. Data were analyzed using directed content analysis.

Results: We found that demand for substandard and falsified BP lowering medications in Nigeria was driven by high out-of-pocket costs and stockouts of quality-assured BP lowering medications. High out-of-pocket costs of BP lowering medications were driven by low in-country production and high import taxes. Stockouts were driven by low in-country production, poor supply chain management, poor stock storage and management, and weak procurement systems. Supply of low-quality BP lowering medications was driven by limited in-country manufacturing capacity, non-adherence to good manufacturing and distribution practices, under-resourced drug regulatory systems, ineffective healthcare facility operations, poor distribution practices, limited number of trained pharmacists, and the Covid-19 pandemic which led to stockouts. Central medicine store procurement procedures, active pharmaceutical ingredient quality check, and availability of trained pharmacists were existing strategies perceived to lower the risk of supply and demand of substandard and falsified BP lowering medications.

Conclusion: Our findings suggest that demand for and supply of substandard and falsified BP lowering medications in Nigeria is driven by multi-level, interrelated factors. Multi-pronged

strategies need to target stakeholders and systems involved in drug production, distribution, prescription, consumption, regulation, and pricing.

KEY QUESTIONS

What is already known?

- Substandard and falsified ((SS/F) medicines are a global problem but are more prevalent in low- and middle-income countries (LMICs).
- Most pharmaco-surveillance and supply chain strengthening programs in LMICs like Nigeria focus on communicable diseases rather than non-communicable diseases including cardiovascular disease.

What are the new findings?

- Demand and supply of substandard and falsified blood pressure (BP) lowering medications in Nigeria is driven by multi-level, interrelated factors. Factors driving demand for SS/F BP lowering medicines include high out-of-pocket costs and stockouts of quality-assured blood pressure lowering medications.
- Supply of SS/F BP lowering medications in Nigeria is driven by unfavorable government policies, non-adherence to good manufacturing and distribution practices, weak regulatory systems due to limited resources, non-adherence to good manufacturing practices, and Covid-19 pandemic.
- Strategies in place to address the risk of substandard and falsified medicines in Nigeria include procurement quality checks and good supply chain management practices by central medical stores; availability of analytical laboratory to conduct quality tests on active pharmaceutical ingredients (APIs), and; serialization (i.e., tracing a medicine by using a unique serial number from the manufacturer right to the patient) and authentication (by the National Agency for Food and Drug Administration and Control) to confirm the quality of medicines at the endpoint. Strategies which were also suggested to reduce the risk of low-quality BP lowering medications include public awareness on how to identify substandard and falsified

BP lowering medications, strengthening post-marketing surveillance to ensure adherence to good manufacturing practices, equipping all borders with necessary equipment to test the active pharmaceutical ingredients of imported medicines, and tax reductions on imported BP lowering medications to reduce cost and ensure broader availability of quality BP lowering medications across Nigeria.

What do the new findings imply?

- Reducing the demand for and supply of poor-quality BP lowering medications in Nigeria requires multi-pronged strategies targeting stakeholders involved in drug production, distribution, prescription, consumption, regulation, and pricing.
- As demand for BP lowering medications grows, this work is needed to ensure that expanding hypertension diagnosis and treatment can meet the potential to reduce morbidity and mortality through ensuring quality and effective drugs.

INTRODUCTION

Elevated blood pressure (BP) is a leading modifiable risk factor for global cardiovascular disease (CVD) morbidity and mortality,[1–3] including in Nigeria which is the most populous country in Africa.[4,5] Hypertension control programs need reliable and affordable supplies of quality, generic BP lowering medicines to achieve widespread hypertension control.[6] However, there is suboptimal availability of affordable and quality BP lowering medicines in most low- and middle-income countries (LMICs), including Nigeria, a challenge which may increase as rates of hypertension continue to grow.[7–10] As a result, there is a risk for falsified or substandard medications entering the supply chain, posing a threat to patients and health systems.[11]

The World Health Organization (WHO) defined falsified medicines as products that are fraudulently manufactured with their identity misrepresented and distributed with bad intent, while substandard medications are products that are registered by the regulatory authorities but fail to meet quality standards.[12] Although substandard and falsified medications are a global problem, they are pervasive in LMICs with the burden estimated to be as high as 10% of all medicines.[12–15] Some LMICs are targets for manufacturers of substandard and falsified medicines because of gaps in under-resourced regulatory systems, poor governance, and shortage of health products.[14,16–19] These risks are largely attributed to misalignment between supply chain market drivers of pharmaceutical manufacturing and distribution, and out-of-pocket expense, especially in the context of expanding universal health coverage.[20] Stockouts can further incentivize the use of substandard and falsified medicines to fill the void.[20] Pisani et al. showed that other factors driving substandard and falsified medicines in LMICs include: 1) limited technical capacity among producers, 2) buying from informal markets for convenience and affordability due to out-of-pocket payment for medicines, 3) donors activities which undermine national efforts to build sustainable markets, and 4) weak systems to mitigate demand for and supply of substandard and falsified medicines.[18]

When present, most pharmaco-surveillance and supply chain strengthening programs in LMICs like Nigeria focus on communicable diseases rather than non-communicable diseases including cardiovascular disease.[13] In Nigeria for example, the last mapping activity of the Federal Ministry of Health (FMoH) on multilateral, bilateral and non-governmental organizations' support in medicine procurement and distribution was in 2010 and focused on communicable disease.[17] Also, recent investments made by the Nigerian government on supply chain through organizations such as the National Supply Chain Integration Project have focused on medicines for communicable diseases and vaccines. Nevertheless, available evidence has shown that 24.6% of amlodipine and 31.9% of lisinopril in Nigeria[9] and 24.3% of generic BP lowering medications in 10 other African countries[21] are of substandard quality. The last mapping activity conducted by FMoH showed that the procurement and supply of medicines in Nigeria was uncoordinated, fragmented, and unplanned.[17] However, one of the strategic focuses of the National Agency for Food and Drug Administration and Control (NAFDAC) between 2020-2023 is to strengthen Good Distribution Practice of regulated products from pre-shipment and local manufacturers to the end user.[22]

We present the results of a qualitative study of market risk to understand the demand and supply factors driving substandard and falsified BP lowering medications in the Nigeria public sector and the role of strategies to address factors that directly or indirectly increase the risk for substandard and falsified medications. This is the first exploration of the risks and potential interventions for ensuring availability of quality BP lowering medications in Nigeria.

METHODS

Study design and setting

We conducted a cross-sectional qualitative study in the Federal Capital Territory, Nigeria to understand factors driving the risk of falsified and substandard BP lowering medications. The interview guides were adapted from the framework developed by Pisani et al., which was

developed to understand risks of and interventions to prevent substandard and falsified medications in China, Indonesia, Turkey, and Romania.[18] Details of the interview guides are provided in **Supplementary Table 1**.

Study population

Data collection took place between August 2020 and September 2020. We purposefully sampled stakeholders involved in the supply and use of BP lowering medicines and in the management of patients with elevated BP. Participants were purposively sampled from three of the six area councils of the Federal Capital Territory (Abuja Municipal Area Council, Bwari, and Gwagwalada) because they have the largest number of qualified stakeholders among the six area councils. Eleven in-depth interviews (IDIs) were conducted and these included administrators of health facilities (n=4), major manufacturers and distributors of BP lowering medications (n=3), primary and secondary healthcare facilities and community pharmacists (n=2), and regulators of medicines supply from Pharmacists' Council of Nigeria (PCN) and from the National Agency for Food and Drug Administration and Control (NAFDAC) (n=2). While community pharmacists are responsible for dispensing and supplying prescription medicines to community residents, PCN is a Federal Government parastatal responsible for regulating and controlling pharmacy education, training, and practice in Nigeria. NAFDAC regulates and controls the manufacture, importation, exportation, distribution, advertisement, sale and use of Food, Drugs, Cosmetics, Medical Devices, Packaged Water, Chemicals and Detergents in Nigeria. We also conducted seven focus group discussions (FGDs) with a total of 18 participants (FGDs 1-4, 3 stakeholders per group; FGDs 5-7, 2 stakeholders per group) including primary care physicians, pharmacists, and patients.

Interview procedures

Written informed consent for interview and recording was obtained from each participant. The IDIs and FGDs were performed face-to-face with participants on different days in settings

(e.g., participants' clinic and workplace) to ensure confidentiality. Interviews were conducted by study members (two females and two males) trained in qualitative methods, namely four Nigerian co-authors (GS, ENU, PP, and IO), including two interviewers with pharmacy management expertise (GS, ENU). Relationship was established for some of the participants prior to the commencement of the study. The duration of interviews ranged from 32 minutes to 57 minutes. Most interviews were conducted in English language, and one was conducted in colloquial English (Pidgin). Hausa, one of Nigeria's three major languages, was used in the FGD with patients with hypertension. Interviews were audio-recorded, and notes were also taken during the interview sessions with the permission of participants. Participants were informed about the aim of the study and the goal being to understand their perspective on blood pressure lowering hypertensive medications. None of the participants refused to participate or dropped out and we did not return transcripts to participants for comments. We have provided further details about participant recruitment, interviews, and data handling following the COnsolidated criteria for REporting Qualitative research (COREQ) guidelines. A reflexivity statement which outlined authors' roles in the research is provided in **Supplementary Table 2**.

Analysis

All recorded IDIs and FGDs were transcribed verbatim. The FGD in Hausa was translated and transcribed into English by a professional translator. All data and transcripts were anonymized and stored in a secured database at Northwestern University. We analyzed the data using directed content analysis,[23] with the aid of Dedoose (Los Angeles, CA: SocioCultural Research Consultants, LLC www.dedoose.com).[24] The coding process started with the codes that were derived from Pisani et al.'s market risk framework.[18] The deductive coding stage was followed by identification of inductive codes, which focused on new concepts which emerged outside the framework developed by Pisani et al. (**Supplementary Table 3**). Coding of initial transcripts was done as a team led by qualitative researchers (TMO, LRH) with disagreements

resolved by consensus. Final coding was done by GS, ENU and TMO and disagreements were resolved by LRH. sing directed content analysis, we identified factors driving substandard and falsified BP lowering medications into demand and supply sides. Demand side factors focused on drivers of population access and uptake or substandard and falsified BP lowering medicines. Supply side factors focused on the production, distribution, and availability of substandard and falsified BP lowering medications across Nigeria. We also extracted identified strategies that were thought to reduce demand and supply of low-quality BP lowering medications and suggestions for strengthening or new strategies from participants.

Ethical approval

The study was reviewed and approved by the Ethics Committee at the University of Abuja Teaching Hospital with approval number UATH/HREC/PR/2020/001/008. The aim of the study was explained to the stakeholders prior to the start of data collection, and written consent was obtained. During the informed consent process, we assured participants of maintaining their confidentiality.

Patient and public involvement

There was no patient or public involvement in this study.

RESULTS

Participants' characteristics are provided in **Table 1**. A total of 29 people participated in the study with two-thirds (62.1%) females and 58.6% younger than 50 years of age. The largest representation was at the Federal level, and the single largest participant group were pharmacists (34.5%) followed by administrators and regulators (20.7%), patients (17.2%), physicians (17.2%), and manufacturers and distributors (10.3%).

Table 1. Participant characteristics.

Characteristics	IDIs (n= 11) n (%)	FGDs (n=18) n (%)	Total (n=29) n (%)
Sex			
Male	7 (63.6)	11 (61.1)	18 (62.1)
Female	4 (36.4)	7 (38.9)	11 (37.9)
Age, years			
<40	4 (36.4)	4 (22.2)	8 (27.6)
40-49	2 (18.2)	7 (38.9)	9 (31.0)
50-59	5 (45.5)	5 (27.8)	10 (34.5)
>60	0 (0.0)	2 (11.1)	2 (11.1)
Participant type			
Administrators	4 (36.4)	0 (0.0)	4 (13.8)
Regulators	2 (18.2)	0 (0.0)	2 (6.9)
Pharmacists (hospital or community level)	2 (18.2)	8 (44.4)	10 (34.5)
Patients	0 (0.0)	5 (27.8)	5 (17.2)
Physicians	0 (0.0)	5 (27.8)	5 (17.2)
Manufacturers and distributors	3 (27.3)	0 (0.0)	3 (10.3)
Level[a]			
Local	2 (18.2)	2 (11.1)	4 (13.8)
State	3 (27.3)	7 (38.9)	10 (34.5)
Federal	3 (27.3)	9 (50.0)	12 (41.4)

[a] Level does not include participants who were manufacturers and distributors.

The results are divided into three broad sections with each focusing on demand and supply sides: 1) factors driving substandard and falsified hypertension medicines; 2) current actions to minimize demand and supply of substandard and falsified hypertension medicines, and 3) additional potential strategies which can contribute to future work to reduce substandard and falsified hypertension medicines in Nigeria **(Supplementary Table 4)**. A framework for how these demand and supply factors were found to potentially increase and decrease the risk of substandard and falsified BP lowering medications in FCT, Nigeria was then developed (**Figure 1)**.

Factors driving risk of substandard and falsified BP lowering medications

Demand side

We identified two interrelated factors which were associated with increased demand for substandard and falsified BP lowering medications, including: 1) poverty/poor economic condition in Nigeria and high out-of-pocket BP medication costs and 2) stockouts.

Poverty/poor economic condition in Nigeria and high out-of-pocket BP medication costs

Poor economic conditions in Nigeria, including high rates of poverty, and relatively high out-of-pocket cost of quality BP medicine make it difficult for people living with hypertension to afford quality BP lowering medicines. Participants reported that some people living with hypertension are unable to afford quality BP lowering medications, especially more expensive drugs classes like angiotensin receptor blockers, with the resultant effect being increased demand for cheaper but potentially lower quality medicines. Limited affordability of some BP lowering medications may also drive manufacturers and suppliers to produce or import cheaper substandard and falsified medicines. (see below) Additional contributors related to limited financial resources among patients included the lack of health insurance coverage for medications and the chronic nature of hypertension which demands long-term use of BP lowering medications, increasing the impact of out-of-pocket-cost.

"You know, no matter how cost-effective a drug can be, there are people that cannot afford it. And sometimes, they use more than two BP lowering medications. Then for some class of patients, where they have angiotensin receptor blockers (ARBs), that one is always an issue. They are unable to afford it, and most of the time, they really need it, and that's it." (FGD 4, Pharmacist from Secondary Healthcare facility)

Stockouts

Participants noted that stockouts force patients to look outside regular and trusted sources of BP lowering medications. As a result, patients may purchase these medications at sources with higher risks of being substandard or falsified, including informal pharmacy markets. Stockouts also erode trust in facilities especially public sector ones and further push patients to patronize other sources of medications where access to quality of medicines is not assured. Further, we found that stockout can be driven by patients' preference for a particular brand of medicines, which results in a situation where demand for that brand exceeds its supply. This lack of supply chain monitoring contributes to stockouts.

"So, if you talk about fake, we come to the hospital because in the hospital you cannot have fake. And that is why I get annoyed when they say it's out of stock." (FGD 3, Patient from Tertiary Healthcare facility)

Supply side

The supply side factors identified which contribute to the supply of substandard and falsified BP lowering medications across Nigeria include limited in-country manufacturing capacity, non-adherence to good manufacturing and distribution practices, weak systems of drug regulation, inconsistent quality assurance and post-market surveillance process due to limited resources, ineffective healthcare facility operations, poor distribution practices, limited number of trained pharmacists, and the Covid-19 pandemic. These factors also synergized to

create an even greater challenge of supply of substandard and falsified BP lowering medications.

Limited in-country production

Participants mentioned that there is low in-country production of quality BP lowering medications in Nigeria, which provides an opportunity for substandard and falsified BP lowering medications either produced or imported into the country to fill potential gaps from demand or actual stockouts. Participants reported concerns about this reliance on BP lowering drug importation making it difficult to assure quality, including the risk from longer distribution and storage periods compared with locally manufactured medications. Respondents also reported that poor economic policies leading to increased importation and Naira devaluation, as well as unfavorable government policies (e.g., lack of government subsidies for costs of production and high import taxes), may lead some manufacturers and distributors to compromise on good manufacturing, procurement practices, storage, and distribution practices to reduce costs.

Non-adherence to good production and procurement practices

In addition, some pharmaceutical manufacturing and distribution companies were felt to not always adhere to good practices and may prioritize profits over quality practices. Concern about these behaviors was mentioned by patients, pharmacists, supply chain managers, and drug regulators. For example, participants mentioned that some of the pharmaceutical and manufacturing distribution companies capitalize on the high level of poverty in Nigeria by bringing into the country medications that even though may not have the right active pharmaceutical ingredients (APIs) but are affordable by an average Nigerian.

Drug regulation

The system of drug regulation in Nigeria was also identified as contributing to the supply of substandard and falsified BP lowering medications. Some federal drug regulator respondents noted that since most medications are imported, high taxes on imported medicines increased

costs and risk of weakened supply chain of quality BP lowering medicines. While regulations exist, the limited resources of the food and drug regulatory agency facilitate the existence of parallel markets which offer substandard and falsified medications.

Participants also noted that the challenges of routine quality assurance process of NAFDAC due to low laboratory testing capacity. This capacity gap makes it difficult for this regulatory body to maintain the desired level of testing needed to ensure quality medicines which are imported or produced and distributed across Nigeria. Further compromising the existing system, NAFDAC was noted to have inadequate staff strength needed to perform adequate post-market surveillance.

> *"But we also have to look at the various brands in the market, most of these BP lowering medications are numerous. So, for me, I feel it will be very tasking for NAFDAC to really inspect them. I don't think they have enough staff and facilities to do that, so, that might be a loophole where fake drugs can thrive." (FGD 4, Pharmacist from Secondary Healthcare facility).*

Participants noted that the weakness in regulation of the Nigerian healthcare system has led to the proliferation of unlicensed pharmacies. As a result, some people own and operate pharmacies and prescribe medicines without licenses, which increases the demand and supply of substandard and falsified BP lowering medications.

> *"Somebody who is having a pharmacy is treating patients, recommending, and giving medicines, whether it's good or bad. Well, it's not something I can make a lot of comment about because it's part of the society (Nigeria). But if you want to wipe it away, let the hospital, government hospital, be functioning properly, so that people will be ready to come here." (FGD 3).*

Ineffective healthcare facility operation

Some pharmacists mentioned that poor inventory and delays in suppliers' payments due to bureaucracy within the healthcare facility also contribute to stockouts and risk of substandard medications. They noted that poor communication flow between the central medical store and healthcare facilities sometimes leads to drug expiration because healthcare facilities may not be aware that certain medicines are available at the central medical store, at the same time, the central medical store may also not be aware of the' need for medicines at the facilities. This poor communication could result in a situation where certain medicines remain at the central medical store longer than necessary and may even be near expiration before they are supplied., while stockouts occur locally. On other factors which increased the risk of expired medications, a supply chain manager mentioned that change in prescription patterns at the healthcare facility level could lead to reduced demand for in-stock medications and so expiration. This poor function was also identified as a reason why people went to unlicensed pharmacies as noted in the above quote.

Poor storage

The lack of infrastructure to store large quantities of BP lowering medicines resulted in poor storage and was also identified as a risk to medicine quality. For example, some pharmacists noted challenges with getting enough space to store procured BP lowering medications under the required temperature range, threatening medication potency. Finally, since some substandard and falsified BP lowering medications are smuggled into the country to avoid the high taxes, improper storage conditions during this process was identified as also reducing quality of available medications.

Other factors

Respondents noted several other factors including human resources and COVD-19 pandemic. The limited number of trained pharmacists in the country, especially in health facilities, contributes to the supply of substandard and falsified BP lowering medications. For

instance, some private hospitals do not have trained pharmacists to determine the quality of drugs procured and dispensed within the hospitals. Without sufficient pharmacy oversight, such hospitals may risk dispensing substandard and falsified BP lowering medications. Participants also noted that lockdown of health services during the Covid-19 pandemic affected supplies of medicines because some of the BP lowering medications in Nigeria are imported, resulting in stockouts, and also increased demand for substandard and falsified BP lowering medications. Participants also stated that cost of imported BP lowering medications increased during the pandemic and such products were more frequently out of stock than prior to the pandemic, thus increasing market for substandard and falsified BP lowering medications.

Factors and strategies to minimize the risk of demand for and supply of substandard and falsified BP lowering medications

Respondents identified a number of existing factors and strategies in place which reduced the risk of substandard and falsified BP lowering medications, although some needed strengthening as noted below.

Demand side

Participants identified that four factors that lowered the risk of demand for substandard and falsified BP lowering medications, including: 1) availability and affordability of medicines from the central medical store; 2) access to functional national health insurance scheme, which enhances affordability of quality BP lowering medicines for covered individuals; 3) supervision by pharmacists to ascertain appropriateness and quality of medicines and to prevent stockouts; and 4) purchase of medicines at the healthcare facility instead of outside pharmacies.

Supply Side

Participants also identified a number of supply side strategies which reduce the risk of substandard and falsified BP lowering medications in circulation. One strategy was the

procurement quality checks and good supply chain management practices by central medical stores. Participants also remarked that the medicines supplied at central medical stores are NAFDAC-certified and undergo quality control checks, even if capacity for checking all medications was limited. The strategy of serialization (i.e., tracing a medicine by using a unique serial number from the manufacturer right to the patient) and authentication by NAFDAC allows them to be able to confirm the quality of medicines at the endpoint. NAFDAC's capacity with an analytical laboratory available to conduct quality tests on active pharmaceutical ingredients (APIs) was identified as a factor that reduces supply of low-quality BP lowering medications. These actions may help to enhance adherence to good manufacturing and distribution practices.

Further, participants noted that procurement guidelines in healthcare facilities also reduces risk of poor-quality BP medicines facilitated by trainings that pharmacists undergo to identify and prevent procurement of low-quality BP lowering medications. These trainings include effective supply chain management, detection, and monitoring of substandard and falsified medicines, drug procurement. As a result, pharmacists are better able to select medicines based on quality and affordability and purchase from reputable companies. This training also supports the central medical store procurement of quality BP lowering medications.

Suggested additional strategies for reducing substandard and falsified medicines

Demand side

Participants also identified additional actions which could decrease demand for poor quality medicines. They identified a need for strong communication to increase public awareness to purchase medicines from licensed and registered pharmacies and to know the locations of such pharmacies.

Supply Side

Manufacturing, distribution, and importation

Participants suggested that manufacturers should ensure that APIs used for drug production are safe for patients' consumption by adhering to good manufacturing practices. Participants also identified the need for manufacturers to ensure that distributors follow necessary storage procedures, although they identified the challenge of a resulting increase in manufacturers' costs and subsequently, medication prices. An additional strategy identified was establishing an active and passive capture of adverse events by manufacturers and distributors with reliable reporting system. In addition, proper supply chain monitoring of BP lowering medicines should be established across the local, state, and federal government levels.

Regulatory bodies

Much of the input was on strengthening strategies already in existence. For example, they suggested that regulatory bodies should strengthen the system of registering and monitoring pharmaceutical companies to enhance accountability in manufacturing and distribution of BP lowering medications. Reflecting the external sources, they also suggested that regulatory measures are strengthened to check the quality of BP lowering medications at the borders when they are coming in and before they are being distributed across the country which is critical to maintain quality supply chain management and quality of BP lowering medicines. Reflecting the limited resources, they also noted that more officers may be needed to allow NAFDAC to carry out on-site assessments overseas to ensure fidelity to quality control measures.

Local, state, and federal government

Some participants noted that lower import taxes should be considered to increase importation of quality medicines, ensure availability of medicines across Nigeria, and reduce cost of medicines. This approach may reduce both the supply of low-quality BP lowering medications and demand for cheaper and often lower quality drugs. Participants also

recognized the need for strengthening transportation across the country in order to improve the efficiency and speed of the supply chain including reducing risk of substandard medications and prevent stockouts. Finally, they noted the importance of developing a functional health insurance program to cover treatment of noncommunicable diseases, to reduce costs and increase uptake of quality BP lowering medications.

Procurement, dispensing, and storage

Respondents suggested that pharmacists should purchase BP lowering medications from central medical stores at all times because these medicines are cheaper, more affordable, and of reliable quality, reducing availability of substandard and falsified medications. Some participants suggested that selection of companies to supply BP lowering medications by pharmacists should be based on merit of quality and affordability. It was suggested that such companies should be screened first before drugs are supplied and must have license to procure medicines. After this, prices should be compared across different companies and clinical presentations should be done for any new drug moiety. This process would directly reduce the supply of substandard and falsified BP lowering medicines and reduce cost t. Participants stated that drug regulators in Nigeria should ensure that good storage condition are maintained from the manufacturer to the distributor, through the pharmacy and then to the end users. This can be partly achieved by ensuring that appropriate infrastructure such as functional air conditioners and inverters (which give constant alternating current voltage at its output socket when there is no electricity) (due to poor power supply) are in place.

In addition, expansion and strengthening of existing strategies to improve availability of BP lowering medications is needed. For example, functional drug revolving funds, which are based upon a system already existing in the public sector where other drugs are sold with a limited (e.g., 5%) markup above procurement price to cover supply side costs. The subsequent revenue is used to replenish the drug stocks would be a potential way to ensure availability and

affordability for BP lowering medications. However, work needed to strengthen the process was also noted.

DISCUSSION

By interviewing key stakeholders in the Nigeria public sector, our study provides information on factors driving the demand for and supply of substandard and falsified BP lowering medications in Nigeria and outlines the strategies for overcoming these risks. While Nigerian health experts and the community are worried over the existence of low-quality BP lowering medications in the country,[25] these results provide important evidence on the factors driving availability of poor quality of BP lowering medications which can be used to inform strategies to strengthen existing systems or new ones needed to address this growing crisis. Similarities and differences between our study findings and that of Pisani et al are presented in **Table 2**.

Table 2. Similarities and differences between our study findings and that of Pisani et al.

Similarities 1. Our study and that of Pisani et al showed that multi-level and interrelated factors drive the risk of demand and supply of substandard and falsified medicines. 2. Pharmaceutical companies' desire to maximize profits emerged as a key factor which increases the risk of supply of substandard and falsified medicines in Nigeria as well as in China, Indonesia, Turkey, and Romania. 3. Our study and that of Pisani et al showed that patients acquire medications from unregulated supply chain in response to shortages thereby creating market opportunity for falsifiers.
Differences 1. While our study focused on factors driving the risk of demand and supply of substandard and falsified BP lowering medications, Pisani et al study focused on different kinds of medicines.

2. Pisani et al. showed that political promises made by the government in China, Indonesia, Turkey, and Romania to provide universal health coverage led to public procurement policies targeted at lowering prices of medical products; this political promise led to cost-cutting by pharmaceutical companies, and distributors thus increasing the risk of substandard medicines. This theme did not feature in our study.
3. Our study showed that some of the factors driving the risk of supply of substandard and falsified BP lowering medicines across Nigeria included limited in-country manufacturing capacity, weak regulatory systems due to limited resources, poor healthcare facility operations and distribution practices, and limited number of pharmacists. These factors were not mentioned in Pisani et al study.
4. Our study participants cited Covid-19 pandemic as a factor which affected supplies of medicines, thus resulting in stockouts, and an increased demand for substandard and falsified BP lowering medications. However, Covid-19 was not mentioned by Pisani et al because their research was done before the Covid-19 pandemic.

We found that BP lowering medicines are at elevated risk of falsification when there is a high market demand for these medications, further amplified by cost and scarcity of quality medications. The nature of health system financing mechanisms in Nigeria provides a basis for increased demand for low-quality BP lowering medications because healthcare is mostly funded through out-of-pocket payment.[26,27] As a result, it is often difficult for people to sustain access to quality medicines due to poverty, cost, stockouts, low health insurance coverage, and the chronic nature of hypertension management. We found that High out-of-pocket costs pushes people to demand cheaper medicines from 'high risk outlets', which are more likely to sell low-quality BP lowering medications. This finding is similar to another study in Nigeria, which showed that relatively high cost of drugs has made access to quality medicines difficult for many

Nigerians because a large proportion of the population lives below the poverty line.[28] Widening the national health insurance scheme coverage geographically and in terms of the scope of medicines covered may help to reduce out-of-pocket costs. In addition, creating a system where Drug Revolving Fund can thrive will help to improve the availability and affordability of quality-assured BP lowering medications.[29]

Further, our findings showed that stockouts was a major driver of substandard and falsified BP lowering medications in Nigeria and occurred due to low in-country production, poor supply chain management, poor stock storage and management, and weak procurement systems. Implementing policies that increase in-country production and monitor the supply chain for BP lowering medications will go a long way in reducing the risk of demand and supply of substandard and falsified BP lowering medications in Nigeria. In addition, we found that reliance on BP lowering drug importation makes it difficult to assure quality and it increases the risk of longer distribution and storage periods compared with locally manufactured medications. Addressing this challenge may involve repeat testing following storage or longer distribution periods; this approach prioritizes quality over cost.[30]

Our findings showed that supply of substandard and falsified BP lowering medications in Nigeria is driven by unfavorable government policies that limit in-country manufacturing capacity and create over-reliance on drug importation. Coupled with this, there is no clear monitoring of the APIs which came in through the borders indicating that the quality of such BP lowering medications may be unknown. The porous nature of Nigeria's borders creates a potential avenue where substandard and falsified BP lowering medications may gain an entry into the Nigeria market. Other studies have similarly linked the supply of low-quality medicines to drug smuggling cartels who may be motivated to diversify their portfolios.[12,31,32] To improve detection of and prosecution for low-quality BP lowering medications, the Nigerian government may need to have mutual legal assistance or extradition treaties with countries that are major sources of falsified drugs.[12,33]

Further, we found that an under-resourced regulatory system contributes to the supply of low-quality BP lowering medications in Nigeria. Within Nigeria, poor regulation due to low testing capacity and limited post-marketing surveillance create an enabling environment for non-adherence to good manufacturing practices and supply of low-quality BP lowering medications within the country. These findings are consistent with another study in Nigeria, which showed that factors contributing to the supply of low-quality medications including weak law enforcement, proliferation of unlicensed drug dealers, lack of system control, greed, illiteracy, illicit medicine importation, and erratic distribution system.[28] Strengthening the national regulatory systems for BP lowering medicines in Nigeria and protecting patients from low-quality medicines will require a strong political will and putting appropriate legislative frameworks, actionable and enforced policies, human resources, technologies, and quality control networks in place.[12] There is a need to enforce national directives to further address substandard and falsified medicines, including BP lowering medications. An important first step may be passing the bill on counterfeit medication which was presented to the National Assembly in August 2021.[34] This bill can be modeled after the Model Law on Medicine Crime which provides clear guidance on criminalization against supply of low-quality medicines, as well as incentives for governments to strengthen drug regulatory capacity.[35]

Our study identified factors and interventions that may reduce demand for and supply of substandard and falsified BP lowering medications in Nigeria, including central medical store procurement procedures, APIs quality check and availability of trained pharmacists to improve supply chain management. Interventions which encourage the continuance and expansion of these activities will be crucial to minimizing the risk of demand for and supply of low-quality BP lowering medications in Nigeria.

An important intervention to minimize the availability of low-quality medications will be to incentivize and regulate with accountability quality markets and discourage open markets. Open markets are common sources of medicine in Nigeria and provide key opportunities for

counterfeiting. Since 70% of drugs are imported from the two world's major sources of counterfeit medicines (China and India), dismantling the open drug market is necessary to achieve sustained decrease in counterfeit drug circulation in Nigeria.[36]

In addition, participants suggested that risk of low-quality BP lowering medications can be reduced through public awareness on how to identify substandard and falsified BP lowering medications, active post-marketing surveillance to ensure adherence to good manufacturing practices, equipping all borders with necessary equipment to test the APIs of imported medicines, and tax reductions on imported BP lowering medications to reduce cost and ensure broader availability of quality BP lowering medications across Nigeria.

Limitations

Our study includes limitations common to qualitative research. First, our study was based on a purposive sample of stakeholders from the Federal Capital Territory (one out of 37 states in Nigeria) indicating that the results cannot be generalized to the whole of Nigeria. Also, our stopping criterion was not based on data saturation. Nevertheless, we were able to provide a wide range of opinions and experience from major stakeholders involved in the demand for and supply of BP lowering medications, including at the federal level. Second, three of our audio recordings were not audible and could not be transcribed. Even though we used the field notes taken during these interviews in our analysis, participants may have mentioned other factors driving low-quality BP lowering medication, which were not captured in our analysis. In addition, transcripts were not returned to participants for comments and/or corrections Despite these limitations, our study is the first study to map out the factors driving the risk of substandard and falsified BP lowering medications in Nigeria and potential areas for strengthening new strategies to reduce this risk.

CONCLUSION

Our findings suggest that multi-level and interrelated factors drive the demand for and supply of substandard and falsified BP lowering medications in Nigeria. Multi-faceted strategies to address these factors need to target all stakeholders involved in drug production, distribution, prescription, consumption, regulation, and pricing. Also, suggested strategies to lower the risks of substandard and falsified medicines in Nigeria, as highlighted by the stakeholders, show the potential for combating the proliferation of low-quality medicines in the country. Progress on safeguarding the quality of medicines and combating low-quality medicines is crucial to achieving the Sustainable Development Goal (SDG) on 'improving access to safe, effective, quality, and affordable medicines and vaccines' (SDG 3). Thus, the Nigerian government can strengthen the political will to implement national directives that address low-quality BP lowering medications to reduce the burden of hypertension-related disease in Nigeria.

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Competing Interests

Non declared

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Contributors

MDH, DBO, AV and LRH conceptualized and designed the study. ENU, GS, PP, and IO collected the data. OAS, GS, TMO, ENU and LRH conducted the analysis. GS, OAS, ENU drafted the manuscript. All authors reviewed the manuscript and provided important intellectual

content. All authors read and approved the final manuscript. LRH is responsible for the overall content as guarantor.

Ethics approval

This research was conducted with approval from the University of Abuja Teaching hospital (UATH) Health Research Ethics Committee (HREC) (Approval number: UATH/HREC/PR/2020/001/008).

Data availability statement

Data are available upon reasonable request

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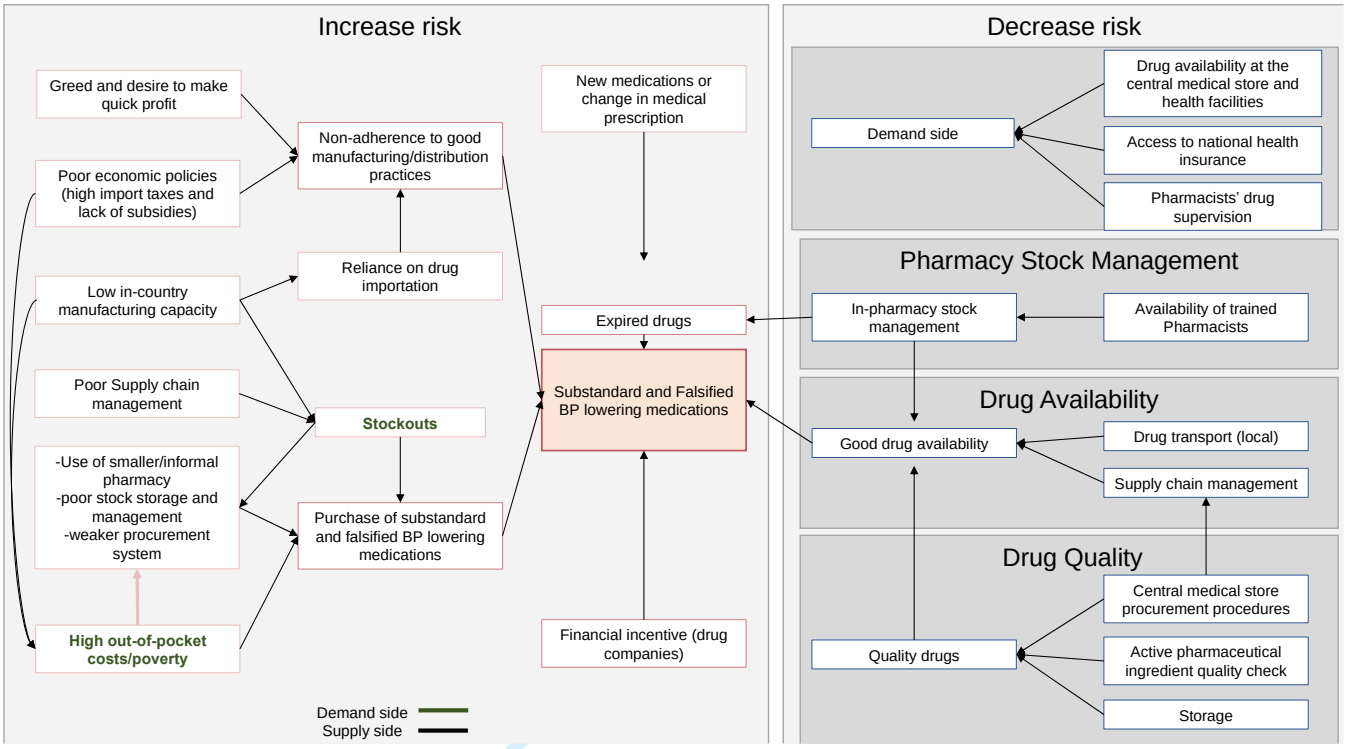

Figure 1: Factors identified as driving risk of substandard and falsified blood pressure lowering medications in Nigeria.

Supplementary Table 1: Interview guides.

Blood pressure lowering medicine mapping in Nigeria: A Pilot Study
In-depth Interview and Focus Group Discussion Guide

Introduction:
Thank you, Sir/Ma, for accepting to meet with me today. My name is_____. I am working with the Cardiovascular Research Unit of University of Abuja and University of Abuja Teaching Hospital, Gwagwalada, Abuja.

We are assessing the status of blood pressure lowering medications used in Nigeria towards improved supply chain and treatment outcomes. This interview will take about 30 minutes. To get your valuable comments, I would like to request your permission to record the session and taking some notes as well. Be assured that your responses will be kept confidential, and we will ensure that any information to be included in our report does not identify you as the respondent. We can stop the recording at any time.

Please Sir/Ma, do you have any questions on what I have just explained? Are you willing to participate in this interview? If so, then kindly review and sign this consent form.

Questions:

1. Please, tell me about yourself and your organization.

2. What is your view on the availability of anti -hypertensive medicines for patients in your setting?

3. How has cost of medicines affected patients' access to anti -hypertensive medicines?

4. What can you say about the quality of anti-hypertensive medicines in circulation?
   Probes:
   i. What factors drive the flow of fake and counterfeit anti-hypertensive medicines in our environment?
   ii. Do you notice batches of fake/counterfeit medicines?
   iii. What measures do you take to check the proliferation of these fake or substandard products?)

5. **In selecting and engaging suppliers**, can you describe what procedure do you use?
   Probes:
   i. For a typical BP medication, how many suppliers do you engage at a time?
   ii. What would cause you to go to a new supplier?
   iii. What are the problems encountered in the process?
   iv. How are such problems usually resolved?

6. Kindly describe your process of quantification for anti -hypertensive medicines.
   Probes:
   i. Are there challenges of suppliers not meeting the supply lead-times?
   ii. Do you experience challenges with incomplete deliveries?
   iii. What monitoring procedures do you adopt to ensure to prompt complete deliveries of ordered medicines?

7. Ensuring you receive quality anti-hypertensive medicines is key to successful blood pressure control. Please tell us your experience.
   Probe:
   i. Describe any quality assurance processes that are or are planned to be put into place.

8. How do you handle medicines storage in your facility?
   Probe:
   i. Are there issues of space, temperature/humidity control?

9. What are your product transportation choices like?
   Probes:
   i. How about cost?
   ii. Do you engage third party logistics providers?

10. What inventory management process do you employ for anti-hypertensive medicines?
    Probes:
    i. How do you determine your ordering strategy (i.e., how do you estimate demand?)
    ii. What causes demand spikes?
    iii. How much buffer of stock of inventory do you have for anti-hypertensive medicines?
    iv. What are the costs of holding stock?
    v. Any issues on warehousing?
    vi. Are there moments of stockout of anti-hypertensive medicines? If so, then describe the typical reasons.
    vii. Any issues of expiration of products? If so, then describe the typical reasons.
    viii. What have you tried to avoid stockout and expiration occurrences?

11. Can you discuss the nature of your anti-hypertensive medications stock?
    Probe:
    i. Which type of anti-=hypertensives do you usually stock?

12. How is information flow and communication along your supply chain?
    Probes:
    i. Are any data (e.g. paper/electronic, orders/customer demand) available?
    ii. What is the nature of feedback from end-users of blood pressure lowering medicines?
    iii. Are there complaints on medicine side effects or adverse drug reactions?

13. Patient compliance ultimately drives positive blood pressure control. Sir/Ma, what has been the experience so for far in your setting?

14. Please what is your final note on improving the supply chain of antihypertensive medicines in the country?

Conclusion: Thank you very much for your time. Your knowledge and insight will be very helpful to us. We will keep in touch with you, Sir/Ma.

Supplementary Table 2. Reflexivity statement

1. How does this study address local research and policy priorities?

Elevated blood pressure (BP) is a leading modifiable risk factor for global cardiovascular disease (CVD) morbidity and mortality, including in Nigeria which is the most populous country in Africa. One of the key factors that account for hypertension complications is the use of substandard and falsified blood pressure (BP) lowering medications. This study is the first exploration of the risks and potential interventions for ensuring availability of quality BP lowering medications in Nigeria.

2. How were local researchers involved in study design?

This study was conducted in Nigeria. The first category of local researchers involved were those with extensive experience of conducting, leading and publishing qualitative research on hypertension (DBO, GS, GS, TMO). The second category were local researchers with ongoing experience in qualitative research (PP, IO). A researcher (OAS) who is currently a migrant in a high-income country, but with experience in qualitative research was also involved in the study. In addition, there were high-income country researchers with extensive experience of conducting, leading, or publishing qualitative research (LRH, MDH, AV). Many of the authors have diverse cultural heritages originating from Nigeria and are more represented on the list of authors of this article. This representation was because the study was conducted in Nigeria and because we are interested in addressing inequities through 'parachute research'.

3. How has funding been used to support the local research team?

This project funding has been used to support local researchers (based in Nigeria) to conduct and lead qualitative research publication.

4. How are research staff who conducted data collection acknowledged?

All the research staff who participated in the data collection also met the authorship criteria as outlined by the International Committee of Medical Journal Editors (ICMJE) and so were listed as co-authors.

5. Do all members of the research partnership have access to study data?

All members of the research partnership have access to data.

6. How was data used to develop analytical skills within the partnership?

Majority of the coding was done by local researchers (GS, ENU, TMO) and were trained by senior researchers (DBO, MDH, LRH). Some of the data were coded together in order to leverage the skill sets of the senior researchers.

7. How have research partners collaborated in interpreting study data?

Weekly team meetings were held to discuss the data as well as emerging themes. Two members of the research team (GS, OAS) drafted the results, and the results formed the basis for discussing

the findings during the team's weekly meetings where all the team members agree on the interpretation of the study findings.

8. How were research partners supported to develop writing skills?

The research team writing this statement is a mix of senior and junior academics. The junior academics (GS, OAS) on the authorship team were supported by senior academics (MDH, DBO, LRH) in drafting the manuscript.

9. How will research products be shared to address local needs?

This paper will be published in open access journal. The findings will also be disseminated to all the key stakeholders including the National Agency for Food and Drug Administration and Control (NAFDAC), Pharmacists' Council of Nigeria (PCN), administrators of health facilities, major manufacturers and distributors of BP lowering medications, primary and secondary healthcare facilities and community pharmacists.

10. How is the leadership, contribution and ownership of this work by LMIC researchers recognised within the authorship?

Authors GS and OS led the draft of this manuscript, and their contribution has been recognised as joint first authors. In addition, the authorship team is predominantly based in a low-and middle-income (LMIC) country. The primary reason for this authorship plan is to strengthen the capacity of researchers in this LMIC in research publication.

11. **How have early career researchers across the partnership been included within the authorship team?**

We have included early career researchers (GS, OAS, PP, IO, AV) within the authorship team and they led the writing of the manuscript. These early career researchers are also mostly based on a LMIC.

12. How has gender balance been addressed within the authorship?

Seven authors are male (OS, TMO, PP, IO, GS, MDH, DBO) and four authors female (GS, ENU, AV, LRH).

13. How has the project contributed to training of LMIC researchers?

The authorship team is primarily composed of early career researchers. Most of the authors based in the low- and middle-income country are especially early career researchers.

14. How has the project contributed to improvements in local infrastructure?

This project has not directly contributed to improvements in local infrastructure.

15. What safeguarding procedures were used to protect local study participants and researchers?

Participation of local study participants was voluntary, and they could stop participation at any time, and not related to their employment or receipt of delivery. All data were deidentified before analysis and stored in secure site.

Supplementary Table 3: Coding structure for the current study with a comparison of code frequencies with Pisani et al.

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
00_Political_economy	**These are codes for the high-level political and economic factors that affect national and regional decision-making.**	**45**	**190**	**8**	**19**
Economic_factors	Economic factors that determine availability of jobs, purchasing power, demand and supply, inflation.	18	39	7	13
Jobs	*Employment status, sector (public versus private)*	*7*	*8*	*1*	*1*
National_income	*Minimum wage, per capita income*	*19*	*33*	*3*	*5*
Political_factors	Type of governance, party manifesto, policies, political actors.	37	147	5	8
Lobbying	*From industry, patient groups or other power blocs*	*16*	*34*	*1*	*1*
Political_promises	*This is for cases where promises made around things like UHC, industrial policy etc shape or constrain policy choices.*	*18*	*32*	*0*	*0*
Political_will	*The political will/determination to implement a system, program, product, etc.*	*10*	*19*	*5*	*6*
Votes		*11*	*22*	-	-
01_Market_opportunity	**These codes broadly map to what the GSMS report describes as "Access", though they mostly lead to opportunities by creating situations where demand outstrips supply**	**103**	**1063**	**14**	**98**
1_Supply_side	Factors related to supply of medications	71	364	13	49
Conflict_or_disaster	*External interruption to supply, e.g. because of conflict, natural disaster, industrial accident.*	*2*	*2*	*1*	*1*
Distorting_regulation	*Regulations which either restrict or mandate the availability of certain items. e.g. restriction to contraception for religious reasons (see also 07_Motivator/Perverse_incentives)*	*19*	*41*	-	-

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Infrastructure	*Poor infrastructure as a routine barrier to product supply or distribution*	*8*	*17*	*10*	*19*
Limited_manufacturing_capacity	*Comments about limitations on manufacturing capacity in Nigeria*	*13*	*14*	*3*	*3*
Procurement_practices	*Practices or rules such as obligation to procure only on price, which may affect product choice or quality*	*34*	*132*	*10*	*39*
Producer_incentives	*Incentives and disincentives which affect market entry and promotion of particular items*	*38*	*119*	*3*	*3*
Supply_chain_incentives	*Incentives and disincentives which affect distribution of particular items, including to remote areas*	*5*	*10*	*3*	*3*
2_Demand_side	Comments related to factors from the perspective of consumers	81	402	15	65
Affordability_OOP	*Affordability as an issue at the patient level*	*38*	*73*	*15*	*53*
Affordability_UHC_insurance	*Affordability at the level of the health system or insurer*	*38*	*73*	*8*	*14*
Incentive_structures_eg_prescription	*Incentive structures that determine the likelihood that a product will be covered, prescribed or otherwise proposed to pharmacists or patients (potential driver of irrational demand).*	*38*	*66*	*2*	*0*
Patient_preference	*Cultural or personal preference for particular products or brands*	*55*	*164*	*6*	*12*
Unexpected_demand	*Sudden, unforeseen spike in demand e.g. because of disease outbreak*	*6*	*8*	*8*	*10*
3_Market_regulation	**areas related to regulation of the market externally**	**58**	**290**	**3**	**3**
Clawback_tax		13	31	-	-
Price_related	Regulations or policies such as reference pricing, global budgeting, which affect prices in national market	51	188	2	2
Trade_related	Including free trade agreements, import restrictions, local content requirements and other measures to protect local industry	28	60	0	0

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
02_Market_dynamics	**A grouping of codes to tag different types of trade and target markets**	**54**	**266**	**7**	**9**
Domestic_consumption	Demand for medications(low/high) in the country	12	15	3	3
Export	Policies on export(does it favour local retention over export or viceversa), quality assurance.	32	53	0	0
Import	Taxation imported medicines, and products, substitution, regulations,	23	53	5	8
Parallel_trade	Availability of black markets, online markets,	29	100	2	3
Transit	Mode of transport, source, availability of middle men in the supply chain, handling/storage.	13	20	4	5
03_Actors	**Institutions or groups influencing production, trade and consumption of medical products**	**95**	**1028**	**15**	**130**
1_Macro	Institutions/organisations that influence policy or practice at a supra-national or national level, or operate outside the formal national supply chain	57	281	3	9
Global_health_funders	*e.g. GAVI, Global Fund, Gates etc*	*5*	*13*	*1*	*3*
Government	*National government agencies other than MoH/MRA whose policies affect trade, health financing and health systems*	*27*	*70*	*6*	*11*
MoH	*Ministry of Health, as distinct from Medicine Regulator (see 6_Regulators)*	*38*	*93*	*4*	*4*
Organised_crime	*This covers even small-scale deliberately criminal operations*	*12*	*31*	*0*	*0*
Other_international_org	*Includes multilaterals who influence pharmaceutical policy eg. UNICEF, WTO, World Bank, IFC etc*	*6*	*24*	*0*	*0*
Procurement_agency	*Specialised state procurement agencies*	*4*	*10*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
WHO	*World Health Organization*	*7*	*35*	*0*	*0*
2_Producers (see also 10)	This groups all manufacturers of medical products, with a sub for unlicensed. See under 10_Category_of_meds for subtypes	51	189	7	9
Packaging	*Presentation/look,location, size, cost*	*9*	*19*	*1*	*1*
Unlicensed	*Off-label used, unregistered medication, illegal production, irrational use.*	*6*	*7*	*0*	*0*
3_Supply_chain	Actors and factors involved in the movement of medicines.	8	50	13	62
Brokers		*8*	*18*	-	-
Central_medical_stores	*Availability, proximity,storage capacity and condition, management, payment system.*	*3*	*7*	*10*	*26*
Distributors	*capacity, coverage of distribution, (global, regional, national, sub-nation.*	*33*	*78*	*7*	*12*
NGOs	*Drug availability, type(for profit versus non-profit),coverage,*	*5*	*10*	*2*	*2*
Smugglers (illegal imports)	*Illegal importers*	*3*	*6*	*0*	*0*
Transportation	*Nature, cost, condition.*	*7*	*9*	*7*	*10*
Unlicensed	*Unlicensed distributors in country*	*2*	*7*	*2*	*2*
Pharmacy	*Actions that occur at a pharmacy*	-	-	*7*	*19*
Wholesalers	*Volume of stock, warehousing, inventory management*	*14*	*61*	*6*	*14*
4_Healthcare_professionals	Setting where the supply is being discussed	65	333	14	53
Clinic	*Availability, setting, waiting time, price for consultation.*	*8*	*15*	*1*	*1*
Hospital	*Availability, setting, waiting time, price for consultation*	*25*	*45*	*6*	*8*
Insurers	*Availability, degree of coverage, availability of medicines.*	*28*	*68*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Pharmacy	*Any person who works in a pharmacy Availability, Medicine stock, pricing, waiting time, counseling services.*	*33*	*111*	*12*	*34*
5_Patient_market_interface	This covers places where patients can access medicines directly, potentially without the mediation of any regulated organisation. Broadly equivalent to unregulated market	8	38	3	3
Internet	*Availability of online presence of conventional pharmacies.*	*17*	*55*	*0*	*0*
Market	*Availability of open markets(licensed/unlicensed)*	*11*	*17*	*1*	*1*
6_Regulators		45	136	10	23
Customs	*Customs actions related to preventing or enabling falsified or substandard medications*	*3*	*5*	*2*	*3*
Judiciary		*1*	*1*	*0*	*0*
NAFDAC_MRA	*National medicine regulatory agency (National Agency for Food and Drugs, Administration. And Control)*	*36*	*78*	*10*	*19*
NDLEA	*Nigerian Drug Law Enforcement Agency*	*-*	*-*	*1*	*2*
PCN	*Pharmacists Council of Nigeria*	*-*	*-*	*3*	*4*
Police		*9*	*23*	*-*	*-*
04_Levels	**These codes try to capture the geopolitical level at which an influencing factor operates**	**36**	**128**	**3**	**3**
Global		*9*	*17*	*1*	*1*
Mismatch	*Flags comments on the mismatch between level of activity and level of regulation, e.g. inability of national regulators to regulate exports for global market*	*17*	*24*	*0*	*0*
National		*13*	*23*	*3*	*3*
Regional		*21*	*54*	*-*	*-*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Sub_national		*4*	*5*	*0*	*0*
05_Intent	This marks information about the intent of the person manufacturing or selling the product; it is here mostly for equivalence with GSMS database coding.	0	0	6	6
Accidental	*The deficit in quality was due to a genuine accident*	*3*	*6*	*0*	*0*
Deliberate	*The deficit in quality was deliberate*	*7*	*12*	*4*	*4*
No_information	*Not enough information to determine whether it was deliberate or accidental*	*1*	*1*	*1*	*1*
Unknowing	*At this level of the supply chain, the handler had no knowledge of the quality deficit*	*0*	*0*	*0*	*0*
06_Facilitator	**Factors facilitating the trade in substandard and falsified medical products. Most of the aspects of "poor governance" and "limited technical capacity" in the GSMS report map to these codes.**	**90**	**738**	**12**	**26**
Corruption	Covers rent-seeking, grossly unethical behaviour, and the deliberate subversion of good practice for personal gain.	40	110	9	15
Conflict_of_interest	*e.g. lax regulation in order to maximise income from product registrations; prescription of innovator products to maximise hospital profits.*	*13*	*26*	*0*	*0*
In_law_enforcement_or_judiciary		*1*	*2*	*0*	*0*
Protecting_economic_interests	*e.g. deliberately lax regulation to favour state-owned companies*	*20*	*33*	*0*	*0*
Protecting_political_interests	*e.g. procurement of products from politically-connected firms without due regulatory diligence*	*11*	*14*	*0*	*0*
Disruption_&_adaptation	*Events or processes which create changes that facilitate trade in falsified medical productss, and market adaptation to those changes*	*5*	*14*	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
New_technologies		*13*	*23*	*-*	*-*
Pricing_and_or_medicine shortage	*Particular disruptions such as huge increase in tax, currency fluctuations etc that affect price, or e.g. factory closures affecting supply.*	*35*	*125*	*1*	*2*
Limited_capacity	capacity to carry out regulatory duties,	56	198	3	7
Financial_resources	*Financial resources to regulator to carry out regulatory work*	*18*	*35*	*1*	*1*
Human_resources	*Includes adequate training as well as head-count*	*36*	*110*	*3*	*7*
Technology	*Including laboratory capacity and access to reference standards etc.*	*21*	*38*	*1*	*2*
Systemic_failure	Weaknesses or failures which exceed the scope of a single actor or agency, or which are embedded in broader health systems.	69	398	6	17
No_due_dilligence	*Deliberate or accidental neglect of basic quality-assurance processes as medicines pass between actors through the supply chain.*	*27*	*49*	*1*	*2*
Poor_coordination	*Failure of necessary coordination between agencies or across borders, including failure to consider effects of enforcement of e.g. customs delays on medicine supply.*	*38*	*128*	*1*	*1*
Poor_planning	*Poor prediction of demand, supply or budget*	*39*	*164*	*1*	*2*
07_Motivator	**Factors motivating people to make or trade in substandard or falsified medicines, deliberately or through negligence. [Motivations for consumption of poor quality meds are covered under "market opportunity"]**	**61**	**274**	**12**	**18**
1_Legal_profit	Desire to make money or stay in business, using legal [though not always ethical] means. [See also 01_Market_opportunity/1_Supply_sde/Producer_incentives.]	38	120	0	0
Arbitrage	*Exploiting price differences between markets. Includes parallel trade*	*15*	*27*	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
	within free trade areas.				
Competitive_advantage	*Actions to increase market share, e.g. providing free samples, selling below cost.*	*15*	*33*	*0*	*0*
Cost_reduction	*Cost-cutting, including around production, packaging, distribution.*	*14*	*24*	*2*	*2*
Tax_avoidance	*Actions done to avoid taxes*	*1*	*1*	*0*	*0*
2_Illegal_or_liminal_profit	Desire to make lots of money, illegal or grey areas. Often co-coded with 1_Legal_profit/Cost_cutting, because intention is hard to determine.	19	49	10	13
Access_to_meds	*Increasing access in situations of extreme need and shortage. e.g. extending expiry dates of recently expired medicines in conflict zones*	*14*	*19*	*3*	*3*
Avoid_red_tape_or_laziness		*7*	*11*	*2*	*2*
Fraud_&_Money_laundering	*Generating money in a black economy (e.g. reimbursement fraud)*	*10*	*25*	*0*	*0*
Need	*Economic pressures on individuals to make a living*	*12*	*19*	*3*	*4*
Perverse_incentives	*Disproportionate, excessive or non-sensical regulations incentivise opacity or liminal behaviour. E.g. requirement of "halal" certification for raw ingredients may lead to faked paperwork. See also "Avoid_red_tape"*	*16*	*29*	*1*	*1*
08_Deterent	**Factors deterring people from making, selling, consuming substandard and falsified medicines. Most of the factors described in the "Prevent, Detect. Respond" approach in the GSMS report map on to these codes.**	**92**	**599**	**13**	**55**
1_Product_regulation		59	228	8	16
GDP	*Good distribution practice, and its enforcement.*	*16*	*32*	*4*	*7*
GMP	*Good manufacturing practice, and its enforcement.*	*19*	*46*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Inspection	*Inspection of manufacturing plants and warehouses and other distribution facilities.*	*24*	*36*	*4*	*6*
Licensing_&_market_authorisation		*27*	*37*	*2*	*2*
Prequalification	*WHO prequalification procedures which certify the quality of specific products made in specific factories.*	*7*	*8*	*1*	*1*
SOP	*Standard Operating Procedures*	*3*	*3*	*3*	*3*
2_Detection		45	171	12	34
Laboratory		*13*	*17*	*5*	*7*
Reporting_systems	*Post-market surveillance, and systems and technologies that allow for the rapid and efficient reporting of suspect products, and their recall.*	*14*	*22*	*3*	*8*
Risk_assesment	*Systems that anticipate likely shortages, extreme price pressures, or other factors that guide rapid pre and post-market interventions.*	*5*	*8*	*0*	*0*
Track_and_trace	*Technologies which allow legitimate products to be traced through the regulated supply chain.*	*30*	*88*	*5*	*6*
Whistleblowing_regs	*Rules, systems and culture that support the reporting of suspect products.*	*3*	*7*	*4*	*5*
3_Criminal_justice	Description of criminal justice system	11	13	0	0
Effective_policing	*Investigation of suspected falsification that is honest, capable and adequately resourced*	*3*	*3*	*0*	*0*
Impartial_judiciary	*Current state of judicial system and its ability to be impartial*	*1*	*1*	*0*	*0*
4_Transparency	Flags actions which aim to reduce fraud or falsification by increasing the transparency of procurement or the supply chain.	29	62	1	1
5_Systemic_approach	Covers active prevention working long term through health systems	41	112	5	11

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Avoid_production_shortages	*Steps to foresee demand and avoid shortages, e.g. effective demand forecasting, incentivising multiple prequalified generics of essential medicines.*	*22*	*133*	*4*	*7*
Clinical_guideline	*Clinical guidelines which reduce the likelihood of/opportunity for irrational prescribing.*	*9*	*21*	*2*	*2*
HTA	*Health Technology Assessment — cost-benefit assessment that aim to maximise availability of cost-effective, clinically indicated products.*	*0*	*0*	*3*	*4*
Champions	Individuals who actively promote med quality agenda, and who make a difference through their own persistance	6	8	3	4
09_Legislation	**Laws relevant to substandard and falsified products**	**35**	**123**	**4**	**6**
Definitions	Flags discussions over definitions and language	8	10	0	0
Law_type	Applicable law related to medicine regulation	14	29	1	1
General_trade_law	*Laws that are generally related to trade*	*3*	*4*	*0*	*0*
Medicine-specific-laws	*Laws that are specific to medicines*	*7*	*13*	*1*	*1*
Medicrime	*Refers specifically to the Medicrime Convention.*	*4*	*8*	-	-
Penalties	Penalties for breaking laws	21	64	4	4
Enforcement	*Type and method of enforcement*	*9*	*15*	*4*	*9*
Penalties_for_other_falsification	*Penalties for other types of falsification*	*4*	*8*	*1*	*1*
Penalties_for_pharma_crime	*Penalties for medicine crime*	*11*	*28*	*0*	*0*
Trade_and_IP	Legislation related to trade, patents or intellectual property. This also flags examples where patent violations are deliberately conflated with medicine quality issues	8	15	0	0
10_Quality	**Specifies the particular nature of the quality violation. These**	**61**	**373**	**8**	**19**

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
	nodes are principally for comparison with GSMS database codes				
Falsified	*Fake medicine that has been intentionally altered and may contain no active ingredient, the wrong active ingredient or the wrong amount of the correct active ingredient*	49	211	6	8
Criminal_substandard	*Medicines that were intentionally made out of specification*	*5*	*8*	*3*	*3*
Expiry_date_extended	*Change in expiry date*	*4*	*5*	*2*	*2*
Quality_but_falsely_labelled	*The medicine is produced based on quality standards but is falsely labeled based on dose, expiry date, or other labeling change*	*1*	*1*	*0*	*0*
Repackaged_as_different_product	*The product has been repackaged as a different product*	*5*	*14*	*0*	*0*
Total_fake	*Falsified medicine that is easily recognized as fake*	*21*	*56*	*0*	*0*
Meets_standards	medicines that meet manufacturing standards but aim to subvert regulated market	7	9	2	6
Other_illegal	Other forms of illegal manufacturing or distribution	13	39	0	0
Stolen_or_diverted	*Medicines that are stolen or diverted*	*6*	*16*	*0*	*0*
Unregistered	*Medicines that are available for sale but have not been registered with NAFDAC*	*6*	*15*	*0*	*0*
Substandard	Low-quality medicines	24	96	9	14
Contaminated	*Medicines that are contaminated*	*3*	*5*	*0*	*0*
Degraded	*Medicines that are degraded*	*10*	*18*	*1*	*1*
Failed_dissolution	*Medicines that fail dissolution tests*	*1*	*1*	*0*	*0*
Wrong_amount_of_API	*Wrong amount of active pharmaceutical ingredient*	*2*	*2*	*0*	*0*
Wrong_API	*Wrong active pharmaceutical ingredient*	*1*	*1*	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
10a_Category_of_meds	**Categorises medicines according to producer type or therapeutic group. Used in combination with other codes**	**73**	**369**	**12**	**37**
Producer_type		60	199	3	4
API	*Type of med based on active pharmaceutical ingredient*	*18*	*34*	*6*	*10*
Contract	*Manufacturers who produce medicines under contract for license holders or other clients.*	*5*	*6*	*1*	*1*
Generic	*Generic medicine*	*32*	*97*	*4*	*7*
Branded				*9*	*17*
Innovator		*20*	*27*	-	-
Therapeutic_class	Therapeutic class of medicine	46	168	12	23
Blood pressure lowering	*Blood pressure lowering medicine*			13	36
Anti-microbial		*6*	*7*	-	-
Biosimilars		*1*	*1*	-	-
Lifestyle		*9*	*14*	-	-
NCD	*Medications mentioned for other noncommunicable diseases, including cardiovascular diseases*	*12*	*18*	*0*	*0*
Other	*Medications mentioned that are not blood pressure lowering*	*7*	*12*	-	-
Sexual_health		*3*	*3*	-	-
Vaccines		*23*	*99*	-	-
Important/notable Excerpts	*Notable excerpts from interviews to be set aside as quotations*	-	-	*13*	*41*
Improvement ideas_actions	*Ideas or actions underway aimed to reduce the risk of substandard and falsified drugs*	-	-	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Demand	*Ideas or action targeting patients*	-	-	*0*	*0*
Supply	*Ideas or action targeting supply side including dispensing*	-	-	*0*	*0*
15_Sub-study		**0**	**0**	**-**	**-**
China		10	37	-	-
GSMS	Flags public access data from GSMS cases, used to validate framework.	0	0	-	-
Indonesia		12	26	-	-
Romania		6	7	-	-
Tool	Flags info for risk-assessment framework	1	3	-	-
Turkey		5	5	-	-

Supplementary Table 4: Factors driving the risk of substandard and falsified BP lowering medications in Nigeria.

Factors	Definitions	Illustrative quotes
Demand side	Factors which increase or reduce demand for substandard and falsified BP lowering medications	
1. Poverty/poor economic condition (+)	Lack of financial resources and high out-of-pocket costs which limit purchasing power and increase demand for low quality medicines.	*You know, no matter how cost-effective a drug can be, there are people that cannot afford it. And sometimes, they use more than two BP lowering s. Then for some class of patients, where they have Angiotensin receptor blockers (ARBs), that one is always an issue. They are unable to afford it, and most of the time, they really need it, and that's it (FGD 4, Pharmacist from Secondary Healthcare facility).* *For instance, now, if you see branded products from (manufacturers), they are of very high quality, everybody knows it, but the prices are high; it's only for the rich in the society. So, the general populace is made of not too rich/low-income group. So, they will buy, they will prefer to buy things that are cheaper. (FGD 4, Pharmacist from Secondary Healthcare facility).*
2. Stockouts (+)	Lack of availability of BP lowering medications anywhere along the supply chain (from the manufacturer to the point of dispensing).	*So, if you talk about fake medicines, we come to the hospital because in the hospital you cannot have fake. And that is why I get annoyed when they say it's out of stock. (FGD 3, Tertiary Healthcare facility patients).* *Certain patients, they go on a particular type of drug over a long period of time, and they tell you that, that is the only drug that works for them. And even if the doctors, or the pharmacists try to convince them about how efficacious other drugs are, they tend to not agree with them. So, if it is not that particular drug, they would prefer to go outside; so, the, the demand on such drugs can be so high, and that can lead to out-of-stock syndrome (FGD 2, Federal level Medical Officers).*

3. Availability of medicines from the Central Medical Store (-)	Availability of BP lowering medications from the Central Medical Store indicating access to timely quality medicines	*Based on the drugs, the tablet, the BP lowering s we collect, because we collect them from the Central Medical Store. So far, so good, the brands and the products they give, they are relatively cheap and affordable for the common man to use (FGD 4, Pharmacist from Secondary Healthcare facility).*
4. National health insurance (-)	Access to national health insurance at the Federal Capital Territory which enhances affordability of quality BP lowering medications	*I say this with utmost confidence because at least we have a larger set of our population utilizing their National Health Insurance Scheme, and the one that is domiciled with the FCT, which is, FCT Health Insurance Scheme. So, for that reason, the cost has not been our own major problem. I think too, let's give credit to the system that patients are able to access their BP lowering drugs. (IDI 9, State Pharmacy Administrator)*
5. Pharmacists' supervision (-)	Availability of pharmacists at healthcare facilities to ensure appropriateness and quality of medicines.	*Because we say that every procurement must be handled by pharmacist, every document for procurement, any company that is engaged, to supply drugs, to any institution must come through a pharmacist, and we must see the license of that pharmacist (IDI 11, State level Administrator).* *Yes, so you have to ask them to go and buy outside [when BP lowering medications are out-of-stock with the hospital]. What I normally do if they prescribe [BP lowering medications] to them and we don't have, I will tell them "bring it let me see". This is so that we [Pharmacists] know whether this is the right medication prescribed for the patient (IDI 2, PHC Pharmacist)*
6. Drug availability at healthcare facility (-)	Availability of BP lowering medications within the healthcare facility instead of outside the healthcare facility ensures access to quality medicines.	*Because going to the hospital to collect drugs, is better than going to any pharmacy outside to buy. Most of them are fake (FGD 3, Tertiary Healthcare facility patients).*
Supply side	Factors which increase or reduce supply of substandard and falsified BP lowering medications.	

1. Limited in-country manufacturing capacity (+)	Limitations on manufacturing capacity for BP lowering medications in Nigeria.	*Actually, the factor is just policy. One, in the country where, will I say, up to eighty to eighty-five percent of our drug consumption is still dependent on importation. You can't guarantee a mere quality (IDI 9, State level supply chain manager)*
2. Non-adherence to good manufacturing and distribution practices (+)	Wrong motives (greed and desire to make quick profit) for market entry, promotion and distribution of BP lowering medications.	*You know, there are so many reasons why you have fake drugs in circulation. One of it is the suppliers; the second one is economic gain from those that are producing these products. Some of the suppliers, you give them Local Purchase Order for instance to supply drugs, and rather than go to the actual companies at the source, they will go to the side, and maybe go to Onitsha market or somewhere and buy these drugs...(IDI 1, Federal level Administrator).* *So, each time there is fall in the price in dollars, it affects the cost of all these goods that come in, because the marketers will never want to lose their money. So, the only option left will be probably to compromise on quality (IDI 9, State level supply chain manager)*
3. Drug regulation (+)	Regulations which either restrict or mandate the availability of certain BP lowering medications. This also includes poor quality assurance process due to low testing capacity of available laboratories and limited staff strength to conduct post-market surveillance.	*Then, when we are not regulating…we are not stringent on regulation, or we don't have the technology or the manpower to be able to man our porous borders… And I think the government instituted that drugs are only to be imported through air. But you find out that most of these drugs find their way in through the land borders. And once that is done, there's no check (IDI 7, federal level drug regulator)* *But we also have to look at the various brands in the market, most of these BP lowering s are numerous. So, for me, I feel it will be very tasking for NAFDAC to really inspect them. I don't think they have enough staff and facilities to do that, so, that might be a loophole where fake drugs can thrive. (FGD 4, Pharmacist from Secondary Healthcare facility).*

4. Ineffective healthcare facility operation (+)	Poor inventory of BP lowering medications, poor communication flow, change in prescription pattern, and delay in suppliers' payment which often led to stockouts	*Prior to now, the communication flow was, was not adequate; that's from Central Medical Stores to the facilities. And err, it led to even the Central Medical Stores having drugs that were expiring. Because the facilities are not aware that they have such drugs" (FGD 4, Pharmacist from Secondary Healthcare facility)* *And, apart from that too, sometimes, before now, we were getting list from the pharmacy point on drugs that are close to expiration, and that if we don't, if we don't exhaust these drugs, in good time, the hospital stands the chance of losing so much (FGD 2, Federal level Medical Officers).* *Expiration of drugs is inherent to the pharmaceutical business. Take for instance, change in the pattern of prescription will cause your own stock to expire. I have based my projection on the previous consumption pattern and the request, but if there is sudden change in the pattern, of, you understand, of consumption at the facility level or, for whatever reason, or response (IDI9, state level supply chain manager)*
5. Poor storage (+)	Inability to store procured BP lowering medications under the required temperature, driven by limited space and use of illegal drug supply sources.	*…we all know what drug moieties are all about. For instance, a drug can still be potent and exported to deliver efficaciously its own, I mean, activities, but because of ordinary storage condition, it can lose its potency, long before the expiration date. And as long as we import, you cannot guarantee storage condition during the course of importation. So, some potency could have long been lost (IDI 9, state level supply chain manager).* *Yes, I think once in a while, we have problems with storage because, one, where we store our large quantities of drugs, which is what they call the Bulk Store, you know, they have a problem of space, and they have a problem of aeration. So, once in a while, we have*

		some challenges (IDI 1, Federal level Administrator).
6. Limited number of trained pharmacists (+)	Limited number of trained pharmacists leading to limited of pharmacists available in healthcare facilities, especially in private hospitals.	*Now, our profession, pharmacy profession is one of those profession that up till today is still growing at a very slow rate. If you go to most universities and you compare the population medical students, medical lab scientists to pharmacy students, you will be shocked that there is a gap in the professional need (IDI 9, state level supply chain manager).* *And then, even the situation whereby everybody is a pharmacist; we have private hospitals, they don't have pharmacist in their system, they go to anywhere, buy their drugs, dispensers – they are the dispensers, they are the everything IDI1, Federal level Administrator).*
7. Covid-19 pandemic (+)	Interruption to supply chain due to Covid-19 pandemic.	*Again, unforeseen circumstances, the COVID has given us a typical example. Our stock was meant to last for February and March, and by March, there was lockdown and patients could not access hospitals. So, if I have a stock of short life, you understand…, they will definitely expire (IDI 9, state level supply chain manager).*
8. Central Medical Store procurement quality check (-)	Availability of BP lowering medicines improves supply chain management and availability of quality medicines which are NAFDAC certified.	*We get most of our drugs from the Central Medical Store; and the people there, there are a lot of pharmacists with experience. So, they look into, the brands of drugs they buy. It might not be branded, but they look at the company that has been in the market for a long time, so it has a name already, when they are getting those anti hypertensives. So, most of the time, the brands we get, they are good brands (FGD 4, Pharmacist from Secondary Healthcare facility)* *Because like the Central Medical Store, most of the BP lowering s they buy, they are NAFDAC-certified. So, they hardly collect or procure any medicines that NAFDAC has not certified. And to certain extent, most of the time, they have their own quality control unit in the store,*

		which if they go for bidding, they will collect samples and check (FGD 4, Pharmacist from Secondary Healthcare facility)
9. NAFDAC equipment and operations (-)	Availability of analytical laboratories to conduct quality tests on active pharmaceutical ingredients and use of barcodes which allows the possibility of confirming BP lowering medications at endpoint.	*Because when you are dealing directly with the real source, then the possibility of buying fake will be, at least reduced or eliminated. Because I will not expect a company to fake its own products, or if you are the one distributing, you are bringing it from whatever country, I don't expect you to bring in anything fake. But we also have an analytical lab, but right now, I don't know what they are able to test, or what they are able to check when they receive the drugs (IDI11, Administrator State level).*
10. Healthcare facilities guidelines (-)	Availability of guidelines in health care facilities which facilitates procurement of quality and affordable BP lowering medications	*We have a Central Procurement Unit, where all the hospitals under FCTA collect their drugs and consumables; and there's a process which they follow, the quantification, bidding, and; for us here, even the ones we get for ourselves, we normally get through companies, reliable companies. And, with that we are certain that the qualities are of a standard. So, we have not really come across any substandard, and we have not gotten any feedback from patients that these drugs are not effective, nor from the physicians (FGD 4, Pharmacist from Secondary Healthcare facility)*

(+) Factors contributing to increase in demand for and supply of substandard and falsified BP lowering medications

(-) Actions contributing to decline in demand for and supply of substandard and falsified BP lowering medications

Research Checklist: COREQ (COnsolidated criteria for REporting Qualitative research)

Checklist

Topic	Item No.	Guide Questions/Description	Page Number
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	9
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	9
Occupation	3	What was their occupation at the time of the study?	9
Gender	4	Was the researcher male or female?	9
Experience and training	5	What experience or training did the researcher have?	9
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	9
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	9
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	9
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	9
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	8
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	8
Sample size	12	How many participants were in the study?	8
Non-participation	13	How many people refused to participate or dropped out? Reasons?	9
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	9
Presence of nonparticipants	15	Was anyone else present besides the participants and researchers?	9
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	10-11
Data collection			

Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	8
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	7
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	9
Field notes	20	Were field notes made during and/or after the interview or focus group?	25
Duration	21	What was the duration of the interviews or focus group?	9
Data saturation	22	Was data saturation discussed?	8
Transcripts returned	23	Were transcripts returned to participants for comment and/or correction?	9
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	9-10
Description of the coding tree	25	Did authors provide a description of the coding tree?	9-10
Derivation of themes	26	Were themes identified in advance or derived from the data?	9
Software	27	What software, if applicable, was used to manage the data?	9
Participant checking	28	Did participants provide feedback on the findings?	9
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	12-16
Data and findings consistent	30	Was there consistency between the data presented and the findings?	12-24
Clarity of major themes	31	Were major themes clearly presented in the findings?	12-20
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	12-20

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Stakeholder perspectives on the demand and supply factors driving substandard and falsified blood pressure lowering medications in Nigeria: a qualitative study

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Stakeholder perspectives on the demand and supply factors driving substandard and falsified blood pressure lowering medications in Nigeria: a qualitative study

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ABSTRACT

Objectives: Although substandard and falsified (SF) blood pressure lowering (BP) medications are a global problem, qualitative research exploring factors driving this in Nigeria has not been reported. This study provides information on factors driving demand for and supply of low-quality BP lowering medications in Nigeria and potential strategies to address these factors.

Methods: This was a cross-sectional qualitative study. Between August 2020 and September 2020, we conducted 11 in-depth interviews and 7 focus group discussions with administrators of health facilities, major manufacturers and distributors of BP lowering medications, pharmacists, drug regulators, patients, and primary care physicians purposively sampled from the Federal Capital Territory, Nigeria. Data were analyzed using directed content analysis, with the aid of Dedoose.

Results: We found that demand for SF BP lowering medications in Nigeria was driven by high OOP expenditure and stockouts of quality-assured BP lowering medications. Supply of low-quality BP lowering medications was driven by limited in-country manufacturing capacity, non-adherence to good manufacturing and distribution practices, under-resourced drug regulatory systems, ineffective healthcare facility operations, poor distribution practices, limited number of trained pharmacists, and the Covid-19 pandemic which led to stockouts. Central medicine store procurement procedures, active pharmaceutical ingredient quality check, and availability of trained pharmacists were existing strategies perceived to lower the risk of supply and demand of SF BP lowering medications.

Conclusion: Our findings suggest that demand for and supply of SF BP lowering medications in Nigeria is driven by multi-level, interrelated factors. Multi-pronged strategies need to target stakeholders and systems involved in drug production, distribution, prescription, consumption, regulation, and pricing.

Strengths and limitations of this study

- The qualitative approach contributes to an in-depth understanding of the factors driving the risk of substandard and falsified blood pressure lowering medications in Nigeria and potential areas for strengthening new strategies to reduce this risk.
- Unique insights from this paper are information from Nigeria and a focus on blood pressure lowering medications which have not been the focus of previous qualitative research on substandard and falsified medications.
- The current study identified potential effects of COVID on the supply of substandard and falsified blood pressure lowering medications.
- The purposive sampling frame means that the results cannot be generalized to the whole of Nigeria.
- Experiences of all stakeholders involved in the supply and use of BP lowering medicines in all the 37 states in Nigeria were not captured because the sample was limited to stakeholders in the Federal Capital Territory (one out of 37 states in Nigeria).

INTRODUCTION

Elevated blood pressure (BP) is a leading modifiable risk factor for global cardiovascular disease (CVD) morbidity and mortality,[1–3] including in Nigeria which is the most populous country in Africa.[4,5] Hypertension control programs need reliable and affordable supplies of quality, generic BP lowering medicines to achieve widespread hypertension control.[6] However, there is suboptimal availability of affordable and quality BP lowering medicines in most low- and middle-income countries (LMICs), including Nigeria, a challenge which may increase as rates of hypertension continue to grow.[7–10] As a result, there is a risk for falsified or substandard medications entering the supply chain, posing a threat to patients and health systems.[11]

The World Health Organization (WHO) defined falsified medicines as products that are fraudulently manufactured with their identity misrepresented and distributed with bad intent, while substandard medications are products that are registered by the regulatory authorities but fail to meet quality standards.[12] Although substandard and falsified (SF) medications are a global problem, they are pervasive in LMICs with the burden estimated to be as high as 10% of all medicines.[12–15] Some LMICs are targets for manufacturers of SF medicines because of gaps in under-resourced regulatory systems, poor governance, and shortage of health products.[14,16–19] These risks are largely attributed to misalignment between supply chain market drivers of pharmaceutical manufacturing and distribution, and out-of-pocket (OOP) expenditure, especially in the context of expanding universal health coverage.[20] Stockouts can further incentivize the use of SF medicines to fill the void.[20] Pisani et al. showed that other factors driving SF medicines in LMICs include: 1) limited technical capacity among producers, 2) buying from informal markets for convenience and affordability due to OOP payment for medicines, 3) donors activities which undermine national efforts to build sustainable markets, and 4) weak systems to mitigate demand for and supply of SF medicines.[18]

When present, most pharmaco-surveillance and supply chain strengthening programs in LMICs like Nigeria focus on communicable diseases rather than non-communicable diseases

including cardiovascular disease.[13] In Nigeria for example, the last mapping activity of the Federal Ministry of Health (FMoH) on multilateral, bilateral and non-governmental organizations' support in medicine procurement and distribution was in 2010 and focused on communicable disease.[17] Also, recent investments made by the Nigerian government on supply chain through organizations such as the National Supply Chain Integration Project have focused on medicines for communicable diseases and vaccines. Nevertheless, available evidence has shown that 24.6% of amlodipine and 31.9% of lisinopril in Nigeria[9] and 24.3% of generic BP lowering medications in 10 other African countries[21] are of substandard quality. The last mapping activity conducted by FMoH showed that the procurement and supply of medicines in Nigeria was uncoordinated, fragmented, and unplanned.[17] However, one of the strategic focuses of the National Agency for Food and Drug Administration and Control (NAFDAC) between 2020-2023 is to strengthen Good Distribution Practice of regulated products from pre-shipment and local manufacturers to the end user.[22]

National drug distribution guidelines were embarked upon by the Government to revamp the drug distribution method in Nigeria. Suggestions were made to dismantle the open drug market to achieve a sustainable decrease in the circulation of counterfeit drugs across the country and sub-Saharan Africa.[23] Nigeria is also about to implement a track-and-trace surveillance system under the leadership of NAFDAC. As the most populous country with a high burden of SF medicines, understanding upstream drivers of SF medicines will be useful for maximizing the success of strategies like track-and-trace. We present the results of a qualitative study of market risk to understand the demand and supply factors driving SF BP lowering medications in the Nigeria public sector and the role of strategies to address factors that directly or indirectly increase the risk for SF medications. To our knowledge, this is the first qualitative exploration of the risks and potential interventions for ensuring availability of quality BP lowering medications in Nigeria. Blood pressure lowering medications have not been a focus in previous qualitative research related to SF medications. Addressing SF BP lowering medications is

important to minimize the burden of hypertension and hypertension complications like hypertensive heart failure, stroke, and chronic kidney disease.

METHODS

Study design and setting

We conducted a cross-sectional qualitative study in the Federal Capital Territory, Nigeria to understand factors driving the risk of falsified and substandard BP lowering medications. The interview guides were adapted from the framework developed by Pisani et al., which was developed to understand risks of and interventions to prevent SF medications in China, Indonesia, Turkey, and Romania.[18] Details of the interview guides are provided in **Supplementary Table 1**.

Study population

Data collection took place between August 2020 and September 2020. We purposefully sampled stakeholders involved in the supply and use of BP lowering medicines and in the management of patients with elevated BP. Participants were purposively sampled from three of the six area councils of the Federal Capital Territory (Abuja Municipal Area Council, Bwari, and Gwagwalada) because they have the largest number of qualified stakeholders among the six area councils. Eleven in-depth interviews (IDIs) were conducted and these included administrators of health facilities (n=4), major manufacturers and distributors of BP lowering medications (n=3), primary and secondary healthcare facilities and community pharmacists (n=2), and regulators of medicines supply from Pharmacists' Council of Nigeria (PCN) and from the National Agency for Food and Drug Administration and Control (NAFDAC) (n=2). While community pharmacists are responsible for dispensing and supplying prescription medicines to community residents, PCN is a Federal Government parastatal responsible for regulating and controlling pharmacy education, training, and practice in Nigeria. NAFDAC regulates and controls the manufacture, importation, exportation, distribution, advertisement, sale and use of

food, drugs, cosmetics, medical devices, packaged water, chemicals and detergents in Nigeria. We also conducted seven focus group discussions (FGDs) with a total of 18 participants (FGDs 1-4, 3 stakeholders per group; FGDs 5-7, 2 stakeholders per group) including primary care physicians, pharmacists, and patients. The type of number of interviews conducted in this study was determined by stakeholder mapping. We conducted a mapping of stakeholders who can influence the demand and supply of quality and SF blood pressure lowering medications in Nigeria. We identified 29 participants who were in seven FGDs and 11 IDIs. All identified stakeholders who were approached consented to participate in this study, and they were consequently interviewed.

Interview procedures

Written informed consent for interview and recording was obtained from each participant. The IDIs and FGDs were performed face-to-face with participants on different days in settings (e.g., participants' clinic and workplace) to ensure confidentiality. Interviews were conducted by study members (two females and two males) trained in qualitative methods, namely four Nigerian co-authors (GS, ENU, PP, and IO), including two interviewers with pharmacy management expertise (GS, ENU). We established rapport with some of the participants prior to the commencement of the study building on preexisting relationships. The duration of interviews ranged from 32 minutes to 57 minutes. Most interviews were conducted in English language, one was conducted in Hausa (one of Nigeria's three major languages) and one was conducted in colloquial English (Pidgin). The interviews in Hausa and Pidgin were conducted by interviewers who were fluent in these languages. Interviews were audio-recorded, and notes were also taken during the interview sessions with the permission of participants. Participants were informed about the aim of the study and the goal being to understand their perspective on blood pressure lowering hypertensive medications. None of the participants refused to participate or dropped out and we did not return transcripts to participants for comments. We have provided further details about participant recruitment, interviews, and data handling

following the COnsolidated criteria for REporting Qualitative research (COREQ) guidelines. A reflexivity statement which outlined authors' roles in the research is provided in **Supplementary Table 2**.

Analysis

All recorded IDIs and FGDs were transcribed verbatim. The FGDs in Hausa and colloquial English (Pidgin) were translated and transcribed into English by a professional translator. All data and transcripts were anonymized and stored in a secured database at Northwestern University. We analyzed the data using directed content analysis,[24] with the aid of Dedoose (Los Angeles, CA: SocioCultural Research Consultants, LLC www.dedoose.com).[25] The coding process started with the codes that were derived from Pisani et al.'s market risk framework.[18] The Pisani codebook was adapted as a starting point for our deductive analysis because the study focused on factors driving SF medicines in four low-and middle-income countries (China, Indonesia, Turkey, and Romania) just like Nigeria. We also saw the Pisani et al's framework as a comprehensive framework to guide country-specific, system-wide analysis. The deductive coding stage was followed by identification of inductive codes, which focused on new concepts which emerged outside the framework developed by Pisani et al. (**Supplementary Table 3**).

Coding of initial transcripts was done as a team led by qualitative researchers (TMO, LRH) with disagreements resolved by consensus. Final coding was done by GS, ENU and TMO and disagreements were resolved by LRH using directed content analysis, we identified factors driving SF BP lowering medications into demand and supply sides. Demand side factors focused on drivers of population access and uptake or SF BP lowering medicines. Supply side factors focused on the production, distribution, and availability of SF BP lowering medications across Nigeria. We also extracted identified strategies that were thought to reduce demand and supply of low-quality BP lowering medications and suggestions for strengthening or new strategies from participants.

Ethical approval

The study was reviewed and approved by the Ethics Committee at the University of Abuja Teaching Hospital with approval number UATH/HREC/PR/2020/001/008. The aim of the study was explained to the stakeholders prior to the start of data collection, and written consent was obtained. During the informed consent process, we assured participants of maintaining their confidentiality.

Patient and public involvement

Patients or participants were not involved in the design, intervention, research question or outcome measures of the current study but were contributors to data.

RESULTS

Participants' characteristics are provided in **Table 1**. A total of 29 people participated in the study with two-thirds (62.1%) females and 58.6% younger than 50 years of age. The largest representation was at the Federal level, and the single largest participant group were pharmacists (34.5%) followed by administrators and regulators (20.7%), patients (17.2%), physicians (17.2%), and manufacturers and distributors (10.3%).

Table 1. Participant characteristics.

Characteristics	IDIs (n= 11) n (%)	FGDs (n=18) n (%)	Total (n=29) n (%)
Sex			
Male	7 (63.6)	11 (61.1)	18 (62.1)
Female	4 (36.4)	7 (38.9)	11 (37.9)
Age, years			
<40	4 (36.4)	4 (22.2)	8 (27.6)
40-49	2 (18.2)	7 (38.9)	9 (31.0)

50-59	5 (45.5)	5 (27.8)	10 (34.5)
>60	0 (0.0)	2 (11.1)	2 (11.1)
Participant type			
Administrators	4 (36.4)	0 (0.0)	4 (13.8)
Regulators	2 (18.2)	0 (0.0)	2 (6.9)
Pharmacists (hospital or community level)	2 (18.2)	8 (44.4)	10 (34.5)
Patients	0 (0.0)	5 (27.8)	5 (17.2)
Physicians	0 (0.0)	5 (27.8)	5 (17.2)
Manufacturers and distributors	3 (27.3)	0 (0.0)	3 (10.3)
Level[a]			
Local	2 (18.2)	2 (11.1)	4 (13.8)
State	3 (27.3)	7 (38.9)	10 (34.5)
Federal	3 (27.3)	9 (50.0)	12 (41.4)

[a] Level does not include participants who were manufacturers and distributors.

The results are divided into three broad sections with each focusing on demand and supply sides: 1) factors driving SF hypertension medicines; 2) current actions to minimize demand and supply of SF hypertension medicines, and 3) additional potential strategies which can contribute to future work to reduce SF hypertension medicines in Nigeria **(Supplementary Table 4)**. A framework for how these demand and supply factors were found to potentially increase and decrease the risk of SF BP lowering medications in FCT, Nigeria was then developed (**Figure 1)**.

Factors driving risk of substandard and falsified BP lowering medications

Demand side

We identified two interrelated factors which were associated with increased demand for SF BP lowering medications, including: 1) poverty/poor economic condition in Nigeria and high OOP BP medication expenditure and 2) stockouts.

Poverty/poor economic condition in Nigeria and high OOP BP medication expenditure

Participants reported that poor economic conditions in Nigeria, including high rates of poverty, and relatively high OOP expenditure of quality BP medicine make it difficult for people living with hypertension to afford quality BP lowering medicines. Participants reported that some people living with hypertension are unable to afford quality BP lowering medications, especially more expensive drugs classes like angiotensin receptor blockers, with the resultant effect being increased demand for cheaper but potentially lower quality medicines. Limited affordability of some BP lowering medications may also drive manufacturers and suppliers to produce or import cheaper SF medicines. (see below) Additional contributors related to limited financial resources among patients included the lack of health insurance coverage for medications and the chronic nature of hypertension which demands long-term use of BP lowering medications, increasing the impact of OOP expenditure.

> *"You know, no matter how cost-effective a drug can be, there are people that cannot afford it. And sometimes, they use more than two BP lowering medications. Then for some class of patients, where they have angiotensin receptor blockers (ARBs), that one is always an issue. They are unable to afford it, and most of the time, they really need it, and that's it." (FGD 4, Pharmacist from Secondary Healthcare facility)*

Stockouts

Participants noted that stockouts force patients to look outside regular and trusted sources of BP lowering medications. As a result, patients may purchase these medications at sources

with higher risks of being substandard or falsified, including informal pharmacy markets. Stockouts also erode trust in facilities especially public sector ones and further push patients to patronize other sources of medications where access to quality of medicines is not assured. Further, we found that stockout can be driven by patients' preference for a particular brand of medicines, which results in a situation where demand for that brand exceeds its supply. This lack of supply chain monitoring contributes to stockouts.

> *"So, if you talk about fake, we come to the hospital because in the hospital you cannot have fake. And that is why I get annoyed when they say it's out of stock." (FGD 3, Patient from Tertiary Healthcare facility)*

Supply side

The supply side factors identified which contribute to the supply of SF BP lowering medications across Nigeria include limited in-country manufacturing capacity, non-adherence to good manufacturing and distribution practices, weak systems of drug regulation, inconsistent quality assurance and post-market surveillance process due to limited resources, ineffective healthcare facility operations, poor distribution practices, limited number of trained pharmacists, and the Covid-19 pandemic. Participants mentioned that these factors also combined to create an even greater challenge of supply of SF BP lowering medications than individual factors.

Limited in-country production

Participants mentioned that there is low in-country production of quality BP lowering medications in Nigeria, which provides an opportunity for SF BP lowering medications either produced or imported into the country to fill potential gaps from demand or actual stockouts. Participants reported concerns about this reliance on BP lowering drug importation making it difficult to assure quality and increasing the risk of substandard medications, including the risk from longer distribution and storage periods compared with locally manufactured medications. Respondents also reported that poor economic policies leading to increased importation and

Naira devaluation, as well as unfavorable government policies (e.g., lack of government subsidies for costs of production and high import taxes), may lead some manufacturers and distributors to compromise on good manufacturing, procurement practices, storage, and distribution practices to reduce costs which can increase the risk of falsified medications as well as for substandard products at the point of consumption.

Non-adherence to good production and procurement practices

In addition, some pharmaceutical manufacturing and distribution companies were felt to not always adhere to good practices and may prioritize profits over quality practices. Concern about these behaviors was mentioned by patients, pharmacists, supply chain managers, and drug regulators. For example, participants mentioned that some of the pharmaceutical and manufacturing distribution companies capitalize on the high level of poverty in Nigeria by bringing into the country medications that even though may not have the right active pharmaceutical ingredients (APIs) but are affordable by an average Nigerian.

Drug regulation

The system of drug regulation in Nigeria was also identified as contributing to the supply of SF BP lowering medications. Some federal drug regulator respondents noted that since most medications are imported, high taxes on imported medicines increased costs and risk of weakened supply chain of quality BP lowering medicines. While regulations exist, the limited resources of the food and drug regulatory agency facilitate the existence of parallel markets which offer SF medications.

Participants also noted that the challenges of routine quality assurance process of NAFDAC due to low laboratory testing capacity. This capacity gap makes it difficult for this regulatory body to maintain the desired level of testing needed to ensure quality medicines which are imported or produced and distributed across Nigeria. Further compromising the

existing system, NAFDAC was noted to have inadequate staff strength needed to perform adequate post-market surveillance.

> *"But we also have to look at the various brands in the market, most of these BP lowering medications are numerous. So, for me, I feel it will be very tasking for NAFDAC to really inspect them. I don't think they have enough staff and facilities to do that, so, that might be a loophole where fake drugs can thrive." (FGD 4, Pharmacist from Secondary Healthcare facility).*

Participants noted that the weakness in regulation of the Nigerian healthcare system has led to the proliferation of unlicensed pharmacies. As a result, some people own and operate pharmacies and prescribe medicines without licenses, which increases the demand and supply of SF BP lowering medications.

> *"Somebody who is having a pharmacy is treating patients, recommending, and giving medicines, whether it's good or bad. Well, it's not something I can make a lot of comment about because it's part of the society (Nigeria). But if you want to wipe it away, let the hospital, government hospital, be functioning properly, so that people will be ready to come here." (FGD 3).*

Ineffective healthcare facility operation

Some pharmacists mentioned that poor inventory and delays in suppliers' payments due to bureaucracy within the healthcare facility also contribute to stockouts and risk of substandard medications. They noted that poor communication flow between the central medical store and healthcare facilities sometimes leads to drug expiration because healthcare facilities may not be aware that certain medicines are available at the central medical store, at the same time, the central medical store may also not be aware of the' need for medicines at the facilities. This poor communication could result in a situation where certain medicines remain at the central medical store longer than necessary and may even be near expiration before they are supplied.,

while stockouts occur locally. On other factors which increased the risk of expired medications, a supply chain manager mentioned that change in prescription patterns at the healthcare facility level could lead to reduced demand for in-stock medications and so expiration. This poor function was also identified as a reason why people went to unlicensed pharmacies as noted in the above quote.

Poor storage

The lack of infrastructure to store large quantities of BP lowering medicines resulted in poor storage and was also identified as a risk to medicine quality. For example, some pharmacists noted challenges with getting enough space to store procured BP lowering medications under the required temperature range, threatening medication potency. Finally, since some SF BP lowering medications are smuggled into the country to avoid the high taxes, improper storage conditions during this process was identified as also reducing quality of available medications.

Other factors

Respondents noted several other factors including human resources and COVD-19 pandemic. The limited number of trained pharmacists in the country, especially in health facilities, contributes to the supply of SF BP lowering medications. For instance, some private hospitals do not have trained pharmacists to determine the quality of drugs procured and dispensed within the hospitals. Without sufficient pharmacy oversight, such hospitals may risk dispensing SF BP lowering medications. Participants also noted that lockdown of health services during the Covid-19 pandemic affected supplies of medicines because some of the BP lowering medications in Nigeria are imported, resulting in stockouts, which further exacerbated the supply-demand mismatch and consequently increase in SF BP lowering medications. Participants also stated that cost of imported BP lowering medications increased

during the pandemic and such products were more frequently out of stock than prior to the pandemic, thus increasing market for SF BP lowering medications.

Factors and strategies to minimize the risk of demand for and supply of substandard and falsified BP lowering medications

Respondents identified a number of existing factors and strategies in place which reduced the risk of SF BP lowering medications, although some needed strengthening as noted below.

Demand side

Participants identified that four factors that lowered the risk of demand for SF BP lowering medications, including: 1) availability and affordability of medicines from the central medical store; 2) access to functional national health insurance scheme, which enhances affordability of quality BP lowering medicines for covered individuals; 3) supervision by pharmacists to ascertain appropriateness and quality of medicines and to prevent stockouts; and 4) purchase of medicines at the healthcare facility instead of outside pharmacies.

Supply Side

Participants also identified a number of supply side strategies which reduce the risk of SF BP lowering medications in circulation. One strategy was the procurement quality checks and good supply chain management practices by central medical stores. Participants also remarked that the medicines supplied at central medical stores are NAFDAC-certified and undergo quality control checks, even if capacity for checking all medications was limited. The strategy of serialization (i.e., tracing a medicine by using a unique serial number from the manufacturer right to the patient) and authentication by NAFDAC allows them to be able to confirm the quality of medicines at the endpoint. NAFDAC's capacity with an analytical laboratory available to conduct quality tests on active pharmaceutical ingredients (APIs) was identified as a factor that

reduces supply of low-quality BP lowering medications. These actions may help to enhance adherence to good manufacturing and distribution practices.

Further, participants noted that procurement guidelines in healthcare facilities also reduces risk of poor-quality BP medicines facilitated by trainings that pharmacists undergo to identify and prevent procurement of low-quality BP lowering medications. These trainings include effective supply chain management, detection, and monitoring of SF medicines, drug procurement. As a result, pharmacists are better able to select medicines based on quality and affordability and purchase from reputable companies. This training also supports the central medical store procurement of quality BP lowering medications.

Suggested additional strategies for reducing substandard and falsified medicines

Demand side

Participants also identified additional actions which could increase the market demand for less expensive medications, which may have a higher risk of being SF. They identified a need for strong communication to increase public awareness to purchase medicines from licensed and registered pharmacies and to know the locations of such pharmacies.

Supply Side

Manufacturing, distribution, and importation

Participants suggested that manufacturers should ensure that APIs used for drug production are safe for patients' consumption by adhering to good manufacturing practices. Good manufacturing practice that involves quality assurance of materials and processes as well as good packaging will also ensure safe effective medicines. Participants also identified the need for manufacturers to ensure that distributors follow necessary storage procedures, although they identified the challenge of a resulting increase in manufacturers' costs and subsequently, medication prices. An additional strategy identified was establishing an active and passive capture of adverse events by manufacturers and distributors with reliable reporting system. In

addition, proper supply chain monitoring of BP lowering medicines should be established across the local, state, and federal government levels.

Regulatory bodies

Much of the input was on strengthening strategies already in existence. For example, they suggested that regulatory bodies should strengthen the system of registering and monitoring pharmaceutical companies to enhance accountability in manufacturing and distribution of BP lowering medications. Reflecting the external sources, they also suggested that regulatory measures are strengthened to check the quality of BP lowering medications at the borders when they are coming in and before they are being distributed across the country which is critical to maintain quality supply chain management and quality of BP lowering medicines. Reflecting the limited resources, they also noted that more officers may be needed to allow NAFDAC to carry out on-site assessments overseas to ensure fidelity to quality control measures.

Local, state, and federal government

Some participants noted that lower import taxes should be considered to increase importation of quality medicines, ensure availability of medicines across Nigeria, and reduce cost of medicines. This approach may reduce both the supply of low-quality BP lowering medications and demand for cheaper and often lower quality drugs. Participants also recognized the need for strengthening transportation across the country in order to improve the efficiency and speed of the supply chain including reducing risk of substandard medications and prevent stockouts. Finally, they noted the importance of developing a functional health insurance program to cover treatment of noncommunicable diseases, to reduce costs and increase uptake of quality BP lowering medications.

Procurement, dispensing, and storage

Respondents suggested that pharmacists should purchase BP lowering medications from central medical stores at all times because these medicines are cheaper, more affordable, and

of reliable quality, reducing availability of SF medications. Some participants suggested that selection of companies to supply BP lowering medications by pharmacists should be based on merit of quality and affordability. It was suggested that such companies should be screened first before drugs are supplied and must have license to procure medicines. After this, prices should be compared across different companies and clinical presentations should be done for any new drug moiety. This process would directly reduce the supply of SF BP lowering medicines and reduce cost. Participants stated that drug regulators in Nigeria should ensure that good storage condition are maintained from the manufacturer to the distributor, through the pharmacy and then to the end users. This can be partly achieved by ensuring that appropriate infrastructure such as functional air conditioners and inverters (which give constant alternating current voltage at its output socket when there is no electricity) (due to poor power supply) are in place.

In addition, expansion and strengthening of existing strategies to improve availability of BP lowering medications is needed. For example, functional drug revolving funds, which are based upon a system already existing in the public sector where other drugs are sold with a limited (e.g., 5%) markup above procurement price to cover supply side costs. The subsequent revenue is used to replenish the drug stocks would be a potential way to ensure availability and affordability for BP lowering medications. However, work needed to strengthen the process was also noted.

DISCUSSION

By interviewing key stakeholders in the Nigeria public sector, our study provides information on factors driving the demand for and supply of SF BP lowering medications in Nigeria and outlines the strategies for overcoming these risks. Even though the factors driving SF BP lowering medicines were classified under broad factors, the narratives in the results captured the dynamics of how the factors driving substandard medicines were different from falsified medicines. For instance, participants noted that limited in-country production increased

reliance on drug importation thus increasing the risk of substandard medications through longer distribution and storage periods. On the other hand, participants mentioned that poor economic and unfavorable government policies encouraged cost cutting by pharmaceutical companies to protect profit margins and meet local demands, and which consequently increase the risk of drug falsification. While Nigerian health experts and the community are worried over the existence of low-quality BP lowering medications in the country,[26] these results provide important evidence on the factors driving availability of poor quality of BP lowering medications which can be used to inform strategies to strengthen existing systems or new ones needed to address this growing crisis. Similarities and differences between our study findings and that of Pisani et al are presented in **Table 2**. Our findings were compared with that of Pisani et al to show what was found in the countries studied by Pisani et al and what emerged from this study of SF BP lowering medications in Nigeria.

Table 2. Similarities and differences between our study findings and that of Pisani et al.

Similarities
1. Our study and that of Pisani et al showed that multi-level and interrelated factors drive the risk of demand and supply of SF medicines.
2. Pharmaceutical companies' desire to maximize profits emerged as a key factor which increases the risk of supply of SF medicines in Nigeria as well as in China, Indonesia, Turkey, and Romania.
3. Our study and that of Pisani et al showed that patients acquire medications from unregulated supply chain in response to shortages thereby creating market opportunity for falsifiers.
Differences
1. While our study focused on factors driving the risk of demand and supply of SF BP lowering medications, Pisani et al study focused on different kinds of medicines.

2. Pisani et al. showed that political promises made by the government in China, Indonesia, Turkey, and Romania to provide universal health coverage led to public procurement policies targeted at lowering prices of medical products; this political promise led to cost-cutting by pharmaceutical companies, and distributors thus increasing the risk of substandard medicines. This theme did not feature in our study.
3. Our study showed that some of the factors driving the risk of supply of SF BP lowering medicines across Nigeria included limited in-country manufacturing capacity, weak regulatory systems due to limited resources, poor healthcare facility operations and distribution practices, and limited number of pharmacists. These factors were not mentioned in Pisani et al study.
4. Our study participants cited Covid-19 pandemic as a factor which affected supplies of medicines, thus resulting in stockouts, and an increased demand for SF BP lowering medications. However, Covid-19 was not mentioned by Pisani et al because their research was done before the Covid-19 pandemic.

We found that BP lowering medicines are at elevated risk of falsification when there is a high market demand for these medications, further amplified by cost and scarcity of quality medications. The nature of health system financing mechanisms in Nigeria provides a basis for increased demand for low-quality BP lowering medications because healthcare is mostly funded through OOP payment.[27,28] As a result, it is often difficult for people to sustain access to quality medicines due to poverty, cost, stockouts, low health insurance coverage, and the chronic nature of hypertension management. We found that High OOP expenditure pushes people to demand cheaper medicines from 'high risk outlets', which are more likely to sell low-quality BP lowering medications. This finding is similar to another study in Nigeria, which showed that relatively high cost of drugs has made access to quality medicines difficult for many Nigerians because a large proportion of the population lives below the poverty line.[29] Widening the

national health insurance scheme coverage geographically and in terms of the scope of medicines covered may help to reduce OOP expenditure. Also, creating a system where Drug Revolving Fund can thrive will help to improve the availability and affordability of quality-assured BP lowering medications.[30] Also, evidence shows that the prices of generic and brand BP lowering medications in SSA[31] and other LMICs[32] are many times higher than international reference prices. An application of international reference prices on BP lowering medications in Nigeria may therefore help to improve adherence and reduce OOP expenditure.

Further, our findings showed that stockouts was a major driver of SF BP lowering medications in Nigeria and occurred due to low in-country production, poor supply chain management, poor stock storage and management, and weak procurement systems. Implementing policies that increase in-country production and monitor the supply chain for BP lowering medications will go a long way in reducing the risk of demand and supply of SF BP lowering medications in Nigeria. In addition, we found that reliance on BP lowering drug importation makes it difficult to assure quality and it increases the risk of longer distribution and storage periods compared with locally manufactured medications. Addressing this challenge may involve repeat testing following storage or longer distribution periods; this approach prioritizes quality over cost.[33]

Our findings showed that supply of SF BP lowering medications in Nigeria is driven by unfavorable government policies that limit in-country manufacturing capacity and create over-reliance on drug importation. Coupled with this, there is no clear monitoring of the APIs which came in through the borders indicating that the quality of such BP lowering medications may be unknown. The porous nature of Nigeria's borders creates a potential avenue where SF BP lowering medications may gain an entry into the Nigeria market. Other studies have similarly linked the supply of low-quality medicines to drug smuggling cartels who may be motivated to diversify their portfolios.[12,34,35] To improve detection of and prosecution for low-quality BP

lowering medications, the Nigerian government may need to have mutual legal assistance or extradition treaties with countries that are major sources of falsified drugs.[12,36]

Further, we found that an under-resourced regulatory system contributes to the supply of low-quality BP lowering medications in Nigeria. Within Nigeria, poor regulation due to low testing capacity and limited post-marketing surveillance create an enabling environment for non-adherence to good manufacturing practices and supply of low-quality BP lowering medications within the country. These findings are consistent with another study in Nigeria, which showed that factors contributing to the supply of low-quality medications including weak law enforcement, proliferation of unlicensed drug dealers, lack of system control, greed, illiteracy, illicit medicine importation, and erratic distribution system.[29] Strengthening the national regulatory systems for BP lowering medicines in Nigeria and protecting patients from low-quality medicines will require a strong political will and putting appropriate legislative frameworks, actionable and enforced policies, human resources, technologies, and quality control networks in place.[12] There is a need to enforce national directives to further address SF medicines, including BP lowering medications. An important first step may be passing the bill on counterfeit medication which was presented to the National Assembly in August 2021.[37] This bill can be modeled after the Model Law on Medicine Crime which provides clear guidance on criminalization against supply of low-quality medicines, as well as incentives for governments to strengthen drug regulatory capacity.[38]

Our study identified factors and interventions that may reduce demand for and supply of SF BP lowering medications in Nigeria, including central medical store procurement procedures, APIs quality check and availability of trained pharmacists to improve supply chain management. Interventions which encourage the continuance and expansion of these activities will be crucial to minimizing the risk of demand for and supply of low-quality BP lowering medications in Nigeria. Even though participants mentioned that pharmacists are able to select and purchase quality medicines from reputable companies to reduce the risk of SF medications, there is

evidence that even reputable pharmaceuticals are not immune to SF medicines due to difficulty in maintaining a high-quality and reliable manufacturing and distribution system.[39] To minimize supply of SF medicines, reputable pharmaceuticals may need to maintain a supply chain of their own to eliminate supply by unauthorized distributors.

An important intervention to minimize the availability of low-quality medications will be to incentivize and regulate with accountability quality markets and discourage open markets. Open markets are common sources of medicine in Nigeria and provide key opportunities for counterfeiting. Since 70% of drugs are imported from the two world's major sources of counterfeit medicines (China and India), dismantling the open drug market is necessary to achieve sustained decrease in counterfeit drug circulation in Nigeria.[40]

In addition, participants suggested that risk of low-quality BP lowering medications can be reduced through public awareness on how to identify SF BP lowering medications, active post-marketing surveillance to ensure adherence to good manufacturing practices, equipping all borders with necessary equipment to test the APIs of imported medicines, and tax reductions on imported BP lowering medications to reduce cost and ensure broader availability of quality BP lowering medications across Nigeria. These strategies are similar to what previous studies have suggested.[41,42]

Limitations

Our study includes limitations common to qualitative research. First, our study was based on a purposive sample of stakeholders from the Federal Capital Territory (one out of 37 states in Nigeria) indicating that the results cannot be generalized to the whole of Nigeria. Also, our stopping criterion was not based on data saturation. Nevertheless, we were able to provide a wide range of opinions and experience from major stakeholders involved in the demand for and supply of BP lowering medications, including at the federal level. Second, three of our audio recordings were not audible and could not be transcribed. Even though we used the field notes

taken during these interviews in our analysis, participants may have mentioned other factors driving low-quality BP lowering medication, which were not captured in our analysis. In addition, transcripts were not returned to participants for comments and/or corrections. Despite these limitations, our study is the first study to map out the factors driving the risk of SF BP lowering medications in Nigeria and potential areas for strengthening new strategies to reduce this risk.

CONCLUSION

Our findings suggest that multi-level and interrelated factors drive the demand for and supply of SF BP lowering medications in Nigeria. Multi-faceted strategies to address these factors need to target all stakeholders involved in drug production, distribution, prescription, consumption, regulation, and pricing. Also, suggested strategies to lower the risks of SF medicines in Nigeria, as highlighted by the stakeholders, show the potential for combating the proliferation of low-quality medicines in the country. Progress on safeguarding the quality of medicines and combating low-quality medicines is crucial to achieving the Sustainable Development Goal (SDG) on 'improving access to safe, effective, quality, and affordable medicines and vaccines' (SDG 3). Thus, the Nigerian government can strengthen the political will to implement national directives that address low-quality BP lowering medications to reduce the burden of hypertension-related disease in Nigeria.

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Competing Interests

Non declared

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Contributors

MDH, DBO, AV and LRH conceptualized and designed the study. ENU, GS, PP, and IO collected the data. OAS, GS, TMO, ENU and LRH conducted the analysis. GS, OAS, ENU drafted the manuscript. All authors reviewed the manuscript and provided important intellectual content. All authors read and approved the final manuscript. LRH is responsible for the overall content as guarantor.

Ethics approval

This research was conducted with approval from the University of Abuja Teaching hospital (UATH) Health Research Ethics Committee (HREC) (Approval number: UATH/HREC/PR/2020/001/008).

Data availability statement

Data are available upon reasonable request

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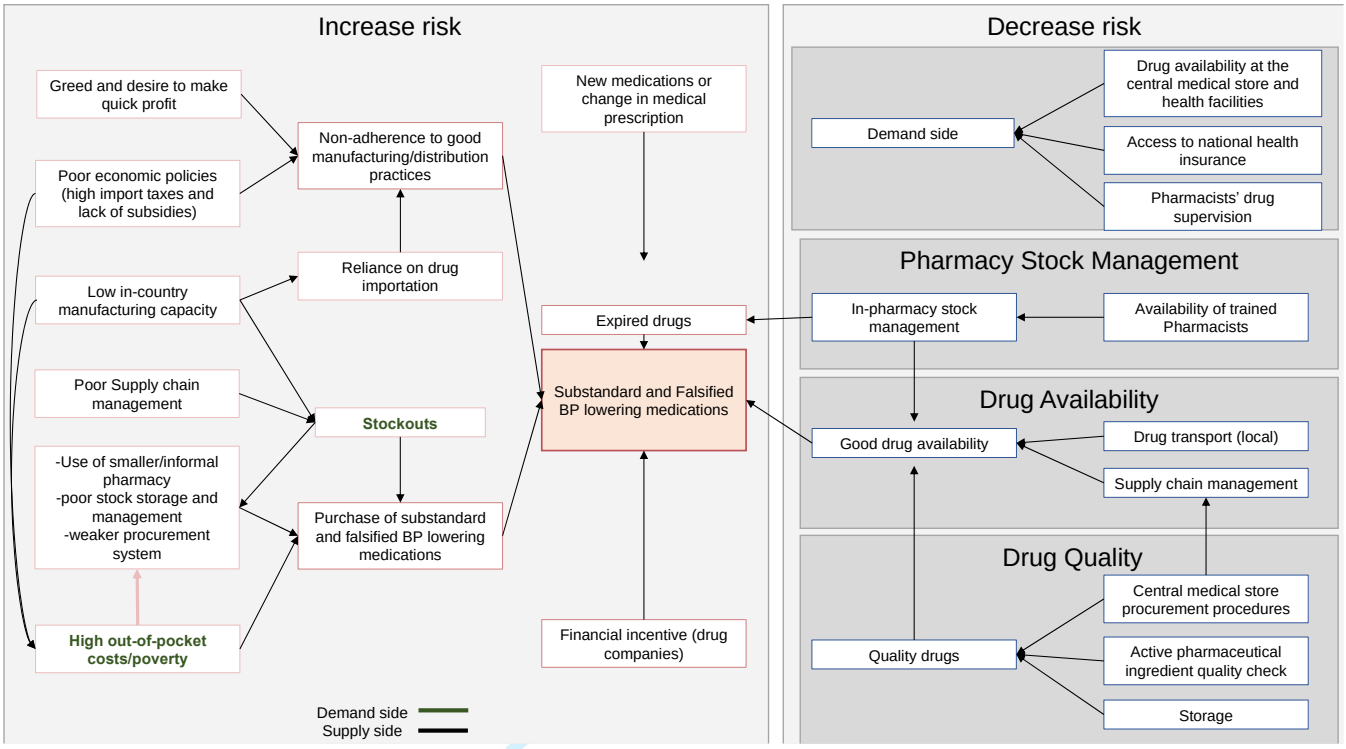

Figure 1: Factors identified as driving risk of substandard and falsified blood pressure lowering medications in Nigeria.

Supplementary Table 1: Interview guides.

Blood pressure lowering medicine mapping in Nigeria: A Pilot Study
In-depth Interview and Focus Group Discussion Guide

Introduction:
Thank you, Sir/Ma, for accepting to meet with me today. My name is_____. I am working with the Cardiovascular Research Unit of University of Abuja and University of Abuja Teaching Hospital, Gwagwalada, Abuja.

We are assessing the status of blood pressure lowering medications used in Nigeria towards improved supply chain and treatment outcomes. This interview will take about 30 minutes. To get your valuable comments, I would like to request your permission to record the session and taking some notes as well. Be assured that your responses will be kept confidential, and we will ensure that any information to be included in our report does not identify you as the respondent. We can stop the recording at any time.

Please Sir/Ma, do you have any questions on what I have just explained? Are you willing to participate in this interview? If so, then kindly review and sign this consent form.

Questions:

1. Please, tell me about yourself and your organization.

2. What is your view on the availability of anti -hypertensive medicines for patients in your setting?

3. How has cost of medicines affected patients' access to anti -hypertensive medicines?

4. What can you say about the quality of anti-hypertensive medicines in circulation?
   Probes:
   i. What factors drive the flow of fake and counterfeit anti-hypertensive medicines in our environment?
   ii. Do you notice batches of fake/counterfeit medicines?
   iii. What measures do you take to check the proliferation of these fake or substandard products?)

5. **In selecting and engaging suppliers**, can you describe what procedure do you use?
   Probes:
   i. For a typical BP medication, how many suppliers do you engage at a time?
   ii. What would cause you to go to a new supplier?
   iii. What are the problems encountered in the process?
   iv. How are such problems usually resolved?

6. Kindly describe your process of quantification for anti -hypertensive medicines.
   Probes:
   i. Are there challenges of suppliers not meeting the supply lead-times?
   ii. Do you experience challenges with incomplete deliveries?
   iii. What monitoring procedures do you adopt to ensure to prompt complete deliveries of ordered medicines?

7. Ensuring you receive quality anti-hypertensive medicines is key to successful blood pressure control. Please tell us your experience.
   Probe:
   i. Describe any quality assurance processes that are or are planned to be put into place.

8. How do you handle medicines storage in your facility?
   Probe:
   i. Are there issues of space, temperature/humidity control?

9. What are your product transportation choices like?
   Probes:
   i. How about cost?
   ii. Do you engage third party logistics providers?

10. What inventory management process do you employ for anti-hypertensive medicines?
    Probes:
    i. How do you determine your ordering strategy (i.e., how do you estimate demand?)
    ii. What causes demand spikes?
    iii. How much buffer of stock of inventory do you have for anti-hypertensive medicines?
    iv. What are the costs of holding stock?
    v. Any issues on warehousing?
    vi. Are there moments of stockout of anti-hypertensive medicines? If so, then describe the typical reasons.
    vii. Any issues of expiration of products? If so, then describe the typical reasons.
    viii. What have you tried to avoid stockout and expiration occurrences?

11. Can you discuss the nature of your anti-hypertensive medications stock?
    Probe:
    i. Which type of anti-=hypertensives do you usually stock?

12. How is information flow and communication along your supply chain?
    Probes:
    i. Are any data (e.g. paper/electronic, orders/customer demand) available?
    ii. What is the nature of feedback from end-users of blood pressure lowering medicines?
    iii. Are there complaints on medicine side effects or adverse drug reactions?

13. Patient compliance ultimately drives positive blood pressure control. Sir/Ma, what has been the experience so for far in your setting?

14. Please what is your final note on improving the supply chain of antihypertensive medicines in the country?

Conclusion: Thank you very much for your time. Your knowledge and insight will be very helpful to us. We will keep in touch with you, Sir/Ma.

Supplementary Table 2. Reflexivity statement

1. How does this study address local research and policy priorities?

Elevated blood pressure (BP) is a leading modifiable risk factor for global cardiovascular disease (CVD) morbidity and mortality, including in Nigeria which is the most populous country in Africa. One of the key factors that account for hypertension complications is the use of substandard and falsified blood pressure (BP) lowering medications. This study is the first exploration of the risks and potential interventions for ensuring availability of quality BP lowering medications in Nigeria.

2. How were local researchers involved in study design?

This study was conducted in Nigeria. The first category of local researchers involved were those with extensive experience of conducting, leading and publishing qualitative research on hypertension (DBO, GS, GS, TMO). The second category were local researchers with ongoing experience in qualitative research (PP, IO). A researcher (OAS) who is currently a migrant in a high-income country, but with experience in qualitative research was also involved in the study. In addition, there were high-income country researchers with extensive experience of conducting, leading, or publishing qualitative research (LRH, MDH, AV). Many of the authors have diverse cultural heritages originating from Nigeria and are more represented on the list of authors of this article. This representation was because the study was conducted in Nigeria and because we are interested in addressing inequities through 'parachute research'.

3. How has funding been used to support the local research team?

This project funding has been used to support local researchers (based in Nigeria) to conduct and lead qualitative research publication.

4. How are research staff who conducted data collection acknowledged?

All the research staff who participated in the data collection also met the authorship criteria as outlined by the International Committee of Medical Journal Editors (ICMJE) and so were listed as co-authors.

5. Do all members of the research partnership have access to study data?

All members of the research partnership have access to data.

6. How was data used to develop analytical skills within the partnership?

Majority of the coding was done by local researchers (GS, ENU, TMO) and were trained by senior researchers (DBO, MDH, LRH). Some of the data were coded together in order to leverage the skill sets of the senior researchers.

7. How have research partners collaborated in interpreting study data?

Weekly team meetings were held to discuss the data as well as emerging themes. Two members of the research team (GS, OAS) drafted the results, and the results formed the basis for discussing

the findings during the team's weekly meetings where all the team members agree on the interpretation of the study findings.

8. How were research partners supported to develop writing skills?

The research team writing this statement is a mix of senior and junior academics. The junior academics (GS, OAS) on the authorship team were supported by senior academics (MDH, DBO, LRH) in drafting the manuscript.

9. How will research products be shared to address local needs?

This paper will be published in open access journal. The findings will also be disseminated to all the key stakeholders including the National Agency for Food and Drug Administration and Control (NAFDAC), Pharmacists' Council of Nigeria (PCN), administrators of health facilities, major manufacturers and distributors of BP lowering medications, primary and secondary healthcare facilities and community pharmacists.

10. How is the leadership, contribution and ownership of this work by LMIC researchers recognised within the authorship?

Authors GS and OS led the draft of this manuscript, and their contribution has been recognised as joint first authors. In addition, the authorship team is predominantly based in a low-and middle-income (LMIC) country. The primary reason for this authorship plan is to strengthen the capacity of researchers in this LMIC in research publication.

11. **How have early career researchers across the partnership been included within the authorship team?**

We have included early career researchers (GS, OAS, PP, IO, AV) within the authorship team and they led the writing of the manuscript. These early career researchers are also mostly based on a LMIC.

12. How has gender balance been addressed within the authorship?

Seven authors are male (OS, TMO, PP, IO, GS, MDH, DBO) and four authors female (GS, ENU, AV, LRH).

13. How has the project contributed to training of LMIC researchers?

The authorship team is primarily composed of early career researchers. Most of the authors based in the low- and middle-income country are especially early career researchers.

14. How has the project contributed to improvements in local infrastructure?

This project has not directly contributed to improvements in local infrastructure.

15. What safeguarding procedures were used to protect local study participants and researchers?

Participation of local study participants was voluntary, and they could stop participation at any time, and not related to their employment or receipt of delivery. All data were deidentified before analysis and stored in secure site.

Supplementary Table 3: Coding structure for the current study with a comparison of code frequencies with Pisani et al.

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
00_Political_economy	**These are codes for the high-level political and economic factors that affect national and regional decision-making.**	**45**	**190**	**8**	**19**
Economic_factors	Economic factors that determine availability of jobs, purchasing power, demand and supply, inflation.	18	39	7	13
Jobs	*Employment status, sector (public versus private)*	*7*	*8*	*1*	*1*
National_income	*Minimum wage, per capita income*	*19*	*33*	*3*	*5*
Political_factors	Type of governance, party manifesto, policies, political actors.	37	147	5	8
Lobbying	*From industry, patient groups or other power blocs*	*16*	*34*	*1*	*1*
Political_promises	*This is for cases where promises made around things like UHC, industrial policy etc shape or constrain policy choices.*	*18*	*32*	*0*	*0*
Political_will	*The political will/determination to implement a system, program, product, etc.*	*10*	*19*	*5*	*6*
Votes		*11*	*22*	-	-
01_Market_opportunity	**These codes broadly map to what the GSMS report describes as "Access", though they mostly lead to opportunities by creating situations where demand outstrips supply**	**103**	**1063**	**14**	**98**
1_Supply_side	Factors related to supply of medications	71	364	13	49
Conflict_or_disaster	*External interruption to supply, e.g. because of conflict, natural disaster, industrial accident.*	*2*	*2*	*1*	*1*
Distorting_regulation	*Regulations which either restrict or mandate the availability of certain items. e.g. restriction to contraception for religious reasons (see also 07_Motivator/Perverse_incentives)*	*19*	*41*	-	-

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Infrastructure	*Poor infrastructure as a routine barrier to product supply or distribution*	*8*	*17*	*10*	*19*
Limited_manufacturing_capacity	*Comments about limitations on manufacturing capacity in Nigeria*	*13*	*14*	*3*	*3*
Procurement_practices	*Practices or rules such as obligation to procure only on price, which may affect product choice or quality*	*34*	*132*	*10*	*39*
Producer_incentives	*Incentives and disincentives which affect market entry and promotion of particular items*	*38*	*119*	*3*	*3*
Supply_chain_incentives	*Incentives and disincentives which affect distribution of particular items, including to remote areas*	*5*	*10*	*3*	*3*
2_Demand_side	Comments related to factors from the perspective of consumers	81	402	15	65
Affordability_OOP	*Affordability as an issue at the patient level*	*38*	*73*	*15*	*53*
Affordability_UHC_insurance	*Affordability at the level of the health system or insurer*	*38*	*73*	*8*	*14*
Incentive_structures_eg_prescription	*Incentive structures that determine the likelihood that a product will be covered, prescribed or otherwise proposed to pharmacists or patients (potential driver of irrational demand).*	*38*	*66*	*2*	*0*
Patient_preference	*Cultural or personal preference for particular products or brands*	*55*	*164*	*6*	*12*
Unexpected_demand	*Sudden, unforeseen spike in demand e.g. because of disease outbreak*	*6*	*8*	*8*	*10*
3_Market_regulation	**areas related to regulation of the market externally**	**58**	**290**	**3**	**3**
Clawback_tax		13	31	-	-
Price_related	Regulations or policies such as reference pricing, global budgeting, which affect prices in national market	51	188	2	2
Trade_related	Including free trade agreements, import restrictions, local content requirements and other measures to protect local industry	28	60	0	0

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
02_Market_dynamics	**A grouping of codes to tag different types of trade and target markets**	**54**	**266**	**7**	**9**
Domestic_consumption	Demand for medications(low/high) in the country	12	15	3	3
Export	Policies on export(does it favour local retention over export or viceversa), quality assurance.	32	53	0	0
Import	Taxation imported medicines, and products, substitution, regulations,	23	53	5	8
Parallel_trade	Availability of black markets, online markets,	29	100	2	3
Transit	Mode of transport, source, availability of middle men in the supply chain, handling/storage.	13	20	4	5
03_Actors	**Institutions or groups influencing production, trade and consumption of medical products**	**95**	**1028**	**15**	**130**
1_Macro	Institutions/organisations that influence policy or practice at a supra-national or national level, or operate outside the formal national supply chain	57	281	3	9
Global_health_funders	*e.g. GAVI, Global Fund, Gates etc*	*5*	*13*	*1*	*3*
Government	*National government agencies other than MoH/MRA whose policies affect trade, health financing and health systems*	*27*	*70*	*6*	*11*
MoH	*Ministry of Health, as distinct from Medicine Regulator (see 6_Regulators)*	*38*	*93*	*4*	*4*
Organised_crime	*This covers even small-scale deliberately criminal operations*	*12*	*31*	*0*	*0*
Other_international_org	*Includes multilaterals who influence pharmaceutical policy eg. UNICEF, WTO, World Bank, IFC etc*	*6*	*24*	*0*	*0*
Procurement_agency	*Specialised state procurement agencies*	*4*	*10*	*3*	*3*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
WHO	*World Health Organization*	*7*	*35*	*0*	*0*
2_Producers (see also 10)	This groups all manufacturers of medical products, with a sub for unlicensed. See under 10_Category_of_meds for subtypes	51	189	7	9
Packaging	*Presentation/look,location, size, cost*	*9*	*19*	*1*	*1*
Unlicensed	*Off-label used, unregistered medication, illegal production, irrational use.*	*6*	*7*	*0*	*0*
3_Supply_chain	Actors and factors involved in the movement of medicines.	8	50	13	62
Brokers		*8*	*18*	-	-
Central_medical_stores	*Availability, proximity,storage capacity and condition, management, payment system.*	*3*	*7*	*10*	*26*
Distributors	*capacity, coverage of distribution, (global, regional, national, sub-nation.*	*33*	*78*	*7*	*12*
NGOs	*Drug availability, type(for profit versus non-profit),coverage,*	*5*	*10*	*2*	*2*
Smugglers (illegal imports)	*Illegal importers*	*3*	*6*	*0*	*0*
Transportation	*Nature, cost, condition.*	*7*	*9*	*7*	*10*
Unlicensed	*Unlicensed distributors in country*	*2*	*7*	*2*	*2*
Pharmacy	*Actions that occur at a pharmacy*	-	-	*7*	*19*
Wholesalers	*Volume of stock, warehousing, inventory management*	*14*	*61*	*6*	*14*
4_Healthcare_professionals	Setting where the supply is being discussed	65	333	14	53
Clinic	*Availability, setting, waiting time, price for consultation.*	*8*	*15*	*1*	*1*
Hospital	*Availability, setting, waiting time, price for consultation*	*25*	*45*	*6*	*8*
Insurers	*Availability, degree of coverage, availability of medicines.*	*28*	*68*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Pharmacy	*Any person who works in a pharmacy Availability, Medicine stock, pricing, waiting time, counseling services.*	*33*	*111*	*12*	*34*
5_Patient_market_interface	This covers places where patients can access medicines directly, potentially without the mediation of any regulated organisation. Broadly equivalent to unregulated market	8	38	3	3
Internet	*Availability of online presence of conventional pharmacies.*	*17*	*55*	*0*	*0*
Market	*Availability of open markets(licensed/unlicensed)*	*11*	*17*	*1*	*1*
6_Regulators		45	136	10	23
Customs	*Customs actions related to preventing or enabling falsified or substandard medications*	*3*	*5*	*2*	*3*
Judiciary		*1*	*1*	*0*	*0*
NAFDAC_MRA	*National medicine regulatory agency (National Agency for Food and Drugs, Administration. And Control)*	*36*	*78*	*10*	*19*
NDLEA	*Nigerian Drug Law Enforcement Agency*	*-*	*-*	*1*	*2*
PCN	*Pharmacists Council of Nigeria*	*-*	*-*	*3*	*4*
Police		*9*	*23*	*-*	*-*
04_Levels	**These codes try to capture the geopolitical level at which an influencing factor operates**	**36**	**128**	**3**	**3**
Global		*9*	*17*	*1*	*1*
Mismatch	*Flags comments on the mismatch between level of activity and level of regulation, e.g. inability of national regulators to regulate exports for global market*	*17*	*24*	*0*	*0*
National		*13*	*23*	*3*	*3*
Regional		*21*	*54*	*-*	*-*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Sub_national		*4*	*5*	*0*	*0*
05_Intent	This marks information about the intent of the person manufacturing or selling the product; it is here mostly for equivalence with GSMS database coding.	0	0	6	6
Accidental	*The deficit in quality was due to a genuine accident*	*3*	*6*	*0*	*0*
Deliberate	*The deficit in quality was deliberate*	*7*	*12*	*4*	*4*
No_information	*Not enough information to determine whether it was deliberate or accidental*	*1*	*1*	*1*	*1*
Unknowing	*At this level of the supply chain, the handler had no knowledge of the quality deficit*	*0*	*0*	*0*	*0*
06_Facilitator	**Factors facilitating the trade in substandard and falsified medical products. Most of the aspects of "poor governance" and "limited technical capacity" in the GSMS report map to these codes.**	**90**	**738**	**12**	**26**
Corruption	Covers rent-seeking, grossly unethical behaviour, and the deliberate subversion of good practice for personal gain.	40	110	9	15
Conflict_of_interest	*e.g. lax regulation in order to maximise income from product registrations; prescription of innovator products to maximise hospital profits.*	*13*	*26*	*0*	*0*
In_law_enforcement_or_judiciary		*1*	*2*	*0*	*0*
Protecting_economic_interests	*e.g. deliberately lax regulation to favour state-owned companies*	*20*	*33*	*0*	*0*
Protecting_political_interests	*e.g. procurement of products from politically-connected firms without due regulatory diligence*	*11*	*14*	*0*	*0*
Disruption_&_adaptation	*Events or processes which create changes that facilitate trade in falsified medical productss, and market adaptation to those changes*	*5*	*14*	*0*	*0*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
New_technologies		*13*	*23*	-	-
Pricing_and_or_medicine shortage	*Particular disruptions such as huge increase in tax, currency fluctuations etc that affect price, or e.g. factory closures affecting supply.*	*35*	*125*	*1*	*2*
Limited_capacity	capacity to carry out regulatory duties,	56	198	3	7
Financial_resources	*Financial resources to regulator to carry out regulatory work*	*18*	*35*	*1*	*1*
Human_resources	*Includes adequate training as well as head-count*	*36*	*110*	*3*	*7*
Technology	*Including laboratory capacity and access to reference standards etc.*	*21*	*38*	*1*	*2*
Systemic_failure	Weaknesses or failures which exceed the scope of a single actor or agency, or which are embedded in broader health systems.	69	398	6	17
No_due_dilligence	*Deliberate or accidental neglect of basic quality-assurance processes as medicines pass between actors through the supply chain.*	*27*	*49*	*1*	*2*
Poor_coordination	*Failure of necessary coordination between agencies or across borders, including failure to consider effects of enforcement of e.g. customs delays on medicine supply.*	*38*	*128*	*1*	*1*
Poor_planning	*Poor prediction of demand, supply or budget*	*39*	*164*	*1*	*2*
07_Motivator	**Factors motivating people to make or trade in substandard or falsified medicines, deliberately or through negligence. [Motivations for consumption of poor quality meds are covered under "market opportunity"]**	**61**	**274**	**12**	**18**
1_Legal_profit	Desire to make money or stay in business, using legal [though not always ethical] means. [See also 01_Market_opportunity/1_Supply_sde/Producer_incentives.]	38	120	0	0
Arbitrage	*Exploiting price differences between markets. Includes parallel trade*	*15*	*27*	*0*	*0*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
	within free trade areas.				
Competitive_advantage	*Actions to increase market share, e.g. providing free samples, selling below cost.*	*15*	*33*	*0*	*0*
Cost_reduction	*Cost-cutting, including around production, packaging, distribution.*	*14*	*24*	*2*	*2*
Tax_avoidance	*Actions done to avoid taxes*	*1*	*1*	*0*	*0*
2_Illegal_or_liminal_profit	Desire to make lots of money, illegal or grey areas. Often co-coded with 1_Legal_profit/Cost_cutting, because intention is hard to determine.	19	49	10	13
Access_to_meds	*Increasing access in situations of extreme need and shortage. e.g. extending expiry dates of recently expired medicines in conflict zones*	*14*	*19*	*3*	*3*
Avoid_red_tape_or_laziness		*7*	*11*	*2*	*2*
Fraud_&_Money_laundering	*Generating money in a black economy (e.g. reimbursement fraud)*	*10*	*25*	*0*	*0*
Need	*Economic pressures on individuals to make a living*	*12*	*19*	*3*	*4*
Perverse_incentives	*Disproportionate, excessive or non-sensical regulations incentivise opacity or liminal behaviour. E.g. requirement of "halal" certification for raw ingredients may lead to faked paperwork. See also "Avoid_red_tape"*	*16*	*29*	*1*	*1*
08_Deterent	**Factors deterring people from making, selling, consuming substandard and falsified medicines. Most of the factors described in the "Prevent, Detect. Respond" approach in the GSMS report map on to these codes.**	**92**	**599**	**13**	**55**
1_Product_regulation		59	228	8	16
GDP	*Good distribution practice, and its enforcement.*	*16*	*32*	*4*	*7*
GMP	*Good manufacturing practice, and its enforcement.*	*19*	*46*	*3*	*3*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Inspection	*Inspection of manufacturing plants and warehouses and other distribution facilities.*	*24*	*36*	*4*	*6*
Licensing_&_market_authorisation		*27*	*37*	*2*	*2*
Prequalification	*WHO prequalification procedures which certify the quality of specific products made in specific factories.*	*7*	*8*	*1*	*1*
SOP	*Standard Operating Procedures*	*3*	*3*	*3*	*3*
2_Detection		45	171	12	34
Laboratory		*13*	*17*	*5*	*7*
Reporting_systems	*Post-market surveillance, and systems and technologies that allow for the rapid and efficient reporting of suspect products, and their recall.*	*14*	*22*	*3*	*8*
Risk_assesment	*Systems that anticipate likely shortages, extreme price pressures, or other factors that guide rapid pre and post-market interventions.*	*5*	*8*	*0*	*0*
Track_and_trace	*Technologies which allow legitimate products to be traced through the regulated supply chain.*	*30*	*88*	*5*	*6*
Whistleblowing_regs	*Rules, systems and culture that support the reporting of suspect products.*	*3*	*7*	*4*	*5*
3_Criminal_justice	Description of criminal justice system	11	13	0	0
Effective_policing	*Investigation of suspected falsification that is honest, capable and adequately resourced*	*3*	*3*	*0*	*0*
Impartial_judiciary	*Current state of judicial system and its ability to be impartial*	*1*	*1*	*0*	*0*
4_Transparency	Flags actions which aim to reduce fraud or falsification by increasing the transparency of procurement or the supply chain.	29	62	1	1
5_Systemic_approach	Covers active prevention working long term through health systems	41	112	5	11

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Avoid_production_shortages	*Steps to foresee demand and avoid shortages, e.g. effective demand forecasting, incentivising multiple prequalified generics of essential medicines.*	*22*	*133*	*4*	*7*
Clinical_guideline	*Clinical guidelines which reduce the likelihood of/opportunity for irrational prescribing.*	*9*	*21*	*2*	*2*
HTA	*Health Technology Assessment — cost-benefit assessment that aim to maximise availability of cost-effective, clinically indicated products.*	*0*	*0*	*3*	*4*
Champions	Individuals who actively promote med quality agenda, and who make a difference through their own persistance	6	8	3	4
09_Legislation	**Laws relevant to substandard and falsified products**	**35**	**123**	**4**	**6**
Definitions	Flags discussions over definitions and language	8	10	0	0
Law_type	Applicable law related to medicine regulation	14	29	1	1
General_trade_law	*Laws that are generally related to trade*	*3*	*4*	*0*	*0*
Medicine-specific-laws	*Laws that are specific to medicines*	*7*	*13*	*1*	*1*
Medicrime	*Refers specifically to the Medicrime Convention.*	*4*	*8*	-	-
Penalties	Penalties for breaking laws	21	64	4	4
Enforcement	*Type and method of enforcement*	*9*	*15*	*4*	*9*
Penalties_for_other_falsification	*Penalties for other types of falsification*	*4*	*8*	*1*	*1*
Penalties_for_pharma_crime	*Penalties for medicine crime*	*11*	*28*	*0*	*0*
Trade_and_IP	Legislation related to trade, patents or intellectual property. This also flags examples where patent violations are deliberately conflated with medicine quality issues	8	15	0	0
10_Quality	**Specifies the particular nature of the quality violation. These**	**61**	**373**	**8**	**19**

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
	nodes are principally for comparison with GSMS database codes				
Falsified	*Fake medicine that has been intentionally altered and may contain no active ingredient, the wrong active ingredient or the wrong amount of the correct active ingredient*	49	211	6	8
Criminal_substandard	*Medicines that were intentionally made out of specification*	*5*	*8*	*3*	*3*
Expiry_date_extended	*Change in expiry date*	*4*	*5*	*2*	*2*
Quality_but_falsely_labelled	*The medicine is produced based on quality standards but is falsely labeled based on dose, expiry date, or other labeling change*	*1*	*1*	*0*	*0*
Repackaged_as_different_product	*The product has been repackaged as a different product*	*5*	*14*	*0*	*0*
Total_fake	*Falsified medicine that is easily recognized as fake*	*21*	*56*	*0*	*0*
Meets_standards	medicines that meet manufacturing standards but aim to subvert regulated market	7	9	2	6
Other_illegal	Other forms of illegal manufacturing or distribution	13	39	0	0
Stolen_or_diverted	*Medicines that are stolen or diverted*	*6*	*16*	*0*	*0*
Unregistered	*Medicines that are available for sale but have not been registered with NAFDAC*	*6*	*15*	*0*	*0*
Substandard	Low-quality medicines	24	96	9	14
Contaminated	*Medicines that are contaminated*	*3*	*5*	*0*	*0*
Degraded	*Medicines that are degraded*	*10*	*18*	*1*	*1*
Failed_dissolution	*Medicines that fail dissolution tests*	*1*	*1*	*0*	*0*
Wrong_amount_of_API	*Wrong amount of active pharmaceutical ingredient*	*2*	*2*	*0*	*0*
Wrong_API	*Wrong active pharmaceutical ingredient*	*1*	*1*	*0*	*0*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
10a_Category_of_meds	**Categorises medicines according to producer type or therapeutic group. Used in combination with other codes**	**73**	**369**	**12**	**37**
Producer_type		60	199	3	4
API	*Type of med based on active pharmaceutical ingredient*	*18*	*34*	*6*	*10*
Contract	*Manufacturers who produce medicines under contract for license holders or other clients.*	*5*	*6*	*1*	*1*
Generic	*Generic medicine*	*32*	*97*	*4*	*7*
Branded				*9*	*17*
Innovator		*20*	*27*	-	-
Therapeutic_class	Therapeutic class of medicine	46	168	12	23
Blood pressure lowering	*Blood pressure lowering medicine*			13	36
Anti-microbial		*6*	*7*	-	-
Biosimilars		*1*	*1*	-	-
Lifestyle		*9*	*14*	-	-
NCD	*Medications mentioned for other noncommunicable diseases, including cardiovascular diseases*	*12*	*18*	*0*	*0*
Other	*Medications mentioned that are not blood pressure lowering*	*7*	*12*	-	-
Sexual_health		*3*	*3*	-	-
Vaccines		*23*	*99*	-	-
Important/notable Excerpts	*Notable excerpts from interviews to be set aside as quotations*	-	-	*13*	*41*
Improvement ideas_actions	*Ideas or actions underway aimed to reduce the risk of substandard and falsified drugs*	-	-	*0*	*0*

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Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Demand	*Ideas or action targeting patients*	-	-	*0*	*0*
Supply	*Ideas or action targeting supply side including dispensing*	-	-	*0*	*0*
15_Sub-study		**0**	**0**	**-**	**-**
China		10	37	-	-
GSMS	Flags public access data from GSMS cases, used to validate framework.	0	0	-	-
Indonesia		12	26	-	-
Romania		6	7	-	-
Tool	Flags info for risk-assessment framework	1	3	-	-
Turkey		5	5	-	-

Supplementary Table 4: Factors driving the risk of substandard and falsified BP lowering medications in Nigeria.

Factors	Definitions	Illustrative quotes
Demand side	Factors which increase or reduce demand for substandard and falsified BP lowering medications	
1. Poverty/poor economic condition (+)	Lack of financial resources and high out-of-pocket costs which limit purchasing power and increase demand for low quality medicines.	*You know, no matter how cost-effective a drug can be, there are people that cannot afford it. And sometimes, they use more than two BP lowering s. Then for some class of patients, where they have Angiotensin receptor blockers (ARBs), that one is always an issue. They are unable to afford it, and most of the time, they really need it, and that's it (FGD 4, Pharmacist from Secondary Healthcare facility).* *For instance, now, if you see branded products from (manufacturers), they are of very high quality, everybody knows it, but the prices are high; it's only for the rich in the society. So, the general populace is made of not too rich/low-income group. So, they will buy, they will prefer to buy things that are cheaper. (FGD 4, Pharmacist from Secondary Healthcare facility).*
2. Stockouts (+)	Lack of availability of BP lowering medications anywhere along the supply chain (from the manufacturer to the point of dispensing).	*So, if you talk about fake medicines, we come to the hospital because in the hospital you cannot have fake. And that is why I get annoyed when they say it's out of stock. (FGD 3, Tertiary Healthcare facility patients).* *Certain patients, they go on a particular type of drug over a long period of time, and they tell you that, that is the only drug that works for them. And even if the doctors, or the pharmacists try to convince them about how efficacious other drugs are, they tend to not agree with them. So, if it is not that particular drug, they would prefer to go outside; so, the, the demand on such drugs can be so high, and that can lead to out-of-stock syndrome (FGD 2, Federal level Medical Officers).*

3. Availability of medicines from the Central Medical Store (-)	Availability of BP lowering medications from the Central Medical Store indicating access to timely quality medicines	*Based on the drugs, the tablet, the BP lowering s we collect, because we collect them from the Central Medical Store. So far, so good, the brands and the products they give, they are relatively cheap and affordable for the common man to use (FGD 4, Pharmacist from Secondary Healthcare facility).*
4. National health insurance (-)	Access to national health insurance at the Federal Capital Territory which enhances affordability of quality BP lowering medications	*I say this with utmost confidence because at least we have a larger set of our population utilizing their National Health Insurance Scheme, and the one that is domiciled with the FCT, which is, FCT Health Insurance Scheme. So, for that reason, the cost has not been our own major problem. I think too, let's give credit to the system that patients are able to access their BP lowering drugs. (IDI 9, State Pharmacy Administrator)*
5. Pharmacists' supervision (-)	Availability of pharmacists at healthcare facilities to ensure appropriateness and quality of medicines.	*Because we say that every procurement must be handled by pharmacist, every document for procurement, any company that is engaged, to supply drugs, to any institution must come through a pharmacist, and we must see the license of that pharmacist (IDI 11, State level Administrator).* *Yes, so you have to ask them to go and buy outside [when BP lowering medications are out-of-stock with the hospital]. What I normally do if they prescribe [BP lowering medications] to them and we don't have, I will tell them "bring it let me see". This is so that we [Pharmacists] know whether this is the right medication prescribed for the patient (IDI 2, PHC Pharmacist)*
6. Drug availability at healthcare facility (-)	Availability of BP lowering medications within the healthcare facility instead of outside the healthcare facility ensures access to quality medicines.	*Because going to the hospital to collect drugs, is better than going to any pharmacy outside to buy. Most of them are fake (FGD 3, Tertiary Healthcare facility patients).*
Supply side	Factors which increase or reduce supply of substandard and falsified BP lowering medications.	

1. Limited in-country manufacturing capacity (+)	Limitations on manufacturing capacity for BP lowering medications in Nigeria.	*Actually, the factor is just policy. One, in the country where, will I say, up to eighty to eighty-five percent of our drug consumption is still dependent on importation. You can't guarantee a mere quality (IDI 9, State level supply chain manager)*
2. Non-adherence to good manufacturing and distribution practices (+)	Wrong motives (greed and desire to make quick profit) for market entry, promotion and distribution of BP lowering medications.	*You know, there are so many reasons why you have fake drugs in circulation. One of it is the suppliers; the second one is economic gain from those that are producing these products. Some of the suppliers, you give them Local Purchase Order for instance to supply drugs, and rather than go to the actual companies at the source, they will go to the side, and maybe go to Onitsha market or somewhere and buy these drugs...(IDI 1, Federal level Administrator).* *So, each time there is fall in the price in dollars, it affects the cost of all these goods that come in, because the marketers will never want to lose their money. So, the only option left will be probably to compromise on quality (IDI 9, State level supply chain manager)*
3. Drug regulation (+)	Regulations which either restrict or mandate the availability of certain BP lowering medications. This also includes poor quality assurance process due to low testing capacity of available laboratories and limited staff strength to conduct post-market surveillance.	*Then, when we are not regulating…we are not stringent on regulation, or we don't have the technology or the manpower to be able to man our porous borders… And I think the government instituted that drugs are only to be imported through air. But you find out that most of these drugs find their way in through the land borders. And once that is done, there's no check (IDI 7, federal level drug regulator)* *But we also have to look at the various brands in the market, most of these BP lowering s are numerous. So, for me, I feel it will be very tasking for NAFDAC to really inspect them. I don't think they have enough staff and facilities to do that, so, that might be a loophole where fake drugs can thrive. (FGD 4, Pharmacist from Secondary Healthcare facility).*

4. Ineffective healthcare facility operation (+)	Poor inventory of BP lowering medications, poor communication flow, change in prescription pattern, and delay in suppliers' payment which often led to stockouts	*Prior to now, the communication flow was, was not adequate; that's from Central Medical Stores to the facilities. And err, it led to even the Central Medical Stores having drugs that were expiring. Because the facilities are not aware that they have such drugs" (FGD 4, Pharmacist from Secondary Healthcare facility)* *And, apart from that too, sometimes, before now, we were getting list from the pharmacy point on drugs that are close to expiration, and that if we don't, if we don't exhaust these drugs, in good time, the hospital stands the chance of losing so much (FGD 2, Federal level Medical Officers).* *Expiration of drugs is inherent to the pharmaceutical business. Take for instance, change in the pattern of prescription will cause your own stock to expire. I have based my projection on the previous consumption pattern and the request, but if there is sudden change in the pattern, of, you understand, of consumption at the facility level or, for whatever reason, or response (IDI9, state level supply chain manager)*
5. Poor storage (+)	Inability to store procured BP lowering medications under the required temperature, driven by limited space and use of illegal drug supply sources.	*…we all know what drug moieties are all about. For instance, a drug can still be potent and exported to deliver efficaciously its own, I mean, activities, but because of ordinary storage condition, it can lose its potency, long before the expiration date. And as long as we import, you cannot guarantee storage condition during the course of importation. So, some potency could have long been lost (IDI 9, state level supply chain manager).* *Yes, I think once in a while, we have problems with storage because, one, where we store our large quantities of drugs, which is what they call the Bulk Store, you know, they have a problem of space, and they have a problem of aeration. So, once in a while, we have*

		some challenges (IDI 1, Federal level Administrator).
6. Limited number of trained pharmacists (+)	Limited number of trained pharmacists leading to limited of pharmacists available in healthcare facilities, especially in private hospitals.	*Now, our profession, pharmacy profession is one of those profession that up till today is still growing at a very slow rate. If you go to most universities and you compare the population medical students, medical lab scientists to pharmacy students, you will be shocked that there is a gap in the professional need (IDI 9, state level supply chain manager).* *And then, even the situation whereby everybody is a pharmacist; we have private hospitals, they don't have pharmacist in their system, they go to anywhere, buy their drugs, dispensers – they are the dispensers, they are the everything IDI1, Federal level Administrator).*
7. Covid-19 pandemic (+)	Interruption to supply chain due to Covid-19 pandemic.	*Again, unforeseen circumstances, the COVID has given us a typical example. Our stock was meant to last for February and March, and by March, there was lockdown and patients could not access hospitals. So, if I have a stock of short life, you understand…, they will definitely expire (IDI 9, state level supply chain manager).*
8. Central Medical Store procurement quality check (-)	Availability of BP lowering medicines improves supply chain management and availability of quality medicines which are NAFDAC certified.	*We get most of our drugs from the Central Medical Store; and the people there, there are a lot of pharmacists with experience. So, they look into, the brands of drugs they buy. It might not be branded, but they look at the company that has been in the market for a long time, so it has a name already, when they are getting those anti hypertensives. So, most of the time, the brands we get, they are good brands (FGD 4, Pharmacist from Secondary Healthcare facility)* *Because like the Central Medical Store, most of the BP lowering s they buy, they are NAFDAC-certified. So, they hardly collect or procure any medicines that NAFDAC has not certified. And to certain extent, most of the time, they have their own quality control unit in the store,*

		which if they go for bidding, they will collect samples and check (FGD 4, Pharmacist from Secondary Healthcare facility)
9. NAFDAC equipment and operations (-)	Availability of analytical laboratories to conduct quality tests on active pharmaceutical ingredients and use of barcodes which allows the possibility of confirming BP lowering medications at endpoint.	*Because when you are dealing directly with the real source, then the possibility of buying fake will be, at least reduced or eliminated. Because I will not expect a company to fake its own products, or if you are the one distributing, you are bringing it from whatever country, I don't expect you to bring in anything fake. But we also have an analytical lab, but right now, I don't know what they are able to test, or what they are able to check when they receive the drugs (IDI11, Administrator State level).*
10. Healthcare facilities guidelines (-)	Availability of guidelines in health care facilities which facilitates procurement of quality and affordable BP lowering medications	*We have a Central Procurement Unit, where all the hospitals under FCTA collect their drugs and consumables; and there's a process which they follow, the quantification, bidding, and; for us here, even the ones we get for ourselves, we normally get through companies, reliable companies. And, with that we are certain that the qualities are of a standard. So, we have not really come across any substandard, and we have not gotten any feedback from patients that these drugs are not effective, nor from the physicians (FGD 4, Pharmacist from Secondary Healthcare facility)*

(+) Factors contributing to increase in demand for and supply of substandard and falsified BP lowering medications
(-) Actions contributing to decline in demand for and supply of substandard and falsified BP lowering medications

Research Checklist: COREQ (COnsolidated criteria for REporting Qualitative research)

Checklist

Topic	Item No.	Guide Questions/Description	Page Number
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	9
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	9
Occupation	3	What was their occupation at the time of the study?	9
Gender	4	Was the researcher male or female?	9
Experience and training	5	What experience or training did the researcher have?	9
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	9
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	9
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	9
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	9
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	8
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	8
Sample size	12	How many participants were in the study?	8
Non-participation	13	How many people refused to participate or dropped out? Reasons?	9
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Presence of nonparticipants	15	Was anyone else present besides the participants and researchers?	9
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	10-11
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Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	9
Field notes	20	Were field notes made during and/or after the interview or focus group?	25
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Domain 3: analysis and findings			
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Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	12-16
Data and findings consistent	30	Was there consistency between the data presented and the findings?	12-24
Clarity of major themes	31	Were major themes clearly presented in the findings?	12-20
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	12-20

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Stakeholder perspectives on the demand and supply factors driving substandard and falsified blood pressure lowering medications in Nigeria: a qualitative study

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Stakeholder perspectives on the demand and supply factors driving substandard and falsified blood pressure lowering medications in Nigeria: a qualitative study

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ABSTRACT

Objectives: Although substandard and falsified (SF) blood pressure lowering (BP) medications are a global problem, qualitative research exploring factors driving this in Nigeria has not been reported. This study provides information on factors driving demand for and supply of low-quality BP lowering medications in Nigeria and potential strategies to address these factors.

Methods: This was a cross-sectional qualitative study. Between August 2020 and September 2020, we conducted 11 in-depth interviews and 7 focus group discussions with administrators of health facilities, major manufacturers and distributors of BP lowering medications, pharmacists, drug regulators, patients, and primary care physicians purposively sampled from the Federal Capital Territory, Nigeria. Data were analyzed using directed content analysis, with the aid of Dedoose.

Results: We found that demand for SF BP lowering medications in Nigeria was driven by high out-of-pocket (OOP) expenditure and stockouts of quality-assured BP lowering medications. Supply of low-quality BP lowering medications was driven by limited in-country manufacturing capacity, non-adherence to good manufacturing and distribution practices, under-resourced drug regulatory systems, ineffective healthcare facility operations, poor distribution practices, limited number of trained pharmacists, and the Covid-19 pandemic which led to stockouts. Central medicine store procurement procedures, active pharmaceutical ingredient quality check, and availability of trained pharmacists were existing strategies perceived to lower the risk of supply and demand of SF BP lowering medications.

Conclusion: Our findings suggest that demand for and supply of SF BP lowering medications in Nigeria is driven by multi-level, interrelated factors. Multi-pronged strategies need to target stakeholders and systems involved in drug production, distribution, prescription, consumption, regulation, and pricing.

Strengths and limitations of this study

- The qualitative approach contributes to an in-depth understanding of the factors driving the risk of substandard and falsified blood pressure lowering medications in Nigeria and potential areas for strengthening new strategies to reduce this risk.
- Unique insights from this paper are information from Nigeria and a focus on blood pressure lowering medications which have not been the focus of previous qualitative research on substandard and falsified medications.
- The current study identified potential effects of the COVID-19 pandemic on the supply of substandard and falsified blood pressure lowering medications.
- The purposive sampling frame means that the results cannot be generalized to the whole of Nigeria.
- Experiences of all stakeholders involved in the supply and use of BP lowering medicines in all the 37 states in Nigeria were not captured because the sample was limited to stakeholders in the Federal Capital Territory (one out of 37 states in Nigeria).

INTRODUCTION

Elevated blood pressure (BP) is a leading modifiable risk factor for global cardiovascular disease (CVD) morbidity and mortality,[1–3] including in Nigeria which is the most populous country in Africa.[4,5] Hypertension control programs need reliable and affordable supplies of quality, generic BP lowering medicines to achieve widespread hypertension control.[6] However, there is suboptimal availability of affordable and quality BP lowering medicines in most low- and middle-income countries (LMICs), including Nigeria, a challenge which may increase as rates of hypertension continue to grow.[7–10] As a result, there is a risk for falsified or substandard medications entering the supply chain, posing a threat to patients and health systems.[11]

The World Health Organization (WHO) defined falsified medicines as products that are fraudulently manufactured with their identity misrepresented and distributed with bad intent, while substandard medications are products that are registered by the regulatory authorities but fail to meet quality standards.[12] Although substandard and falsified (SF) medications are a global problem, they are pervasive in LMICs with the burden estimated to be as high as 10% of all medicines.[12–15] Some LMICs are targets for manufacturers of SF medicines because of gaps in under-resourced regulatory systems, poor governance, and shortage of health products.[14,16–19] These risks are largely attributed to misalignment between supply chain market drivers of pharmaceutical manufacturing and distribution, and out-of-pocket (OOP) expenditure, especially in the context of expanding universal health coverage.[20] Stockouts can further incentivize the use of SF medicines to fill the void.[20] Pisani et al. showed that other factors driving SF medicines in LMICs include: 1) limited technical capacity among producers, 2) buying from informal markets for convenience and affordability due to OOP payment for medicines, 3) donors activities which undermine national efforts to build sustainable markets, and 4) weak systems to mitigate demand for and supply of SF medicines.[18]

When present, most pharmaco-surveillance and supply chain strengthening programs in LMICs like Nigeria focus on communicable diseases rather than non-communicable diseases

including cardiovascular disease.[13] In Nigeria for example, the last mapping activity of the Federal Ministry of Health (FMoH) on multilateral, bilateral and non-governmental organizations' support in medicine procurement and distribution was in 2010 and focused on communicable disease.[17] Also, recent investments made by the Nigerian government on supply chain through organizations such as the National Supply Chain Integration Project have focused on medicines for communicable diseases and vaccines. Nevertheless, available evidence has shown that 24.6% of amlodipine and 31.9% of lisinopril in Nigeria[9] and 24.3% of generic BP lowering medications in 10 other African countries[21] are of substandard quality. The last mapping activity conducted by FMoH showed that the procurement and supply of medicines in Nigeria was uncoordinated, fragmented, and unplanned.[17] However, one of the strategic focuses of the National Agency for Food and Drug Administration and Control (NAFDAC) between 2020-2023 is to strengthen Good Distribution Practice of regulated products from pre-shipment and local manufacturers to the end user.[22]

National drug distribution guidelines were embarked upon by the Government to revamp the drug distribution method in Nigeria. Suggestions were made to dismantle the open drug market to achieve a sustainable decrease in the circulation of counterfeit drugs across the country and sub-Saharan Africa.[23] Nigeria is also about to implement a track-and-trace surveillance system under the leadership of NAFDAC. As the most populous country with a high burden of SF medicines, understanding upstream drivers of SF medicines will be useful for maximizing the success of strategies like track-and-trace. We present the results of a qualitative study of market risk to understand the demand and supply factors driving SF BP lowering medications in the Nigeria public sector and the role of strategies to address factors that directly or indirectly increase the risk for SF medications. To our knowledge, this is the first qualitative exploration of the risks and potential interventions for ensuring availability of quality BP lowering medications in Nigeria. Blood pressure lowering medications have not been a focus in previous qualitative research related to SF medications. Addressing SF BP lowering medications is

important to minimize the burden of hypertension and hypertension complications like hypertensive heart failure, stroke, and chronic kidney disease.

METHODS

Study design and setting

We conducted a cross-sectional qualitative study in the Federal Capital Territory, Nigeria to understand factors driving the risk of falsified and substandard BP lowering medications. The interview guides were adapted from the framework developed by Pisani et al., which was developed to understand risks of and interventions to prevent SF medications in China, Indonesia, Turkey, and Romania.[18] Details of the interview guides are provided in **Supplementary Table 1**.

Study population

Data collection took place between August 2020 and September 2020. We purposefully sampled stakeholders involved in the supply and use of BP lowering medicines and in the management of patients with elevated BP. Participants were purposively sampled from three of the six area councils of the Federal Capital Territory (Abuja Municipal Area Council, Bwari, and Gwagwalada) because they have the largest number of qualified stakeholders among the six area councils. Eleven in-depth interviews (IDIs) were conducted and these included administrators of health facilities (n=4), major manufacturers and distributors of BP lowering medications (n=3), primary and secondary healthcare facilities and community pharmacists (n=2), and regulators of medicines supply from Pharmacists' Council of Nigeria (PCN) and from the National Agency for Food and Drug Administration and Control (NAFDAC) (n=2). While community pharmacists are responsible for dispensing and supplying prescription medicines to community residents, PCN is a Federal Government parastatal responsible for regulating and controlling pharmacy education, training, and practice in Nigeria. NAFDAC regulates and controls the manufacture, importation, exportation, distribution, advertisement, sale and use of

food, drugs, cosmetics, medical devices, packaged water, chemicals and detergents in Nigeria. We also conducted seven focus group discussions (FGDs) with a total of 18 participants (FGDs 1-4, 3 stakeholders per group; FGDs 5-7, 2 stakeholders per group) including primary care physicians, pharmacists, and patients. The number of interviews conducted in this study was determined by stakeholder mapping and the feasibility of the number of stakeholders we were able to interview within the study timeframe. We conducted a mapping of stakeholders who can influence the demand and supply of quality and SF blood pressure lowering medications in Nigeria. We identified 29 participants who were in seven FGDs and 11 IDIs. All identified stakeholders who were approached consented to participate in this study, and they were consequently interviewed.

Interview procedures

Written informed consent for interview and recording was obtained from each participant. The IDIs and FGDs were performed face-to-face with participants on different days in settings (e.g., participants' clinic and workplace) to ensure confidentiality. Interviews were conducted by study members (two females and two males) trained in qualitative methods, namely four Nigerian co-authors (GJS, ENU, PP, and IO), including two interviewers with pharmacy management expertise (GJS, ENU). We established rapport with some of the participants prior to the commencement of the study building on preexisting relationships. The duration of interviews ranged from 32 minutes to 57 minutes. Most interviews were conducted in English language, one was conducted in Hausa (one of Nigeria's three major languages) and one was conducted in colloquial English (Pidgin). The interviews in Hausa and Pidgin were conducted by interviewers who were fluent in these languages. Interviews were audio-recorded, and notes were also taken during the interview sessions with the permission of participants. Participants were informed about the aim of the study and the goal being to understand their perspective on blood pressure lowering hypertensive medications. None of the participants refused to participate or dropped out and we did not return transcripts to participants for comments. We

have provided further details about participant recruitment, interviews, and data handling following the COnsolidated criteria for REporting Qualitative research (COREQ) guidelines. A reflexivity statement which outlined authors' roles in the research is provided in **Supplementary Table 2**.

Analysis

All recorded IDIs and FGDs were transcribed verbatim. The FGDs in Hausa and colloquial English (Pidgin) were translated and transcribed into English by a professional translator who was fluent in English, Hausa, and Pidgin. To minimize bias, fluent speakers (GJS and ENU) reviewed the transcripts of the interviews conducted in Hausa and Pidgin for both linguistic and content translation. All data and transcripts were anonymized and stored in a secured database at Northwestern University. We analyzed the data using directed content analysis,[24] with the aid of Dedoose (Los Angeles, CA: SocioCultural Research Consultants, LLC www.dedoose.com).[25] The coding process started with the codes that were derived from Pisani et al.'s market risk framework.[18] The Pisani codebook was adapted as a starting point for our deductive analysis because the study focused on factors driving SF medicines in four low-and middle-income countries (China, Indonesia, Turkey, and Romania) just like Nigeria. We also saw the Pisani et al's framework as a comprehensive framework to guide country-specific, system-wide analysis. The deductive coding stage was followed by identification of inductive codes, which focused on new concepts which emerged outside the framework developed by Pisani et al. (**Supplementary Table 3**).

Coding of initial transcripts was done as a team led by qualitative researchers (TMO, LRH) with disagreements resolved by consensus. Final coding was done by GJS, ENU and TMO and disagreements were resolved by LRH using directed content analysis, we identified factors driving SF BP lowering medications into demand and supply sides. Demand side factors focused on drivers of population access and uptake or SF BP lowering medicines. Supply side

factors focused on the production, distribution, and availability of SF BP lowering medications across Nigeria. We also extracted identified strategies that were thought to reduce demand and supply of low-quality BP lowering medications and suggestions for strengthening or new strategies from participants.

Ethical approval

The study was reviewed and approved by the Ethics Committee at the University of Abuja Teaching Hospital with approval number UATH/HREC/PR/2020/001/008. The aim of the study was explained to the stakeholders prior to the start of data collection, and written consent was obtained. During the informed consent process, we assured participants of maintaining their confidentiality.

Patient and public involvement

Patients or participants were not involved in the design, intervention, research question or outcome measures of the current study but were contributors to data.

RESULTS

Participants' characteristics are provided in **Table 1**. A total of 29 people participated in the study with two-thirds (62.1%) females and 58.6% younger than 50 years of age. The largest representation was at the Federal level, and the single largest participant group were pharmacists (34.5%) followed by administrators and regulators (20.7%), patients (17.2%), physicians (17.2%), and manufacturers and distributors (10.3%).

Table 1. Participant characteristics.

Characteristics	IDIs (n= 11) n (%)	FGDs (n=18) n (%)	Total (n=29) n (%)
Sex	7 (63.6)	11 (61.1)	18 (62.1)
Male	4 (36.4)	7 (38.9)	11 (37.9)

Female			
Age, years			
<40	4 (36.4)	4 (22.2)	8 (27.6)
40-49	2 (18.2)	7 (38.9)	9 (31.0)
50-59	5 (45.5)	5 (27.8)	10 (34.5)
>60	0 (0.0)	2 (11.1)	2 (11.1)
Participant type			
Administrators	4 (36.4)	0 (0.0)	4 (13.8)
Regulators	2 (18.2)	0 (0.0)	2 (6.9)
Pharmacists (hospital or community level)	2 (18.2)	8 (44.4)	10 (34.5)
Patients	0 (0.0)	5 (27.8)	5 (17.2)
Physicians	0 (0.0)	5 (27.8)	5 (17.2)
Manufacturers and distributors	3 (27.3)	0 (0.0)	3 (10.3)
Level[a]			
Local	2 (18.2)	2 (11.1)	4 (13.8)
State	3 (27.3)	7 (38.9)	10 (34.5)
Federal	3 (27.3)	9 (50.0)	12 (41.4)

[a] Level does not include participants who were manufacturers and distributors.

The results are divided into three broad sections with each focusing on demand and supply sides: 1) factors driving SF hypertension medicines; 2) current actions to minimize demand and supply of SF hypertension medicines, and 3) additional potential strategies which can contribute to future work to reduce SF hypertension medicines in Nigeria **(Supplementary Table 4)**. A framework for how these demand and supply factors were found to potentially

increase and decrease the risk of SF BP lowering medications in FCT, Nigeria was then developed (**Figure 1)**.

Factors driving risk of substandard and falsified BP lowering medications

Demand side

We identified two interrelated factors which were associated with increased demand for SF BP lowering medications, including: 1) poverty/poor economic condition in Nigeria and high OOP BP medication expenditure and 2) stockouts.

Poverty/poor economic condition in Nigeria and high OOP BP medication expenditure

Participants reported that poor economic conditions in Nigeria, including high rates of poverty, and relatively high OOP expenditure of quality BP medicine make it difficult for people living with hypertension to afford quality BP lowering medicines. Participants reported that some people living with hypertension are unable to afford quality BP lowering medications, especially more expensive drugs classes like angiotensin receptor blockers, with the resultant effect being increased demand for cheaper but potentially lower quality medicines. Limited affordability of some BP lowering medications may also drive manufacturers and suppliers to produce or import cheaper SF medicines. (see below) Additional contributors related to limited financial resources among patients included the lack of health insurance coverage for medications and the chronic nature of hypertension which demands long-term use of BP lowering medications, increasing the impact of OOP expenditure.

> *"You know, no matter how cost-effective a drug can be, there are people that cannot afford it. And sometimes, they use more than two BP lowering medications. Then for some class of patients, where they have angiotensin receptor blockers (ARBs), that one is always an issue. They are unable to afford it, and most of the time, they really need it, and that's it." (FGD 4, Pharmacist from Secondary Healthcare facility)*

Stockouts

Participants noted that stockouts force patients to look outside regular and trusted sources of BP lowering medications. As a result, patients may purchase these medications at sources with higher risks of being substandard or falsified, including informal pharmacy markets. Stockouts also erode trust in facilities especially public sector ones and further push patients to patronize other sources of medications where access to quality of medicines is not assured. Further, we found that stockout can be driven by patients' preference for a particular brand of medicines, which results in a situation where demand for that brand exceeds its supply. This lack of supply chain monitoring contributes to stockouts.

> *"So, if you talk about fake, we come to the hospital because in the hospital you cannot have fake. And that is why I get annoyed when they say it's out of stock." (FGD 3, Patient from Tertiary Healthcare facility)*

Supply side

The supply side factors identified which contribute to the supply of SF BP lowering medications across Nigeria include limited in-country manufacturing capacity, non-adherence to good manufacturing and distribution practices, weak systems of drug regulation, inconsistent quality assurance and post-market surveillance process due to limited resources, ineffective healthcare facility operations, poor distribution practices, limited number of trained pharmacists, and the Covid-19 pandemic. Participants mentioned that these factors also combined to create an even greater challenge of supply of SF BP lowering medications than individual factors.

Limited in-country production

Participants mentioned that there is low in-country production of quality BP lowering medications in Nigeria, which provides an opportunity for SF BP lowering medications either produced or imported into the country to fill potential gaps from demand or actual stockouts. Participants reported concerns about this reliance on BP lowering drug importation making it difficult to assure quality and increasing the risk of substandard medications, including the risk

from longer distribution and storage periods compared with locally manufactured medications. Respondents also reported that poor economic policies leading to increased importation and Naira devaluation, as well as unfavorable government policies (e.g., lack of government subsidies for costs of production and high import taxes), may lead some manufacturers and distributors to compromise on good manufacturing, procurement practices, storage, and distribution practices to reduce costs which can increase the risk of falsified medications as well as for substandard products at the point of consumption.

> *Actually, the factor is just policy. One, in the country where, will I say, up to eighty to eighty-five percent of our drug consumption is still dependent on importation. You can't guarantee a mere quality (IDI 9, State level supply chain manager)*

Non-adherence to good production and procurement practices

In addition, some pharmaceutical manufacturing and distribution companies were felt to not always adhere to good practices and may prioritize profits over quality practices. Concern about these behaviors was mentioned by patients, pharmacists, supply chain managers, and drug regulators. For example, participants mentioned that some of the pharmaceutical and manufacturing distribution companies capitalize on the high level of poverty in Nigeria by bringing into the country medications that even though may not have the right active pharmaceutical ingredients (APIs) but are affordable by an average Nigerian.

> *So, each time there is fall in the price in dollars, it affects the cost of all these goods that come in, because the marketers will never want to lose their money. So, the only option left will be probably to compromise on quality (IDI 9, State level supply chain manager)*

Drug regulation

The system of drug regulation in Nigeria was also identified as contributing to the supply of SF BP lowering medications. Some federal drug regulator respondents noted that since most medications are imported, high taxes on imported medicines increased costs and risk of

weakened supply chain of quality BP lowering medicines. While regulations exist, the limited resources of the food and drug regulatory agency facilitate the existence of parallel markets which offer SF medications.

Participants also noted that the challenges of routine quality assurance process of NAFDAC due to low laboratory testing capacity. This capacity gap makes it difficult for this regulatory body to maintain the desired level of testing needed to ensure quality medicines which are imported or produced and distributed across Nigeria. Further compromising the existing system, NAFDAC was noted to have inadequate staff strength needed to perform adequate post-market surveillance.

> *"But we also have to look at the various brands in the market, most of these BP lowering medications are numerous. So, for me, I feel it will be very tasking for NAFDAC to really inspect them. I don't think they have enough staff and facilities to do that, so, that might be a loophole where fake drugs can thrive." (FGD 4, Pharmacist from Secondary Healthcare facility).*

Participants noted that the weakness in regulation of the Nigerian healthcare system has led to the proliferation of unlicensed pharmacies. As a result, some people own and operate pharmacies and prescribe medicines without licenses, which increases the demand and supply of SF BP lowering medications.

> *"Somebody who is having a pharmacy is treating patients, recommending, and giving medicines, whether it's good or bad. Well, it's not something I can make a lot of comment about because it's part of the society (Nigeria). But if you want to wipe it away, let the hospital, government hospital, be functioning properly, so that people will be ready to come here." (FGD 3).*

Ineffective healthcare facility operation

Some pharmacists mentioned that poor inventory and delays in suppliers' payments due to bureaucracy within the healthcare facility also contribute to stockouts and risk of substandard medications. They noted that poor communication flow between the central medical store and healthcare facilities sometimes leads to drug expiration because healthcare facilities may not be aware that certain medicines are available at the central medical store, at the same time, the central medical store may also not be aware of the' need for medicines at the facilities.

> *Prior to now, the communication flow between health facilities and Central Medical Stores was not adequate. And it led to even the Central Medical Stores having drugs that were expiring because the health facilities are not aware that they have such drugs" (FGD 4, Pharmacist from Secondary Healthcare facility)*

This poor communication could result in a situation where certain medicines remain at the central medical store longer than necessary and may even be near expiration before they are supplied., while stockouts occur locally. On other factors which increased the risk of expired medications, a supply chain manager mentioned that change in prescription patterns at the healthcare facility level could lead to reduced demand for in-stock medications and so expiration. This poor function was also identified as a reason why people went to unlicensed pharmacies as noted in the above quote.

Poor storage

The lack of infrastructure to store large quantities of BP lowering medicines resulted in poor storage and was also identified as a risk to medicine quality. For example, some pharmacists noted challenges with getting enough space to store procured BP lowering medications under the required temperature range, threatening medication potency. Finally, since some SF BP lowering medications are smuggled into the country to avoid the high taxes,

improper storage conditions during this process was identified as also reducing quality of available medications.

> *We all know what drug moieties are all about. For instance, a drug can still be potent at the point of importation, but because of ordinary storage condition, it can lose its potency, long before the expiration date. And as long as we import, you cannot guarantee storage condition during the course of importation. So, some potency could have long been lost (IDI 9, state level supply chain manager).*

Other factors

Respondents noted several other factors including human resources and COVD-19 pandemic. The limited number of trained pharmacists in the country, especially in health facilities, contributes to the supply of SF BP lowering medications. For instance, some private hospitals do not have trained pharmacists to determine the quality of drugs procured and dispensed within the hospitals. Without sufficient pharmacy oversight, such hospitals may risk dispensing SF BP lowering medications. Participants also noted that lockdown of health services during the Covid-19 pandemic affected supplies of medicines because some of the BP lowering medications in Nigeria are imported, resulting in stockouts, which further exacerbated the supply-demand mismatch and consequently increase in SF BP lowering medications. Participants also stated that cost of imported BP lowering medications increased during the pandemic and such products were more frequently out of stock than prior to the pandemic, thus increasing market for SF BP lowering medications.

Factors and strategies to minimize the risk of demand for and supply of substandard and falsified BP lowering medications

Respondents identified a number of existing factors and strategies in place which reduced the risk of SF BP lowering medications, although some needed strengthening as noted below.

Demand side

Participants identified that four factors that lowered the risk of demand for SF BP lowering medications, including: 1) availability and affordability of medicines from the central medical store; 2) access to functional national health insurance scheme, which enhances affordability of quality BP lowering medicines for covered individuals; 3) supervision by pharmacists to ascertain appropriateness and quality of medicines and to prevent stockouts; and 4) purchase of medicines at the healthcare facility instead of outside pharmacies.

Supply Side

Participants also identified a number of supply side strategies which reduce the risk of SF BP lowering medications in circulation. One strategy was the procurement quality checks and good supply chain management practices by central medical stores. Participants also remarked that the medicines supplied at central medical stores are NAFDAC-certified and undergo quality control checks, even if capacity for checking all medications was limited. The strategy of serialization (i.e., tracing a medicine by using a unique serial number from the manufacturer right to the patient) and authentication by NAFDAC allows them to be able to confirm the quality of medicines at the endpoint. NAFDAC's capacity with an analytical laboratory available to conduct quality tests on active pharmaceutical ingredients (APIs) was identified as a factor that reduces supply of low-quality BP lowering medications. These actions may help to enhance adherence to good manufacturing and distribution practices.

Further, participants noted that procurement guidelines in healthcare facilities also reduces risk of poor-quality BP medicines facilitated by trainings that pharmacists undergo to identify and prevent procurement of low-quality BP lowering medications. These trainings include effective supply chain management, detection, and monitoring of SF medicines, drug procurement. As a result, pharmacists are better able to select medicines based on quality and affordability and

purchase from reputable companies. This training also supports the central medical store procurement of quality BP lowering medications.

Suggested additional strategies for reducing substandard and falsified medicines

Demand side

Participants also identified additional actions which could increase the market demand for less expensive medications, which may have a higher risk of being SF. They identified a need for strong communication to increase public awareness to purchase medicines from licensed and registered pharmacies and to know the locations of such pharmacies.

Supply Side

Manufacturing, distribution, and importation

Participants suggested that manufacturers should ensure that APIs used for drug production are safe for patients' consumption by adhering to good manufacturing practices. Good manufacturing practice that involves quality assurance of materials and processes as well as good packaging will also ensure safe effective medicines. Participants also identified the need for manufacturers to ensure that distributors follow necessary storage procedures, although they identified the challenge of a resulting increase in manufacturers' costs and subsequently, medication prices. An additional strategy identified was establishing an active and passive capture of adverse events by manufacturers and distributors with reliable reporting system. In addition, proper supply chain monitoring of BP lowering medicines should be established across the local, state, and federal government levels.

Regulatory bodies

Much of the input was on strengthening strategies already in existence. For example, they suggested that regulatory bodies should strengthen the system of registering and monitoring pharmaceutical companies to enhance accountability in manufacturing and distribution of BP lowering medications. Reflecting the external sources, they also suggested that regulatory

measures are strengthened to check the quality of BP lowering medications at the borders when they are coming in and before they are being distributed across the country which is critical to maintain quality supply chain management and quality of BP lowering medicines. Reflecting the limited resources, they also noted that more officers may be needed to allow NAFDAC to carry out on-site assessments overseas to ensure fidelity to quality control measures.

Local, state, and federal government

Some participants noted that lower import taxes should be considered to increase importation of quality medicines, ensure availability of medicines across Nigeria, and reduce cost of medicines. This approach may reduce both the supply of low-quality BP lowering medications and demand for cheaper and often lower quality drugs. Participants also recognized the need for strengthening transportation across the country in order to improve the efficiency and speed of the supply chain including reducing risk of substandard medications and prevent stockouts. Finally, they noted the importance of developing a functional health insurance program to cover treatment of noncommunicable diseases, to reduce costs and increase uptake of quality BP lowering medications.

Procurement, dispensing, and storage

Respondents suggested that pharmacists should purchase BP lowering medications from central medical stores at all times because these medicines are cheaper, more affordable, and of reliable quality, reducing availability of SF medications. Some participants suggested that selection of companies to supply BP lowering medications by pharmacists should be based on merit of quality and affordability. It was suggested that such companies should be screened first before drugs are supplied and must have license to procure medicines. After this, prices should be compared across different companies and clinical presentations should be done for any new drug moiety. This process would directly reduce the supply of SF BP lowering medicines and reduce cost. Participants stated that drug regulators in Nigeria should ensure that good storage

condition are maintained from the manufacturer to the distributor, through the pharmacy and then to the end users. This can be partly achieved by ensuring that appropriate infrastructure such as functional air conditioners and inverters (which give constant alternating current voltage at its output socket when there is no electricity) (due to poor power supply) are in place.

In addition, expansion and strengthening of existing strategies to improve availability of BP lowering medications is needed. For example, functional drug revolving funds, which are based upon a system already existing in the public sector where other drugs are sold with a limited (e.g., 5%) markup above procurement price to cover supply side costs. The subsequent revenue is used to replenish the drug stocks would be a potential way to ensure availability and affordability for BP lowering medications. However, work needed to strengthen the process was also noted.

DISCUSSION

By interviewing key stakeholders in the Nigeria public sector, our study provides information on factors driving the demand for and supply of SF BP lowering medications in Nigeria and outlines the strategies for overcoming these risks. Even though the factors driving SF BP lowering medicines were classified under broad factors, the narratives in the results captured the dynamics of how the factors driving substandard medicines were different from falsified medicines. For instance, participants noted that limited in-country production increased reliance on drug importation thus increasing the risk of substandard medications through longer distribution and storage periods. On the other hand, participants mentioned that poor economic and unfavorable government policies encouraged cost cutting by pharmaceutical companies to protect profit margins and meet local demands, and which consequently increase the risk of drug falsification. While Nigerian health experts and the community are worried over the existence of low-quality BP lowering medications in the country,[26] these results provide important evidence on the factors driving availability of poor quality of BP lowering medications

which can be used to inform strategies to strengthen existing systems or new ones needed to address this growing crisis. Similarities and differences between our study findings and that of Pisani et al are presented in **Table 2**. Our findings were compared with that of Pisani et al to show what was found in the countries studied by Pisani et al and what emerged from this study of SF BP lowering medications in Nigeria.

Table 2. Similarities and differences between our study findings and that of Pisani et al.

Similarities

1. Our study and that of Pisani et al showed that multi-level and interrelated factors drive the risk of demand and supply of SF medicines.
2. Pharmaceutical companies' desire to maximize profits emerged as a key factor which increases the risk of supply of SF medicines in Nigeria as well as in China, Indonesia, Turkey, and Romania.
3. Our study and that of Pisani et al showed that patients acquire medications from unregulated supply chain in response to shortages thereby creating market opportunity for falsifiers.

Differences

1. While our study focused on factors driving the risk of demand and supply of SF BP lowering medications, Pisani et al study focused on different kinds of medicines.
2. Pisani et al. showed that political promises made by the government in China, Indonesia, Turkey, and Romania to provide universal health coverage led to public procurement policies targeted at lowering prices of medical products; this political promise led to cost-cutting by pharmaceutical companies, and distributors thus increasing the risk of substandard medicines. This theme did not feature in our study.
3. Our study showed that some of the factors driving the risk of supply of SF BP lowering medicines across Nigeria included limited in-country manufacturing capacity, weak regulatory

systems due to limited resources, poor healthcare facility operations and distribution practices, and limited number of pharmacists. These factors were not mentioned in Pisani et al study.

4. Our study participants cited Covid-19 pandemic as a factor which affected supplies of medicines, thus resulting in stockouts, and an increased demand for SF BP lowering medications. However, Covid-19 was not mentioned by Pisani et al because their research was done before the Covid-19 pandemic.

We found that BP lowering medicines are at elevated risk of falsification when there is a high market demand for these medications, further amplified by cost and scarcity of quality medications. The nature of health system financing mechanisms in Nigeria provides a basis for increased demand for low-quality BP lowering medications because healthcare is mostly funded through OOP payment.[27,28] As a result, it is often difficult for people to sustain access to quality medicines due to poverty, cost, stockouts, low health insurance coverage, and the chronic nature of hypertension management. We found that High OOP expenditure pushes people to demand cheaper medicines from 'high risk outlets', which are more likely to sell low-quality BP lowering medications. This finding is similar to another study in Nigeria, which showed that relatively high cost of drugs has made access to quality medicines difficult for many Nigerians because a large proportion of the population lives below the poverty line.[29] Widening the national health insurance scheme coverage geographically and in terms of the scope of medicines covered may help to reduce OOP expenditure. Also, creating a system where Drug Revolving Fund can thrive will help to improve the availability and affordability of quality-assured BP lowering medications.[30] Also, evidence shows that the prices of generic and brand BP lowering medications in SSA[31] and other LMICs[32] are many times higher than international reference prices. An application of international reference prices on BP lowering medications in Nigeria may therefore help to improve adherence and reduce OOP expenditure.

Further, our findings showed that stockouts was a major driver of SF BP lowering medications in Nigeria and occurred due to low in-country production, poor supply chain management, poor stock storage and management, and weak procurement systems. Implementing policies that increase in-country production and monitor the supply chain for BP lowering medications will go a long way in reducing the risk of demand and supply of SF BP lowering medications in Nigeria. In addition, we found that reliance on BP lowering drug importation makes it difficult to assure quality and it increases the risk of longer distribution and storage periods compared with locally manufactured medications. Addressing this challenge may involve repeat testing following storage or longer distribution periods; this approach prioritizes quality over cost.[33]

Our findings showed that supply of SF BP lowering medications in Nigeria is driven by unfavorable government policies that limit in-country manufacturing capacity and create over-reliance on drug importation. Coupled with this, there is no clear monitoring of the APIs which came in through the borders indicating that the quality of such BP lowering medications may be unknown. The porous nature of Nigeria's borders creates a potential avenue where SF BP lowering medications may gain an entry into the Nigeria market. Other studies have similarly linked the supply of low-quality medicines to drug smuggling cartels who may be motivated to diversify their portfolios.[12,34,35] To improve detection of and prosecution for low-quality BP lowering medications, the Nigerian government may need to have mutual legal assistance or extradition treaties with countries that are major sources of falsified drugs.[12,36]

Further, we found that an under-resourced regulatory system contributes to the supply of low-quality BP lowering medications in Nigeria. Within Nigeria, poor regulation due to low testing capacity and limited post-marketing surveillance create an enabling environment for non-adherence to good manufacturing practices and supply of low-quality BP lowering medications within the country. These findings are consistent with another study in Nigeria, which showed that factors contributing to the supply of low-quality medications including weak law

enforcement, proliferation of unlicensed drug dealers, lack of system control, greed, illiteracy, illicit medicine importation, and erratic distribution system.[29] Strengthening the national regulatory systems for BP lowering medicines in Nigeria and protecting patients from low-quality medicines will require a strong political will and putting appropriate legislative frameworks, actionable and enforced policies, human resources, technologies, and quality control networks in place.[12] There is a need to enforce national directives to further address SF medicines, including BP lowering medications. An important first step may be passing the bill on counterfeit medication which was presented to the National Assembly in August 2021.[37] This bill can be modeled after the Model Law on Medicine Crime which provides clear guidance on criminalization against supply of low-quality medicines, as well as incentives for governments to strengthen drug regulatory capacity.[38]

Our study identified factors and interventions that may reduce demand for and supply of SF BP lowering medications in Nigeria, including central medical store procurement procedures, APIs quality check and availability of trained pharmacists to improve supply chain management. Interventions which encourage the continuance and expansion of these activities will be crucial to minimizing the risk of demand for and supply of low-quality BP lowering medications in Nigeria. Even though participants mentioned that pharmacists are able to select and purchase quality medicines from reputable companies to reduce the risk of SF medications, there is evidence that even reputable pharmaceuticals are not immune to SF medicines due to difficulty in maintaining a high-quality and reliable manufacturing and distribution system.[39] To minimize supply of SF medicines, reputable pharmaceuticals may need to maintain a supply chain of their own to eliminate supply by unauthorized distributors.

An important intervention to minimize the availability of low-quality medications will be to incentivize and regulate with accountability quality markets and discourage open markets. Open markets are common sources of medicine in Nigeria and provide key opportunities for counterfeiting. Since 70% of drugs are imported from the two world's major sources of

counterfeit medicines (China and India), dismantling the open drug market is necessary to achieve sustained decrease in counterfeit drug circulation in Nigeria.[40]

In addition, participants suggested that risk of low-quality BP lowering medications can be reduced through public awareness on how to identify SF BP lowering medications, active post-marketing surveillance to ensure adherence to good manufacturing practices, equipping all borders with necessary equipment to test the APIs of imported medicines, and tax reductions on imported BP lowering medications to reduce cost and ensure broader availability of quality BP lowering medications across Nigeria. These strategies are similar to what previous studies have suggested.[41,42]

Limitations

Our study includes limitations common to qualitative research. First, our study was based on a purposive sample of stakeholders from the Federal Capital Territory (one out of 37 states in Nigeria) indicating that the results cannot be generalized to the whole of Nigeria. Also, our stopping criterion was not based on data saturation. Nevertheless, we were able to provide a wide range of opinions and experience from major stakeholders involved in the demand for and supply of BP lowering medications, including at the federal level. Second, three of our audio recordings were not audible and could not be transcribed. Even though we used the field notes taken during these interviews in our analysis, participants may have mentioned other factors driving low-quality BP lowering medication, which were not captured in our analysis. In addition, transcripts were not returned to participants for comments and/or corrections. Despite these limitations, our study is the first study to map out the factors driving the risk of SF BP lowering medications in Nigeria and potential areas for strengthening new strategies to reduce this risk.

CONCLUSION

Our findings suggest that multi-level and interrelated factors drive the demand for and supply of SF BP lowering medications in Nigeria. Multi-faceted strategies to address these

factors need to target all stakeholders involved in drug production, distribution, prescription, consumption, regulation, and pricing. Also, suggested strategies to lower the risks of SF medicines in Nigeria, as highlighted by the stakeholders, show the potential for combating the proliferation of low-quality medicines in the country. Progress on safeguarding the quality of medicines and combating low-quality medicines is crucial to achieving the Sustainable Development Goal (SDG) on 'improving access to safe, effective, quality, and affordable medicines and vaccines' (SDG 3). Thus, the Nigerian government can strengthen the political will to implement national directives that address low-quality BP lowering medications to reduce the burden of hypertension-related disease in Nigeria.

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Competing Interests

Non declared

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Contributors

MDH, DBO, AV, GLS and LRH conceptualized and designed the study. ENU, GJS, PP, and IO collected the data. OAS, GJS, TMO, GLS, ENU and LRH conducted the analysis. OAS, GJS, and ENU drafted the manuscript. All authors reviewed the manuscript and provided important intellectual content. All authors read and approved the final manuscript. LRH is responsible for the overall content as guarantor.

Ethics approval

This research was conducted with approval from the University of Abuja Teaching hospital (UATH) Health Research Ethics Committee (HREC) (Approval number: UATH/HREC/PR/2020/001/008).

Data availability statement

Data are available upon reasonable request

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Figure 1: Factors identified as driving risk of substandard and falsified blood pressure lowering medications in Nigeria.

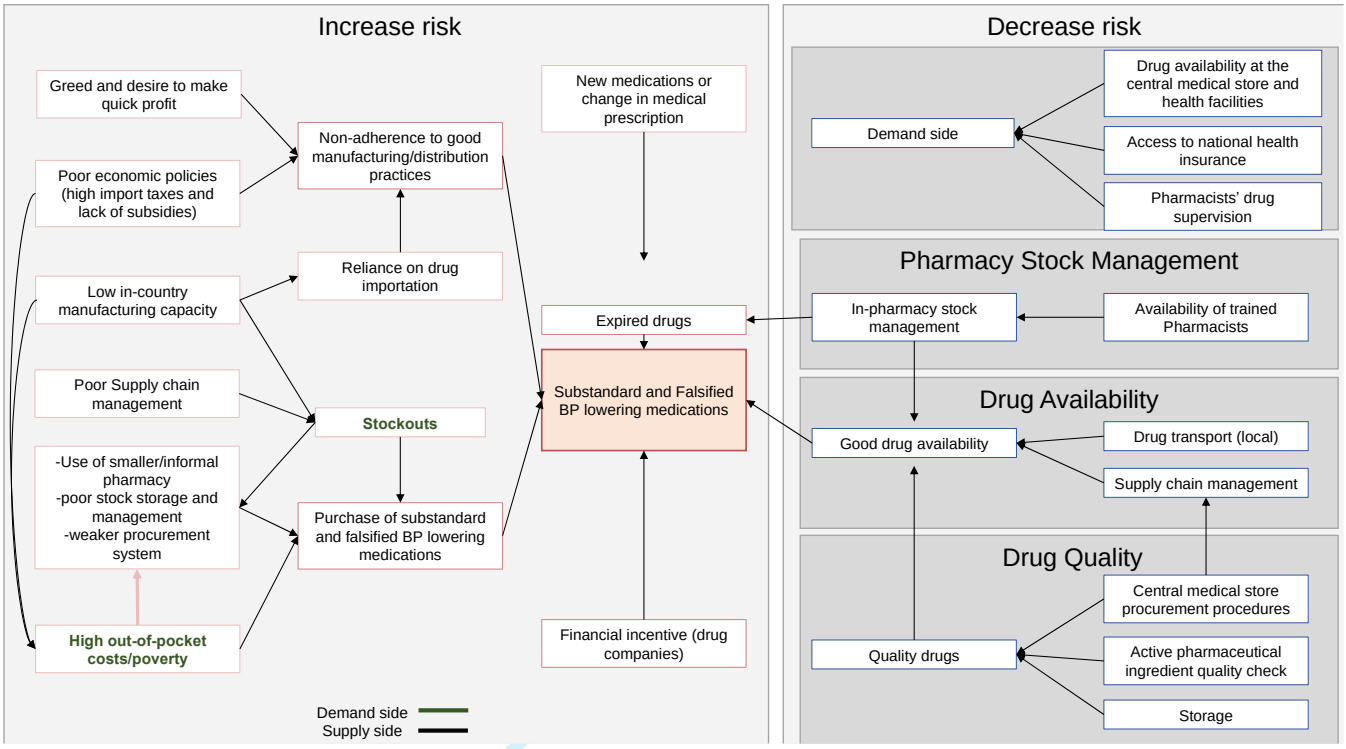

Figure 1: Factors identified as driving risk of substandard and falsified blood pressure lowering medications in Nigeria.

Supplementary Table 1: Interview guides.

Blood pressure lowering medicine mapping in Nigeria: A Pilot Study
In-depth Interview and Focus Group Discussion Guide

Introduction:
Thank you, Sir/Ma, for accepting to meet with me today. My name is_____. I am working with the Cardiovascular Research Unit of University of Abuja and University of Abuja Teaching Hospital, Gwagwalada, Abuja.

We are assessing the status of blood pressure lowering medications used in Nigeria towards improved supply chain and treatment outcomes. This interview will take about 30 minutes. To get your valuable comments, I would like to request your permission to record the session and taking some notes as well. Be assured that your responses will be kept confidential, and we will ensure that any information to be included in our report does not identify you as the respondent. We can stop the recording at any time.

Please Sir/Ma, do you have any questions on what I have just explained? Are you willing to participate in this interview? If so, then kindly review and sign this consent form.

Questions:

1. Please, tell me about yourself and your organization.

2. What is your view on the availability of anti -hypertensive medicines for patients in your setting?

3. How has cost of medicines affected patients' access to anti -hypertensive medicines?

4. What can you say about the quality of anti-hypertensive medicines in circulation?
   Probes:
   i. What factors drive the flow of fake and counterfeit anti-hypertensive medicines in our environment?
   ii. Do you notice batches of fake/counterfeit medicines?
   iii. What measures do you take to check the proliferation of these fake or substandard products?)

5. **In selecting and engaging suppliers**, can you describe what procedure do you use?
   Probes:
   i. For a typical BP medication, how many suppliers do you engage at a time?
   ii. What would cause you to go to a new supplier?
   iii. What are the problems encountered in the process?
   iv. How are such problems usually resolved?

6. Kindly describe your process of quantification for anti -hypertensive medicines.
   Probes:
   i. Are there challenges of suppliers not meeting the supply lead-times?
   ii. Do you experience challenges with incomplete deliveries?
   iii. What monitoring procedures do you adopt to ensure to prompt complete deliveries of ordered medicines?

7. Ensuring you receive quality anti-hypertensive medicines is key to successful blood pressure control. Please tell us your experience.
   Probe:
   i. Describe any quality assurance processes that are or are planned to be put into place.

8. How do you handle medicines storage in your facility?
   Probe:
   i. Are there issues of space, temperature/humidity control?

9. What are your product transportation choices like?
   Probes:
   i. How about cost?
   ii. Do you engage third party logistics providers?

10. What inventory management process do you employ for anti-hypertensive medicines?
    Probes:
    i. How do you determine your ordering strategy (i.e., how do you estimate demand?)
    ii. What causes demand spikes?
    iii. How much buffer of stock of inventory do you have for anti-hypertensive medicines?
    iv. What are the costs of holding stock?
    v. Any issues on warehousing?
    vi. Are there moments of stockout of anti-hypertensive medicines? If so, then describe the typical reasons.
    vii. Any issues of expiration of products? If so, then describe the typical reasons.
    viii. What have you tried to avoid stockout and expiration occurrences?

11. Can you discuss the nature of your anti-hypertensive medications stock?
    Probe:
    i. Which type of anti-=hypertensives do you usually stock?

12. How is information flow and communication along your supply chain?
    Probes:
    i. Are any data (e.g. paper/electronic, orders/customer demand) available?
    ii. What is the nature of feedback from end-users of blood pressure lowering medicines?
    iii. Are there complaints on medicine side effects or adverse drug reactions?

13. Patient compliance ultimately drives positive blood pressure control. Sir/Ma, what has been the experience so for far in your setting?

14. Please what is your final note on improving the supply chain of antihypertensive medicines in the country?

Conclusion: Thank you very much for your time. Your knowledge and insight will be very helpful to us. We will keep in touch with you, Sir/Ma.

Supplementary Table 2. Reflexivity statement

1. How does this study address local research and policy priorities?

Elevated blood pressure (BP) is a leading modifiable risk factor for global cardiovascular disease (CVD) morbidity and mortality, including in Nigeria which is the most populous country in Africa. One of the key factors that account for hypertension complications is the use of substandard and falsified blood pressure (BP) lowering medications. This study is the first exploration of the risks and potential interventions for ensuring availability of quality BP lowering medications in Nigeria.

2. How were local researchers involved in study design?

This study was conducted in Nigeria. The first category of local researchers involved were those with extensive experience of conducting, leading and publishing qualitative research on hypertension (DBO, GS, GS, TMO). The second category were local researchers with ongoing experience in qualitative research (PP, IO). A researcher (OAS) who is currently a migrant in a high-income country, but with experience in qualitative research was also involved in the study. In addition, there were high-income country researchers with extensive experience of conducting, leading, or publishing qualitative research (LRH, MDH, AV). Many of the authors have diverse cultural heritages originating from Nigeria and are more represented on the list of authors of this article. This representation was because the study was conducted in Nigeria and because we are interested in addressing inequities through 'parachute research'.

3. How has funding been used to support the local research team?

This project funding has been used to support local researchers (based in Nigeria) to conduct and lead qualitative research publication.

4. How are research staff who conducted data collection acknowledged?

All the research staff who participated in the data collection also met the authorship criteria as outlined by the International Committee of Medical Journal Editors (ICMJE) and so were listed as co-authors.

5. Do all members of the research partnership have access to study data?

All members of the research partnership have access to data.

6. How was data used to develop analytical skills within the partnership?

Majority of the coding was done by local researchers (GS, ENU, TMO) and were trained by senior researchers (DBO, MDH, LRH). Some of the data were coded together in order to leverage the skill sets of the senior researchers.

7. How have research partners collaborated in interpreting study data?

Weekly team meetings were held to discuss the data as well as emerging themes. Two members of the research team (GS, OAS) drafted the results, and the results formed the basis for discussing

the findings during the team's weekly meetings where all the team members agree on the interpretation of the study findings.

8. How were research partners supported to develop writing skills?

The research team writing this statement is a mix of senior and junior academics. The junior academics (GS, OAS) on the authorship team were supported by senior academics (MDH, DBO, LRH) in drafting the manuscript.

9. How will research products be shared to address local needs?

This paper will be published in open access journal. The findings will also be disseminated to all the key stakeholders including the National Agency for Food and Drug Administration and Control (NAFDAC), Pharmacists' Council of Nigeria (PCN), administrators of health facilities, major manufacturers and distributors of BP lowering medications, primary and secondary healthcare facilities and community pharmacists.

10. How is the leadership, contribution and ownership of this work by LMIC researchers recognised within the authorship?

Authors GS and OS led the draft of this manuscript, and their contribution has been recognised as joint first authors. In addition, the authorship team is predominantly based in a low-and middle-income (LMIC) country. The primary reason for this authorship plan is to strengthen the capacity of researchers in this LMIC in research publication.

11. **How have early career researchers across the partnership been included within the authorship team?**

We have included early career researchers (GS, OAS, PP, IO, AV) within the authorship team and they led the writing of the manuscript. These early career researchers are also mostly based on a LMIC.

12. How has gender balance been addressed within the authorship?

Seven authors are male (OS, TMO, PP, IO, GS, MDH, DBO) and four authors female (GS, ENU, AV, LRH).

13. How has the project contributed to training of LMIC researchers?

The authorship team is primarily composed of early career researchers. Most of the authors based in the low- and middle-income country are especially early career researchers.

14. How has the project contributed to improvements in local infrastructure?

This project has not directly contributed to improvements in local infrastructure.

15. What safeguarding procedures were used to protect local study participants and researchers?

Participation of local study participants was voluntary, and they could stop participation at any time, and not related to their employment or receipt of delivery. All data were deidentified before analysis and stored in secure site.

Supplementary Table 3: Coding structure for the current study with a comparison of code frequencies with Pisani et al.

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
00_Political_economy	**These are codes for the high-level political and economic factors that affect national and regional decision-making.**	**45**	**190**	**8**	**19**
Economic_factors	Economic factors that determine availability of jobs, purchasing power, demand and supply, inflation.	18	39	7	13
Jobs	*Employment status, sector (public versus private)*	*7*	*8*	*1*	*1*
National_income	*Minimum wage, per capita income*	*19*	*33*	*3*	*5*
Political_factors	Type of governance, party manifesto, policies, political actors.	37	147	5	8
Lobbying	*From industry, patient groups or other power blocs*	*16*	*34*	*1*	*1*
Political_promises	*This is for cases where promises made around things like UHC, industrial policy etc shape or constrain policy choices.*	*18*	*32*	*0*	*0*
Political_will	*The political will/determination to implement a system, program, product, etc.*	*10*	*19*	*5*	*6*
Votes		*11*	*22*	-	-
01_Market_opportunity	**These codes broadly map to what the GSMS report describes as "Access", though they mostly lead to opportunities by creating situations where demand outstrips supply**	**103**	**1063**	**14**	**98**
1_Supply_side	Factors related to supply of medications	71	364	13	49
Conflict_or_disaster	*External interruption to supply, e.g. because of conflict, natural disaster, industrial accident.*	*2*	*2*	*1*	*1*
Distorting_regulation	*Regulations which either restrict or mandate the availability of certain items. e.g. restriction to contraception for religious reasons (see also 07_Motivator/Perverse_incentives)*	*19*	*41*	-	-

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Infrastructure	*Poor infrastructure as a routine barrier to product supply or distribution*	*8*	*17*	*10*	*19*
Limited_manufacturing_capacity	*Comments about limitations on manufacturing capacity in Nigeria*	*13*	*14*	*3*	*3*
Procurement_practices	*Practices or rules such as obligation to procure only on price, which may affect product choice or quality*	*34*	*132*	*10*	*39*
Producer_incentives	*Incentives and disincentives which affect market entry and promotion of particular items*	*38*	*119*	*3*	*3*
Supply_chain_incentives	*Incentives and disincentives which affect distribution of particular items, including to remote areas*	*5*	*10*	*3*	*3*
2_Demand_side	Comments related to factors from the perspective of consumers	81	402	15	65
Affordability_OOP	*Affordability as an issue at the patient level*	*38*	*73*	*15*	*53*
Affordability_UHC_insurance	*Affordability at the level of the health system or insurer*	*38*	*73*	*8*	*14*
Incentive_structures_eg_prescription	*Incentive structures that determine the likelihood that a product will be covered, prescribed or otherwise proposed to pharmacists or patients (potential driver of irrational demand).*	*38*	*66*	*2*	*0*
Patient_preference	*Cultural or personal preference for particular products or brands*	*55*	*164*	*6*	*12*
Unexpected_demand	*Sudden, unforeseen spike in demand e.g. because of disease outbreak*	*6*	*8*	*8*	*10*
3_Market_regulation	**areas related to regulation of the market externally**	**58**	**290**	**3**	**3**
Clawback_tax		13	31	-	-
Price_related	Regulations or policies such as reference pricing, global budgeting, which affect prices in national market	51	188	2	2
Trade_related	Including free trade agreements, import restrictions, local content requirements and other measures to protect local industry	28	60	0	0

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
02_Market_dynamics	**A grouping of codes to tag different types of trade and target markets**	**54**	**266**	**7**	**9**
Domestic_consumption	Demand for medications(low/high) in the country	12	15	3	3
Export	Policies on export(does it favour local retention over export or viceversa), quality assurance.	32	53	0	0
Import	Taxation imported medicines, and products, substitution, regulations,	23	53	5	8
Parallel_trade	Availability of black markets, online markets,	29	100	2	3
Transit	Mode of transport, source, availability of middle men in the supply chain, handling/storage.	13	20	4	5
03_Actors	**Institutions or groups influencing production, trade and consumption of medical products**	**95**	**1028**	**15**	**130**
1_Macro	Institutions/organisations that influence policy or practice at a supra-national or national level, or operate outside the formal national supply chain	57	281	3	9
Global_health_funders	*e.g. GAVI, Global Fund, Gates etc*	*5*	*13*	*1*	*3*
Government	*National government agencies other than MoH/MRA whose policies affect trade, health financing and health systems*	*27*	*70*	*6*	*11*
MoH	*Ministry of Health, as distinct from Medicine Regulator (see 6_Regulators)*	*38*	*93*	*4*	*4*
Organised_crime	*This covers even small-scale deliberately criminal operations*	*12*	*31*	*0*	*0*
Other_international_org	*Includes multilaterals who influence pharmaceutical policy eg. UNICEF, WTO, World Bank, IFC etc*	*6*	*24*	*0*	*0*
Procurement_agency	*Specialised state procurement agencies*	*4*	*10*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
WHO	*World Health Organization*	*7*	*35*	*0*	*0*
2_Producers (see also 10)	This groups all manufacturers of medical products, with a sub for unlicensed. See under 10_Category_of_meds for subtypes	51	189	7	9
Packaging	*Presentation/look,location, size, cost*	*9*	*19*	*1*	*1*
Unlicensed	*Off-label used, unregistered medication, illegal production, irrational use.*	*6*	*7*	*0*	*0*
3_Supply_chain	Actors and factors involved in the movement of medicines.	8	50	13	62
Brokers		*8*	*18*	-	-
Central_medical_stores	*Availability, proximity,storage capacity and condition, management, payment system.*	*3*	*7*	*10*	*26*
Distributors	*capacity, coverage of distribution, (global, regional, national, sub-nation.*	*33*	*78*	*7*	*12*
NGOs	*Drug availability, type(for profit versus non-profit),coverage,*	*5*	*10*	*2*	*2*
Smugglers (illegal imports)	*Illegal importers*	*3*	*6*	*0*	*0*
Transportation	*Nature, cost, condition.*	*7*	*9*	*7*	*10*
Unlicensed	*Unlicensed distributors in country*	*2*	*7*	*2*	*2*
Pharmacy	*Actions that occur at a pharmacy*	-	-	*7*	*19*
Wholesalers	*Volume of stock, warehousing, inventory management*	*14*	*61*	*6*	*14*
4_Healthcare_professionals	Setting where the supply is being discussed	65	333	14	53
Clinic	*Availability, setting, waiting time, price for consultation.*	*8*	*15*	*1*	*1*
Hospital	*Availability, setting, waiting time, price for consultation*	*25*	*45*	*6*	*8*
Insurers	*Availability, degree of coverage, availability of medicines.*	*28*	*68*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Pharmacy	*Any person who works in a pharmacy Availability, Medicine stock, pricing, waiting time, counseling services.*	*33*	*111*	*12*	*34*
5_Patient_market_interface	This covers places where patients can access medicines directly, potentially without the mediation of any regulated organisation. Broadly equivalent to unregulated market	8	38	3	3
Internet	*Availability of online presence of conventional pharmacies.*	*17*	*55*	*0*	*0*
Market	*Availability of open markets(licensed/unlicensed)*	*11*	*17*	*1*	*1*
6_Regulators		45	136	10	23
Customs	*Customs actions related to preventing or enabling falsified or substandard medications*	*3*	*5*	*2*	*3*
Judiciary		*1*	*1*	*0*	*0*
NAFDAC_MRA	*National medicine regulatory agency (National Agency for Food and Drugs, Administration. And Control)*	*36*	*78*	*10*	*19*
NDLEA	*Nigerian Drug Law Enforcement Agency*	*-*	*-*	*1*	*2*
PCN	*Pharmacists Council of Nigeria*	*-*	*-*	*3*	*4*
Police		*9*	*23*	*-*	*-*
04_Levels	**These codes try to capture the geopolitical level at which an influencing factor operates**	**36**	**128**	**3**	**3**
Global		*9*	*17*	*1*	*1*
Mismatch	*Flags comments on the mismatch between level of activity and level of regulation, e.g. inability of national regulators to regulate exports for global market*	*17*	*24*	*0*	*0*
National		*13*	*23*	*3*	*3*
Regional		*21*	*54*	*-*	*-*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Sub_national		*4*	*5*	*0*	*0*
05_Intent	This marks information about the intent of the person manufacturing or selling the product; it is here mostly for equivalence with GSMS database coding.	0	0	6	6
Accidental	*The deficit in quality was due to a genuine accident*	*3*	*6*	*0*	*0*
Deliberate	*The deficit in quality was deliberate*	*7*	*12*	*4*	*4*
No_information	*Not enough information to determine whether it was deliberate or accidental*	*1*	*1*	*1*	*1*
Unknowing	*At this level of the supply chain, the handler had no knowledge of the quality deficit*	*0*	*0*	*0*	*0*
06_Facilitator	**Factors facilitating the trade in substandard and falsified medical products. Most of the aspects of "poor governance" and "limited technical capacity" in the GSMS report map to these codes.**	**90**	**738**	**12**	**26**
Corruption	Covers rent-seeking, grossly unethical behaviour, and the deliberate subversion of good practice for personal gain.	40	110	9	15
Conflict_of_interest	*e.g. lax regulation in order to maximise income from product registrations; prescription of innovator products to maximise hospital profits.*	*13*	*26*	*0*	*0*
In_law_enforcement_or_judiciary		*1*	*2*	*0*	*0*
Protecting_economic_interests	*e.g. deliberately lax regulation to favour state-owned companies*	*20*	*33*	*0*	*0*
Protecting_political_interests	*e.g. procurement of products from politically-connected firms without due regulatory diligence*	*11*	*14*	*0*	*0*
Disruption_&_adaptation	*Events or processes which create changes that facilitate trade in falsified medical productss, and market adaptation to those changes*	*5*	*14*	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
New_technologies		*13*	*23*	-	-
Pricing_and_or_medicine shortage	*Particular disruptions such as huge increase in tax, currency fluctuations etc that affect price, or e.g. factory closures affecting supply.*	*35*	*125*	*1*	*2*
Limited_capacity	capacity to carry out regulatory duties,	56	198	3	7
Financial_resources	*Financial resources to regulator to carry out regulatory work*	*18*	*35*	*1*	*1*
Human_resources	*Includes adequate training as well as head-count*	*36*	*110*	*3*	*7*
Technology	*Including laboratory capacity and access to reference standards etc.*	*21*	*38*	*1*	*2*
Systemic_failure	Weaknesses or failures which exceed the scope of a single actor or agency, or which are embedded in broader health systems.	69	398	6	17
No_due_dilligence	*Deliberate or accidental neglect of basic quality-assurance processes as medicines pass between actors through the supply chain.*	*27*	*49*	*1*	*2*
Poor_coordination	*Failure of necessary coordination between agencies or across borders, including failure to consider effects of enforcement of e.g. customs delays on medicine supply.*	*38*	*128*	*1*	*1*
Poor_planning	*Poor prediction of demand, supply or budget*	*39*	*164*	*1*	*2*
07_Motivator	**Factors motivating people to make or trade in substandard or falsified medicines, deliberately or through negligence. [Motivations for consumption of poor quality meds are covered under "market opportunity"]**	**61**	**274**	**12**	**18**
1_Legal_profit	Desire to make money or stay in business, using legal [though not always ethical] means. [See also 01_Market_opportunity/1_Supply_sde/Producer_incentives.]	38	120	0	0
Arbitrage	*Exploiting price differences between markets. Includes parallel trade*	*15*	*27*	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
	within free trade areas.				
Competitive_advantage	*Actions to increase market share, e.g. providing free samples, selling below cost.*	*15*	*33*	*0*	*0*
Cost_reduction	*Cost-cutting, including around production, packaging, distribution.*	*14*	*24*	*2*	*2*
Tax_avoidance	*Actions done to avoid taxes*	*1*	*1*	*0*	*0*
2_Illegal_or_liminal_profit	Desire to make lots of money, illegal or grey areas. Often co-coded with 1_Legal_profit/Cost_cutting, because intention is hard to determine.	19	49	10	13
Access_to_meds	*Increasing access in situations of extreme need and shortage. e.g. extending expiry dates of recently expired medicines in conflict zones*	*14*	*19*	*3*	*3*
Avoid_red_tape_or_laziness		*7*	*11*	*2*	*2*
Fraud_&_Money_laundering	*Generating money in a black economy (e.g. reimbursement fraud)*	*10*	*25*	*0*	*0*
Need	*Economic pressures on individuals to make a living*	*12*	*19*	*3*	*4*
Perverse_incentives	*Disproportionate, excessive or non-sensical regulations incentivise opacity or liminal behaviour. E.g. requirement of "halal" certification for raw ingredients may lead to faked paperwork. See also "Avoid_red_tape"*	*16*	*29*	*1*	*1*
08_Deterent	**Factors deterring people from making, selling, consuming substandard and falsified medicines. Most of the factors described in the "Prevent, Detect. Respond" approach in the GSMS report map on to these codes.**	**92**	**599**	**13**	**55**
1_Product_regulation		59	228	8	16
GDP	*Good distribution practice, and its enforcement.*	*16*	*32*	*4*	*7*
GMP	*Good manufacturing practice, and its enforcement.*	*19*	*46*	*3*	*3*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Inspection	*Inspection of manufacturing plants and warehouses and other distribution facilities.*	*24*	*36*	*4*	*6*
Licensing_&_market_authorisation		*27*	*37*	*2*	*2*
Prequalification	*WHO prequalification procedures which certify the quality of specific products made in specific factories.*	*7*	*8*	*1*	*1*
SOP	*Standard Operating Procedures*	*3*	*3*	*3*	*3*
2_Detection		45	171	12	34
Laboratory		*13*	*17*	*5*	*7*
Reporting_systems	*Post-market surveillance, and systems and technologies that allow for the rapid and efficient reporting of suspect products, and their recall.*	*14*	*22*	*3*	*8*
Risk_assesment	*Systems that anticipate likely shortages, extreme price pressures, or other factors that guide rapid pre and post-market interventions.*	*5*	*8*	*0*	*0*
Track_and_trace	*Technologies which allow legitimate products to be traced through the regulated supply chain.*	*30*	*88*	*5*	*6*
Whistleblowing_regs	*Rules, systems and culture that support the reporting of suspect products.*	*3*	*7*	*4*	*5*
3_Criminal_justice	Description of criminal justice system	11	13	0	0
Effective_policing	*Investigation of suspected falsification that is honest, capable and adequately resourced*	*3*	*3*	*0*	*0*
Impartial_judiciary	*Current state of judicial system and its ability to be impartial*	*1*	*1*	*0*	*0*
4_Transparency	Flags actions which aim to reduce fraud or falsification by increasing the transparency of procurement or the supply chain.	29	62	1	1
5_Systemic_approach	Covers active prevention working long term through health systems	41	112	5	11

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Avoid_production_shortages	*Steps to foresee demand and avoid shortages, e.g. effective demand forecasting, incentivising multiple prequalified generics of essential medicines.*	*22*	*133*	*4*	*7*
Clinical_guideline	*Clinical guidelines which reduce the likelihood of/opportunity for irrational prescribing.*	*9*	*21*	*2*	*2*
HTA	*Health Technology Assessment — cost-benefit assessment that aim to maximise availability of cost-effective, clinically indicated products.*	*0*	*0*	*3*	*4*
Champions	Individuals who actively promote med quality agenda, and who make a difference through their own persistance	6	8	3	4
09_Legislation	**Laws relevant to substandard and falsified products**	**35**	**123**	**4**	**6**
Definitions	Flags discussions over definitions and language	8	10	0	0
Law_type	Applicable law related to medicine regulation	14	29	1	1
General_trade_law	*Laws that are generally related to trade*	*3*	*4*	*0*	*0*
Medicine-specific-laws	*Laws that are specific to medicines*	*7*	*13*	*1*	*1*
Medicrime	*Refers specifically to the Medicrime Convention.*	*4*	*8*	-	-
Penalties	Penalties for breaking laws	21	64	4	4
Enforcement	*Type and method of enforcement*	*9*	*15*	*4*	*9*
Penalties_for_other_falsification	*Penalties for other types of falsification*	*4*	*8*	*1*	*1*
Penalties_for_pharma_crime	*Penalties for medicine crime*	*11*	*28*	*0*	*0*
Trade_and_IP	Legislation related to trade, patents or intellectual property. This also flags examples where patent violations are deliberately conflated with medicine quality issues	8	15	0	0
10_Quality	**Specifies the particular nature of the quality violation. These**	**61**	**373**	**8**	**19**

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
	nodes are principally for comparison with GSMS database codes				
Falsified	*Fake medicine that has been intentionally altered and may contain no active ingredient, the wrong active ingredient or the wrong amount of the correct active ingredient*	49	211	6	8
Criminal_substandard	*Medicines that were intentionally made out of specification*	*5*	*8*	*3*	*3*
Expiry_date_extended	*Change in expiry date*	*4*	*5*	*2*	*2*
Quality_but_falsely_labelled	*The medicine is produced based on quality standards but is falsely labeled based on dose, expiry date, or other labeling change*	*1*	*1*	*0*	*0*
Repackaged_as_different_product	*The product has been repackaged as a different product*	*5*	*14*	*0*	*0*
Total_fake	*Falsified medicine that is easily recognized as fake*	*21*	*56*	*0*	*0*
Meets_standards	medicines that meet manufacturing standards but aim to subvert regulated market	7	9	2	6
Other_illegal	Other forms of illegal manufacturing or distribution	13	39	0	0
Stolen_or_diverted	*Medicines that are stolen or diverted*	*6*	*16*	*0*	*0*
Unregistered	*Medicines that are available for sale but have not been registered with NAFDAC*	*6*	*15*	*0*	*0*
Substandard	Low-quality medicines	24	96	9	14
Contaminated	*Medicines that are contaminated*	*3*	*5*	*0*	*0*
Degraded	*Medicines that are degraded*	*10*	*18*	*1*	*1*
Failed_dissolution	*Medicines that fail dissolution tests*	*1*	*1*	*0*	*0*
Wrong_amount_of_API	*Wrong amount of active pharmaceutical ingredient*	*2*	*2*	*0*	*0*
Wrong_API	*Wrong active pharmaceutical ingredient*	*1*	*1*	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
10a_Category_of_meds	**Categorises medicines according to producer type or therapeutic group. Used in combination with other codes**	**73**	**369**	**12**	**37**
Producer_type		60	199	3	4
API	*Type of med based on active pharmaceutical ingredient*	*18*	*34*	*6*	*10*
Contract	*Manufacturers who produce medicines under contract for license holders or other clients.*	*5*	*6*	*1*	*1*
Generic	*Generic medicine*	*32*	*97*	*4*	*7*
Branded				*9*	*17*
Innovator		*20*	*27*	-	-
Therapeutic_class	Therapeutic class of medicine	46	168	12	23
Blood pressure lowering	*Blood pressure lowering medicine*			13	36
Anti-microbial		*6*	*7*	-	-
Biosimilars		*1*	*1*	-	-
Lifestyle		*9*	*14*	-	-
NCD	*Medications mentioned for other noncommunicable diseases, including cardiovascular diseases*	*12*	*18*	*0*	*0*
Other	*Medications mentioned that are not blood pressure lowering*	*7*	*12*	-	-
Sexual_health		*3*	*3*	-	-
Vaccines		*23*	*99*	-	-
Important/notable Excerpts	*Notable excerpts from interviews to be set aside as quotations*	-	-	*13*	*41*
Improvement ideas_actions	*Ideas or actions underway aimed to reduce the risk of substandard and falsified drugs*	-	-	*0*	*0*

		Pisani et al.		Nigeria	
Name	**Description**	**Media**	**Code Freq (n)**	**Media**	**Code Freq (n)**
Demand	*Ideas or action targeting patients*	-	-	*0*	*0*
Supply	*Ideas or action targeting supply side including dispensing*	-	-	*0*	*0*
15_Sub-study		**0**	**0**	**-**	**-**
China		10	37	-	-
GSMS	Flags public access data from GSMS cases, used to validate framework.	0	0	-	-
Indonesia		12	26	-	-
Romania		6	7	-	-
Tool	Flags info for risk-assessment framework	1	3	-	-
Turkey		5	5	-	-

Supplementary Table 4: Factors driving the risk of substandard and falsified BP lowering medications in Nigeria.

Factors	Definitions	Illustrative quotes
Demand side	Factors which increase or reduce demand for substandard and falsified BP lowering medications	
1. Poverty/poor economic condition (+)	Lack of financial resources and high out-of-pocket costs which limit purchasing power and increase demand for low quality medicines.	*You know, no matter how cost-effective a drug can be, there are people that cannot afford it. And sometimes, they use more than two BP lowering s. Then for some class of patients, where they have Angiotensin receptor blockers (ARBs), that one is always an issue. They are unable to afford it, and most of the time, they really need it, and that's it (FGD 4, Pharmacist from Secondary Healthcare facility).* *For instance, now, if you see branded products from (manufacturers), they are of very high quality, everybody knows it, but the prices are high; it's only for the rich in the society. So, the general populace is made of not too rich/low-income group. So, they will buy, they will prefer to buy things that are cheaper. (FGD 4, Pharmacist from Secondary Healthcare facility).*
2. Stockouts (+)	Lack of availability of BP lowering medications anywhere along the supply chain (from the manufacturer to the point of dispensing).	*So, if you talk about fake medicines, we come to the hospital because in the hospital you cannot have fake. And that is why I get annoyed when they say it's out of stock. (FGD 3, Tertiary Healthcare facility patients).* *Certain patients, they go on a particular type of drug over a long period of time, and they tell you that, that is the only drug that works for them. And even if the doctors, or the pharmacists try to convince them about how efficacious other drugs are, they tend to not agree with them. So, if it is not that particular drug, they would prefer to go outside; so, the, the demand on such drugs can be so high, and that can lead to out-of-stock syndrome (FGD 2, Federal level Medical Officers).*

3. Availability of medicines from the Central Medical Store (-)	Availability of BP lowering medications from the Central Medical Store indicating access to timely quality medicines	*Based on the drugs, the tablet, the BP lowering s we collect, because we collect them from the Central Medical Store. So far, so good, the brands and the products they give, they are relatively cheap and affordable for the common man to use (FGD 4, Pharmacist from Secondary Healthcare facility).*
4. National health insurance (-)	Access to national health insurance at the Federal Capital Territory which enhances affordability of quality BP lowering medications	*I say this with utmost confidence because at least we have a larger set of our population utilizing their National Health Insurance Scheme, and the one that is domiciled with the FCT, which is, FCT Health Insurance Scheme. So, for that reason, the cost has not been our own major problem. I think too, let's give credit to the system that patients are able to access their BP lowering drugs. (IDI 9, State Pharmacy Administrator)*
5. Pharmacists' supervision (-)	Availability of pharmacists at healthcare facilities to ensure appropriateness and quality of medicines.	*Because we say that every procurement must be handled by pharmacist, every document for procurement, any company that is engaged, to supply drugs, to any institution must come through a pharmacist, and we must see the license of that pharmacist (IDI 11, State level Administrator).* *Yes, so you have to ask them to go and buy outside [when BP lowering medications are out-of-stock with the hospital]. What I normally do if they prescribe [BP lowering medications] to them and we don't have, I will tell them "bring it let me see". This is so that we [Pharmacists] know whether this is the right medication prescribed for the patient (IDI 2, PHC Pharmacist)*
6. Drug availability at healthcare facility (-)	Availability of BP lowering medications within the healthcare facility instead of outside the healthcare facility ensures access to quality medicines.	*Because going to the hospital to collect drugs, is better than going to any pharmacy outside to buy. Most of them are fake (FGD 3, Tertiary Healthcare facility patients).*
Supply side	Factors which increase or reduce supply of substandard and falsified BP lowering medications.	

1. Limited in-country manufacturing capacity (+)	Limitations on manufacturing capacity for BP lowering medications in Nigeria.	*Actually, the factor is just policy. One, in the country where, will I say, up to eighty to eighty-five percent of our drug consumption is still dependent on importation. You can't guarantee a mere quality (IDI 9, State level supply chain manager)*
2. Non-adherence to good manufacturing and distribution practices (+)	Wrong motives (greed and desire to make quick profit) for market entry, promotion and distribution of BP lowering medications.	*You know, there are so many reasons why you have fake drugs in circulation. One of it is the suppliers; the second one is economic gain from those that are producing these products. Some of the suppliers, you give them Local Purchase Order for instance to supply drugs, and rather than go to the actual companies at the source, they will go to the side, and maybe go to Onitsha market or somewhere and buy these drugs...(IDI 1, Federal level Administrator).* *So, each time there is fall in the price in dollars, it affects the cost of all these goods that come in, because the marketers will never want to lose their money. So, the only option left will be probably to compromise on quality (IDI 9, State level supply chain manager)*
3. Drug regulation (+)	Regulations which either restrict or mandate the availability of certain BP lowering medications. This also includes poor quality assurance process due to low testing capacity of available laboratories and limited staff strength to conduct post-market surveillance.	*Then, when we are not regulating…we are not stringent on regulation, or we don't have the technology or the manpower to be able to man our porous borders… And I think the government instituted that drugs are only to be imported through air. But you find out that most of these drugs find their way in through the land borders. And once that is done, there's no check (IDI 7, federal level drug regulator)* *But we also have to look at the various brands in the market, most of these BP lowering s are numerous. So, for me, I feel it will be very tasking for NAFDAC to really inspect them. I don't think they have enough staff and facilities to do that, so, that might be a loophole where fake drugs can thrive. (FGD 4, Pharmacist from Secondary Healthcare facility).*

4. Ineffective healthcare facility operation (+)	Poor inventory of BP lowering medications, poor communication flow, change in prescription pattern, and delay in suppliers' payment which often led to stockouts	*Prior to now, the communication flow between health facilities and Central Medical Stores was not adequate. And it led to even the Central Medical Stores having drugs that were expiring because the health facilities are not aware that they have such drugs" (FGD 4, Pharmacist from Secondary Healthcare facility)* *And, apart from that too, sometimes, before now, we were getting list from the pharmacy point on drugs that are close to expiration, and that if we don't, if we don't exhaust these drugs, in good time, the hospital stands the chance of losing so much (FGD 2, Federal level Medical Officers).* *Expiration of drugs is inherent to the pharmaceutical business. Take for instance, change in the pattern of prescription will cause your own stock to expire. I have based my projection on the previous consumption pattern and the request, but if there is sudden change in the pattern, of, you understand, of consumption at the facility level or, for whatever reason, or response (IDI9, state level supply chain manager)*
5. Poor storage (+)	Inability to store procured BP lowering medications under the required temperature, driven by limited space and use of illegal drug supply sources.	*We all know what drug moieties are all about. For instance, a drug can still be potent at the point of importation, but because of ordinary storage condition, it can lose its potency, long before the expiration date. And as long as we import, you cannot guarantee storage condition during the course of importation. So, some potency could have long been lost (IDI 9, state level supply chain manager)* *Yes, I think once in a while, we have problems with storage because, one, where we store our large quantities of drugs, which is what they call the Bulk Store, you know, they have a problem of space, and they have a problem of aeration. So, once in a while, we have*

		some challenges (IDI 1, Federal level Administrator).
6. Limited number of trained pharmacists (+)	Limited number of trained pharmacists leading to limited of pharmacists available in healthcare facilities, especially in private hospitals.	*Now, our profession, pharmacy profession is one of those profession that up till today is still growing at a very slow rate. If you go to most universities and you compare the population medical students, medical lab scientists to pharmacy students, you will be shocked that there is a gap in the professional need (IDI 9, state level supply chain manager).* *And then, even the situation whereby everybody is a pharmacist; we have private hospitals, they don't have pharmacist in their system, they go to anywhere, buy their drugs, dispensers – they are the dispensers, they are the everything IDI1, Federal level Administrator).*
7. Covid-19 pandemic (+)	Interruption to supply chain due to Covid-19 pandemic.	*Again, unforeseen circumstances, the COVID has given us a typical example. Our stock was meant to last for February and March, and by March, there was lockdown and patients could not access hospitals. So, if I have a stock of short life, you understand…, they will definitely expire (IDI 9, state level supply chain manager).*
8. Central Medical Store procurement quality check (-)	Availability of BP lowering medicines improves supply chain management and availability of quality medicines which are NAFDAC certified.	*We get most of our drugs from the Central Medical Store; and the people there, there are a lot of pharmacists with experience. So, they look into, the brands of drugs they buy. It might not be branded, but they look at the company that has been in the market for a long time, so it has a name already, when they are getting those anti hypertensives. So, most of the time, the brands we get, they are good brands (FGD 4, Pharmacist from Secondary Healthcare facility)* *Because like the Central Medical Store, most of the BP lowering s they buy, they are NAFDAC-certified. So, they hardly collect or procure any medicines that NAFDAC has not certified. And to certain extent, most of the time, they have their own quality control unit in the store,*

		which if they go for bidding, they will collect samples and check (FGD 4, Pharmacist from Secondary Healthcare facility)
9. NAFDAC equipment and operations (-)	Availability of analytical laboratories to conduct quality tests on active pharmaceutical ingredients and use of barcodes which allows the possibility of confirming BP lowering medications at endpoint.	*Because when you are dealing directly with the real source, then the possibility of buying fake will be, at least reduced or eliminated. Because I will not expect a company to fake its own products, or if you are the one distributing, you are bringing it from whatever country, I don't expect you to bring in anything fake. But we also have an analytical lab, but right now, I don't know what they are able to test, or what they are able to check when they receive the drugs (IDI11, Administrator State level).*
10. Healthcare facilities guidelines (-)	Availability of guidelines in health care facilities which facilitates procurement of quality and affordable BP lowering medications	*We have a Central Procurement Unit, where all the hospitals under FCTA collect their drugs and consumables; and there's a process which they follow, the quantification, bidding, and; for us here, even the ones we get for ourselves, we normally get through companies, reliable companies. And, with that we are certain that the qualities are of a standard. So, we have not really come across any substandard, and we have not gotten any feedback from patients that these drugs are not effective, nor from the physicians (FGD 4, Pharmacist from Secondary Healthcare facility)*

(+) Factors contributing to increase in demand for and supply of substandard and falsified BP lowering medications

(-) Actions contributing to decline in demand for and supply of substandard and falsified BP lowering medications

Research Checklist: COREQ (COnsolidated criteria for REporting Qualitative research)

Checklist

Topic	Item No.	Guide Questions/Description	Page Number
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	9
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	9
Occupation	3	What was their occupation at the time of the study?	9
Gender	4	Was the researcher male or female?	9
Experience and training	5	What experience or training did the researcher have?	9
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	9
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	9
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	9
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	9
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	8
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	8
Sample size	12	How many participants were in the study?	8
Non-participation	13	How many people refused to participate or dropped out? Reasons?	9
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	9
Presence of nonparticipants	15	Was anyone else present besides the participants and researchers?	9
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	10-11
Data collection			

Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	8
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	7
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	9
Field notes	20	Were field notes made during and/or after the interview or focus group?	25
Duration	21	What was the duration of the interviews or focus group?	9
Data saturation	22	Was data saturation discussed?	8
Transcripts returned	23	Were transcripts returned to participants for comment and/or correction?	9
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	9-10
Description of the coding tree	25	Did authors provide a description of the coding tree?	9-10
Derivation of themes	26	Were themes identified in advance or derived from the data?	9
Software	27	What software, if applicable, was used to manage the data?	9
Participant checking	28	Did participants provide feedback on the findings?	9
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	12-16
Data and findings consistent	30	Was there consistency between the data presented and the findings?	12-24
Clarity of major themes	31	Were major themes clearly presented in the findings?	12-20
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	12-20