Innovative Private Pharmacy Distribution Channels: Implications on Medicine Quality in Zambia

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Declaration

I, Scott Kaba Matafwali, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

Poor-quality medicines represent a profound public health risk, contributing to increased morbidity, mortality, and global health challenges such as antimicrobial resistance. The complexity of pharmaceutical supply chains, particularly in low- and middle-income countries (LMICs), may exacerbate inequalities in access to quality-assured medicines. The multiple stages of the supply chain, from the procurement of active pharmaceutical ingredients to the final distribution of medicines, present numerous points of entry for suspect medicines (substandard and falsified). This problem is particularly acute in rural areas where lengthy supply chains and multiple storage points increase the risk of medicine degradation. Added to which, the lack of access to medicines in public facilities can lead to out-of-pocket purchases from potentially unlicensed private facilities, where the quality of medicines is often questionable.

In response to these challenges, entrepreneurs are leveraging innovative technologies and business models with the potential to enhance the availability, affordability, and quality of medicines. However, research on these innovations has primarily focused on their financial and business benefits, with no investigation of their impact on medicine quality. This PhD thesis investigated this gap by comparing quality of the commonly used antimalarial (sulfadoxine/pyrimethamine) and antibiotic (amoxicillin) available in pharmacies supplied by innovative pharmacy chains with those in independent pharmacies served by traditional supply chains.

A mixed-method approach comprising standardised surveys, key informant interviews, and laboratory analyses of samples to assess their quality, was undertaken to appreciate if innovative supply chains provide better quality medicines in Zambia.

The findings of this thesis revealed that no falsified medicines were detected in the SP and amoxicillin samples analysed. However, there were some inconsistencies in the content analysis, yet all samples conformed to the USP tolerance limits for bioavailability. Notably, no statistically significance difference was found in medicine quality between samples purchased from the innovative and traditional independent pharmacies. This research further revealed that innovative pharmacies, characterised by more streamlined supply chains, adopted digital record-keeping and better transportation practices. Nevertheless, gaps in professional training and storage practices, were evident in both types of pharmacies, indicating that innovation alone is not a panacea. However, this research underscores the potential advantages of incorporating innovative distribution channels to ensure the consistent delivery of good-quality medicines to patients. Merging these innovative strategies with established trust in traditional pharmacies could offer a novel approach to mitigating the challenges of poor-quality medicines in LMICs.

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I would like to express my profound gratitude to my family for their unwavering support and encouragement throughout my PhD journey. My heartfelt appreciation goes to my wife Pipina, my two children, siblings, nephews, nieces, and especially to my mother Anna, who has been a constant source of love and motivation. Your steadfast presence and belief in me have been truly invaluable, and I cannot express how deeply your support resonated with me during this time.

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Additionally, I am grateful for the insightful contributions from my advisory team, Prof Virginia Bond and Prof Ron Behrens, who have played a pivotal role in refining my work. I also appreciate Prof Catherine Goodman for her unique perspectives on private pharmacy and research methodology, and Prof Charles Opondo for his invaluable assistance with the statistical facets of my research. Their collective input significantly enriched my work.

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Dedication

I dedicate this thesis to my cherished children, Eliana and Demetrius. May the passion and perseverance embodied in this work inspire you to pursue your dreams and aspirations. It is my deepest wish that you live lives rich in purpose, fulfilment, and happiness.

List of publications

Proposed publications from the thesis

1. Characteristics of Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: A Descriptive Comparison (paper 1).
2. Assessment of medicine Procurement, Transportation, and Storage Practices in Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: Implications on medicine quality (paper 2).
3. Comparative Analysis of Medicine Quality Surveillance between Innovative and Traditional Independent Pharmacies in Lusaka, Zambia (paper 3).
4. Medicine Quality in Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: Factors Influencing the Quality of Amoxicillin and Sulfadoxine/Pyrimethamine (paper 4).
5. Stakeholder Perceptions on Innovative Private Pharmacy Distribution Channels and Implications for Medicine Quality in Zambia (paper 5).

Additional relevant publications not included in the thesis.

- Lalani M, **Matafwali SK**, Ndiaye AD, Webster J, Clarke SE, Kaur H. An absence of evidence breeds contempt: a qualitative study of health system stakeholder perceptions of the quality of medicines available in Senegal. PLOS Glob Public Health. 2023 Jul 12;3(7):e0002004. doi: 10.1371/journal.pgph.0002004. PMID: 37437003; PMCID: PMC10337888.
- Chabalenge, B., Jere, E., Nanyangwe, N., Hikaambo, C., Mudenda, S., Banda, M., Kalungia, A., & **Matafwali, S**. (2022). Substandard and falsified medical product recalls in Zambia from 2018 to 2021 and implications on the quality surveillance systems. The Journal of Medicine Access. https://doi.org/10.1177/27550834221141767
- LSHTM AMR blog: https://www.lshtm.ac.uk/research/centres/amr/news/382986/crisis-substandard-and-falsified-antibiotics-africa-catalyst-antimicrobial

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Abbreviations

ACT	Artemisinin-based combination therapy
AMR	Antimicrobial Resistance
CHAZ	Churches Health Association of Zambia
GMPs	Good Manufacturing Practices
HPCZ	Health Professions Council of Zambia
HPLC	High-Performance Liquid Chromatography
LMICs	Low- and Middle-Income Countries
MoH	Ministry of Health
NQCL	National Quality Control Laboratory
SDGs	Sustainable Development Goals
SF	Substandard and Falsified
UHC	Universal Health Coverage
USAID	United States Agency for International Development
WHA	World Health Assembly
WHO	World Health Organization
ZAMMSA	Zambia Medicines and Medical Supplies Agency
ZAMRA	Zambia Medicines Regulatory Authority

Chapter 1: Introduction

1.1 Quality of Medicines

Public Health need for Good Quality Medicine

The provision of quality-assured medicines plays a crucial role in public health by guaranteeing safe and effective treatment for individuals. With the aid of recent scientific and technological advancements, the production of these medicines has been enhanced, resulting in increased drug safety and efficacy. These advancements have facilitated significant progress in the prevention, diagnosis, and treatment of various diseases [1].

For medicines to effectively serve their intended purpose, they must consistently demonstrate quality, efficacy, and safety. The availability of good-quality and effective medicines, vaccines, and medical equipment underpins a robust health system. Quality-assured medicines are fundamental to good health services. As such, ensuring the quality of medicines is pivotal for realising Universal Health Coverage (UHC), a significant component emphasised in the United Nations Sustainable Development Goal (SDG) 3 [2,3]. Specifically, SDG 3 promotes ensuring healthy lives and the well-being of all ages. Among its multiple targets, target 3.8 states: "Achieve universal health coverage, including financial risk protection, access to quality essential healthcare services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all" [2]. Although the role of quality medicines is highlighted in SDG 3.8, it is not explicitly used as a progress indicator for UHC. It is crucial to view the access to medicines through multiple lenses, considering aspects such as availability, affordability, and quality. Overcoming challenges related to medicine quality is essential to fulfilling the vision of UHC, ensuring that everyone receives quality-assured medicines [3,4].

What are Good Quality Medicines?

The term "good quality medicines" refers to pharmaceutical products that meet the established criteria for potency, quality, purity, packaging, or labelling. Generally, a product's quality, including medicines, can be defined as meeting customer requirements for performance, quality, durability, appearance, and intended use/purpose [5]. The characteristics of good quality medicines include adherence to approved standards for potency, purity, and uniformity of dosage units, as well as other quality attributes such as bioavailability, which is the proportion of medicines that enter circulation after ingestion, leading to its intended therapeutic effect [6]. The fundamental idea that quality should be inherently designed for a product was highlighted by Juran, who pointed out that most quality deficiencies stem from product design [7]. This notion resonates deeply with pharmaceutical products: the essence of quality should be intrinsically integrated during the developmental and manufacturing phases [7]. For a medicine to be classified as 'good quality', it must have been registered by regulatory

authorities and undergone rigorous visual inspection. In the context of this thesis, "good quality medicines" are defined as those containing an acceptable stated amount of active pharmaceutical ingredients (SAPIs) in accordance with the pharmacopoeia and meeting other essential quality attributes [8,9].

Definitions of Poor-Quality Medicine

The World Health Organization (WHO) has historically used substandard, spurious, falsely labelled, falsified, and counterfeit (SSFFC) to describe a broad range of poor-quality medicine issues [10,11]. The WHO defined substandard medicines as authorised medical products that do not meet their quality standards, specifications, or both. Counterfeit medicines as products that are fraudulently mislabelled with respect to identity and/or source. Counterfeiting can be applied to both branded and generic products, and counterfeit products may include products with the correct ingredients, wrong ingredients, without active ingredients, with an insufficient quantity of active ingredients, or fake packaging [11]. The umbrella term SSFFC was criticised for its ambiguity as it lumped all poor-quality medicine issues into one term, suggesting that their deficiencies are the same, although they are very different from their causes and solutions. The confusion in terminology describing different types of poor-quality medicines hampered the global fight against poor-quality medicines [12–14]. The confusion was due to the tension between the defence of commercial interests and the public health importance of enhanced access to good quality medicines in developing countries [15]. Counterfeit medicines had been viewed "primarily as intellectual property (IP) rather than public health concerns, and the innovative pharmaceutical industry was using action against counterfeit medicines to impede the trade in competing generics" [12,14].

Hence, the World Health Assembly (WHA) agreed in 2017 to adapt the definitions of poor-quality medicines as substandard, unregistered, and falsified medicines [16]. Substandard medicines are those that fail to meet their quality standards or specifications. Unregistered medicines are products that have not undergone evaluation and/or approval by the national or regional regulatory authority for the market in which they are marketed/distributed or used. Falsified medicines are those that deliberately or fraudulently misrepresent their identity, composition, or source. This research will use the WHO definitions to define poor-quality medicines, where a substandard medicine fails to meet the authorised pharmacopoeia tolerance limits stated in the authorised monograph and contains less than or more than the authorised SAPI of the specified formulation [8,9]. Falsified medicines are the ones that deliberately or fraudulently misrepresent their identity, composition, or source.

Why should we be concerned about Substandard and Falsified Medicines?

Substandard and falsified (SF) medical products present a complex global challenge with serious implications for both public health and patient safety. SF medical products have been linked to various detrimental outcomes, ranging from prolonged illness to an increased risk of mortality, thereby escalating healthcare expenditures [16–18]. A recent case of this issue manifested in The Gambia, where contaminated pediatric syrups led to the tragic loss of at least 60 children, primarily under the age of five [19–21]. Additionally, the misuse or overuse of substandard antibiotics poses a particularly serious threat as it can be a significant driver for the development of antimicrobial resistance (AMR) [22–24]. The presence of subtherapeutic doses of these antibiotics allows bacteria to adapt and develop resistance, which has long-term consequences for effective disease management.

These challenges extend beyond physical health to undermine the credibility and functioning of healthcare systems. The circulation of SF medical products can erode the confidence of both healthcare providers and patients, leading to overtreatment and unnecessary strain on healthcare resources [22]. This is especially pertinent in LMICs, where a significant portion of healthcare expenditure is out-of-pocket and directed towards medicines. The economic ramifications are equally profound [25,26]. For example, in Zambia, SF antimalarials have been modelled to cause 2,610 deaths in children under the age of five, corresponding to an estimated annual economic burden of $141.5 million [27]. The economic implications on a global scale are significant, with estimates suggesting that the annual market for falsified medicines falls between $75 and $200 billion [18,28].

Causes of Substandard and Falsified Medicines

Substandard and falsified medicines arise from various factors. One primary cause is non-compliance with good manufacturing practices (GMPs). Failure to adhere to these guidelines during manufacturing can lead to medicines containing incorrect dosages of API [6,29]. Ensuring adherence to GMPs is pivotal for maintaining the quality of medicines and reducing production errors.

The global API market, which is primarily influenced by India and China, has experienced significant price fluctuations [30,31]. As costs rise, manufacturers, especially those from smaller firms, may be compelled to prioritise cost over the quality of APIs [32]. This challenge was further accentuated during the COVID-19 pandemic, exposing vulnerabilities in the global pharmaceutical supply chain [33,34]. Notably, dominant producers, such as India and China, imposed export restrictions, potentially pushing other manufacturers toward less reliable suppliers. Furthermore, many LMICs rely heavily on imports for their medicines, which increases the risk of substandard drug imports.

Another crucial factor is the degradation of the medicines during storage and transportation. Properly manufactured drugs can deteriorate when exposed to extreme temperature, moisture, or light [35,36].

Ensuring adherence to guidelines, including good storage, transportation, and distribution practices, is vital for preserving medicine integrity.

Finally, criminal activity plays a significant role in the proliferation of falsified medicines [29,37]. Such illicit activities are often straightforward and inexpensive, requiring only basic equipment and processes. Unfortunately, these operations are rampant in areas with weak regulatory oversight and high corruption levels, leading to an influx of poor-quality, potentially harmful medicines into the market.

Drivers of Substandard and Falsified Medicines

Overlapping drivers contributing to the proliferation of SF medicines include limited access to medicines, weak regulatory governance, lack of political will and corruption, and a lack of awareness among health professionals and the public.

Lack of access to medicines

Limited access to medicines significantly contributes to the prevalence of SF medicines, particularly in LMICs. In these regions, there is substantial demand for essential medicines, often resulting in frequent stockouts, as depicted in Figure 1 [38–40]. This scarcity is further exacerbated by fragmented supply chains, disruptions, and the lack of comprehensive national policies to ensure access to affordable, quality medical products [4,41]. The COVID-19 pandemic has magnified the risks of medicine shortages and stockouts because of the disruption of supply chains [33,34]. The greater demand for medicines in areas with a high burden of diseases can lead to an increased likelihood of patients purchasing poor-quality medicine [38,39,42]. When demand exceeds supply, a market for SF medical products is created. Public sector stockouts can also prompt consumers to seek alternative sources of medicines, including unregulated entities such as drugstores, which may sell poor-quality medical products. Additionally, the lack of access to safe and effective antimicrobials due to poor-quality medicines threatens global health security and may contribute to the developing of AMR [43].

Weak regulatory governance

Weak regulatory governance is another significant driver in SF medicine. Limited resources, a lack of technical capacity, and weak regulatory systems compromise the security of pharmaceutical supply chains and reduce a country's capacity to protect its population's health [16,18]. Many countries lack a consistent and effective legal and judicial framework to provide effective quality assurance, and many have limited capacity in certified laboratories to detect SF medical products in the supply chain [44,45]. Additionally, it is estimated that at least 30 per cent of the global National Medicine Regulatory Authorities (NMRAs), especially in LMICs, cannot effectively fulfil their primary responsibilities [46].

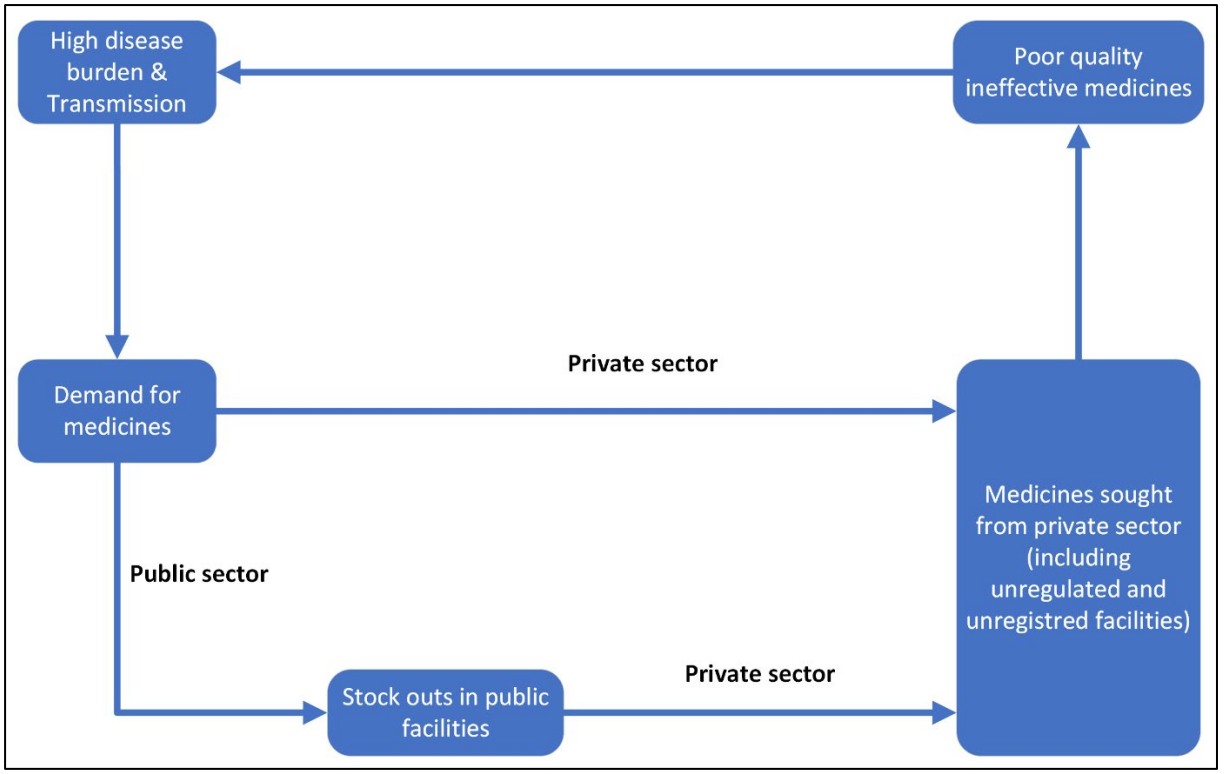

Figure 1: The vicious cycle of the lack of access to medicines

Lack of political will and corruption

The lack of political will, weak penalties for crimes related to SF medicines, and corruption have also contributed to the sustained flow of poor-quality medicines in legitimate supply chains [44]. Politicians do not prioritise quality assurance programmes mainly because of a lack of surveillance data on mortality and morbidity caused by poor-quality medicines in many LMICs. Instead, the leaders prioritise other seemingly more quantifiable programmes, and some high-level politicians in several LMICs have been implicated in the corrupt procurement of medicines, which can explain the unwillingness to tackle poor-quality medicines [47,48].

Lack of awareness

Both health professionals and the public often lack awareness regarding SF medicines. Health professionals might not recognise the risks or realise that they are handling poor-quality products, and timely warnings about SF products entering their markets might be absent [44,49–51]. This oversight can jeopardise patient safety. Meanwhile, the public may be unaware of the dangers of purchasing such products. Furthermore, there is a notable deficiency in the training and engagement of health workers to combat the issue of SF medicines [52].

Determining the Quality of Medicine

The detection of SF medicines is essential for regulatory action. Chemical analysis is pivotal because falsifiers can replicate genuine packaging convincingly [53]. A well-equipped medicine quality control laboratory (MQCL) with trained personnel and appropriate sample sizes is necessary for accurate testing. Portable devices can serve as screening tools when MQCLs are unavailable. Challenges arise owing to highly replicable packaging and various types of falsification, making uniform detection methods difficult across locations. Barcodes, QR codes, and other markings aid medicine tracking during distribution. However, falsifiers can reuse packaging and pharmacovigilance methods remain inadequate in many areas. Examples of the advantages and disadvantages of screening and confirmatory tests are listed in Table 1.

Analytical methods used to assess medicine quality

Medicine quality assessment methods can be categorised into screening devices and confirmatory tests. Screening devices, which are portable and designed for field use, require further analysis using advanced equipment, such as high-performance liquid chromatography (HPLC) or gas chromatography (GC), combined with detection systems, such as UV spectroscopy or mass spectrometry.

Table 1: Screening vs. Confirmatory Tests

Analytical Method	Advantages	Disadvantages
Confirmatory (e.g., HPLC)	High specificity and sensitivity; Quantitative & Objective	Expensive (capital and maintenance costs); Requires expertise
Screening (e.g., GPHF Minilab®)	Rapid; Simple to operate; Portable; Minimal training; Sensitive to picking out falsified medicines	Not quantitative; Subjective interpretation of results; Less specific for substandard medicines

Screening devices

Several technologies such as Near-Infrared (NIR) spectrometers, Raman spectrometers, Mid-Infrared (MIR) spectrometers, Paper-based analytical devices (PADs,) and Global Health Pharma Fund (GHPF) Minilab® have been employed for medicine quality assessment [54–59]. Their effectiveness varies, but portable devices have shown potential to support regulatory authorities. Awareness of these limitations is vital. NIR spectrometers offer rapid, mobile, and nondestructive chemical analyses, but might have limited spectral ranges and occasional misidentifications. Raman spectrometers are advantageous in distinguishing genuine from falsified medicines but are setup-sensitive and can sometimes damage samples. MIR spectrometers can pinpoint substandard medicines; however, samples often require crushing, and transparent packaging can hinder their effectiveness. Paper-based analytical devices are cost-effective devices that determine medicine quality using colour

patterns. However, interpretation can be challenging, and sometimes requires software assistance. The Artemisinin Derivatives Test (ADT) is a cost-effective method for detecting the artemisinin derivative component of the artemisinin combination therapy. The GPHF Minilab® is a field-ready portable lab, but its sensitivity and interpretation of results are limited.

Confirmatory Tests

Confirmatory tests, such as the 'gold standard' high performance liquid chromatography (HPLC), reinforce the accuracy of initial screening. They are essential for ensuring reliability of the results, especially in the medical and scientific domains [60,61]. They validate the outcomes, ensuring authenticity and alignment with scientific expectations.

Substandard and Falsified Antimalarials and Antibiotics in LMICs

In recent years, a pronounced emphasis has been placed on investigating the global prevalence of SF medicines, primarily to devise preventative and responsive measures to address this escalating concern. An analysis by the WHO, which evaluated 100 articles from 2001 to 2016, encompassing regions such as Africa, Asia, and Latin America, concluded that approximately 10% of medicines in LMICs are categorised as SF [16,18]. Antimalarials were notably compromised, with 11.8% falling under the SF category, followed by antibiotics (7.2 %). It is significant to note that Africa showed the highest prevalence of these medicines. A systematic review and meta-analysis confirmed these estimates, finding that 13.6% of essential medicines sampled in LMICs failed the quality analysis [62].

Quality of Antimalarials

In a review of antimalarial medicines in Southeast Asia (SEA), 35% of drug samples from seven countries failed quality assessments, with an equivalent percentage falsified [63]. The situation in Sub-Saharan Africa (SSA) was similar, presenting a 35% failure rate with 20% identified as falsified. Another systematic review by the Worldwide Antimalarial Resistance Network (WWARN) found that 30.1% of samples failed quality tests, with 39.1% classified as falsified [64]. The two reviews used similar methodologies and databases, and the results indicated that many falsified antimalarials were circulating in the LMICs.

Further highlighting this challenge, research in Afghanistan provided evidence of the availability of substandard antimalarials [65]. In the study, 7,740 individual and packaged tablets, ampoules, and syrups were obtained from various public and private outlets. The analysis showed that 26% of the samples failed the MiniLab® disintegration test, and upon further assessment using in vitro dissolution testing, 32% of the sulfadoxine/pyrimethamine (SP) and quinine samples did not comply with the tolerance

limits. Such localised studies underscore the nature of this issue, highlighting the need for continuous drug quality monitoring across various settings.

In a surveillance effort, the Artemisinin Combination Therapy (ACT) Consortium undertook systematic assessments in regions such as Enugu metropolis, Nigeria, Bioko Island, and Equatorial Guinea [8]. They employed varied sampling methods, including convenience, mystery client, and overt sampling. In Enugu, convenience sampling showed a higher prevalence of poor-quality antimalarials than the more representative mystery and overt sampling methods [66]. Similarly, on Bioko Island, falsified artemisinin-containing antimalarials ranged from 6.1% to 16.1%, depending on the sampling approach [67]. Notably, the study also revealed the presence of artesunate monotherapies, a significant portion of which were falsified (did not contain SAPI). These findings from the ACT Consortium emphasise the crucial role of a representative sampling approach in unveiling the true prevalence of SF medicines, highlighting the broader challenges in combatting poor-quality antimalarials in endemic regions. However, this consensus underscores the paramount need for heightened surveillance and more robust regulatory frameworks in LMICs.

Quality of Antibiotics

The prevalence of SF antibiotics in LMICs poses a significant threat to the global public health. Addressing and improving the quality of antibiotics are crucial for the effective treatment of bacterial infections. Studies have investigated the global prevalence of poor-quality medicines and underscored the challenge of SF antibiotics as a potential driver of AMR. For instance, a survey in Lao PDR found no evidence of antibiotics being falsified. However, a significant proportion was deemed substandard. 19.6% of samples fell outside the 90%-110% content range, and 60.2% deviated from the International Pharmacopoeia uniformity limit [68]. Similarly, an investigation of amoxicillin in the DRC found that 28% of the samples were out of specification, with units outside the US Pharmacopoeia uniformity limit [69].

In Haiti, where antibiotics were purchased from the streets, 22.4% of the samples were substandard due to insufficient Raman spectral match with reference products [70]. In a study by Fadeyi et al.[71], samples of amoxicillin and co-trimoxazole purchased from Kintampo, Ghana, were analysed for quality. The study revealed that 10% of amoxicillin and 20% of co-trimoxazole samples failed the quality tests. HPLC analysis showed that all amoxicillin samples complied with US Pharmacopeia tolerance limits. However, 60% of the co-trimoxazole samples purchased in Ghana and Nigeria did not meet these standards, indicating a high prevalence of substandard co-trimoxazole in these regions.

A systematic review assessing the global prevalence of SF antibiotics evaluated 106 surveys, predominantly from the LMICs. Of the 13,555 samples reviewed, 17.4% failed at least one quality test, with a median failure frequency (FF) per survey recorded at 19.6% per survey. The most frequently

surveyed antibiotics were amoxicillin, sulfamethoxazole/trimethoprim, and ciprofloxacin [72]. These findings underscore the extent of the issue of poor-quality antibiotics in LMICs.

1.2 Traditional Pharmaceutical Supply Chains

Ensuring the delivery of quality medicines through a robust pharmaceutical supply chain is pivotal for global health and the achievement of SDGs. Traditional pharmaceutical supply chains, however, are intricate, often making it difficult to guarantee the safety and efficacy of medicines [73]. This complexity arises from the multifaceted interactions between manufacturers, wholesale distributors, and retail pharmacies. Enright [74] provides a compelling depiction of the convoluted nature of the supply chain: APIs might be produced in China, combined into a final product in India, labelled in Senegal, and packaged in Malaysia. Such a product could eventually find its way to a patient in Vietnam, after passing through multiple countries and regulatory landscapes. This intricate web emphasises the need for enhanced transparency and accountability to counteract the influx of SF medicines. The simplified medicine supply chain process is illustrated in Figure 2.

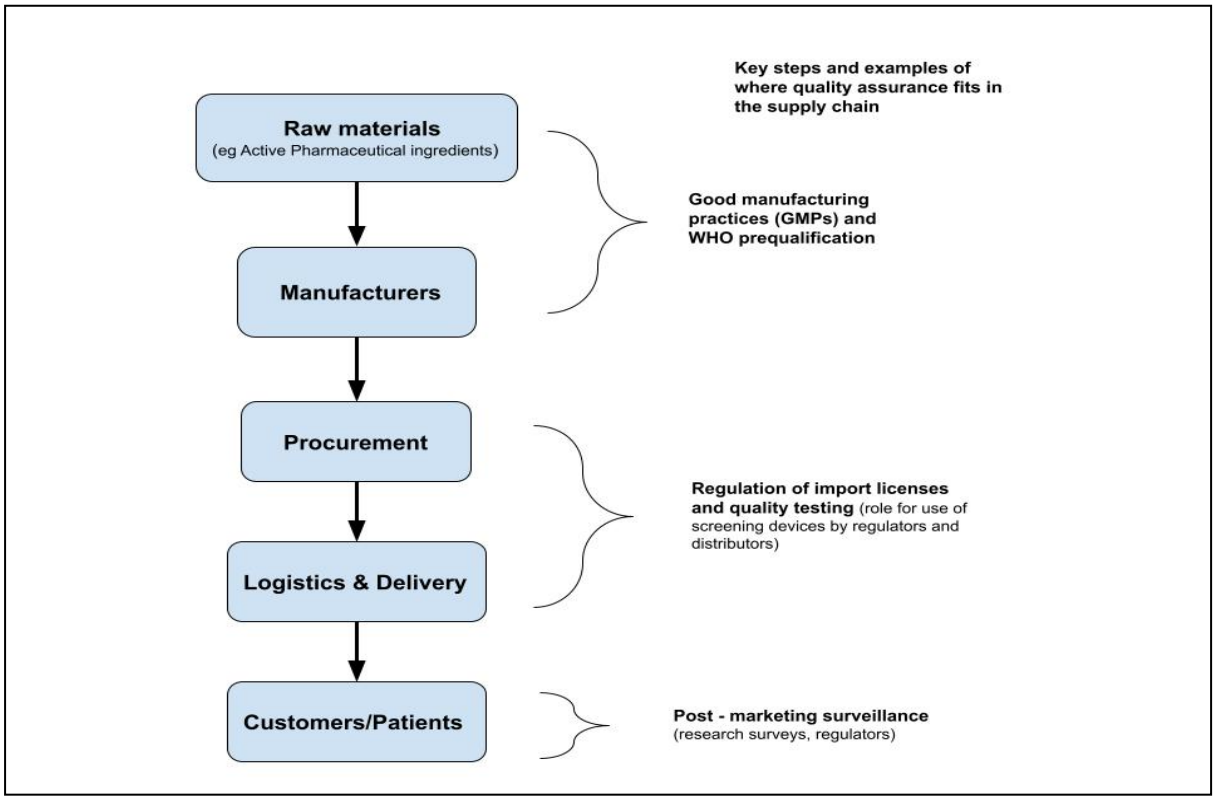

Figure 2: A concise overview of the medicine supply chain process, emphasising key quality assurance junctures.

Challenges of Medicine Distribution in LMICs

Medicine distribution in LMICs is particularly complex, often involving many importers, wholesalers, and pharmacies (simplified depiction of complex routes in Figure 3) [75,76]. While nuances exist between countries, a general flow sees the importer liaising with manufacturers, followed by distribution

through pharmacies. Multiple barriers, including obscured supply routes, elevated costs, and limited accessibility undermine the efficient functioning of this system [29,76]. Furthermore, the intricacies of existing pharmaceutical supply chains, combined with recurrent procurement events and various storage points, amplify the risk of SF medicine infiltration.

Traditional Pharmacies in LMICs

In many LMICs, retail pharmacies serve as the primary health touchpoints, especially in remote locales [77–79]. While they offer ready access to medicines and rudimentary health advice, the quality of service often falters, with many establishments prioritising profit over patient well-being. Non-adherence to prescription norms, sidestepping of guidelines, and inadequate disease awareness further undermine their reputation [75,77,80]. Such challenges, paired with high out-of-pocket expenses and the potential risk of SF medicines, underscore the urgency of enhancing the quality standards in LMIC pharmacies.

Traditional Independent Pharmacies

Traditional independent pharmacies, typically owned and operated by individual pharmacists, emphasise personalised care and foster community relationships [77]. Often termed "mom-and-pop" shops, these entities play a vital role in healthcare within their communities. This research identifies them as private outlets, primarily sourced from traditional supply chains.

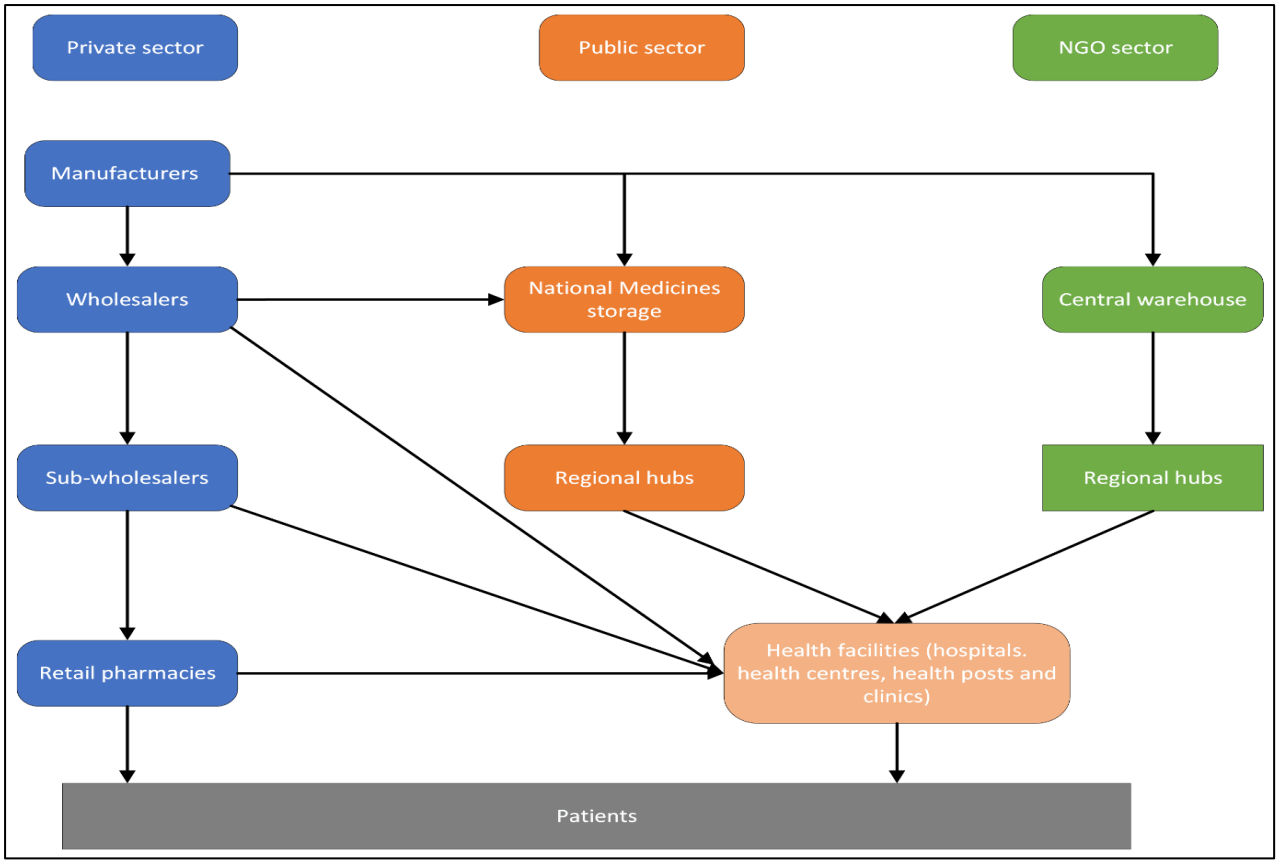

Figure 3: A representation of medicine distribution in LMICs, delineating the private, public, and NGO sectors.

Pharmacy Chains, Franchises, and Social Franchises

The transition from independent 'mom and pop' shops to organised pharmacy chains and franchises in LMICs represents a significant shift in the pharmaceutical sector. Historically, independent pharmacies have dominated the market in these regions, but a combination of economic growth and a need for better-quality pharmaceutical services has led to the expansion of chain pharmacies [77,81]. This evolution raises important questions about the implications for public health and whether such changes lead to improved pharmacy practices or better access to medicines [82]. The last two decades have seen a substantial change in the pharmacy market, characterised by consolidation and the emergence of new forms of pharmacies, including chains and franchises [83,84]. The scholarly discourse, with contributions from studies like those by Miller et al. [77], has illuminated the operational efficiencies and quality control mechanisms that are often more systematic within these larger-scale establishments. These entities typically maintain rigorous procurement protocols and robust quality assurance processes, purportedly surpassing the capabilities of their independent counterparts. Consequently, they are hypothesised to offer services of a superior quality and due to economies of scale, potentially at a greater affordability.

Performance Differences

When scrutinising the performance of these emerging entities, the literature presents mixed findings. Studies by Smith [78] and Miller et al.[77] highlight the improved standardisation and quality control in pharmacy chains. There is evidence to suggest that these larger organisations may enhance the availability and cost-effectiveness of medicines. However, the actual quality of the medicines provided through these new pharmacy models has not been thoroughly investigated. Although it is commonly posited that chain pharmacies in LMICs offer higher-quality services than independents, this assertion remains speculative. The literature also identifies a complex nexus between the size of pharmacy operations and the affordability of medicines, revealing that the presumed cost benefits from larger scales are not consistently passed on to consumers in the form of reduced prices.

The critique extends to the methodological approaches of existing studies. The prevalent reliance on cross-sectional analyses may not capture the dynamic and evolving nature of pharmacy services in LMICs, where rapid changes in regulation, economics, and societal factors can have significant effects. Thus, there is a need for longitudinal research that could provide a deeper and more enduring understanding of how the advantages of scale are actualised over time in these settings. While current scholarship indicates that larger pharmacy entities have the potential to better availability and affordability of medicines, the degree to which these theoretical benefits are realised in the delivery of quality-assured medicines is yet to be determined with certainty.

1.3 Innovative Private Pharmacy Distribution Channels

Innovative private pharmacy distribution channels represent a paradigm shift in pharmaceutical practice. They prioritise accessibility, affordability, and quality of medicines, especially in LMICs [84–86]. By integrating technology, these channels are optimising the supply chain and significantly boosting transparency in the distribution process. A few notable innovations have emerged in this transformative space. Mobile health (mHealth) solutions, for instance, empower patients to conveniently order and receive medications at their doorsteps using their mobile devices. E-commerce platforms have carved a niche by establishing online bridges that connect consumers directly to pharmacies and medicine manufacturers. Additionally, the advent of last-mile delivery services, leveraging drones, and other cutting-edge technologies ensures that even the most remote and hard-to-reach areas are not left behind in the quest for better healthcare [84,87].

Other innovations in this arena include inventory management tools, retail partnerships, and systems for detecting falsified medicines. Such transformative services not only reduce costs, but also enhance product availability [85]. Social enterprise and community-based pharmacies are examples that merge healthcare with social responsibility, serving areas such as Kenya, Nigeria, Ghana, and Zambia. Overall, innovative private pharmacy distribution channels have the potential to improve medicine quality by simplifying supply chains, improving inventory management, increasing supply chain transparency, and providing convenient and accessible pharmacy services to patients.

Figure 4: Logos of some of the innovative companies in Africa

Types of Innovative Pharmacy Companies

According to a report by Salient Advisory and engagements with key stakeholders, innovative pharmacy companies in sub-Saharan Africa can be classified into three primary categories [84].

Table 2: Summary of innovative pharmacy companies and services provided.

Category	Innovation in distribution to providers	Innovation in distribution to customers	Product data and medicines authentication
Description	Technology-driven services for hospitals, clinics, and pharmacies	Tech-enabled services for patients	Data on product authenticity
Services Provided	Pharmacy inventory-management software, Vendor-managed inventory services, Business-to-business (B2B), Marketplace, Fulfilment, Stock financing	Direct-to-consumer distribution, Telemedicine, Product Locators, Patient engagement	Falsified medicine screening, Track and trace, Data analytic services
Intended Benefits	Less expired drugs, reduced wastage, affordable medicines	Access to medicines, Quality and safe medicines	Enhanced medicine quality, pharmacovigilance
Potential for effect on medicine quality	A simplified supply chain reduces time on the shelf and in transit, decreasing the risk of degradation; Improved profitability means providers can afford to stock better-quality products.	Consumers are more knowledgeable and more likely to seek authentic products; Medicines can be traced better.	Substandard and falsified products are more likely to be detected and removed from the supply chain; Consumers are more knowledgeable and more likely to seek authentic products.
Examples of companies	mPharma, SwipeRx, MaishaMeds, Shelf Life	MYDAWA, Kasha, ePharmacy mPharma, SwipeRx, MaishaMeds	Sproxil, PharmaSecure, mPedigree, Chekkit, RxAll
Companies operating in Zambia	mPharma, ViaGlobalhealth	RightePharmacy, HnG online pharmacy, mPharma	mPedigree

Innovation in distribution to providers (pharmacies)

These companies focus on refining the traditional supply chain. Companies such as mPharma connect to the pharmaceutical sector, reduce costs, and improve patient care [85,88]. Others such as Shelf Life and MaishaMeds, use technology and models 'pay as you sell' consignment inventory to retail pharmacies as a subscription service, which helps pharmacies to forecast and optimise inventory without overstocking medicine and expiries [84,89] to optimise inventory. Additionally, they connect patients to local pharmacies and use technology-based systems.

Innovation in distribution to customers (ePharmacies)

E-pharmacies, which are gaining popularity in LMICs, are revolutionising how health products are accessed. These ePharmacies incorporate aspects of telepharmacy, online services, and delivery, and

employ innovative features such as agent-led delivery, digitally enabled direct-to-consumer (D2C) distribution, smart ATMs and lockers, reverse price auctions, and retail partnerships [84]. Companies such as RightePharmacy employ technological innovations such as medication-automated teller medicine machines (ATMs), while Healthy Entrepreneurs empower community health workers with access to generics [90].

Innovation in product data and medicines authentication

Companies such as mPedigree and Sproxil have developed mobile authentication systems to verify the authenticity of medicines and detect falsified medicines. Such systems include product locators, quality scanners, and track-and-trace features to ensure that consumers receive genuine products [91,92]. Others, such as PharmaSecure, use a scalable, cost-effective approach for the mass authentication of pharmaceutical products [84,93]. The company uses unique alphanumeric coding and encryption-based technologies that comply with GS1 standards, which are global standards for item identification and data sharing, enabling both track-and-trace capabilities and consumer authentication [94].

Defining Innovative Pharmacies

Innovative pharmacies diverge from traditional pharmacies by incorporating technologies into their services. They may offer avenues, such as e-pharmacy, telepharmacy, and smartphone app functionalities. Typically, these pharmacies might utilise computerised inventory systems and medicine authentication tools. This thesis focuses on innovations in distribution to providers (pharmacies).

Potential Benefits of Innovative Pharmacy Distribution Channels on Medicine Quality

Innovative private pharmacy distribution channels have the potential to improve the availability of good quality medicine to patients. One potential benefit is simplification of the supply chain. A more straightforward and streamlined process reduces the risk of medicine degradation by ensuring that medicines spend minimal time in transit or storage [85]. In addition, integrating modern technology platforms facilitates the maintenance of efficient inventory management. innovations, such as blockchain technology, adopted by some innovators, aim to promote a more transparent supply chain. Such efforts could potentially aid in monitoring and addressing the presence of falsified medicines [95,96]. The integration of artificial intelligence (AI) by some innovators further augments these efforts. By potentially detecting irregular transactions and predicting areas susceptible to falsified drugs, AI aims to enhance the chances that quality medicines will reach end-users [97]. Furthermore, some AI systems have been designed to assist in distinguishing potentially substandard medicines, especially when paired with smartphones and colourimetric screening devices [98,99]. These devices, which can present challenges for human interpretation due to subtle colour variations, can benefit from AI's precision in differentiating colours.

Impact of Digital Innovations on Pharmaceutical Practice

The advent of digital innovations has spurred a shift in pharmaceutical practice, particularly within the context of LMICs. These advancements, as described by Heerdegen et al.[100], represent a fundamental shift in the delivery of pharmaceutical services and the accessibility of medicines. The integration of mHealth solutions transforms the patient-pharmacist dynamic, enhancing convenience and immediacy in healthcare service delivery. The widespread adoption of mobile devices can enable mHealth applications to facilitate remote consultations, prescription services, and home delivery of medications, thus overcoming historical geographic and logistical barriers [101,102].

E-commerce platforms can transform the landscape by establishing direct-to-consumer channels that circumvent traditional supply chain intermediaries, fostering transparency in procurement and the potential for more competitive pricing of medicines. Complementing these consumer-facing innovations are last-mile delivery technologies, such as drones, which promise to ensure equitable access to quality medicines for even the most remote and underserved communities. Backend digital tools are also enhancing the operational efficiency of pharmacies [103]. Advanced inventory management systems, utilising AI and data analytics, allow pharmacies to optimise stock levels, reduce drug waste, and maintain a consistent supply of essential medicines [104]. Blockchain technology is playing a pivotal role in safeguarding against counterfeit medicines, offering a secure and verifiable record of pharmaceutical provenance and supply chain transactions [105].

The potential of digital technologies to enhance the quality and accessibility of medicines is indeed substantial. Nonetheless, the realisation of this potential is neither automatic nor uniform across different settings. Heerdegen et al. [100] emphasise the importance of critically evaluating the efficacy of these innovations through empirical research, pointing out that while individual successes are reported, comprehensive studies are needed to measure the tangible impact of these innovations on medicine quality and the broader performance of the pharmaceutical sector. The research in this thesis contributes to that vital discourse, presenting a systematic assessment of the quality of medicines within innovative private pharmacy distribution channels in Zambia.

The infusion of technology into the pharmaceutical sector has initiated various innovative approaches to medicine distribution. Empirical assessment of these models is essential to determine their actual impact, which may differ from the potential benefits often proclaimed by technology proponents. Yadav and Glassman [85] suggest that the strategic application of new technologies and data analytics could significantly enhance medicine availability and affordability, urging global health stakeholders to engage with technology innovators to strengthen access to essential health products. Concurrently, the Salient Advisory report [84] notes that the COVID-19 pandemic has accelerated the adoption of

technology-enabled systems for health product and information delivery, highlighting a critical need for investment to improve medicine availability, particularly in rural settings. Furthermore, Miller et al. [106] observe the rapid expansion of ePharmacy in low- and middle-income countries, offering a novel avenue to expand medicine access. Nevertheless, they highlight a lag in regulatory adaptation to accommodate these technological advancements, which could impede their integration into the healthcare system. Collectively, these studies underscore the promise of innovative distribution channels while cautioning against overestimating their efficacy without careful consideration of regulatory and implementation challenges.

1.4 Hypothesis and Study Objectives

Research hypothesis

It is hypothesised that pharmacies supplied using innovative private pharmacy distribution channels have better quality of medicine than those available in independent pharmacies that use traditional supply chains.

Aim

This PhD research aimed to compare the quality of medicines (antimalarials and antibiotics) available in innovative pharmacies with those available in independent pharmacies that use traditional supply chains.

Objectives

Specific objectives to achieve the aim are as follows.

i. Assess and compare medicine procurement practices in innovative and independent pharmacies.
ii. Assess and compare medicine storage and transport practices in innovative and independent pharmacies.
iii. Assess and compare the knowledge, availability, and usability of screening technologies for medicine quality in innovative and independent pharmacies.
iv. Determine and compare the prevalence of poor-quality antimalarials and antibiotics sold in innovative and independent pharmacies.
v. Determine the shortcomings of the innovative pharmacy approach and the improvements needed to ensure that the patient receives good quality medicine.

1.5 Research Justification

Investigating the effects of innovative pharmacy distribution channels on medicine quality is critical and has far-reaching implications for global medicine policy. A notable gap exists in understanding

regarding the extent to which these channels influence medicine quality, presenting significant challenges for policy development aimed at enhancing access to quality assured medicines. There is an urgent need for research that not only quantifies the impact of these channels but also highlights potential risks and challenges.

Innovative pharmacy distribution channels offer a promising avenue for enhancing medicine quality (Figure 5). These channels have the potential to streamline supply chains, minimise intermediaries, and integrate trace and tracking technologies. This can lead to decreased waste and improved quality of medicine throughout the supply chain. The effectiveness of these channels is closely tied to improvements in medicine storage, transport, procurement, robust regulation, sourcing practices, and the tracking and tracing of medicines. A clear understanding of their impact on medicine quality is vital to inform policymaking that will increase access to good-quality medicines globally.

Proponents of digital innovation within the pharmaceutical sector advocate for the transformative potential of such technologies. Claims suggest that digital tools could significantly enhance the supply chain's efficiency, reliability, and transparency, potentially improving medicine quality [85,107]. However, these assertions must be weighed against peer-reviewed research findings to ensure a balanced perspective. Technologies like blockchain are acclaimed for their ability to provide indelible records of transactions, potentially curtailing the prevalence of counterfeit medicines. Likewise, artificial intelligence is posited as a means to forecast and mitigate supply chain disruptions and substandard products, enhancing the safety and quality of consumer medicines. While these propositions are persuasive, they require rigorous empirical validation.

The current literature reveals a scarcity of specific research on the impact of these technological innovations on medicine quality, representing a hurdle for crafting policies that enhance medicine accessibility. While some studies have explored the financial and accessibility aspects of these channels, the literature on their effect on medicine quality remains sparse, potentially hindering policy initiatives aimed at improving medicine accessibility. For instance, research in India [108] suggests that chain pharmacies may improve medicine quality through enhanced sourcing and quality verification technologies, motivated by profit. Conversely, a study in Uganda [109] observed a decrease in the sale of substandard and falsified (SF) antimalarials following the entry of an NGO providing higher quality alternatives. These instances highlight the necessity of a nuanced evaluation of the claims presented by technology proponents. A comprehensive understanding of digital innovations' implications on medicine quality is indispensable for policymakers to devise effective strategies that secure access to quality medicines globally.

Moreover, the emergence of new pharmacy distribution channels could result in a regulatory void, potentially compromising medicine quality. In several jurisdictions, existing legal frameworks are not well-suited to innovative channels like e-pharmacies and telepharmacy, which may not adhere to regulations designed for traditional brick-and-mortar operations, thereby placing patients at risk [106].

While a few publications address the quality of medicines in Zambia, comprehensive data on the extent of the SF medicine issue is lacking. To bridge this knowledge gap, this PhD research evaluated the quality of medicines from pharmacies supplied by innovative distribution channels in Zambia compared to those supplied through traditional supply chains. This research particularly focused on two widely used medicines – sulfadoxine/pyrimethamine (SP) and amoxicillin. Factors such as storage, transportation, procurement, sourcing, regulation, and use of screening technologies were examined.

This research offers insights into the impact of new distribution models on medicine quality, enriching knowledge on the role of innovative pharmacy distribution in LMICs. Ultimately, it aids in advancing access to good quality-assured medicines by highlighting the effects of these innovative channels and equipping stakeholders and policymakers with data-driven solutions.

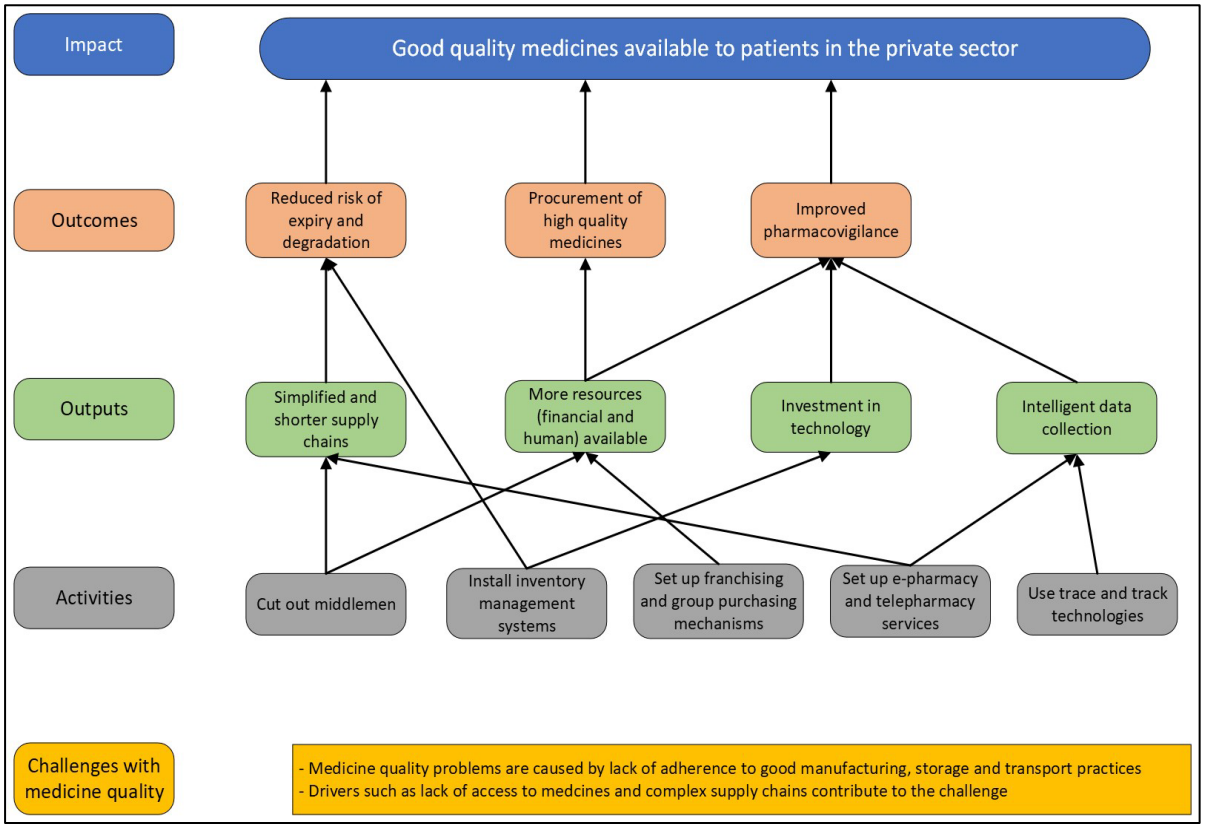

Figure 5: A logic model to describe the theory of change as it regards the potential benefits of innovative distribution channels

1.6 Study Setting

The research was conducted in the city of Lusaka, the capital of Zambia. Zambia, a landlocked country in sub-Saharan Africa, is classified as a low-middle-income nation with an approximate population of 19 million [110]. Zambia is divided into ten provinces, which are subdivided into districts, constituencies, and wards. Most of the population lives in rural areas and is dependent on an agriculturally based economy, with copper and cobalt exports driving the economy [111]. In 2019, 44% of the population lived in the urban areas. According to the World Bank, Zambia faces several health challenges, including a life expectancy at birth of 64 years, a maternal mortality rate of 213 deaths per 100, 000 live births, and a child mortality ratio of 62 deaths per 1, 000 live births [110]. Lusaka Province has a population of approximately three million people, with around 80% residing in the Lusaka district. Generally, the province has higher average household income, education level, and access to healthcare services than many other parts of Zambia [111].

Figure 6: Map of Zambia showing the location of Lusaka Province, where the study was conducted.

Disease Burden in Zambia: Spotlight on Malaria and Pneumonia

Globally, malaria, diarrhoea, and pneumonia account for 45% of deaths in children below five years, with 41% of these fatalities occurring in sub-Saharan Africa [112,113]. In Zambia, pneumonia and malaria are the leading causes of morbidity and mortality in this age group [114–116]. Swift diagnoses and suitable treatments, such as amoxicillin for pneumonia and artemisinin-based combination therapy (ACT) for malaria, can substantially mitigate these effects. Sulfadoxine/pyrimethamine can be used to prevent malaria during pregnancy.

Malaria: Despite innovations in treatment and prevention, malaria remains a critical concern in countries such as Zambia [117,118]. All Zambians face the risk of this fever-inducing illness, primarily propagated by the female Anopheles mosquito that transmits Plasmodium parasites. Plasmodium falciparum is the deadliest form in the region, and is treatable with ACT [119]. Quinine is the primary remedy in severe cases. With support from international organisations, such as the President's Malaria Initiative, the World Bank, and the Global Fund, the Zambian government has implemented strategies such as long-lasting insecticidal net distribution and intermittent preventive treatments [120,121]. However, the grip of malaria remains tenacious in various Zambian regions.

Pneumonia: This respiratory disease is a leading cause of mortality and morbidity among children under five, but it also threatens immunocompromised adults and seniors with existing health concerns [115,116]. Co-infection with HIV and tuberculosis (TB) often exacerbates community-acquired pneumonia (CAP) in Zambia. The causes of CAP can include fungi and viruses such as Mycobacterium tuberculosis, especially among HIV patients. Treatments typically involve oral antibiotics; however, severe instances may necessitate hospital stay and intravenous drugs. Addressing pneumonia also means accounting for coexisting conditions such as HIV or TB. The Integrated Community Case Management (ICCM) strategy in Zambia involves community health workers managing pneumonia, referring severe cases to health facilities for intensive care [114,116].

The Organisation of the Health System

The healthcare system in Zambia comprises public, private-for-profit, and private non-profit providers. The Ministry of Health oversees the coordination and administration of the entire health sector with sector coordination structures established at the national, provincial, district, and community levels to facilitate effective coordination. Healthcare services are organised in a pyramidal structure, with primary healthcare services at the community level, hospitals at the district and provincial levels, and tertiary services at the national level [122,123].

Level 1 healthcare providers include health posts, health centres, mini-hospitals, and district hospitals that primarily serve catchment populations of 500 - 10,000 households for health posts and health centres in rural areas. Mini-hospitals and district hospitals can serve a catchment population between 50,000 - 80,000 households. Level 2 hospitals provide secondary care and curative care in paediatrics, obstetrics and gynaecology, and general surgery. They can serve catchment populations of 200,000 - 800,000 households. Level 3 comprised tertiary hospitals with a catchment population of at least 800,000.

Apart from the public healthcare system, private and non-profit health facilities are registered throughout the country by the Health Professions Council of Zambia (HPCZ). These include primary

health centres and Level 1 hospitals in Lusaka. The private sector also includes retail pharmacies that form part of the health structure registered by the Zambia Medicines Regulatory (ZAMRA). According to the ZAMRA 2020 registry [124], there are 641 registered pharmacies in Zambia, with 66% in Lusaka province. In 2016, ZAMRA developed guidelines to transform unregistered drug shops into health shops and open new health shops [125]. However, several unregistered drug shops, particularly those in high-density areas, were not included in this research.

Medicines Distribution in Zambia

The distribution of medicine in Zambia involves both public and private sectors. The government, through the Ministry of Health (MoH), provides approximately 60% of all medicines to the public sector with support from cooperating partners such as the United Nations Development Program (UNDP), Churches Health Association of Zambia (CHAZ), United Nations Children's Fund (UNICEF), and the United States Agency for International Development (USAID) [126,127]. On the other hand, the private sector supplies approximately 40% of the medicines due to medicine shortages in the public sector [128].

The selection and quantification of medicines in the public sector are based on budgetary and cost-benefit analyses, guided by the National Essential Drug List (EML). The selection committee comprises staff from the MoH, Zambia Medicines Regulatory Authority (ZAMRA), and Zambia Medicines and Medical Supplies Agency (ZAMMSA) [129], with support from cooperating partners such as the Global Fund, PEPFAR, and USAID. ZAMRA, the national regulator, is responsible for product registration, licencing pharmaceutical facilities, and post-marketing surveillance [124].

The government procures medicines through the MoH with the participation of ZAMRA, ZAMMSA, and cooperating partners. ZAMMSA specialises in the storage and distribution of medical supplies and manages the storage of medicines on behalf of the MoH. The Agency then distributes the medicines according to a schedule to all public health facilities, with ZAMRA ensuring the quality of medicines stored in both ZAMMSA and health facilities.

The distribution of private sector medicine in Zambia involves importers, wholesalers, sub-wholesalers, pharmacies, health shops, and drug stores [76]. Pharmaceutical importers and wholesalers serve as intermediaries between pharmaceutical manufacturers, mainly located outside Zambia, and retail pharmacies and hospitals. Although Zambia has about five leading local manufacturers of pharmaceutical products, they fulfil only about 10-15% of the demand for pharmaceuticals. Zambia largely depends on imports from other countries, especially India, for 80% of essential medicines [126,130].

Pharmaceutical wholesalers provide both a distribution and stockholding function, which allows retail pharmacies to be supplied with adequate quantities to meet their daily needs. This also ensures that pharmacies do not have to maintain large stocks, mainly because of the lack of storage space.

Approximately six major wholesalers account for a significant portion of this volume [76,124]. Wholesalers and sub-wholesalers rely mainly on three primary distribution methods: delivery by wholesaler vehicles, private couriers, and customer pick-up. Although distribution by wholesaler vehicles is typically concentrated in the capital city and a few principal towns, some wholesalers use smaller vans to distribute beyond the main roads and into rural areas. Some wholesalers use public transportation methods, including minibuses, to deliver their products to distant customers.

Innovative Medicine Distribution in Zambia

In recent years, several innovative companies have emerged in Zambia to improve medicine distribution. These companies include mPharma, Right ePharmacy, ViaGlobalHealth, HnG Online Pharmacy, and mPedigree. For example, mPharma manages about 30 pharmaceutical inventories in Lusaka, including six of its own Kumera pharmacies and around 22 Mutti pharmacies, through its franchise mechanism. HnG Online Pharmacy has an online platform that allows retail pharmacies and individuals to order and purchase medicines delivered in Lusaka. mPedigree is currently using its authentication technology in the agriculture sector for agro-inputs and expanding into human medicines. RightePharmacy, on the other hand, operates three parcel collection units and has been identified as a potential service provider for the centralised chronic medicine dispensing and distribution (CCMDD) IT system by EQUIP. Other companies offer diverse services within the pharmaceutical sector in Zambia. For instance, MEDSEARCH Zambia specialises in providing direct pharmaceutical education and online pharmacy services. MEDGET Zambia offers specialised courier services, connecting brick-and-mortar pharmacies with customers seeking medical deliveries. Additionally, a few independent and chain retail pharmacies, such as Link Pharmacy, are exploring online delivery and telepharmacy services in Lusaka.

Role of Private Pharmacies in Health-Seeking Behaviours

In Zambia, residents are generally encouraged to use the health centre or health post nearest to them as their initial contact with the health system. From there, they may be referred to a hospital if further care is required. Although primary care is free at these health centres or posts, patients will incur a bypassing fee if they proceed directly to a hospital [123].

Despite the incentives to utilise lower-level facilities, there is evidence indicating that many bypass these centres entirely [111,122,131]. Instead, they directly seek care from retail pharmacies or opt for other hospitals and clinics in the private sector. Factors driving this behaviour might include geographical constraints, prolonged waiting times or tendencies towards self-prescribing [80,125,12]. Furthermore, although antimalarials and antibiotics are provided at no charge in public health institutions, they

occasionally run out of stock. This scarcity often pushes patients towards private outlets for their medicinal needs [25,122,132].

In Zambia, as seen in several LMICs, both the informal and private sectors contribute significantly to addressing the population's health needs. These include community health workers, drug sellers, traditional healers, and private retail outlets. Notably, private retail outlets frequently become the primary, if not sole, resource for the treatment of ailments such as malaria and pneumonia [133]. A study in Lusaka involving 620 households discovered that 71% of adults and 59% of children bypassed primary care facilities for treatment [122]. A significant portion of children, about 21%, were treated at drug shops or pharmacies, pointing to a strong reliance on the informal sector for child health.

Substandard and Falsified Medicines in Zambia

The Zambia Medicines Regulatory Authority shoulders the responsibility of ensuring that medicines and related substances in Zambia meet the quality, safety, and efficacy standards [134]. To achieve this, ZAMRA deploys both active and passive surveillance techniques. Active measures include post-marketing inspections, visual assessments, label evaluations, and rapid field screenings using tools such as GHPF-Minilab® [135]. The National Quality Control Laboratory (NQCL) also assists in analysing medicine samples. Passive surveillance involves alerts from global entities, other regulatory bodies, patients, and the pharmaceutical sector.

Although there is a dearth of precise data on the prevalence of substandard medicines in Zambia, a few studies have provided insights. Bate et al.[136] investigated the quality of medicines in several African cities, including Lusaka, and discovered that the prevalence of substandard medicine sampled in Lusaka between 2008 and 2009 was 10.3% (8/78). The research evaluated antimalarial and antibiotic samples using the Minilab® and found that the overall prevalence in Africa was 18.6% (ranging between 3.6% to 31.1% across cities). The ACT-watch consortium worked with the national malaria control programs in six African countries, conducting outlet surveys between 2008 and 2014 [132,137]. In Zambia, the surveys revealed that the percentage of public facilities that stocked non-quality assured ACTs increased from less than 5% in 2008 to 31.6% in 2014. A 2017 study analysed three vials of propofol from two different batches using gas chromatography-mass spectrometry methods and found that none of the analysed vials contained the stated amount of propofol and, therefore, were substandard [138]. The study was conducted as a result of clinicians throughout Zambia noting unpredictable adverse events after the administration of propofol.

In 2019, ZAMRA piloted the use of the Minilab® in post-market surveillance at hospitals in three provinces [135]. The survey found that 17.6% (22/125) of essential medicine sampled, including antimalarials, did not pass. An impact assessment using an agent-based model, SF antimalarial

research impact (SAFARI), estimated that eliminating substandard and falsified antimalarials in Zambia would result in an 8.1% reduction in under-five deaths, prevent 937 hospitalisations, and save $8.5 million [27]. Furthermore, a recent study in 2022 reviewed the product recalls issued by ZAMRA between January 2018 and December 2021 [139]. Most of the pharmaceutical products recalled in this period were substandard products caused by manufacturing laboratory control issues. Antiseptics (20.5%) and antibiotics (16.9%) represented the most recalled products, and many of them were manufactured in India (38.6%), followed by Zambia (25.3%).

1.7 Thesis Structure

This thesis is structured into seven chapters, beginning with an introduction and concluding with a general discussion and recommendations.

Chapter 1: (Introduction) provides a comprehensive overview of innovative private pharmacy distribution channels in Zambia, presenting background information, a literature review, and insights into the study setting. It also includes the research aim, objectives, and guiding hypotheses.

Chapter 2: (Characteristics of Innovative and Traditional Independent Pharmacies in Lusaka, Zambia) ventures into a descriptive comparison of the two pharmacy types. It investigates a spectrum of attributes, from physical appearance and location to staff qualifications.

Chapter 3: (Assessment of Medicine Storage, Transportation and Procurement Practices) The practices in innovative and traditional pharmacies in Lusaka are juxtaposed to determine their implications on medicine quality.

Chapter 4 (Comparative Analysis of Medicine Quality Surveillance) delves into the technological aspects and reporting practices adopted by pharmacies and contemplates the repercussions of these practices on overall medicine quality surveillance.

Chapter 5 (Quality of Medicines) focuses on the quality of medicine quality and factors that may influence the quality. Using amoxicillin and sulfadoxine/pyrimethamine as case studies, this chapter explored the potential variations between the two types of pharmacies.

Chapter 6 (Stakeholder Perceptions on Innovative Private Pharmacy Distribution Channels) is a qualitative exploration of the perspectives of various Zambian stakeholders. This chapter reveals the insights gained from pharmaceutical professionals, innovators, wholesalers, and retailers.

Finally, *Chapter 7 (General Discussion)* offers a comprehensive research summary, discussing significant findings, implications, and limitations of the study. Recommendations for stakeholders and reflections on the broader consequences of Zambia's healthcare system are also presented.

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Chapter 2: Research Paper 1 - Characteristics of Outlets

Chapter Introduction

The second chapter of this thesis explores the characteristics of innovative and traditional independent pharmacies in Lusaka, Zambia. As stated in the Introduction, the pharmaceutical sector in Africa, including Zambia, is transforming. Entrepreneurs are introducing innovative strategies, such as telepharmacy, delivery services, and e-pharmacies, diversifying the pharmaceutical supply chain. However, there is a gap in the academic literature on the impact of these innovations.

This chapter bridges this gap by providing a descriptive comparison between innovative and traditional independent pharmacies. This study scrutinises an array of attributes, from pharmacy organisation and physical appearance to geographical location and staff qualifications.

Employing a mixed-methods approach, the research combines quantitative surveys and qualitative narratives from key informants to provide a comprehensive view of the pharmaceutical landscape. These insights are not only academically significant but also inform public health policy decisions, presenting a detailed understanding of the current state of pharmacies in Zambia and highlighting areas warranting further research.

Adhering to the structure outlined for biomedical journals, this chapter, a cornerstone of this thesis, comprises an introduction, methods, results, and discussion sections. The research narrative will be submitted to BMJ Public Health.

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1403479	**Title**	Mr
First Name(s)	Scott Kaba		
Surname/Family Name	Matafwali		
Thesis Title	Innovative Private Pharmacy Distribution Channels: Implications on Medicine Quality in Zambia		
Primary Supervisor	Dr Harparkash Kaur		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	BMJ Public Health under BMJ Journals
Please list the paper's authors in the intended authorship order:	Scott Kaba Matafwali, Ron Behrens, Sian Clarke, Harparkash Kaur
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conceptualised the study and developed the protocol with methodological guidance from my supervisors and advisory team. Additionally, I conducted the fieldwork, analysed the data, and wrote the first drafts of the manuscript. I also revised the manuscript based on feedback from co-authors.

SECTION E

Student Signature	[redacted]
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Supervisor Signature	[redacted]
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Characteristics of Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: A Descriptive Comparison

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Abstract

Introduction: In LMICs, entrepreneurs are using innovative technology and business models to improve traditional pharmaceutical supply chains, with the goal of increasing access to affordable, quality-assured medicines. This study compares innovative and traditional independent pharmacies in Lusaka, Zambia, to provide insights into their operations and contributions to healthcare access and patient safety in the country.

Methods: A cross-sectional survey was conducted among 52 pharmacies in Lusaka, Zambia, with an equal representation of innovative and traditional independent pharmacies. Data collection encompassed store appearance, location, organisation, and services offered. Additionally, information on the characteristics of the available amoxicillin and sulfadoxine/pyrimethamine medicines was gathered.

Results: Innovative pharmacies in Lusaka demonstrated a broader spectrum of services, including delivery (65.4%), ePharmacy (61.5%), and telepharmacy (76.9%). In contrast, only a limited percentage of traditional independent pharmacies offer delivery (7.7%) and telepharmacy (3.8%) services, with none providing ePharmacy. These innovative pharmacies often occupy shopping malls (46.2%), have better aesthetic features, and employ franchise models. Approximately half of the traditional independent pharmacies are located in peri-urban areas. Moreover, innovative pharmacies stock amoxicillin sourced from a more diverse set of countries (six in total) than their traditional counterparts, which primarily originate from four countries, with some medicines having unknown origins. Notably, amoxicillin's unit price was higher in innovative pharmacies, with an average of 49.50 Kwacha, compared to the 29.25 Kwacha average in traditional pharmacies.

Conclusion: Both innovative and traditional independent pharmacies play a crucial role in providing access to quality-assured medicines in Zambia. Innovative pharmacies present certain advantages in terms of appearance, organisation, location, and services. However, the study did not explore the potential impact of these characteristics on the quality of medicines, patient outcomes, and

satisfaction in depth. Future research should further investigate these aspects to enhance the quality of healthcare services and access to medicine in Zambia.

Keywords: Medicine Quality, Innovative, Traditional, Independent, Pharmacy, Substandard, Falsified, Characteristics, Zambia

Introduction

Private pharmacies in low- and middle-income countries (LMICs) play a crucial role in providing access to healthcare for communities, which is an important step toward achieving universal health coverage (UHC). They are often the first point of contact for individuals seeking healthcare advice and medication [1,2]. Furthermore, private pharmacies in many LMICs are often the only source of healthcare for individuals living in remote or rural areas where access to healthcare facilities is limited [3,4]. These private pharmacies provide several advantages, such as longer opening hours and not requiring appointments, making them a convenient option for individuals who may have difficulty accessing healthcare during regular business hours [2,5]. In addition, private pharmacies are typically well-stocked with all essential medicines, whereas public health facilities often struggle to maintain an adequate supply [6,7]. This scarcity often arises because of various factors, including irregular funding and a lack of proper supply chain management.

Furthermore, private pharmacies are responsible for ensuring that the medicines they dispense are quality assured [8]. Ensuring the quality of essential medicines is crucial to ensure patient safety and outcomes. Therefore, pharmacy personnel, including pharmacists in these private pharmacies, are crucial for improving and maintaining pharmacy practices [9,10]. They must have adequate knowledge about medicines and patients must receive accurate and appropriate information about their medicines.

Despite their essential role in providing access to healthcare advice and medicines in LMICs, private pharmacies in these countries often operate below acceptable standards and focus more on profit than on patient care [2,11]. These challenges include the presence of poor quality [substandard or falsified (SF)] medicines, poor storage of medicines, and the sale of medicines, such as antibiotics and other medicines without prescriptions. Indiscriminate use of antimicrobials is a major driver of antimicrobial resistance (AMR) [12–15]. These challenges can undermine the quality of the service they provide and pose a significant risk to patient safety [16,17].

The pharmaceutical landscape in Africa, including Zambia, is beginning to show signs of an emergent transformation [18]. This nascent shift, while not yet widespread, is being catalysed by entrepreneurs who are leveraging innovative technologies and business models to tackle the challenges endemic to traditional pharmaceutical supply chains [19]. Although comprehensive data specific to Zambia is limited, these changes echo broader trends observed across the continent, suggesting a potential for significant evolution in the sector. These entrepreneurial initiatives primarily focus on enhancing availability and affordability of medicines. Various services have been introduced to achieve this, including advanced inventory management systems, strategic retail pharmacy partnerships, and

counterfeit detection systems. The implementation of these innovations is expected to curtail healthcare costs and improve the availability of essential health products, heralding a promising shift in the accessibility and affordability of healthcare commodities.

In Zambia, the public sector, backed by cooperative partners, is responsible for supplying approximately 60% of all medicines, with the private sector contributing the remainder [20]. The distribution of medicine in Zambia's private sector is carried out through a network of importers, wholesalers, sub-wholesalers, pharmacies, health shops and drug stores [21]. The private retail sector comprises small-scale informal providers, private pharmacies at clinics, drug stores, and formal private pharmacies [22]. The number of independent pharmacies in Lusaka, the capital of Zambia, has increased over time. Additionally, there has been a steady increase in innovative pharmacies that leverage technology and business models to address challenges in traditional pharmaceutical supply chains.

This study aimed to fill this gap in the literature by investigating the characteristics of innovative and traditional independent pharmacies in the private sector. Despite their growing prevalence, innovative pharmacies remain largely under documented. By comparing these two types of pharmacies, this study aimed to understand their role in providing access to medicine and how they compare the quality of medicine. No study has examined the characteristics of the two groups of private pharmacies. By gaining a deeper understanding of the unique characteristics of these pharmacies in Lusaka, this study hopes to contribute to the development of strategies for improving access to healthcare and ensuring patient safety in the country.

Methods

Study Design and Setting

A cross-sectional survey was conducted from August to September 2022 in Lusaka, the capital and most populous city of Zambia, with an estimated three million inhabitants. Lusaka serves as a central hub for the nation's economic, political, and healthcare activities, and it boasts a diverse population with a wide range of socioeconomic backgrounds. The city's urban centres, often characterised by shopping malls and commercial districts. These areas typically feature a variety of services and amenities that cater to a relatively affluent clientele [23,24]. In contrast, Lusaka's peri-urban areas are home to communities with lower socioeconomic status [25,26]. These rapidly growing zones often face challenges in healthcare access, primarily due to limited resources and infrastructure, a situation that particularly affects residents in low-income areas [27]. This study specifically chose Lusaka because its large population and diverse healthcare settings provided a representative sample of innovative and independent pharmacies. At the time of the study, the absence of innovative pharmacies outside Lusaka further validated this choice.

Study population

Definitions of pharmacies

In this study, pharmacies refer to registered entities in Zambia that are registered with the Zambia Medicines Regulatory Authority (ZAMRA) and are required by law to have a full-time pharmacist. The sizes and structures of these pharmacies can vary. According to the guidelines set by the ZAMRA for establishing a pharmaceutical retail business, the outlet should have certain features, including a pharmacy size of at least 50 square meters, an adequate dispensary area, and a functioning refrigerator [28].

Defining Traditional Independent Pharmacies

Traditional independent pharmacies refer to privately-owned pharmacies that are not part of a larger chain or corporation [29,30]. These pharmacies are typically operated by a pharmacist or a group of pharmacists who prioritise providing personalised care and building relationships with their customers. These pharmacies are commonly referred to as "mom-and-pop" shops and are considered essential healthcare resources in local communities. In this study, traditional independent pharmacies were defined as privately owned outlets typically owned by an individual and supplied by traditional supply chains.

Defining Innovative Pharmacies

Innovative pharmacies in this study are those that stand apart from traditional models by integrating technology into their operations. These include services aimed at healthcare providers such as hospitals, clinics, and pharmacies, with a focus on technology-driven solutions including pharmacy inventory-management software, vendor-managed inventory services, fulfilment services, and stock financing. The innovative pharmacies selected for this study are representative of a prevalent model within the Zambian context, with the majority (24/26) being part of a single, dominant company known for innovating in distribution to providers (at the pharmacy level).

Eligible population

The sampling frame was pharmacies registered with ZAMRA and the latest master list was obtained from the ZAMRA website. Pharmacies were selected using two-stage sampling by first stratifying them according to whether they were supplied by innovative pharmacy distribution channels or traditional supply chains. Innovative pharmacies were identified with the assistance of a medical information and education company called Medsearch Zambia, and KIs in the pharmaceutical sector. The pharmacies were then cross-checked against the characteristics described in Salient Advisory reports [19].

Inclusion criteria: The study includes traditional independent pharmacies are defined as privately owned outlets that are typically owned by an individual and supplied by conventional supply chains.

It also includes innovative pharmacies that are registered as independent but are predominantly part of a single company that exemplifies the innovative model under investigation. These pharmacies are selected for their use of advanced technological solutions in distribution and patient engagement, which distinguish them from traditional setups.

Exclusion Criteria: The study did not include chain outlets, health shops, or drug stores. Chain pharmacies have been excluded from this study due to their fundamentally different operational structures, which often involve more standardised processes and centralised management. These larger entities to have different operational constraints and resources, which could confound the assessment of practices in traditional pharmacies.

Sampling of the pharmacies

A sampling of the pharmacies was conducted in two stages. First, an exhaustive sample of all pharmacies (n=333) in Lusaka was obtained from the Zambia Medicines Regulatory Authority (ZAMRA). Chain outlets (n=96) were then excluded from the list, leaving 273 innovative and traditional independent pharmacies. The list was then stratified into two groups: innovative pharmacies (n=26) and traditional independent pharmacies (n=247). All 26 pharmacies classified as innovative were selected for this study, while a random sample of 26 traditional independent pharmacies were included. Four traditional independent pharmacies refusals were encountered. For each refusal, an alternative pharmacy in close geographical proximity was selected to ensure integrity and representation of the original stratification. Figure 2 shows the flowchart pharmacy outlet selection.

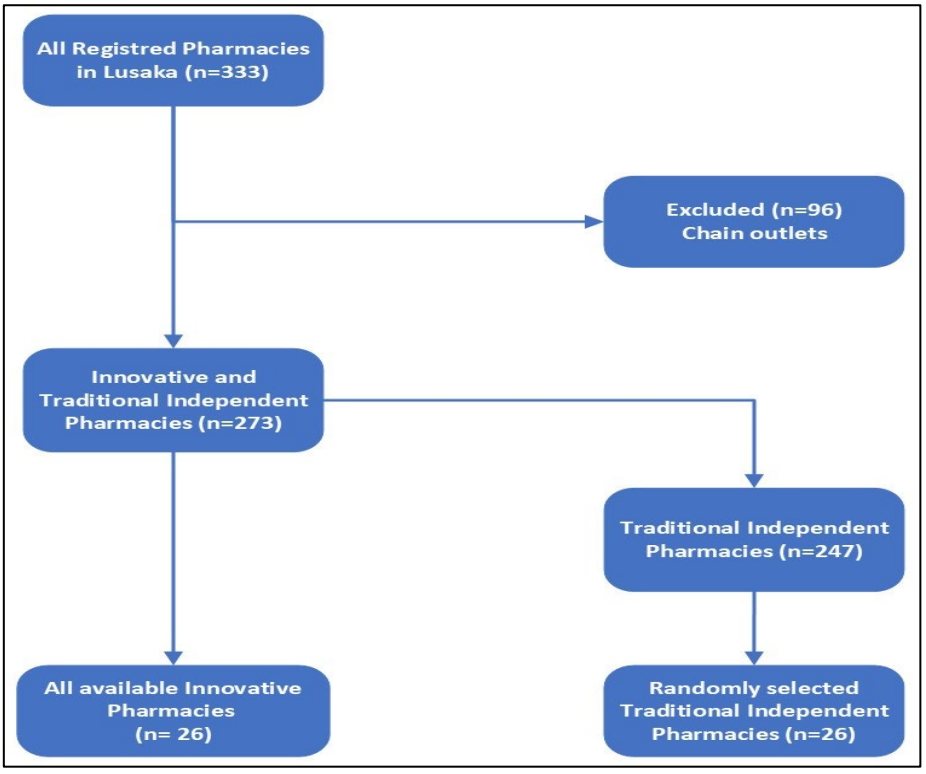

Figure 2: A flowchart of the selection of pharmacies

Rationale for focus on a predominant Innovative company: The decision to concentrate on pharmacies primarily associated with one company was influenced by practical constraints as much as by the company's leading role in shaping recent innovative pharmacy practices in Zambia. At the time of the study, 26 of innovative pharmacies listed by ZAMRA were operational, and 24/26 of these were affiliated with this particular company. This prevalence underscores the company's significant influence in implementing technological innovations at scale. Although the choice was partly dictated by the limited availability of diverse innovative pharmacy models, focusing on this company provides a valuable case study for understanding the impact and scalability of such innovations in Zambia. This approach allows for a concentrated examination of how technological advances are being adopted at the pharmacy level and their implications for healthcare service delivery in the region.

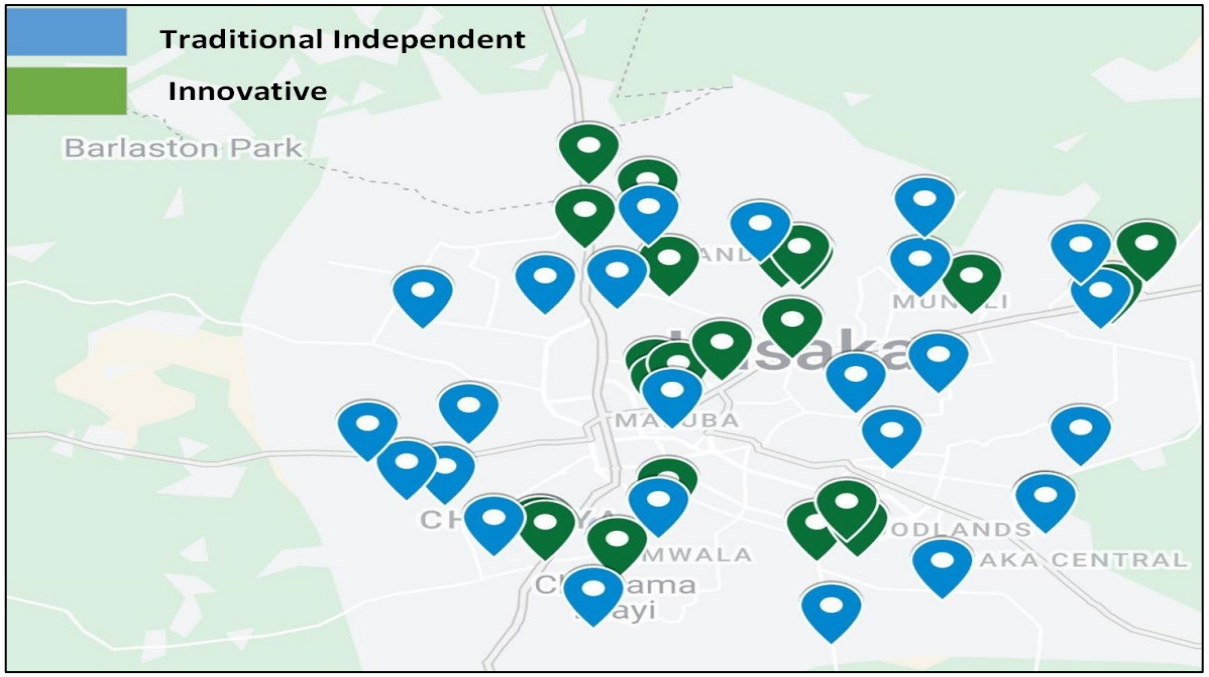

Figure 1: A map of Lusaka was created to show the distribution of pharmacies visited, with blue dots representing traditional independent pharmacies and green dots representing innovative pharmacies.

Study Participants

The participants in the survey consisted of pharmacy-qualified personnel, including pharmacists and pharmacy technologists, who were present in the outlet on the day of the survey. In cases where no pharmacy personnel were present, the study engaged with the most qualified individuals available, such as pharmacy managers or shop assistants.

Questionnaire Design and Data collection

A structured questionnaire was used to collect information on various aspects of the pharmacy, including the type of outlet (innovative or traditional independent), location, types of services offered,

outlet demographics (including pharmacy staff present at the time of the survey), qualifications of personnel, and years of work experience. Additionally, an outlet audit was conducted to assess the physical attributes of the pharmacy, such as cleanliness of the outlet, shelves, and storage space. The questionnaire was pre-tested and refined to ensure its validity and reliability. Furthermore, photographs of the outside appearance of the selected pharmacies were obtained. In this study, the details of amoxicillin and sulfadoxine/pyrimethamine (SP) were collected. These medicines, purchased for an accompanying quality analysis study (Chapter 5), were selected as tracer medicines owing to their widespread use and availability in both innovative and traditional independent pharmacies. Their presence across these different types of pharmacies enabled a meaningful comparison of characteristics, such as storage conditions, sourcing, and pricing.

Data Analysis

The data from the questionnaire and observations were transferred from ODK to Microsoft Excel for final cleaning and preparation for analysis. Descriptive statistics were used to present the participants' characteristics and responses to the questionnaire items. Frequencies and percentages were calculated for categorical data and means, and standard deviations were calculated for continuous data. To compare the differences between innovative and traditional independent pharmacies, chi-squared tests were conducted on categorical variables and t-tests were used for continuous variables. Data were analysed using SPSS 24.0, and statistical significance was set at $p < 0.05$.

Ethics Approval

Ethical approval for this study was obtained from the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022) in Zambia and the London School of Hygiene and Tropical Medicine Ethics Committee (Ref:28040) in the UK. Written Informed consent was obtained from all participants. Adherence to strict ethical and professional guidelines was ensured throughout the study to safeguard participants' confidentiality. The identities of the retail outlets and participants were kept anonymous.

Results

Classification and Operational Models of Pharmacies in Lusaka, Zambia

This research identified three distinct categories of pharmacies operating within Lusaka and Zambia: innovative pharmacies, traditional independent pharmacies, and chain pharmacies. Notably, innovative pharmacies were found to operate in two main formats: individual and franchise outlets. This information was gathered through a key informant from one of the companies in this sector. Conversely, traditional independent pharmacies are typically owned and operated by a single individual and typically manage a single outlet. This investigation also confirmed the presence of chain

pharmacies in this region. In a closer examination of the innovative pharmacy model, one company offered a unique "pharmacy in a box". This service represents a comprehensive franchising solution that integrates technology, marketing expertise, and business insights, to assist community pharmacies. Table 1 presents a visual overview of different types of pharmacies available.

Table 1: Types and Operational Models of Pharmacies in Lusaka, Zambia

Pharmacy Type	Sub-category	Included in study
Innovative	Independent	Yes
	Franchise	Yes
Traditional	Independent	Yes
	Chain	No

Appearance of pharmacies

The appearance of pharmacies in Lusaka, Zambia, was evaluated, and the findings showed that innovative pharmacies are generally associated with aesthetic appearance and branding (figure 3). The franchises under the innovative pharmacy company were also refurbished and branded with contemporary décor and signage, which is different from other pharmacies in these areas.

Figure 3: Illustration of the different types of pharmacies in Lusaka and Zambia through various images. Image (A) represents the outside of a typical traditional independent pharmacy, while image (B) represents the outside of a typical innovative pharmacy. Images (C) and (D) represent the internal appearance of the two types of pharmacies. Images A, B and C were taken during the research period (August to September 2022), while image D is a publicly available image [31].

Outlet Demographics and Personnel Characteristics

The distribution of pharmacy outlets in Lusaka, Zambia, is varied (table 2), with the largest proportion located in peri-urban areas 44.2% (23/52) and shopping malls 34.6% (18/52). A larger percentage of innovative pharmacies were located in shopping malls, 46.2% (12/26) than traditional independent pharmacies, 23.1% (6/26), though overallthere was no statistically significant difference in the outlet locations (p=0.301). Geographical representations of some locations shown in Figure 1.

The pharmacy personnel present at the time of the survey were primarily pharmacists 58.8% (28/52) and pharmacy technologists 32.7% (17/52). Pharmacists were more commonly found in innovative pharmacies, 69.2% (18/26), compared to traditional independent pharmacies, 38.5% (10/26), a statistically significant difference (p=0.041). The highest qualifications of personnel ranged from GCSE to Master's level, with the majority holding a degree 51.9% (27/52) or a diploma 40.4% (21/52). Personnel in innovative pharmacies were more likely to hold a degree 69.2% (18/26) than those in traditional independent pharmacies 34.6% (9/26). The difference in the highest qualifications between innovative and traditional independent pharmacies was statistically significant (p=0.032).

Gender distribution across the surveyed pharmacies was skewed towards males, 59.6% (31/52), with a slightly higher proportion in traditional independent pharmacies, 69.2% (18/52), compared to innovative pharmacies, 50.0% (13/26). However, the sex difference was not statistically significant (p=0.258). The mean years of professional experience were 4.19 (SD=2.9) and did not significantly differ between innovative and traditional independent pharmacies (p=0.794). The mean years of experience at the current outlet was slightly higher for personnel in innovative pharmacies 3.27 (SD=2.3) than in traditional independent pharmacies 2.34 (SD=2.1), but this difference was not statistically significant (p=0.139).

Table 2: Outlet demographics and personnel characteristics (Lusaka,2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N = 26	*p*-value
Location of outlets				
City centre	2 (3.8%)	1 (3.8%)	1(3.8%)	0.301[b]
Commercial area	9 (17.3%)	3 (11.5%)	6 (23.1%)	
Shopping mall	18 (34.6%)	12 (46.2%)	6 (23.1%)	
Peri urban	23 (44.2%)	10 (38.5%)	13 (50.0%)	
Personnel present at time of survey				
Pharmacist	28 (58.8%)	18 (69.2%)	10 (38.5%)	**0.041[a]**
Pharmacy technologist	17 (32.7%)	7 (26.9%)	10 (38.5%)	
Others*	7 (13.5%)	1 (3.8%)	6 (23.1%)	
Highest qualifications				
GCSE	1 (1.9%)	0 (0.0%)	1 (3.8%)	**0.032[b]**
Certificate	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Diploma	21 (40.4%)	8 (30.8%)	13 (50.0%)	
Degree	27 (51.9%)	18 (69.2%)	9 (34.6%)	
Masters	1 (1.9%)	0 (0.0%)	1 (3.8%)	

Gender				
Male	31 (59.6%)	13 (50.0%)	18 (69.2%)	0.258[a]
Female	21 (40.4%)	13 (50.0%)	8 (30.8%)	
Years of professional experience	Mean (SD)	4.2 (2.9)	3.9 (3.4)	0.794
Years of experience in the Outlet	Mean (SD)	2.3 (2.1)	3.3 (2.3)	0.139

[a]Pearson Chi-square test, [b]Fishers exact test. Others* The others included registered nurse (1), laboratory technician (1), cosmetician (1), shop assistant (1), pharmacy managers (2), and pharmacy student (1). Bold *p*-values indicate significant statistical differences.

Types of services offered by pharmacy outlets.

The results in Figure 4 show that all innovative and traditional independent pharmacies in this study offered fixed brick-and-mortar services. Additionally, Innovative pharmacies are more likely to offer a wider range of services than traditional independent pharmacies. Specifically, 65.4% of innovative pharmacies offer delivery services, whereas only 7.7% of traditional independent pharmacies offer this service. Similarly, 61.5% of innovative pharmacies offer Internet and ePharmacy services, while none of the traditional, independent pharmacies offer these services. Furthermore, 76.9% of innovative pharmacies offer telepharmacy services, whereas only 3.8% of traditional independent pharmacies offer this service.

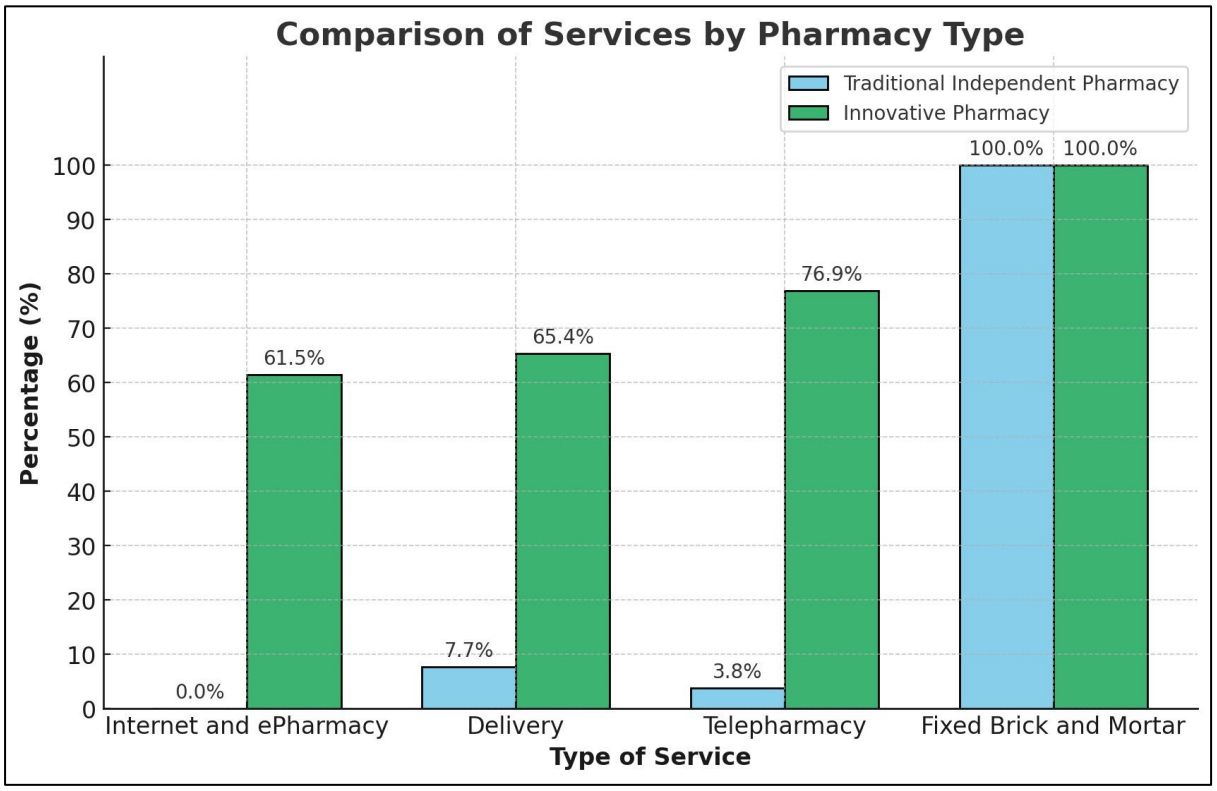

Figure 4: Types of services offered by the two types of pharmacies in Lusaka, Zambia

Medicine Sources and Prices

Amoxicillin

The survey identified 13 amoxicillin brands sold across each type of pharmacy. The amoxicillin available in innovative pharmacies came from six countries, whereas in traditional independent pharmacies from four, with some origins remaining unknown. Notably, Kenya was the most frequently stated country of manufacture, representing 44.7% (51/114) of all amoxicillin purchased. Both traditional independent pharmacies at 46.4% (26/58) and innovative pharmacies at 43.1% (25/56) displayed comparable proportions from Kenya. China accounted for 21.9% (25/114) of the country's total supply. However, its representation was significantly more pronounced in innovative pharmacies 27.6% (16/56) than in traditional pharmacies 16.1% (9/58), with a significant difference (p=0.010). The average price per unit of amoxicillin was higher in innovative pharmacies K49.50 (SD = 52.71) than in traditional independent pharmacies K29.25 (SD = 9.19) (p=0.005).

Sulfadoxine/Pyrimethamine (SP)

The survey identified four SP brands sold across each type of pharmacy. The SP available in innovative pharmacies came from two countries, whereas in traditional independent pharmacies, some origins remain unknown. Notably, the most commonly stated country of manufacture was India, representing 81.1% (43/53) of all SP. The price per unit of SP was slightly higher in traditional independent pharmacies K12.19 (SD=5.04) compared to innovative pharmacies K11.81 (SD=2.73), although this difference was not statistically significant (p=0.735).

Table 3: Medicine sources and prices (Lusaka, 2022)

		Total	Innovative pharmacy	Traditional Independent pharmacy	*p*-value
		N =114	N =58	N =56	
Amoxicillin	**Country of manufacture**				
	Kenya	51 (44.7%)	25 (43.1%)	26 (46.4%)	
	China	25 (21.9%)	16 (27.6%)	9 (16.1%)	**0.010**
	India	21 (18.4%)	9 (15.5%)	12 (21.4%)	
	Germany	5 (4.4%)	5 (8.6%)	0 (0.0%)	
	United Kingdom	3 (2.6%)	2 (3.4%)	1 (1.8%)	
	South Africa	1 (0.9%)	1 (1.7%)	0 (0.0%	
	Unknown	8 (7.0%)	0 (0.0%)	8 (14.3%)	
	Number of brands		13*	13	
	Price/unit(Kwacha)	Mean (SD)	49.5 (52.7)	29.3 (9.2)	**0.005**
		N = 53	**N = 26**	**N = 27**	
Sulfadoxine/pyrimethamine(SP)	**Country of manufacture**				
	India	43 (81.1%)	19 (73.1%)	24 (88.9%)	**0.005**
	Tanzania	7 (6.6%)	7 (26.92%)	0 (0.0%)	
	Unknown	3 (2.8%)	0 (0%)	3 (11.1%)	
	Number of brands		4*	4	
	Price/unit (Kwacha)	Mean (SD)	11.81 (2.73)	12.19 (5.04)	0.735

*For SP, some traditional pharmacies include repackaged SP with unknown brands. 3 brands were common to both Innovative and Traditional outlets, and each outlet type had 1 unique brand. For amoxicillin, some Traditional outlets include unknown brands. 8 brands were common to both groups, and each group had 5 unique brands. 1 Kwacha = 0.052 US dollars. Bold *p*-values indicate significant statistical differences.

Outlet Organisation

Table 4 presents the results of the outlet audit conducted to assess the conditions of innovative and traditional independent pharmacies in Lusaka and Zambia. The majority of the outlets surveyed 86.5% (45/52) were reported to be in good condition, with 100.0 % (26/26) of all innovative pharmacies falling under this category, while 73.1% (19/26) of traditional independent pharmacies were in good condition. This difference was statistically significant (p=0.051). Storage adequacy was reported in 80.8% (42/52) of all outlets, with all innovative pharmacies 100.0% (26/26) having adequate storage compared to 61.5% (16/26) of traditional independent pharmacies. This difference was statistically significant ($p < 0.001$).

Cleanliness of the shelves was observed in 84.6% (44/52) of the outlets. All innovative pharmacies, 100.0% (26/26), had clean shelves, while this was observed in 69.2% (18/26) of the traditional independent pharmacies. This difference was statistically significant (p = 0.004). Regarding storage conditions, 76.9% (40/52) of all outlets reported their shelves to be moisture-free. In innovative pharmacies, 88.5% (23/26) reported moisture-free shelves compared with traditional independent pharmacies 65.4% (17/26), but this difference was not statistically significant (p=0.097). The medicines were stored according to the First-Expiry, First-Out (FEFO) principle in 80.8% (42/52) of the outlets. All innovative pharmacies 100.0% (26/26) reported compliance with the FEFO principle, compared to 61.5% (16/26) of traditional independent pharmacies. This difference was statistically significant ($p < 0.001$).

Table 4: Outlet organisation (Lusaka, 2022)

	Total N =52	Innovative pharmacy N =26	Traditional Independent pharmacy N = 26	*p*-value
Outlet is in good condition				
Yes	45 (86.5%)	26 (100.0%)	19 (73.1%)	**0.051[a]**
No	7 (13.5%)	0 (0.0%)	7 (26.9%)	
Storage had adequate storage				
Yes	42 (80.8%)	26 (100.0%)	16 (61.5%)	**<0.001[a]**
No	10 (19.2%)	0 (0.0%)	10 (38.5%)	
Shelves were clean				
Yes	44 (84.6%)	26 (100.0%)	18 (69.2%)	**0.004[b]**
No	8 (15.4%)	0 (0.0%)	8 (30.8%)	
Shelves moisture-free				
Yes	40 (76.9%)	23 (88.5%)	17 (65.4%)	0.097[a]
No	12 (23.1%)	3 (11.5%)	9 (34.6%)	
Medicines stored according to FEFO				
Yes	42 (80.8%)	26 (100.0%)	16 (61.5%)	**<0.001[a]**
No	10 (19.2%)	0 (0.0%)	10 (38.5%)	

[a]Pearson Chi-square test, [b]Fishers exact test. Bold *p*-values indicate significant statistical differences. FEFO = First Expiry, First-Out

Discussion

This is the first comprehensive survey of innovative and traditional independent pharmacies in Lusaka, Zambia. A key finding of this investigation was the operational divergence between innovative and traditional pharmacy models. This divergence may have practical implications, particularly in how each model approaches the quality and accessibility of medicines. One of the innovative pharmacy companies studied operating retail pharmacies offered a transformative 'pharmacy in a box' service, a tech-enabled franchising solution that includes an inventory management system, marketing expertise, and insights for business growth and profitability. Franchising, such as this 'pharmacy in a box' model, is gaining recognition as a means to improve access to affordable, quality-assured medicines [32,33]. This method allows for the standardisation of processes, training, and quality control, potentially leading to better patient outcomes. Standardisation of pharmacies may significantly impact medicine quality by enhancing the control and regulation of critical aspects such as storage and procurement.

The innovative approach may offer significant benefits to the traditional independent pharmacies and often difficult-to-regulate entities such as drugstores in Zambia, as well as Accredited Drug Dispensing Outlets (ADDOs) in Tanzania and Patent and Proprietary Medicine Vendors (PPMVs) in Nigeria [2,34,35]. The potential for standardised processes and procedures to improve the quality of care and meet customers' changing needs is substantial. However, the potential drawbacks of franchising, such as reduced autonomy and inability to address the root causes of challenges in traditional pharmaceutical supply chains in LMICs, such as inadequate infrastructure and regulatory oversight, should be considered.

The innovative pharmacies in this study had an aesthetic appearance and stronger branding strategy than traditional independent pharmacies. Innovative pharmacies seem to be investing in modern branding techniques and contemporary décor, which creates a distinct and recognisable image for their pharmacies. This finding aligns with innovative pharmacies that aim to create a positive impression on customers and increase the perceived value of the services offered by pharmacies [32,33]. Moreover, franchise outlets under the innovative pharmacy company were refurbished and branded with company branding and signage, which distinguished them from other pharmacies in the area. The implications of these investments, such as their potential influences on customer satisfaction, loyalty, and profitability, present an interesting avenue for future research. This idea is supported by previous studies suggesting a possible relationship between the aesthetic appeal of pharmacies and shopper personality traits [36–38].

This study revealed the differences in operational characteristics, sourcing strategies, and pricing patterns between innovative and traditional independent pharmacies. Notably, innovative pharmacies are often located in shopping malls, potentially targeting high-income customers who could pay more for perceived higher quality. This aligns with findings from previous studies [29,39,40] in India, which suggested that financially better-off customers often patronised chain pharmacies in shopping malls, indicating that a centralised and convenient location may enhance business attraction for innovative pharmacies. Conversely, traditional independent pharmacies were predominantly found in peri-urban areas, likely catering to densely populated regions with a high demand for their services. This study also found that innovative pharmacies stocked various brands, such as amoxicillin, from different countries, resulting in higher prices. This could enhance their appeal to certain demographics. However, a notable challenge for traditional independent pharmacies is dealing with pharmaceutical products of unknown origin or brand, leading to issues in traceability and quality assurance. These differences underscore the need for tailored interventions to improve accessibility, affordability, and quality assurance in both innovative and traditional pharmacies.

This study revealed significant differences between innovative and traditional independent pharmacies in terms of personnel qualifications and presence at the time of the study. Notably, a higher proportion of pharmacists were present in innovative pharmacies during the study period, whereas traditional independent pharmacies had more pharmacy technologists. Furthermore, individuals in innovative pharmacies were more likely to hold degrees, whereas those in traditional independent pharmacies typically held diplomas. The higher presence of pharmacists within innovative pharmacies during the study period has important implications for many aspects of pharmaceutical care, including the quality of medicine, owing to their greater knowledge in areas such as storage, transportation, and surveillance [41,42]. In Zambia, pharmacists undergo an average of 5 years of training, compared to 3 years for pharmacy technologists [43].

The study also revealed instances of traditional independent pharmacies being staffed by individuals with no appropriate qualifications, including a student and cosmetologist, at the time of the study. This corroborates the findings from several studies in many LMICs, including Zambia, where antibiotics are often sold without a prescription or the presence of a pharmacist [15,44]. The presence of unqualified personnel may lead to the improper handling, storage, and dispensing of medicines, potentially resulting in medication errors and adverse patient effects. These findings emphasise the crucial role of appropriately qualified personnel in pharmacies in ensuring the correct handling and dispensing of medicines, contributing to optimal patient care.

The findings of this study revealed that innovative pharmacies in Lusaka, Zambia, offer a more extensive range of services than traditional, independent pharmacies. These services include internet pharmacy, telepharmacy and delivery services. This trend of innovative pharmacies utilising innovation and disruptive technologies to enhance their supply chains in the pharmaceutical sector has also been observed in other countries, such as Nigeria, Ghana, and Kenya [19,45]. This indicates that innovative pharmacies may be better equipped to meet the evolving needs and preferences of customers and adapt to new technologies, potentially leading to improved customer satisfaction, loyalty, and competitive advantage [46–48].

It is also worth noting that the findings of the outlet audit in this study revealed that innovative pharmacies have better storage conditions and practices for medicines than traditional independent pharmacies. This was evidenced by a lower proportion of inadequate storage, medicines not stored according to the first expiry first out (FEFO) system, and dirty shelves in innovative pharmacies. These results align with the observation that innovative pharmacies are often located in shopping malls, which tend to have better store conditions, as seen in other countries, such as India, in terms of chain pharmacies [2,40]. However, the reasons for these differences in storage practices between innovative and traditional pharmacies were not directly assessed in this study. Future research could explore whether factors such as different investment priorities in infrastructure or employee training contribute to these observed differences.

The study also found that innovative pharmacies had a higher proportion of medicines in stock and were stored according to the FEFO system than traditional independent pharmacies. This may be due to the use of modern technologies such as electronic systems and inventory management systems, which improve the accuracy and efficiency of medicine management and alert pharmacies to soon-to-expire medicines [48]. These findings suggest that innovative pharmacies have better practices and conditions for storing and organising medicines.

It is important to acknowledge the limitations of this study. First, the study was conducted in Lusaka, Zambia, and the results may not be generalisable to other locations in Zambia or other countries. An additional limitation is the uniformity of innovators from a single company, limiting the extrapolation of findings to other innovative pharmacy models across Africa. The study included only a small number of innovative and traditional independent pharmacies in the area, and the results may not fully represent the practices and conditions of all pharmacies in Lusaka or Zambia. The cross-sectional design of the study did not allow for the tracking of changes in pharmacy practices and conditions over time. Future studies should consider conducting longitudinal research to track the evolution of pharmacy practices and conditions in Zambia. It is also important to recognise that the study did not examine the economic, political, or regulatory factors that may have impacted the differences

observed. More research is needed to understand the complex interplay between these factors and their impact on the pharmaceutical sector in Zambia. Nevertheless, the study design was effective in gathering comprehensive data on pharmacies and provided a valuable understanding of their characteristics and challenges. Future research should build on these findings and further develop our understanding of the pharmaceutical sector in Zambia, particularly in relation to medicine quality.

Conclusion

The findings from this study underline the critical role that both innovative and traditional independent pharmacies play in providing access to essential medicines in Zambia. Innovative pharmacies distinguish themselves with superior aesthetic appeal, more organised storage, more qualified personnel, strategic location (such as shopping malls), and the application of franchise models. These characteristics, along with a broader range of services, including internet pharmacy, telepharmacy, and delivery services, could potentially improve the accessibility and quality of medicines. However, this study offers only a snapshot of Zambia's current pharmacy services landscape and acknowledges the need for more comprehensive research to fully discern the strengths, weaknesses, and opportunities for improvement for both types of pharmacies. Factors not explored in this study, such as economic, political, and regulatory influences impacting the observed differences in pharmacies, warrant further investigation to fully understand their effect on the country's pharmaceutical sector.

A specific point of interest that emerged from this research was the correlation between pharmacy practices and medicine quality. Innovative pharmacies, with their better storage and organisation practices, more qualified personnel, and adoption of standardised processes under franchising models, potentially contribute to maintaining the quality of dispensed medicines. However, the study identified challenges in traditional independent pharmacies, such as the sale of pharmaceutical products with unknown origins, which could pose a risk to medicine quality. In conclusion, the pivotal role of both innovative and traditional independent pharmacies in ensuring access to quality-assured medicines must be studied and understood. By gaining insight into their strengths and weaknesses, we can strive to enhance pharmacy services' overall quality in Zambia, thereby ensuring the population's access to the best possible healthcare. This objective can be achieved through collaborative efforts among policymakers, healthcare providers, and the private sector to foster an environment conducive to providing quality pharmacy services.

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Chapter 3: Research Paper 2 - Medicine Procurement, Transportation and Storage Practices

Chapter Introduction

The quality of medicines in retail pharmacies is pivotal to public health. Ensuring their safety necessitates the assessment of procurement, transport, and storage, core elements of pharmacovigilance. The pharmacovigilance aspect of healthcare monitors the safety and efficacy of medicines with the aim of detecting, assessing, and preventing adverse effects. Adherence to good procurement, transport, and storage practices mitigates the risk of distributing potentially substandard, falsified, or expired medicines that are detrimental to health. Systematic evaluation of these practices in pharmacy outlets highlights areas for enhancement, helping curb the spread of potentially compromised products and bolster patient trust.

As discussed in Chapter 2, innovative and traditional independent pharmacies in Lusaka, Zambia, have several characteristics that may affect their procurement, transportation, and storage practices. The main objective of this paper-style chapter is to assess and compare the procurement, transportation and storage practices of innovative and traditional independent pharmacies in Lusaka, Zambia. The study aims to provide insights into how these pharmacies store and distribute medicines consumed by the public in Lusaka, Zambia. This chapter delves into practices that could impact the quality of medicines, while the direct assessment of medicine quality is presented in Chapter 5.

The chapter answers two overall research objectives: (1) assess and compare medicine procurement practices in innovative and independent pharmacies, and (2) assess and compare medicine storage and transport practices in innovative and independent pharmacies. This chapter will follow the standard structure for biomedical journals, including an introduction, methods, results, and discussion. The study will be submitted to the Journal of Pharmaceutical Policy and Practice.

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Assessment of Medicine Procurement, Transportation, and Storage Practices in Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: Implications on Medicine Quality

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Abstract

Background: Medicine quality is a critical issue in low- and middle-income countries (LMICs). Innovative pharmacy models in LMICs are designed to address inefficiencies in the pharmaceutical supply chain. This study investigates the procurement, transportation, and storage practices of innovative versus traditional independent pharmacies in Lusaka, Zambia, assessing their implications for medicine quality.

Methods: A cross-sectional study was conducted in Lusaka, Zambia, covering 52 pharmacies: 26 innovative and 26 traditional independent pharmacies. Using a structured survey, we collected data on outlet characteristics and procurement, transportation, and storage practices. Additionally, information on the characteristics of the available amoxicillin and sulfadoxine/pyrimethamine medicines was gathered. Chi-square tests were used to assess differences between the two pharmacy groups. A *p*-value of less than 0.05 was deemed statistically significant throughout the study.

Results: Differences emerged between innovative and traditional independent pharmacies. While 80.8% (21/26) of the innovative pharmacies employed digital inventory and record-keeping systems, only 15.4% (4/26) of the traditional independent pharmacies did the same, with 73.1% (19/26) relying on manual processes. All Innovative outlets mainly procured from parent companies in contrast to traditional pharmacies that sourced extensively from wholesalers (100%) and sub-wholesalers (84.6%). Innovative pharmacies demonstrated a shorter procurement time, with mean times of 9.8 and 7.3 days for the two surveyed medicines.

All innovative pharmacies reported adherence to the first expiry first-out (FEFO) principle and distributor delivery as their primary mode of medicine distribution, compared to 61.5% (16/26) and 19.2% (5/26), respectively, for traditional independent pharmacies. Regarding infrastructure, 90.4% (47/52) of all pharmacies were equipped with a functioning air conditioner and 92.3% had functional refrigerators (48/52). Although 44.2% (23/52) of all outlets experienced power disruptions in the

preceding six months, 76.9% (20/26) of innovative pharmacies possessed a backup power source, compared to 26.9% (7/26) of traditional independent pharmacies.

Conclusion: Both pharmacy types demonstrated unique strengths and areas of improvement. Innovative pharmacies have exhibited advanced practices in inventory management and digital integration that can inform the best practices in Zambia. However, there is a clear need for enhanced training and education to guarantee medicine quality across the board. The results underscore the importance of structured pharmacy practices, emphasising the need for continuous personnel training.

Keywords: Medicine Quality, Innovative, Traditional, Independent, Pharmacy, Substandard, Falsified, Procurement, Transportation, Storage, Practices, Zambia

Introduction

Ensuring the quality of medicines is of utmost importance to prevent harm to individuals and to promote public health. With the globalisation of pharmaceutical production and distribution, regulatory systems worldwide face challenges keeping pace [1,2]. This mismatch has led to multiple pharmaceutical quality standards, particularly in low-income and middle-income countries (LMICs), where many National Medicines Regulatory Authorities (NMRAs) grapple with adequate quality standards [3–5].

Access to quality-assured medicine is paramount to the effectiveness of health systems and public health safety. Despite this, the prevalence of poor-quality medicines, especially in LMICs, is alarmingly high. It is estimated that up to 10% of the global medicine supply could be of substandard quality, leading to several issues such as treatment failure and even mortality [6]. These poor-quality medicines are primarily categorised as either falsified, where they are misrepresented in identity, composition, source [7], or substandard, where they fail to meet quality standards due to unchecked manufacturing issues. The emergence of substandard and falsified (SF) medicines is attributed to a plethora of issues in the supply chain, such as manufacturing defects, inadequate storage, mishandled transportation, and problematic procurement methods [7–9]. The quality and safety of the final product are profoundly influenced by the quality of raw materials, manufacturing processes, storage conditions, and procurement practices [10]. Factors such as extreme temperatures and moisture can compromise medicine integrity [11–13], and improper transportation or procurement from unverified sources further heightens the risk of SF products [8,14–16]. Thus, efficient storage, transportation, and procurement are the pivotal pillars of a resilient pharmaceutical supply chain.

Private pharmacies play an indispensable role in the distribution of medicines. In recent years, the advent of innovative channels within private pharmacies, such as online platforms, franchising, and home delivery services, has reshaped how patients access medicines [17,18]. While these pharmacies utilising modern channels offer enhanced accessibility and convenience, they also introduce new challenges in safeguarding medicine quality. In contrast, traditional independent pharmacies rooted in longstanding distribution practices have their own sets of challenges and advantages [19]. Regardless of the approach, both innovative and traditional private pharmacies must prioritise and maintain the quality of medicine. This not only safeguards public health, but also bolsters trust and credibility in the private healthcare sector.

The pharmaceutical supply chain in Zambia faces unique challenges [20–22]. Given the pivotal impact of procurement, transportation, and storage practices on the quality of medicines, this study aimed to examine and compare these practices across innovative and traditional independent pharmacies in

Lusaka. Through this analysis, this study intends to offer insights into their potential impact on medicine quality, serving as a foundation for informed strategies to curb the spread of substandard and falsified medical products.

Methods

Study Design and Setting

A cross-sectional survey was conducted between August and September 2022 in Lusaka, the capital city of Zambia. As the nation's most populous city, with an estimated three million inhabitants, Lusaka is a crucial hub for economic, political, and healthcare activities. The diverse health care infrastructure within this urban locale offers an ideal backdrop for sampling independent pharmacies. Pharmaceutical distribution in Zambia, predominantly in the private sector, is structured in a tiered manner, starting from importers, moving through wholesalers and sub-wholesalers, and finally reaching pharmacies, health shops, and drug stores [20,23]. Zambia has around five major local pharmaceutical manufacturers, meeting only about 10-15% of the country's pharmaceutical needs. Consequently, there is a heavy reliance on imports, with around 80% of essential medicines predominantly sourced from India [21,22]. Approximately 30 licenced major wholesalers operate within Zambia, ensuring regular supply for retail pharmacies. The wholesale sector predominantly comprises six major companies. Distribution methods vary, ranging from proprietary delivery systems to third-party services, ensuring that medicinal supplies reach both urban centres and peripheral areas.

Study Population

Definitions of pharmacies

In this study, pharmacies refer to registered entities in Zambia that are registered with the Zambia Medicines Regulatory Authority (ZAMRA) and are required by law to have a full-time pharmacist. The sizes and structures of these pharmacies can vary. According to the guidelines set by the ZAMRA for establishing a pharmaceutical retail business, the outlet should have certain features, including a pharmacy size of at least 50 square meters, an adequate dispensary area, and a functioning refrigerator [24].

Defining Traditional Independent Pharmacies

Traditional independent pharmacies refer to privately-owned pharmacies that are not part of a larger chain or corporation [29,30]. These pharmacies are typically operated by a pharmacist or a group of pharmacists who prioritise providing personalised care and building relationships with their customers. These pharmacies are commonly referred to as "mom-and-pop" shops and are considered essential healthcare resources in local communities. In this study, traditional independent pharmacies were defined as privately owned outlets typically owned by an individual and supplied by traditional supply chains.

Defining Innovative Pharmacies

Innovative pharmacies in this study are those that stand apart from traditional models by integrating technology into their operations. These include services aimed at healthcare providers such as hospitals, clinics, and pharmacies, with a focus on technology-driven solutions including pharmacy inventory-management software, vendor-managed inventory services, fulfilment services, and stock financing. The innovative pharmacies selected for this study are representative of a prevalent model within the Zambian context, with the majority (24/26) being part of a single, dominant company known for innovating in distribution to providers (at the pharmacy level).

Eligible population

The sampling frame was pharmacies registered with ZAMRA and the latest master list was obtained from the ZAMRA website. Pharmacies were selected using two-stage sampling by first stratifying them according to whether they were supplied by innovative pharmacy distribution channels or traditional supply chains. Innovative pharmacies were identified with the assistance of a medical information and education company called Medsearch Zambia, and KIs in the pharmaceutical sector. The pharmacies were then cross-checked against the characteristics described in Salient Advisory reports [19].

Inclusion criteria: The study includes traditional independent pharmacies are defined as privately owned outlets that are typically owned by an individual and supplied by conventional supply chains.

It also includes innovative pharmacies that are registered as independent but are predominantly part of a single company that exemplifies the innovative model under investigation. These pharmacies are selected for their use of advanced technological solutions in distribution and patient engagement, which distinguish them from traditional setups.

Exclusion Criteria: The study did not include chain outlets, health shops, or drug stores. Chain pharmacies have been excluded from this study due to their fundamentally different operational structures, which often involve more standardised processes and centralised management. These larger entities to have different operational constraints and resources, which could confound the assessment of practices in traditional pharmacies.

Sampling of the pharmacies

A sampling of the pharmacies was conducted in two stages. First, an exhaustive sample of all pharmacies (n=333) in Lusaka was obtained from the Zambia Medicines Regulatory Authority (ZAMRA). Chain outlets (n=96) were then excluded from the list, leaving 273 innovative and traditional independent pharmacies. The list was then stratified into two groups: innovative pharmacies (n=26) and traditional independent pharmacies (n=247). All 26 pharmacies classified as innovative were selected for this study, while a random sample of 26 traditional independent pharmacies were

included. Four traditional independent pharmacies refusals were encountered. For each refusal, an alternative pharmacy in close geographical proximity was selected to ensure integrity and representation of the original stratification.

Study Participants

The study targeted pharmacy personnel at the selected pharmacies on the day of the interviews. Where multiple staff members were present, preference was given to pharmacists and pharmacy technologists, given their direct involvement in the procurement, storage, and transportation of medicines. If no such personnel were available, the study engaged with the most qualified individuals available, such as pharmacy managers or shop assistants.

Questionnaire Design and Data Collection

To collect data, a questionnaire was adapted from the WHO's established guidelines for good storage and distribution practices (GDSP) and consisted of four sections. Additionally, the methodology was designed to collect data on the procurement and quality assurance practices at the retail pharmacy level. Due to resource and access constraints, the study did not extend to the procurement strategies of parent companies or wholesalers. This delineation was established to maintain a focused approach on the point-of-service, where direct impact on consumer health is observed.

The first section gathered sociodemographic information about the participants, such as their gender and level of education. The second section focused on questions related to the storage and transportation of medicines, including temperature monitoring and mechanisms used for transportation. The third section explored procurement practices and the presence of information systems. The final section comprised an audit and a checklist of pharmacy characteristics. In addition to the questionnaire, a semi-structured questionnaire was administered to a Key Informant from an innovative pharmacy company to help describe pharmaceutical supply chains and procurement aspects. Details of amoxicillin and sulfadoxine/pyrimethamine (SP) purchased for an accompanying study (Chapter 5) that focused on analysing the quality were used to determine aspects such as days from procurement and days to expiry. Amoxicillin and SP were chosen as tracer medicines for this study because of their significant public health relevance, both as commonly used antimicrobials and antimalarials. Given their wide prescription and availability across both innovative and traditional independent pharmacies, they serve as suitable benchmarks for comparing characteristics, such as storage conditions, availability, and pricing. The questionnaire was encoded on the ODK platform. The questionnaire underwent a pilot test in two Lusaka-based retail pharmacies to enhance clarity and relevance. The pilot participants were excluded from the study.

Data Analysis

The collected data from the questionnaire and observations were transferred from ODK to Microsoft Excel for final cleaning and preparation for analysis. Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) version 22. Descriptive and analytical analyses were also performed. Descriptive statistics, such as means and standard deviations (SDs) or medians and interquartile ranges (IQRs), were used to summarise continuous variables, whereas frequencies and percentages were used for categorical variables. Chi-square tests were conducted to compare medicine storage, transportation, and procurement practices between innovative and traditional independent pharmacies and to determine if there were significant differences between the two groups. Differences were considered statistically significant at a p-value < 0.05.

Ethical Approval

Ethical approval for this study was obtained from the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022) in Zambia and the London School of Hygiene and Tropical Medicine Ethics Committee (Ref:28040) in the UK. Written Informed consent was obtained from all participants. Adherence to strict ethical and professional guidelines was ensured throughout the study to safeguard participants' confidentiality. The identities of the retail outlets and participants were kept anonymous.

Results

Outlet Demographics and Training

The results in Table 1 present the demographic characteristics of the sampled outlets, comparing innovative pharmacies to traditional independent pharmacies. In terms of location, both types of pharmacies showed an equal presence in city centres, 3.8% (2/52). However, innovative pharmacies were notably dominant in shopping malls at 46.2% (12/26), compared to traditional ones at 23.1% (6/26). Regarding personnel presence during the survey, only about half of the total number of pharmacies had a pharmacist present at 58.8% (28/52), with innovative pharmacies having a higher presence of pharmacists at 69.2% (18/26). In comparison, traditional pharmacies had more pharmacy technologists, 38.8% (10/26), with a significant difference (p = 0.041).

In terms of training, over half of the participants across both types of pharmacies reported not receiving training in the past year. Among those who received training, procurement emerged as the most common area, 28.8% (15/52), with similar proportions between innovative 30.8% (8/26) and traditional 26.9% (7/26) pharmacies. Other training areas such as pharmacovigilance, storage, information technology, and logistics were less commonly reported, with negligible differences between the two pharmacy types.

Table 1: Outlet demographics (Lusaka, 2022)

	Total N = 52	Innovative pharmacy N =26	Traditional Independent pharmacy N=26	*p*-value
Location of outlets				
City centre	2 (3.8%)	1 (3.8%)	1(3.8%)	
Commercial area	9 (17.3%)	3 (11.5%)	6 (23.1%)	0.301[b]
Shopping mall	18 (34.6%)	12 (46.2%)	6 (23.1%)	
Peri urban	23 (44.2%)	10 (38.5%)	13 (50.0%)	
Personnel present at time of survey				
Pharmacist	28 (58.8%)	18 (69.2%)	10 (38.5%)	
Pharmacy technologist	17 (32.7%)	7 (26.9%)	10 (38.5%)	**0.041[a]**
Others *	7 (13.5%)	1 (3.8%)	6 (23.1%)	
Highest qualifications				
GCSE	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Certificate	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Diploma	21 (40.4%)	8 (30.8%)	13 (50.0%)	**0.032[b]**
Degree	27 (51.9%)	18 (69.2%)	9 (34.6%)	
Masters	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Gender				
Male	31 (59.6%)	13 (50.0%)	18 (69.2%)	0.258[a]
Female	21 (40.4%)	13 (50.0%)	8 (30.8%)	
Years of professional experience	Mean (SD	4.19 (2.9)	3.96 (3.4)	0 .794
Years of experience in the Outlet	Mean (SD)	2.34 (2.1)	3.27 (2.3)	0 .139
Training completed in the past year **				
None	28 (53.8%)	15 (57.7%)	13 (50.0%)	
Procurement	15 (28.8%)	8 (30.8%)	7 (26.9%)	
Pharmacovigilance	5 (9.6%)	3 (11.5%)	2 (7.7%)	0.694[b]
Storage	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Information technology	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Logistics	1 (1.9%)	0 (0.0%)	1 (3.8%)	

[a]Pearson Chi-square test, [b]Fishers exact test. * Others included registered nurse (1), laboratory technician (1), cosmetician (1), shop assistant (1), pharmacy managers (2), and pharmacy student (1). ** Multiple responses were allowed for this question. Bold *p*-values indicate significant statistical differences.

Medicine Suppliers and Procurement Sources

When evaluating medicine suppliers and procurement sources, pharmacies showed different patterns based on their classification as innovative or traditional independent outlets. Figure 1 illustrates the number of medicine suppliers reported by pharmacies. Innovative pharmacies are associated with fewer suppliers (1-4), whereas traditional independent pharmacies have a broader range of suppliers. Most of the surveyed pharmacies (71.2 %) reported engaging to 1-4 suppliers. However, a significant proportion of traditional independent pharmacies also relied on 5-9 suppliers (46.2%), 10-14 (7.7%), and even more than 15 suppliers (3.8%).

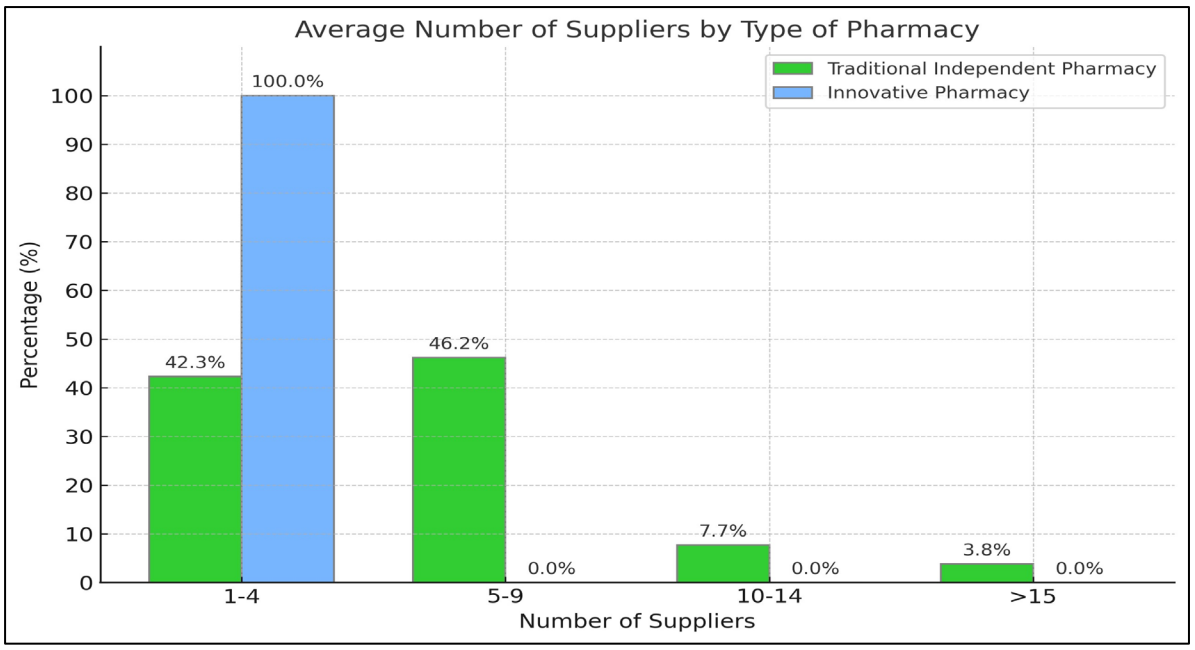

Figure 1: Graph of the average number of medicine suppliers and pharmacy types.

Figure 2 shows the specific sources of medical procurement. Innovative pharmacies uniformly sourced medicines from their parent innovative pharmacy companies, with all responding pharmacies (100%) indicating this. Furthermore, 26.9% of these innovative pharmacies were sourced from wholesalers, especially when facing delayed deliveries from parent companies. Another 30.8% reported importing medicines from international suppliers, and 23.1% procured medicines directly from local manufacturers. In contrast, traditional, independent pharmacies have reported no international procurement. Instead, they predominantly procured from sub-wholesalers (84.6%) and other retailers (15.4%). However, their innovative pharmacies did not reported this.

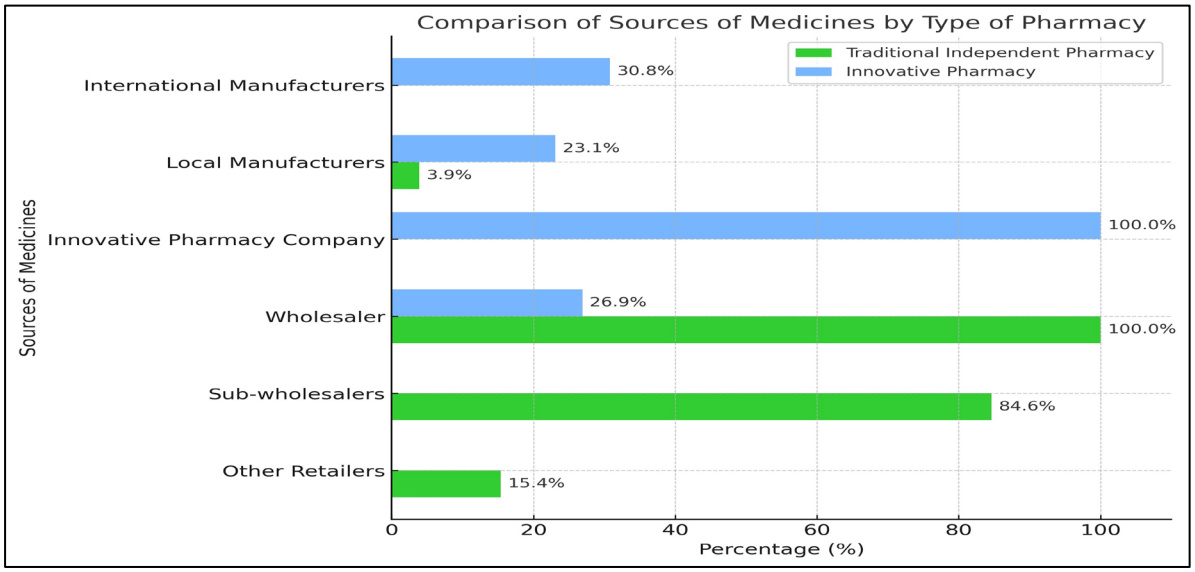

Figure 2: Graph of sources of medicines and types of pharmacies.

Data Recording Practices Across Pharmacies

When analysing the stock update frequency, most pharmacies 65.4% (34/52) updated their stock monthly. With a higher percentage of innovative pharmacies, 73.1% (19/26) compared to traditional independent pharmacies, 57.5% (15/26), with a statistically significant difference (p=0.004). Regarding the type of product data recorded, a significant 90.4% (47/52) of all pharmacies recorded the expiry date of products, with 100 % (26/26) of all innovative pharmacies recording this information. While a notable percentage of 67.3% (35/52) of all pharmacies recorded the batch number, there was a difference between innovative pharmacies 96.2% (25/26) and traditional ones 38.5% (10/26). Additionally, innovative pharmacies 76.9% (20/26) recorded the order number more frequently than traditional independent pharmacies 30.8% (8/26).

Table 2: Data recording practices (Lusaka, 2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N = 26	*p*-value
Stock update frequency				
Weekly	9 (17.3%)	7 (26.9%)	2 (7.7%)	
Monthly	34 (65.4%)	19 (73.1%)	15 (57.7%)	**0.004**[b]
Periodically	4 (7.7%)	0 (0.0%)	4 (15.4%)	
Product data recorded *				
None	3 (5.8%)	0 (0.0%)	3 (11.5%)	
Expiry date	47 (90.4%)	26 (100.0%)	21 (80.8%)	
Lot batch number	35 (67.3%)	25 (96.2%)	10 (38.5%)	
Order number	28 (53.8%)	20 (76.9%)	8 (30.8%)	
Recording system available				
Computerised	25 (48.1%)	21 (80.8%)	4 (15.4%)	
Manual	19 (36.5%)	0 (0.0%)	19 (73.1%)	**<0.001**[b]
Both	8 (15.4%)	5 (19.2%)	3 (11.5%)	
Inventory software used				
None	19 (36.5%)	0 (0.0%)	19 (73.1%)	
Microsoft Excel	3 (5.8%)	1 (3.8%)	2 (7.7%)	**<0.001**[b]
Proprietary software**	30 (57.7%)	25 (96.2%)	5 (19.2%)	
Days from procurement				
Amoxicillin	Mean (SD)	9.8 (4.2)	16.9 (8.5)	**< 0.001**
Sulfadoxine/Pyrimethamine	Mean (SD)	7.3 (2.1)	15.9 (6.8)	**< 0.001**

[a]Pearson Chi-square test, [b]Fishers exact test. ** Multiple answers were allowed for this question. ** Innovative pharmacy companies typically install proprietary software in their pharmacies, and other traditional pharmacies procure software from other companies. Bold *p*-values indicate significant statistical differences.

Regarding recording systems, 48.1% (25/52) of pharmacies employed a computerised system. Innovative pharmacies were more inclined to use a computerised system, 80.8% (21/26), in contrast to traditional pharmacies, where only 15.4% (4/26) used such a system, with the difference being significant (p<0.001). Many traditional independent pharmacies relied on manual recordings 73.1% (19/26). While 57.7% (30/52) of all pharmacies used proprietary software for inventory, a difference was observed between innovative 96.2% (25/26) and traditional independent pharmacies 19.2% (5/26) $p < 0.001$. Finally, days from procurement showed significant variations between the two types

of pharmacies for both amoxicillin and sulfadoxine/pyrimethamine. Innovative pharmacies reported shorter times from procurement for both medicines, with mean times of 9.8 and 7.3 days, respectively. In contrast, traditional independent pharmacies reported longer times, with means of 16.9 and 15.9 days, respectively, and both differences were statistically significant (p< 0.001).

Outlet Organisational Practices and Conditions

The data in table 3 shows that a majority of the total pharmacies, 80.8% (42/52), had adequate storage space, according to ZAMRA recommendations, with all innovative pharmacies and over half of the traditional independent pharmacies, 61.5% (16/26). This difference was statistically significant (p<0.001). Shelf cleanliness was observed in 84.6% (44/52) of all pharmacies. All Innovative pharmacies had clean shelves, while 69.2% (18/26) of traditional independent pharmacies had clean shelves, and this difference was statistically significant (p=0.004). The First-Expiry-First-Out (FEFO) principle was followed by 80.8% (42/52) of the total pharmacies. All innovative pharmacies 100% (26/26) adhered to this principle, while 61.5% (16/26) of the traditional independent pharmacies reported compliance. The difference between the two groups was statistically significant (p<0.001).

Table 3: Outlet organisation (Lusaka, 2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N = 26	*p*-value
Outlet is in good condition				
Yes	45 (86.5%)	26 (100.0%)	19 (73.1%)	**0.051**[a]
No	7 (13.5%)	0 (0.0%)	7 (26.9%)	
Storage had adequate storage*				
Yes	42 (80.8%)	26 (100.0%)	16 (61.5%)	**<0.001**[a]
No	10 (19.2%)	0 (0.0%)	10 (38.5%)	
Shelves were clean				
Yes	44 (84.6%)	26 (100.0%)	18 (69.2%)	**0.004**[b]
No	8 (15.4%)	0 (0.0%)	8 (30.8%)	
Shelves moisture free				
Yes	40 (76.9%)	23 (88.5%)	17 (65.4%)	0.097[a]
No	12 (23.1%)	3 (11.5%)	9 (34.6%)	
Medicines stored according to FEFO				
Yes	42 (80.8%)	26 (100.0%)	16 (61.5%)	**<0.001**[a]
No	10 (19.2%)	0 (0.0%)	10 (38.5%)	

[a]Pearson Chi-square test, [b]Fishers exact test. * Storage conditions comply with ZAMRA recommendations. Bold *p*-values indicate significant statistical differences. FEFO = First Expiry, First-Out

Medicine Transport Conditions and Storage Environment

The medicine distribution methods differed notably between innovative and traditional independent pharmacies (table 4). All innovative pharmacies reported distributor delivery as their primary mode of medicine distribution. In contrast, only 19.2% (5/26) of the traditional independent pharmacies were the same, with 57.7% (15/26) opting to collect medicines directly from the distributor. This difference

was statistically significant (p<0.001). All innovative pharmacies have reported on air conditioning during transport. However, 7.7% (2/26) of the traditional independent pharmacies indicated air conditioning transportation. This difference was statistically significant (p<0.001).

The mean temperature recorded during the survey for innovative pharmacies was 22.69 ± 2.33°C. This recording differed significantly from readings associated with traditional independent pharmacies (p=0.013). Nevertheless, both readings were within the recommended ambient temperature range for medicines (20-25°C). Regarding awareness of ambient temperature, the majority (76.9%) of the personnel perceived it to be within the 20-25°C range. When examining temperature logging practices over the previous three months, an overall average of 69.2% (36/52) maintained complete records. Innovative pharmacies accounted for 84.6% (22/26) of the patients compared to 53.8% (15/26) in the traditional independent group.

Regarding infrastructure, 92.3% (48/52) of all outlets indicated the presence of a functional refrigerator, with all innovative pharmacies having one, and 84.6% (22/26) in the traditional independent pharmacies. Similarly, in an aggregate of all pharmacies, 90.4% (47/52) had a functioning air conditioner, with 96.2% (25/26) in innovative pharmacies and 84.6% (22/26) in traditional independent pharmacies. No statistically significant differences were observed between the pharmacies. Power disruptions in the preceding six months were reported by 44.2% (23/52) of all outlets, with a higher incidence noted among traditional independent pharmacies, 53.8% (14/26). However, 76.9% (20/26) of innovative pharmacies confirmed a backup power source compared with 26.9% (7/26) of their traditional independent pharmacies, resulting in a statistically significant difference (p<0.001). Regarding medicine expiry metrics, amoxicillin had a mean expiry duration of 694.4 days (SD=236.7). In contrast, sulfadoxine/pyrimethamine averaged 529.9 days (SD=165.1), which was not statistically significant.

Table 4: Transport conditions and Storage environment (Lusaka, 2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N = 26	*p*-value
Medicine distribution				
The distributor delivers	31 (59.6%)	26 (100%)	5 (19.2%)	
We pick up from the distributor	15 (28.8%)	0 (0.0%)	15 (57.7%)	**<0.001[b]**
Both	6 (11.5%)	0 (0.0%)	6 (23.1%)	
Air conditioning available on transport				
Yes	28 (53.8%)	26 (100.0%)	2 (7.7%)	
No	22 (42.3%)	0 (0.0%)	22 (84.6%)	**<0.001[b]**
I do not know	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Tracking sensors on transportation				
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	
No	43 (82.7%)	19 (73.1%)	24 (92.3%)	0.140[b]
I do not know	9 (17.3%)	7 (26.9%)	2 (7.7%)	

Temperature reading at the time of survey	Mean (SD)	21.2 (1.7)	22.7 (2.3)	**0.013[a]**
Awareness of medicine ambient temperature				
Below 20 degrees	10 (19.2%)	3 (11.5%)	7 (26.9%)	0.118[b]
Between 20-25 degrees	40 (76.9%)	23 (88.5%)	17 (65.4%)	
Between 26-30 degrees	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Temperature logs for the past 3 months filled in				
Yes, completely filled	36 (69.2%)	22 (84.6%)	14 (53.8%)	
Yes, partially filled.	13 (25.0%)	4 (15.4%)	9 (34.6%)	**0.031[b]**
No	3 (5.8%)	0 (0.0%)	3 (11.5%)	
Functional refrigerator				
Yes	48 (92.3%)	26 (100.0%)	22 (84.6%)	
Yes, but not functional	1 (1.9%)	0 (0.0%)	1 (3.8%)	0.110[b]
No	3 (5.8%)	0 (0.0%)	3 (11.5%)	
Functional air conditioner				
Yes	47 (90.4%)	25 (96.2%)	22 (84.6%)	
Yes, but not functional	1 (1.9%)	1 (3.8%)	0 (0.0%)	0.110[b]
No	4 (7.7%)	0 (0.0%)	4 (15.4%)	
Power cut in past 6 months				
Yes	23 (44.2%)	9 (34.6%)	14 (53.8%)	
No	25 (48.1%)	15 (57.7%)	10 (38.5%)	0.400[b]
I do not know	4 (7.7%)	2 (7.7%)	2 (7.7%)	
Availability of backup power source *				
Yes	27 (51.9%)	20 (76.9%)	7 (26.9%)	
No	25 (48.1%)	6 (23.1%)	19 (73.1%)	**<0.001[a]**
Power backup source available				
None	25 (48.1%)	6 (23.1%)	19 (73.1%)	
Genset	15 (28.8%)	14 (53.8%)	1 (3.8%)	**<0.001[a]**
Inventer	7 (13.5%)	5 (19.2%)	2 (7.7%)	
Solar	5 (9.6%)	1 (3.8%)	4 (15.4%)	
Days to Expiry				
Amoxicillin	Mean (SD)	694.4 (236.7)	783.3 (214.9)	0.412
Sulfadoxine/Pyrimethamine	Mean (SD)	529.9 (165.1)	525.5 (281.5)	0.427

[a]Pearson Chi-square test, [b]Fishers exact test. * Pharmacies operating at a shopping centre with a backup source were categorised as yes. Bold *p*-values indicate significant statistical differences.

Associations Between Personnel Characteristics and Storage Practices in Pharmacies

In examining the link between pharmacy personnel characteristics and storage practices (table 5), the presence of pharmacists in pharmacies resulted in 82.1% compliance with complete temperature logs for the preceding three months. In comparison, pharmacies with pharmacy technologists had a compliance rate of 64.7%, and other personnel types had a compliance rate of 28.6% (p=0.051). Pharmacies overseen by pharmacists had 92.9% adherence to the FEFO protocol, whereas 70.6% was observed in outlets with pharmacy technologists (p=0.043).

In terms of educational qualifications, there was a relationship between the qualification level and adherence to storage practices. Pharmacies with degree holders showed the highest adherence to the FEFO protocol at 96.4%, whereas those managed by diploma holders had a rate of 66.7%. The trends were similar for temperature log maintenance (p=0.0003) and shelf cleanliness (p=0.049).

The role of recent training has also emerged as being significant in certain domains. Specifically, outlets where staff had procurement training in the last year, displayed 80% adherence to the FEFO protocol and 93.3% compliance with shelf cleanliness.

Table 5: Associations between pharmacy personnel characteristics and storage practices

Variables	Temperature logs for the past 3 months completely filled			Medicines stored according to FEFO		Shelves were clean	
	Yes	Partially filled	No	Yes	No	Yes	No
Pharmacy personnel present							
Pharmacists	23 (82.1%)	5 (17.9%)	0 (0.0%)	26 (92.9%)	2 (7.1%)	26 (92.9%)	2 (7.1%)
Pharmacy technologist	11 (64.7%)	4 (23.5%)	2 (11.8%)	12 (70.6%)	5 (29.4%)	13 (76.5%)	4 (23.5%)
Others	2 (28.6%)	4 (57.1%)	1 (14.3%)	4 (57.1%)	3 (42.9%)	5 (71.4%)	2 (28.6%)
		p=**0.051***		*p*=**0.043***		*p*=0.196	
Highest degree qualifications							
GCSE	0 (0.0%)	0 (0.0%)	1 (100.0%)	1 (100%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
Certificate	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	2 (100%)	1 (50.0%)	1 (50.0%)
Diploma	14(66.7%)	5 (23.8%)	2 (9.5%)	14 (66.7%	7 (33.3%)	15 (71.4%)	6 (28.6%)
Degree	21(78.6%)	6 (21.4%)	0 (0.0%)	27 (96.4%)	1 (3.6%)	27 (96.4%)	1 (3.6%)
		P=**0.0003***		*P*=**0.0013***		*P*=**0.049***	
Training completed in the past year							
None	19(67.9%)	6 (21.4%)	3 (10.7%)	21 (75.0%)	7 (25.0%)	23(82.1%)	5 (17.9%)
Procurement	12(80.0%)	3 (20.0%)	0 (0.0%)	13 (80.0%)	2 (20%)	14 (93.3%)	1 (6.7%)
Pharmacovigilance	2(40.0%)	3 (60.0%)	0 (0.0%)	4 (80.0%)	1 (20.0%)	3 (60.0%)	2(40.0%)
Storage	1 (2.8%)	1 (7.7%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)
Information technology	0 (0.0%)	0 (0.0%)	1 (100.0%)	1 (100.0%	0 (0.0%)	1 (100.0%)	0 (0.0%)
Logistics	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
		p = 0.671		*p*=0.864		*P*=0.541	

*Significant difference with *p*-value < 0.05 using Chi square (X2) test. Bold *p*-values indicate significant statistical differences. FEFO = First Expiry, First-Out

Discussion

This study's scope was to examine the operational characteristics of innovative pharmacies in comparison with traditional independent pharmacies in Lusaka, focusing on aspects that could influence medicine quality. Differences were observed in transport conditions, temperature maintenance, power backup provisions, staff qualifications, and training. Procurement methods also vary; innovative pharmacies are generally sourced from fewer suppliers primarily the parent company, and sometimes directly from manufacturers. However, details on the parent company's procurement processes, including pre-qualification of products and suppliers, were beyond the scope of this study. Such an investigation would require access to proprietary company documents and processes that were not available. In contrast, traditional independent pharmacies engage with a broader supplier base and seldom procure directly from manufacturers. The centralised procurement approach of innovative pharmacies suggests the potential for better medicine traceability and quality assurance, which may reduce the risk of substandard or falsified (SF) medicines.

Differences in the procurement-sale timeline for medicines using sulfadoxine/pyrimethamine and amoxicillin as tracers were also observed. Innovative pharmacies showed a shorter gap between procurement and sale and reduced mean days to expiry compared with traditional pharmacies. This suggests that innovative pharmacies may prioritise a tighter, more direct supply chain, aligning with previous research and innovators' claims of reducing intermediaries [17,18]. This finding points to better inventory management in innovative pharmacies, potentially reducing the risk of expiring products before sale. Conversely, traditional independent pharmacies may favour longer expiry durations to avoid potential losses, suggesting more complex supply chains. Hence, diligent supply chain monitoring is crucial to ensure the quality, safety, and efficacy of medicine.

Mirroring the transportation challenges highlighted in this study, well-documented issues with medical product transportation in LMICs exist [26–28]. Challenges such as inadequate temperature control, storage deficiencies, and delivery delays can deteriorate medical product quality [8,9]. Unchecked temperatures can lead to degradation of medicines, and poor handling can compromise packaging. With innovations emerging to address these challenges, it is imperative to prioritise robust transportation and supply chain systems.

In terms of data documentation, innovative pharmacies consistently record essential details such as expiry dates and batch numbers, whereas traditional independent outlets often only note order numbers. Systematic documentation of details promotes improved traceability and product tracking, which is crucial for ensuring medication quality [29–31]. Additionally, while over half of pharmacies, especially innovative ones, have adopted computerised recording systems, traditional pharmacies still rely primarily on manual systems. The use of digital solutions in innovative pharmacies indicates a trend towards technology integration in inventory management and recording. Recognising the potential efficiencies of these systems might be beneficial for traditional independent outlets to consider exploring similar technological adaptations.

Interestingly, both pharmacy types in Lusaka commonly have functional refrigerators and air conditioners, a departure from findings in countries such as Pakistan and Saudi Arabia [32,33]. However, a consistent electricity supply is challenging, as in other LMICs [34,35]. Given Zambia's power outages, "load shedding", the efficacy of refrigeration and air conditioning hinges on consistent power. Innovative pharmacies, often located within malls, have a higher likelihood of backup power provision than traditional, independent pharmacies. Similar findings of low levels of backup power sources have been reported in Libya and Pakistan [33,36,37]. Gensets were the most common among those with backup systems, followed by those with inverters. While such systems can circumvent the challenges of power outages, they introduce new challenges, particularly the financial implications of running on diesel fuel

[38,39]. A continuous power supply is pivotal for preserving the quality of medicine in electricity-sensitive contexts.

A degree in pharmacy was correlated with better storage practices. However, a glaring gap in post-qualification training across both pharmacy types is evident. Continuous professional development (CPD) can enhance pharmacy outcomes and bolster medicine quality practices [40,41]. While the Health Professions Council of Zambia (HPCZ) advocates CPD, its practical effects need to be evaluated. Previous research in Zambia has accentuated the value of locally relevant courses in amplifying pharmaceutical care [41]. Given these observations, a CPD course addressing contemporary procurement, transportation, and storage practices is recommended to ensure the safety of patients and products.

Limitations

This study has several limitations that should be considered when interpreting the results. First, the sample size was relatively small and may not be representative of all pharmacies in Lusaka and Zambia, limiting the generalisability of the findings. Second, the uniformity of innovators from a single company, limiting the extrapolation of findings to other innovative pharmacy models across Africa. Third, although efforts were made to ensure the accuracy of the collected data, the study relied on self-reported information and observations made by the research team. Efforts were made to ensure the accuracy of the collected data, but we did not have access to documents such as procurement receipts to track the procurements and movement of medicines. This reliance on self-reporting and lack of direct documentation may have introduced some inaccuracies and biases, potentially impacting the validity of the findings.

Furthermore, the study did not provide detailed insight into the procurement strategies of the parent companies supplying innovative pharmacies. Access to such data would require transparency and disclosure from the companies, which was not feasible within the context of this study. This is a significant limitation because understanding the procurement strategies, including pre-qualification of products and suppliers, could offer deeper insights into the quality assurance processes. It also points to the potential for future research to explore these upstream processes, potentially employing the 2014 WHO guideline Model Quality Assurance Systems for procurement agencies as a framework.

Finally, while this study examined the impact of medicine storage, transportation, and procurement practices on medicine quality, it did not investigate other factors that may influence medicine quality, such as manufacturing processes or supply chain intermediaries. Nonetheless, this study provides insights into the practices and quality of medicines in both innovative and traditional independent pharmacies in Lusaka, Zambia.

Conclusions

This study compared procurement, transportation, and storage practices between innovative and traditional independent pharmacies in Lusaka, Zambia. The findings revealed distinct operational characteristics, with innovative pharmacies typically adopting advanced inventory systems and prioritising cleanliness standards. However, a consistent area of improvement for both pharmacies is to enhance quality assurance training and education. Centralised procurement and distribution strategies, bolstered by pay-for-sale and franchise models, appear to have potential benefits. These strategies could bolster medicine quality and availability in Zambia, and have implications for other low- and middle-income countries facing similar challenges. An emerging trend from this study is the integration of digital inventory systems in innovative pharmacies, a model that traditional pharmacies could consider.

In light of these findings, this study highlights the need for ongoing quality improvements within the Zambian pharmaceutical sector. It is imperative to focus on optimising storage and transportation mechanisms and to reassess procurement methods to enhance pharmaceutical care. Moreover, as this study has concentrated on the practices of pharmacies, it is recommended that future research efforts delve into the procurement strategies of the parent companies supplying innovative pharmacies. A deeper understanding of their pre-qualification, procurement, and stock control systems could yield valuable insights into the entire supply chain, particularly when framed within robust guidelines such as the WHO Model Quality Assurance Systems.

In summary, enhancing pharmaceutical care in Zambia demands ongoing quality improvements across the pharmaceutical sector. Key focal areas should include the optimisation of storage and transportation mechanisms and a reassessment of procurement methods. Future research should evaluate the impact of these proposed changes and contribute to a broader understanding of the determinants of medicine quality in settings similar to Zambia.

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Chapter 4: Research Paper 3 - Medicine Quality Surveillance

Chapter Introduction

Ensuring the quality of medicines in retail pharmacies is vital to public health. Rapid screening and timely reporting to relevant authorities are fundamental to pharmacovigilance, which focuses on the safety and efficacy of medicines. By gathering and analysing data from diverse sources, pharmacovigilance seeks to detect, evaluate, and address adverse effects or other drug-related concerns. Such practices are instrumental in thwarting the distribution of substandard and falsified medicines, thereby safeguarding patients' health.

Modern screening technologies offer the benefits of speed and precision in identifying compromised medicines, thereby allowing pharmacies to act decisively. These tools often serve as preliminary measures before deploying advanced analytical methods such as high-performance liquid chromatography (HPLC) and mass spectrometry. Prompt and accurate reporting of drug quality issues bolsters the medicine supply chain, enhancing the overall ability of the public health system to pre-empt and tackle risks.

Expanding on the distinct features of innovative and traditional independent pharmacies in Lusaka, Zambia, discussed in Chapters 2 and 3, this chapter delves into their adoption and use of medicine quality screening technologies and reporting mechanisms. In line with the third objective of the broader PhD research, the aim here is to shed light on the ramifications of these practices for medicine quality surveillance and the wider pharmacovigilance framework.

This chapter adheres to the conventional format of biomedical journals, encompassing introduction, methods, results, and discussion sections, with plans to submit this study to the Journal of Pharmaceutical Policy and Practice.

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Thesis Title	Innovative Private Pharmacy Distribution Channels: Implications on Medicine Quality in Zambia		
Primary Supervisor	Dr Harparkash Kaur		

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Comparative Analysis of Medicine Quality Surveillance between Innovative and Traditional Independent Pharmacies in Lusaka, Zambia.

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Abstract

Background: In low- and middle-income countries, poor quality (Substandard and Falsified) medicines pose a mounting threat to public health, with pharmacies being pivotal in safeguarding medicine quality. This study evaluates medicine quality screening technologies and reporting practices across innovative and traditional independent pharmacies in Lusaka, Zambia, analysing their impact on medicine quality surveillance.

Methods: A cross-sectional study was conducted in Lusaka, Zambia, covering 52 pharmacies:26 innovative and 26 traditional independent pharmacies. Using a structured survey, we collected data on outlet characteristics, training related to substandard and falsified medicines, recording systems, inventory management software, and the availability and use of screening technologies and reporting systems. Chi-square tests were used to assess differences between the two pharmacy groups. A *p*-value of less than 0.05 was deemed statistically significant throughout the study.

Results: A majority, 69.2% (36/52) of respondents across both pharmacy types did not receive training on substandard and falsified (SF) medicines. Only 28.9% (15/52) were aware of analytical technologies, notably thin-layer chromatography, with only 3.8% (2/52) having ever used analytical tools. Innovative pharmacies showed an inclination towards computerised systems at 80.8% (21/26) and proprietary inventory software at 96.2% (25/26). In contrast, traditional independent pharmacies primarily relied on manual systems 73.1% (19/26) and had minimal use of proprietary software 19.2%, (5/26), with these differences being statistically significant ($p<0.001$). Of the 55.8% (29/52) suspected of receiving poor-quality medicine from distributors, only 32.7% (17/52) reported these issues. Among those who reported this, 76.5% (13/17) informed the distributors, while 35.3% (6/17) reported it to the NMRA.

Conclusions: The findings emphasise the urgency of targeted initiatives to foster the adoption of modern recording and inventory systems in traditional independent pharmacies. A heightened focus

on exhaustive training of pharmacy staff regarding quality screening and reporting is imperative. Future research should concentrate on formulating effective strategies for promoting these technologies and further examining their efficacy in curtailing the spread of substandard and falsified medicines.

Keywords: Medicine quality, Screening technologies, Reporting practices, Innovative pharmacies, Independent pharmacies, Zambia, Medicine surveillance, Substandard and falsified medicines

Introduction

The availability of quality-assured medicines is critical for ensuring effective treatment and care of patients [1,2]. However, the global prevalence of substandard and falsified (SF) medicines remains a significant public health concern, particularly in low- and middle-income countries (LMICs)[3–5]. The World Health Organization (WHO) estimates that as much as 10% of the global medicine supply is of poor quality, posing significant risks to patients through treatment failure, adverse reactions, and even death [4]. According to WHO, these poor-quality medicines mainly take two forms: falsified and substandard. Falsified medicines are deliberately or fraudulently misrepresented in terms of their identity, composition, or source [6]. Meanwhile, substandard medicines are authorised by National Medicine Regulatory Authorities (NMRAs) but fail to consistently meet the national or international quality standards due to inadequate manufacturing and quality control practices that go undetected by regulators [6]. In Zambia, the prevalence of SF medicines is estimated to be as high as 17.6%, highlighting the need for effective medicine quality surveillance mechanisms [4,7,8].

Pharmacies are critical for providing safe and effective medicines to patients. They serve as the primary distribution channels for pharmaceutical products, making them a crucial point in the healthcare system. Pharmacies play a vital role in ensuring the availability of quality-assured medicines to patients and in monitoring and reporting any issues related to medicine quality [9,10]. Pharmacists and pharmacy personnel are often the first line of defence against SF medicines and are important stakeholders in the fight against the global public health threats posed by these products [11]. Their ability to detect and report suspected cases of poor-quality medicines is essential for quality surveillance, which is a critical component for ensuring the safety and efficacy of medicines.

Various medicine quality screening technologies have been developed and deployed in recent years to address the challenge of SF medicines [12–16]. Screening technologies offer a rapid and cost-effective approach for detecting SF medicines in the field compared with traditional quality control (QC) confirmatory technologies that require significant resources. Screening technologies are designed to be portable and can be easily transported by vehicles or even handheld, thus enabling their use in various settings. These technologies employ a range of tools to assist analysts in making accurate determinations, including colourimetric assays, mid-infrared spectroscopy, near-infrared spectroscopy, Raman spectroscopy, and thin-layer chromatography [13,15,17–19].

The use of screening technologies based on analytical chemistry to detect SF medicines has been a popular approach. However, other medicine authentication tools have also emerged, including mobile applications and messaging services, 2D barcoding with drug safety alert systems, web-based drug safety alerts, radiofrequency identification tags, databases for visual inspection support, and digital

aids [13,20,21]. In addition to these tools, disruptive technologies, such as Artificial Intelligence (AI)-powered systems and blockchain technology, have shown the potential to improve medicine quality screening efficiency and accuracy [22,22–24].

Although the use of AI and blockchain technology in medicine quality surveillance is still nascent, these technologies could markedly enhance the efficacy of existing surveillance systems. They present strengths such as improved tracking capabilities, enhanced data transparency, and potential for real-time quality control. However, their implementation also presents certain challenges. These include the substantial costs associated with adoption, the necessity for specialised expertise for operation, and the requirement for comprehensive regulatory frameworks to govern their use [25–27].

Medicine quality surveillance efficiency hinges not only on screening technologies but also on robust reporting practices. Crucially, a well-structured pharmacovigilance reporting system that enables stakeholders to report suspected substandard and falsified medicines is key for timely identification and remediation [28,29]. In this context, the WHO's Global Surveillance and Monitoring System (GSMS) plays a pivotal role in collecting and responding to reports from stakeholders, such as national medicine regulatory authorities [6].

In recent years, private pharmacies have undergone significant changes, particularly through the adoption of innovative distribution channels such as online platforms, franchising, and home delivery services [30,31]. While these advancements enhance convenience and accessibility for patients, they also pose unique challenges in maintaining the integrity and quality of medicines. On the other hand, traditional independent pharmacies rely on established, conventional distribution systems with a proven track record in managing medicine quality. However, regardless of the model, robust quality control measures are vital in both innovative and traditional settings to ensure the safety and efficacy of the medicines provided. Recognising the essential role of individual shops in frontline quality assurance, especially in light of evidence that many NMRAs in LMICs are often under-resourced [9], it is imperative for pharmacies to adopt practical technologies and procedures. For instance, pharmacies can implement digital systems for monitoring temperature and humidity, ensuring storage conditions meet required standards. They can also conduct regular in-house visual inspections of medicine packaging and physical characteristics, utilize basic testing kits for quick screening of drug quality, and maintain meticulous records of supplier information and batch numbers for traceability. These measures are not merely innovative but necessary, serving to effectively complement the broader surveillance activities of NMRAs and providing a means for independent verification of product integrity at the retail level.

Recognising the global challenge posed by SF medicines, the WHO and the International Pharmaceutical Federation (FIP) have put forth comprehensive guidelines and best practices to ensure the quality of medicines at the dispensing level [32]. WHO Expert Reports and WHO/FIP Good Pharmacy Practices advocate for robust quality assurance and quality control (QA/QC) practices at individual pharmacies, emphasising their critical role within the broader context of national regulatory oversight. This guidance forms the foundational framework within which the role of pharmacies, in concurrence with national regulatory oversight, is assessed and proposed. The implementation of these robust QA/QC practices is particularly pertinent in LMICs like Zambia, which may face significant challenges with SF medicines. Consequently, this study has examined the technologies and techniques employed by both innovative and independent pharmacies in Lusaka, Zambia, and has further explored the reporting systems and their implications for medicine quality surveillance. By pinpointing potential enhancements in these areas, the study offers insights into the operational impact of both types of pharmacies on medicine quality surveillance. The findings contribute to the broader goal of improving the availability of quality-assured medicines in Zambia and other similar settings.

Methods

Study Design and Setting

A cross-sectional survey was conducted from August to September 2022 in Lusaka, the capital and most populous city of Zambia, with an estimated three million inhabitants. Serving as a pivotal hub for economic, political, and healthcare activities, Lusaka boasts of a diverse population and an extensive array of healthcare facilities spanning both the public and private sectors. Despite this, many residents, especially those in low-income areas, face challenges in accessing healthcare [33]. This study specifically chose Lusaka because its large population and diverse healthcare settings provided a representative sample of innovative and independent pharmacies. Notably, the private sector encompasses retail pharmacies integral to the health structure.

Study Population

Definitions of pharmacies

In this study, pharmacies refer to registered entities in Zambia that are registered with the Zambia Medicines Regulatory Authority (ZAMRA) and are required by law to have a full-time pharmacist. The sizes and structures of these pharmacies can vary. According to the guidelines set by the ZAMRA for establishing a pharmaceutical retail business, the outlet should have certain features, including a pharmacy size of at least 50 square meters, an adequate dispensary area, and a functioning refrigerator [34].

Defining Traditional Independent Pharmacies

Traditional independent pharmacies refer to privately-owned pharmacies that are not part of a larger chain or corporation [29,30]. These pharmacies are typically operated by a pharmacist or a group of pharmacists who prioritise providing personalised care and building relationships with their customers. These pharmacies are commonly referred to as "mom-and-pop" shops and are considered essential healthcare resources in local communities. In this study, traditional independent pharmacies were defined as privately owned outlets typically owned by an individual and supplied by traditional supply chains.

Defining Innovative Pharmacies

Innovative pharmacies in this study are those that stand apart from traditional models by integrating technology into their operations. These include services aimed at healthcare providers such as hospitals, clinics, and pharmacies, with a focus on technology-driven solutions including pharmacy inventory-management software, vendor-managed inventory services, fulfilment services, and stock financing. The innovative pharmacies selected for this study are representative of a prevalent model within the Zambian context, with the majority (24/26) being part of a single, dominant company known for innovating in distribution to providers (at the pharmacy level).

Eligible population

The sampling frame was pharmacies registered with ZAMRA and the latest master list was obtained from the ZAMRA website. Pharmacies were selected using two-stage sampling by first stratifying them according to whether they were supplied by innovative pharmacy distribution channels or traditional supply chains. Innovative pharmacies were identified with the assistance of a medical information and education company called Medsearch Zambia, and KIs in the pharmaceutical sector. The pharmacies were then cross-checked against the characteristics described in Salient Advisory reports [19].

Inclusion criteria: The study includes traditional independent pharmacies are defined as privately owned outlets that are typically owned by an individual and supplied by conventional supply chains.

It also includes innovative pharmacies that are registered as independent but are predominantly part of a single company that exemplifies the innovative model under investigation. These pharmacies are selected for their use of advanced technological solutions in distribution and patient engagement, which distinguish them from traditional setups.

Exclusion Criteria: The study did not include chain outlets, health shops, or drug stores. Chain pharmacies have been excluded from this study due to their fundamentally different operational structures, which often involve more standardised processes and centralised management. These larger entities to have different operational constraints and resources, which could confound the assessment of practices in traditional pharmacies.

Sampling of the pharmacies

A sampling of the pharmacies was conducted in two stages. First, an exhaustive sample of all pharmacies (n=333) in Lusaka was obtained from the Zambia Medicines Regulatory Authority (ZAMRA). Chain outlets (n=96) were then excluded from the list, leaving 273 innovative and traditional independent pharmacies. The list was then stratified into two groups: innovative pharmacies (n=26) and traditional independent pharmacies (n=247). All 26 pharmacies classified as innovative were selected for this study, while a random sample of 26 traditional independent pharmacies were included. Four traditional independent pharmacies refusals were encountered. For each refusal, an alternative pharmacy in close geographical proximity was selected to ensure integrity and representation of the original stratification.

Study Participants

The study targeted pharmacy personnel at the selected pharmacies on the day of the interviews. Where multiple staff were present, preference was given to pharmacists and pharmacy technologists, given their knowledge of medicine quality surveillance and reporting. If no such personnel were available, the study engaged with the most qualified individuals available, such as pharmacy managers or shop assistants.

Questionnaire Design and Data Collection

Data were collected using a structured questionnaire, which was adapted from the Good Pharmacovigilance Practices (GVP) of the European Medicines Agency (EMA) [37]. This was complemented by additional guidance from WHO Pharmacovigilance materials [38] and the ZAMRA pharmacovigilance reference manuals [39]. The choice to primarily adapt the EMA's GVP framework was informed by its prominence in the testimonies of key informants and its notable alignment with ZAMRA's standards, as evidenced in the literature. This approach was further reinforced by the comprehensive nature of the EMA's guidance documents, which provide extensive coverage and detailed direction on QA/QC practices. The questionnaire covered various aspects related to medicine quality screening and reporting practices, such as the awareness and usage of different types of medicine quality screening technologies as well as the methods used to receive alerts of circulating substandard and falsified medical products and report quality issues. Additionally, the questionnaire gathered information on the level of training and education of the pharmacy staff regarding quality issues. The questionnaire was administered using ODK, and piloted in two retail pharmacies in Lusaka to test and validate the questionnaire. The participants in the pilot were not included in the final data analysis.

Data Analysis

The data collected from the questionnaire were transferred from ODK to Microsoft Excel for final cleaning and preparation for analysis. Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) version 22. Descriptive and analytical analyses were performed. Descriptive statistics, such as means and standard deviations (SDs) or medians and interquartile ranges (IQRs), were used to summarise continuous variables, whereas frequencies and percentages were used for categorical variables. Chi-square tests were conducted to compare the use and availability of medicine quality screening technologies and reporting systems between innovative and traditional independent pharmacies, and to determine if there were significant differences between the two groups. Differences were considered statistically significant at a p-value < 0.05.

Ethical Approval

Ethical approval for this study was obtained from the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022) in Zambia and the London School of Hygiene and Tropical Medicine Ethics Committee (Ref:28040) in the UK. Written Informed consent was obtained from all participants. Adherence to strict ethical and professional guidelines was ensured throughout the study to safeguard participants' confidentiality. The identities of the retail outlets and participants were kept anonymous.

Results

Demographics, Qualifications, and Sources of Information on Substandard and Falsified (SF) Medicines of Pharmacy Personnel

Table 1 presents the demographics, qualifications, training, and sources of information on SF medicines of the participants. In terms of location, both types of pharmacies showed an equal presence in city centres, 3.8% (2/52). However, innovative pharmacies were notably dominant in shopping malls at 46.2% (12/26), compared to traditional ones at 23.1% (6/26). Regarding personnel presence during the survey, only about half of the total number of pharmacies had a pharmacist present at 58.8% (28/26), with innovative pharmacies having a higher presence of pharmacists at 69.2% (18/26). In comparison, traditional pharmacies had more pharmacy technologists, 38.8% (10/26), a statistically significant difference (p = 0.041). The highest qualifications of personnel ranged from GCSE to Master's level, with the majority holding a degree 51.9% (27/52) or a diploma 40.4% (21/52). Personnel in innovative pharmacies were more likely to hold a degree 69.2% (18/26) than those in traditional independent pharmacies 34.6% (9/26).

Most participants in all the pharmacies surveyed, 69.2% (36/52) reported not receiving any training on SF medicines. Among those who had been trained, the undergraduate course was the most common period, when this training was received by 68.6% (11/16). Regarding information sources on

SF medicines, social media emerged as the dominant platform in 75% (39/52) of cases. Regulatory memos 25% (13/52) and pamphlets 13.5% (7/52) also served as significant sources of information. A smaller group reported obtaining information from 'other sources', 13.5% (7/52), which primarily included academic resources such as journal articles.

Table 1: Demographics, Qualifications, and Sources of Information on Substandard and Falsified Medicines of Pharmacy Personnel (Lusaka,2022)

	Total N = 52	Innovative pharmacy N =26	Traditional Independent pharmacy N =26	*p*-value
Location of outlets				
City centre	2 (3.8%)	1 (3.8%)	1 (3.8%)	
Commercial area	9 (17.3%)	3 (11.5%)	6 (23.1%)	
Shopping mall	18 (34.6%)	12 (46.2%)	6 (23.1%)	0.301[b]
Peri urban	23 (44.2%)	10 (38.5%)	13 (50.0%)	
Personnel present at time of survey				
Pharmacist	28 (58.8%)	18 (69.2%)	10 (38.5%)	**0.041[a]**
Pharmacy technologist	17 (32.7%)	7 (26.9%)	10 (38.5%)	
Others**	7 (13.5%)	1 (3.8%)	6 (23.1%)	
Highest qualifications				
GCSE	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Certificate	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Diploma	21 (40.4%)	8 (30.8%)	13 (50.0%)	**0.032[b]**
Degree	27 (51.9%)	18 (69.2%)	9 (34.6%)	
Masters	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Gender				
Male	31 (59.6%)	13 (50.0%)	18 (69.2%)	0.258[a]
Female	21 (40.4%)	13 (50.0%)	8 (30.8%)	
Training regarding sf medicines				
Yes	16 (30.8%)	9 (34.6%)	7 (26.9%)	0.764[a]
No	36 (69.2%)	17 (65.4%)	19 (73.1%)	
Training timing *(of those that said Yes above)*				
Postgraduate degree	1 (6.25%)	0 (0.0%)	1 (12.5%)	
Undergraduate course	11 (68.75%)	4 (44.4%)	7 (87.5%)	
CPD course	5 (31.25%)	5 (55.6%)	0 (0.0%)	
Source of SF medicine information				
Regulator Memos	13 (25%)	9 (34.6%)	4 (15.4%)	0.106[b]
Pamphlets	7 (13.5%)	4 (15.4%)	3 (11.5%)	0.268[b]
Posters	5 (9.6%)	1 (3.8%)	4 (15.4%)	0.109[b]
Social media	39 (75%)	22 (84.6%)	17 (65.4%)	0.258[b]
Others***	7 (13.5%)	5 (19.2%)	2 (7.7%)	0.102[b]

*[a]Pearson Chi-square test, [b] Fishers exact test. **others in 'Personnel present at time of survey'.***others included registered nurse (1), laboratory technician (1), cosmetician (1), shop assistant (1), pharmacy managers (2), and pharmacy student (1). 'Source of Substandard and Falsified medicine information' would include sources like journal articles. Please note: For some questions, particularly those concerning sources of information, respondents were allowed to select multiple options. Bold *p*-values indicate significant statistical differences.

Recognition of Registered Medicines, Confidence in Medicine Quality, and Use of Technology Among Pharmacies

In Table 2, we observe the practices related to temperature logging, recognition of registered medicines, confidence in medicine quality, and the use of technology among pharmacies. Notably, an

overall average of 69.2% (36/52) of pharmacies maintained complete temperature logs for the past three months, with a higher prevalence in innovative pharmacies 84.6% (22/26) compared to traditional independent pharmacies 53.8% (15/26).

Most participants 94.2% (49/52) identified registered medicines primarily through the presence of a registration number from the National Medicines Regulatory Authority (NMRA). The key features for distinguishing good quality medicine included packaging material 84.6% (44/52), expiry date 75% (39/52), and label 71.2% (37/52). Notably, innovative pharmacies more frequently identified 'country of origin' as a quality marker 76.9% (20/26), whereas traditional independent pharmacies focused on 'expiry date' and 'packing material' 76.9% (20/26). Regarding confidence in the quality of medicines, participants from all types of pharmacies were generally confident, with 36.5% (19/52) reporting being 'very confident'. The differences in confidence levels between innovative and traditional pharmacies were not statistically significant (p = 0.596).

In terms of technology use, only 28.9% (15/52) of respondents were aware of any analytical technologies, with thin-layer chromatography being the most recognized 23.08% (12/52). However, only 3.8% (2/52) of participants reported using any analytical tools, and there were no significant differences between innovative and traditional pharmacies in this regard. None of the surveyed pharmacies reported interactions with authentication technology companies.

Significant differences were observed in recording systems and inventory management software. Overall, 48.1% (25/52) of pharmacies used a computerised system, and 15.4% (8/52) employed both computerised and manual methods. A notable difference was seen between pharmacy types: 80.8% (21/26) of innovative pharmacies used computerised systems, compared to only 15.4% (4/26) of traditional independent pharmacies, which largely relied on manual systems 73.1% (19/26). Regarding inventory management software, 57.7% (30/52) of all surveyed pharmacies used proprietary software, with a significant majority of innovative pharmacies 96.2% (25/26) using it, compared to only 19.2% (5/26) of traditional pharmacies. Finally, an interview with key management staff at an innovative pharmacy company revealed that direct screening with specialized tools for medicine quality is not a standard practice. Instead, there is a reliance on ZAMRA's registration and temperature and humidity monitoring as proxies for quality assurance.

Table 2: Recognition of Registered Medicines, Confidence in Medicine Quality, and Use of Technology Among Pharmacies (Lusaka, 2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N = 26	*p*-value
Temperature logs for the past 3 months filled in				
Yes, completely filled	36 (69.2%)	22 (84.6%)	14 (53.8%)	

Yes, partially filled.	13 (25.0%)	4 (15.4%)	9 (34.6%)	**0.031**[b]
Good quality medicine distinguishing features				
Brand name	35 (67.3%)	19 (73.1%)	16 (61.5%)	
Country of origin	30 (57.7%)	20 (76.9%)	10 (38.5%)	
Expiry date	39 (75.0%)	19 (73.1%)	20 (76.9%)	
ISO certification	18 (34.6%)	11 (42.3%)	7 (26.9%)	
Label	37 (71.2%)	19 (73.1%)	18 (69.2%)	
Packaging material	44 (84.6%)	24 (92.3%)	20 (76.9%)	
Confidence in the quality of medicine in the pharmacy				
Somewhat confident	5 (9.6%)	2 (7.7%)	3 (11.5%)	
Neutral	9 (17.3%)	4 (15.4%)	5 (19.2%)	0.596[b]
Confident	19 (36.5%)	12 (46.2%)	7 (26.9%)	
Very confident	19 (36.5%)	8 (30.8%)	11 (42.3%)	
Aware of any analytical technologies				
Yes	15 (28.9%)	8 (53.3%)	7 (46.7%)	
No	37 (71.2%)	18 (48.6%)	19 (51.4%)	
Analytical technologies aware of				
Colourimetry based	7 (13.46%)	5 (20.8%)	2 (7.7%)	
Thin layer chromatography based	12 (23.08%)	5 (20.8%)	7 (26.9%)	
Raman spectroscopy	3 (5.77%)	2 (8.3%)	1 (3.8%)	
Near-infrared based	3 (5.77%)	2 (8.3%)	1 (3.8%)	
Mid-infrared based	2 (3.85%)	2 (8.3%)	0 (0.0%)	
Fourier transform infrared based	2 (3.85%)	2 (8.3%)	0 (0.0%)	
None	36 (69.23%)	18 (69.2%)	19 (75.0%)	
Analytical technologies used				
Yes	2 (3.8%)	0 (0.0%)	2 (7.7%)	0.490[b]
No	50 (96.2%)	26 (100.0%)	24 (92.3%)	
Work with authentication technology companies*				
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	
No	52 (100.0%)	26 (100.0%)	26 (100.0%)	
Recording system available				
Computerised	25 (48.1%)	21 (80.8%)	4 (15.4%)	
Manual	19 (36.5%)	0 (0.0%)	19 (73.1%)	**<0.001**[b]
Both	8 (15.4%)	5 (19.2%)	3 (11.5%)	
Inventory software used				
None	19 (36.5%)	0 (0.0%)	19 (73.1%)	
Microsoft Excel	3 (5.8%)	1 (3.8%)	2 (7.7%)	**<0.001**[b]
Proprietary software **	30 (57.7%)	25 (96.2%)	5 (19.2%)	

*[b]Fishers exact test was used for statistical analysis. *For 'Analytical technologies aware of' and 'Inventory software used', respondents were allowed to select multiple options. *Proprietary software refers to customised software designed for specific use by a particular entity or organisation. Bold *p*-values indicate significant statistical differences.

Experiences with Suspected Poor-Quality Medicine, Reporting Methods, and National Medicine Regulatory Authority (NMRA) Alerts

A notable finding was that 55.8% (29/52) of the participants reported having received suspected poor-quality medicine from a distributor, and this was more prevalent in traditional independent pharmacies 65.4% (17/26) than in innovative pharmacies 46.2% (12/26). However, these differences were not statistically significant. Regarding the quality concerns experienced, discoloured medicines were the most commonly encountered issue, 44.8% (13/52). The incidence of suspected poor-quality medicine in the past year varied, with 42.3% (22/52) reporting no incidences and 38.5% (20/52) experiencing it once. No significant differences were found between the pharmacy types.

Most respondents, 67.3% (35/52), indicated that they did not report concerns about poor-quality medicine. Of those who did, distributors were primarily informed, accounting for 76.5% (13/17) of the reports. The NMRA was notified in 35.3% (6/17) of instances, while a combination of both distributors and the NMRA received reports in 47.1% (8/17) of cases. To communicate concerns about medicine quality, pharmacy personnel predominantly used phone calls, with 66.7% (12/17) choosing this method.

All surveyed pharmacies confirmed that they had received reports from the NMRA. Concerning receiving alerts about poor-quality medicines from the NMRA, pharmacy personnel primarily relied on social media 73.5% (36/52) and emails 34.7% (17/52). Although the NMRA offers a dedicated mobile application, the 'Adverse Drug Reaction Application (ADRA)', designed to enhance pharmacovigilance, including addressing product quality problems, none of the surveyed pharmacy personnel reported using it.

Table 3: Experiences with Suspected Poor-Quality Medicine, Reporting Methods, and National Medicine Regulatory Authority (NMRA) Alerts (Lusaka,2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N=26	*p*-value
Received suspected poor-quality medicine from a distributor				
Yes	29 (55.8%)	12 (46.2%)	17 (65.4%)	
No	23 (44.2%)	14 (53.8%)	9 (34.6%)	0.264[a]
Medicine quality concerns experienced				
Discoloured medicines	13 (44.8%)	4 (33.3%)	9 (52.9%)	
Expired medicines	8 (27.6%)	2 (16.7%)	6 (35.3%)	
Others	8 (27.6%)	6 (50.0%)	2 (11.8%)	
Number of incidences of suspected poor-quality medicine in the past year experienced				
Zero	22 (42.3%)	12 (46.2%)	10 (38.5%)	
One time	20 (38.5%)	7 (26.9%)	13 (50.0%)	0.103[b]
Two times	9 (17.3%)	7 (26.9%)	2 (7.7%)	
Three times	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Reported poor-quality medicine concern				
Yes	17 (32.7%)	9 (34.6%)	8 (30.8%)	1.000[a]
No	35 (67.3%)	17 (65.4%)	18 (69.2%)	
Who quality concerns were reported *(of those who did)*				
Distributor	13 (76.5%)	5 (55.6%)	8 (100.0%)	
NMRA	6 (35.3%)	2 (22.2%)	4 (50.0%)	
Both	8 (47.1%)	2 (22.2%)	6 (75.0%)	
Receive NMRA reports				
Yes	52 (100.0%)	26 (100.0%)	26 (100.0%)	
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Platform used to report medicine quality issues *(of those who did)*				
Email	4 (22.2%)	3 (33.3%)	1 (9.1%)	
Phone call	12 (66.7%)	6 (66.7%)	6 (54.5%)	
Website	2 (11.1%)	1 (11.1%)	1 (9.1%)	
Other	4 (22.2%)	1 (11.1%)	3 (27.3%)	

Platform used to receive poor-quality medicine alerts from NMRA			
Email	17 (34.7%)	15 (62.5%)	2 (11.8%)
Phone call	3 (6.1%)	1 (4.2%)	2 (11.8%)
Social media	36 (73.5%)	22 (91.7%)	14 (82.4%)
Other	2 (4.1%)	0 (0.0%)	2 (11.8%)

[a]Pearson Chi-square test, [b]Fishers exact test. Social media platforms - mostly WhatsApp, Facebook groups.

Associations between Pharmacy Personnel Characteristics and Awareness of Analytical Technologies and Reporting Poor Quality Medicines

A significant difference was found in the awareness of any analytical technologies among pharmacy personnel (p=0.009). Most pharmacists (86.7%) were aware of these technologies compared to 13.3% of pharmacy technologists and none of the other personnel. No significant difference was found in the use of analytical technologies and reporting of poor-quality medicines across personnel categories. Regarding the highest degree qualifications, degree holders were the most aware of analytical technologies (86.7%) and the only ones who used them. There was a significant difference in the awareness of analytical technologies across qualification groups (p=0.013). However, no significant difference was found in the use of these technologies and reporting of poor-quality medicines. Among those who completed training in the past year, those with no training were more likely to be aware of analytical technologies (46.7%), use them (50%), and report poor-quality medicines (52.9%). However, no significant differences were observed among the different types of training.

Table 4: Associations between pharmacy personnel characteristics, awareness of screening technologies, and reporting of poor-quality medicines

Variables	Aware of any Screening technologies		Screening technologies used		Reported poor quality medicine	
	Yes	No	Yes	No	Yes	No
Pharmacy personnel present						
Pharmacist	13 (86.7%)	15 (40.5%)	2 (100%)	26 (52%)	9 (52.9%)	19 (54.3%
Pharmacy technologist	2 (13.3%)	15 (40.5%)	0 (0.0%)	17 (34%)	7 (41.2%)	10 (28.6%)
Others	0 (0.0%)	7 (18.9%)	0 (0.0%)	7 (14%)	1 (5.9%)	6 (17.1%)
	p=**0.009***		p=0.641		p=0.441	
Highest degree qualifications						
GCSE	0 (0.0%)	1 (2.7%)	0 (0.0%)	1 (2 %)	0 (0.0%)	1 (2.9%)
Certificate	0 (0.0%)	2 (5.4%)	0 (0.0%)	2 (4%)	0 (0.0%)	2 (5.7%)
Diploma	1 (13.3%)	19 (51.4%)	0 (0.0%)	21 (42%)	8 (47.1%)	13 (37.1%)
Degree	13 (86.7%)	14 (37.8%)	2 (100%)	25 (50%)	9 (52.9%)	18 (51.4%)
Masters	0 (0.0%)	1 (2.7%)	0 (0.0%)	1 (2%)	0 (0.0%)	1 (2.9%)
	p=**0.013***		p=0.410		p=0.906	
Training completed in the past year						
None	7 (46.7%)	21 (56.8%)	1 (50%)	27 (54%)	9 (52.9%)	19 (54.3%)
Procurement	6 (40%)	9 (24.3%)	1 (50%)	14 (28%)	5 (29.4%)	10 (28.6%)
Pharmacovigilance	2 (13.3%)	3 (8.1%)	0 (0.0%)	5 (10%)	2 (11.8)	3 (8.6%)
Storage	0 (0.0%)	2 (5.4%)	0 (0.0%)	2 (4%)	0 (0.0%)	2 (5.7%)
Information technology	0 (0.0%)	1 (2.7%)	0 (0.0%)	1 (2%)	1 (5.9%)	0 (0.0%)
Logistics	0 (0.0%)	1 (2.7%)	0 (0.0%)	1 (2%)	0 (0.0%)	1 (2.9%)
	p=0.780		p=1.000		p=0.807	

*Significance was set at p <0.05. 'Others' under 'Pharmacy personnel present' include nurses, pharmacy managers, assistants, laboratory personnel, cosmeticians, and students. Please note that the respondents could select multiple options for some of the questions, particularly in relation to their training completed in the past year. Bold p-values indicate significant statistical differences.

Discussion

This study sheds light on the landscape of medicine quality analytical technologies and reporting practices across innovative and traditional independent pharmacies in Lusaka, Zambia, revealing both the strengths and challenges of this sector. Encountering poor-quality medicines–discoloured, expired, or otherwise deficient–is a shared concern among these pharmacies, underscored by similar observations in prior research and highlighted by product recall alerts from the NMRA. Despite this issue, a disconcerting observation from our study is the consistent underreporting of such medicine quality issues to the NMRA. This low reporting rate underscores a critical hurdle in safeguarding the supply chain's integrity and ensuring medicine's safety and efficacy, necessitating a strategic intervention to address it. As such, the findings of this study call for comprehensive efforts to enhance existing reporting systems and boost training among pharmacy professionals to effectively identify and report poor-quality medicines, ultimately contributing to robust medicine quality surveillance.

Both innovative and traditional independent pharmacies indicated encounters with suspected substandard medicines from distributors, expressing significant apprehensions about their quality. Notably, these pharmacies identified recurring issues such as receiving discoloured or expired medicines. This concern is not isolated; other Zambian pharmacies have similarly flagged such discrepancies, prompting the NMRA to issue product recall alerts [40–42]. For instance, in 2020 and 2021, specific alerts were raised concerning products like Vitamin C and Aspirin, which exhibited discolouration, crumbled upon opening, and emitted an unpleasant odour [41,42]. In a more alarming incident, a local distributor supplied compromised medical products, encompassing items such as condoms, gloves, and paracetamol, to public health facilities [43–45], which subsequently spurred investigations into potential corruption and segregation of the said products. Such episodes underscore the criticality of addressing poor-quality medicines in Zambia as they present grave threats to patient safety.

Despite encountering poor quality medicines, a significant challenge arises from the consistent underreporting of these issues by both innovative and traditional independent pharmacies. Alarmingly, many prefer to relay concerns only to distributors rather than to official regulatory authorities, leading to a gap in effective regulation. This phenomenon is not unique to Zambia; a study from Tanzania also highlighted similar underreporting behaviours, underscoring gaps in addressing medicine quality issues [29]. The importance of robust reporting mechanisms cannot be understated, as they are pivotal in identifying and halting the distribution of poor-quality medicines [9]. Consequently, Zambia needs to fortify its reporting systems and channels, coupled with a push for enhanced awareness and training of pharmacy professionals. Such initiatives would streamline the identification

and reporting of poor-quality medicines and bolster the nation's medicine quality surveillance, ultimately ensuring the consistent availability of good quality-assured medicines.

There is a notable training gap among pharmacy personnel concerning SF medicines. Recognising this, the International Pharmaceutical Federation (FIP), in collaboration with the WHO, introduced a curriculum guide tailored for pharmacy students to bridge the knowledge divide [46]. This initiative echoes a study in which pharmacy students in Sub-Saharan Africa benefited from dedicated SF medicine courses [47]. Notably, Zambian pharmaceutical practitioners have voiced a demand for specialised continuing professional development (CPD) programs encompassing SF medicines [48]. Addressing this training deficiency is pivotal for bolstering medicine quality surveillance in the country.

Pharmacy personnel from both innovative and traditional outlets acknowledged receiving alerts on poor-quality products from the NMRA, primarily through social media platforms, such as WhatsApp, Facebook groups, and email. Direct communication, such as phone calls and emails, dominated the reporting back to the NMRA. Leveraging such diverse communication channels emphasises the potential to reach a broader audience and enhance the reporting of medicine quality concerns. Although the role of social media in conveying poor-quality medicine alerts is significant, its effectiveness and reliability warrant further evaluation [49–51]. Even with the prevalent awareness of NMRA alerts, the underutilisation of tools such as ADRA highlights existing implementation gaps. Addressing these discrepancies is essential for fortifying medicine quality surveillance and safeguarding public health.

Differences in recording systems and inventory management software have emerged between innovative and traditional independent pharmacies. Innovative pharmacies predominantly employ computerised recording systems and proprietary software in line with the practices advocated by innovative pharmacy companies in the retail sector [30,52]. In contrast, traditional independent pharmacies mainly use manual recording systems. The benefits of computerised approaches extend to improved accuracy, reduced errors, and advanced features such as automated ordering and real-time analytics, all of which potentially translate to better patient care, reduced costs, and heightened efficiency [30,53–55]. The reliance on manual systems by traditional outlets underscores the pressing need for interventions that champion modern recording and inventory systems.

Despite notable distinctions in recording and inventory systems, both innovative and traditional independent pharmacies demonstrated a lack of engagement with analytical technologies useful in screening poor-quality medicines. This disengagement is particularly alarming in the context of known SF medicine incidents in the region [7,56–59]. While innovative pharmacies benefit from computerised inventory systems, a substantial portion of both pharmacy types lack access to, or do not employ,

these crucial technologies. In other countries, such technologies have proven indispensable for regulators and pharmacy personnel, ensuring medical products' safety and efficacy [12,17,60]. Factors such as high costs and limited awareness may be contributing to this low adoption[12,13,17]. Strengthening collaboration with authentication technology companies could provide pharmacies with tools that enhance medicine quality screening, traceability, and supply chain tracking.

In the case of the innovative pharmacy company central warehouse, our investigation reveals a reliance on ZAMRA's registration as well as temperature and humidity monitoring as proxies for quality assurance, rather than on direct technological interventions. As indicated in the results, an interview with a manager highlighted that direct screening with specialised tools is not a common practice at the central warehouse. This finding underscores a potential area for strengthening systemic quality checks at the organisational level.

Furthermore, innovative pharmacies, despite their technological advancements, face distinct challenges in maintaining the quality of medicines. These challenges notably include managing the complexities of digital platforms and ensuring the integrity of medicines during delivery processes – a challenge that is not exclusive to them but also pertains to traditional pharmacies. However, unlike traditional pharmacies, which operate within the established parameters of brick-and-mortar establishments and have long-standing systems due to their prolonged presence, the extent of regular inspections and adherence to mandated quality assurance and quality control (QA/QC) measures for innovative pharmacies remains unclear. Traditional pharmacies are typically subject to regular inspections to verify compliance with ZAMRA's licensing requirements, suggesting a need for a more detailed understanding of the inspection and compliance procedures for innovative pharmacies.

In the discussion of quality assurance, it is crucial to recognize the pivotal role that individual pharmacies play in complementing the NMRA’s post-marketing surveillance efforts. For these pharmacies, adopting effective quality screening technologies as part of their standard operating procedures is essential. This includes using portable devices for detecting SF medicines, which allow for quick, on-site verification of drug authenticity and quality; implementing digital systems to monitor environmental factors like temperature and humidity, ensuring optimal storage conditions for medicines; and integrating barcode scanning technology to enhance product verification and traceability. However, it's important to acknowledge that the feasibility of implementing these measures can vary significantly among individual outlets, depending on their available resources, access to technology, and staff training. Pharmacies in resource-limited settings might need to prioritise certain interventions and gradually incorporate more advanced technologies as resources permit. Therefore, while these practices are recommended, the approach to adoption should be

tailored to each pharmacy's specific context, ensuring that enhancements in quality control measures are both practical and sustainable.

Limitations

This study has several limitations. First, the study was conducted in a single city, Lusaka; therefore, the findings may not be applicable to other settings in Zambia or elsewhere. Although it is unlikely that cities and towns outside the capital city, Lusaka, may use screening technologies and report better, there may be differences in the medicine quality screening technologies and reporting practices used in other cities or rural areas. Therefore, caution should be exercised when generalising the findings to other contexts. Second, the uniformity of innovators from a single company, limiting the extrapolation of findings to other innovative pharmacy models across Africa. Third, the study relied on self-reported data, possibly subject to a social desirability bias. This means that the participants' responses may have been influenced by their desire to present themselves in a positive light. To address this limitation, future studies should consider using more objective measures, such as observational studies, to explore medicine quality screening technologies and reporting practices. Finally, the study did not explore the reasons for the reported lack of awareness and use of screening technologies and authentication technology companies. Future studies could examine the barriers to and facilitators of adopting these technologies and services by pharmacy professionals in Zambia. This could include exploring the cost-effectiveness of these technologies and services, identifying the training needs of pharmacy professionals, and investigating the regulatory and policy environments that may influence the adoption of these technologies and services.

Conclusion

In conclusion, the disparities observed between innovative and traditional independent pharmacies in Lusaka, Zambia, underscore the importance of improved medicine quality surveillance. While there is potential for enhanced medicine quality via modern screening technologies, their low adoption remains a concern, possibly because of high costs and limited awareness among pharmacy personnel. Targeted interventions, training programs, and benefits could address this gap.

The pervasive underreporting of substandard medicines poses a significant risk to the healthcare supply chain. Augmenting reporting mechanisms and increasing training for professionals can improve medicine safety. Moreover, the prevalent use of social media for receiving ZAMRA alerts points towards an opportunity to broaden information dissemination, although its efficiency needs assessment. The benefits of computerised systems in innovative pharmacies suggest that extending such advancements to traditional pharmacies can improve healthcare delivery. Ultimately, there is an urgent call for concerted efforts from all stakeholders to improve the quality of medicine in Zambia.

Future research should focus on the practical effects of interventions and continually refine strategies to meet the sector's dynamic requirements.

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Chapter 5: Research paper 4 - Medicine Quality (Amoxicillin and Sulfadoxine/Pyrimethamine)

Chapter Introduction

This chapter, presented as Research Paper 4, investigates the quality of medicines in pharmacies in Lusaka, Zambia, with a specific focus on amoxicillin and sulfadoxine/pyrimethamine (SP). These two medicines are critical to the public health landscape in Zambia. Amoxicillin, an antibiotic, is essential for tackling bacterial infections such as pneumonia, whereas sulfadoxine/pyrimethamine is crucial for preventing and treating malaria, a significant health concern in the country.

Ensuring the quality of medicines is essential, especially for medicines as significant as amoxicillin and SP. Good-quality medicines are not only vital for effective disease management but are also pivotal for achieving the goal of universal health coverage. Quality assurance contributes to improved therapeutic outcomes, reduced risk of drug resistance, and minimised public health threats. Conversely, poor-quality amoxicillin and SP can lead to ineffective treatment outcomes and escalating drug resistance. Additionally, the economic implications of poor-quality medicines can place undue burdens on patients due to the costs of prolonged health care.

While the previous chapters explored the attributes of the outlets, storage and transportation protocols, procurement practices, and the technologies employed to screen poor-quality medicines, they primarily examined the potential for practices and the environment to influence medicine quality. This chapter underscores the real concerns that exist. It establishes the tangible challenges and contrasts in the quality of antimalarials and antibiotics dispensed by innovative and traditional independent pharmacies. This chapter further complements the overarching objectives of the PhD research by transitioning from a theoretical understanding of potential risks to presenting empirical evidence of actual quality discrepancies.

This investigation encompasses laboratory analyses of the medicines for quality, supplemented by insights obtained from surveys conducted with pharmacy staff. These insights could help formulate potential policy interventions to enhance the accessibility and quality of medicines in Zambia.

The structure of this chapter aligns with standard practices for biomedical journals, encompassing sections on introduction, methods, results, and discussion. The intention is to submit the paper to BMC Public Health.

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Student ID Number	1403479	**Title**	Mr
First Name(s)	Scott Kaba		
Surname/Family Name	Matafwali		
Thesis Title	Innovative Private Pharmacy Distribution Channels: Implications on Medicine Quality in Zambia		
Primary Supervisor	Dr Harparkash Kaur		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

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Where is the work intended to be published?	BMC Public Health (published by Springer Nature).
Please list the paper's authors in the intended authorship order:	Scott Kaba Matafwali, Charles Opondo, Sian Clarke, Harparkash Kaur
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conceptualised the study and developed the protocol with methodological guidance from my supervisors and advisory team. Additionally, I conducted the fieldwork, analysed the data, and wrote the first drafts of the manuscript. I also revised the manuscript based on feedback from co-authors.

SECTION E

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Date	17/08/2023

Medicine Quality in Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: Factors Influencing the Quality of Amoxicillin and Sulfadoxine/Pyrimethamine

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Abstract

Introduction: Ensuring the availability and quality of medicines is fundamental for effective treatment and overall health of the population. In Zambia, innovative emerging pharmacy distribution channels could influence the quality of medicines available to the public. This study investigated the impact of these innovative distribution systems, in comparison with traditional independent pharmacies in Lusaka, Zambia, on the quality of two widely used medicines in the region: amoxicillin and sulfadoxine/pyrimethamine.

Methods: In this cross-sectional study, a total of 114 samples of amoxicillin and 53 samples of sulfadoxine/pyrimethamine (SP) were purchased from 52 pharmacies (26 innovative and 26 traditional independent pharmacies).

In addition to sample purchases, pharmacy staff completed questionnaires to enable insights into their practices. The quality of the purchased samples was assessed by visual inspection and laboratory (content and *in vitro* dissolution) analyses according to the authorised United States Pharmacopeia (USP) monographs. The amount of the stated active pharmaceutical ingredient (SAPI) was measured using the technique of high-performance liquid chromatography-diode array detection (HPLC-DAD).The major points for data analyses were sample content expressed as percentage of SAPI and for the dissolution test to pass the USP specified percent of the SAPI needs to be detected.

Results:

It is reassuring that no falsified medicines (absence of SAPIs) were detected amongst the samples of amoxicillin (n=114) and SP (n=53). However, 62.3% (n=71/114) of the amoxicillin samples and none (n=53/53) of the SP samples complying with these limits. Overall, the amounts of SAPI detected in samples of amoxicillin and SP were more than USP specified limits of 120% and 110%, respectively.

Notably, all samples complied with the USP tolerance limits for bioavailability. Furthermore, no difference was observed (p=0.799) when comparing medicine quality between innovative and traditional independent pharmacies.

Conclusion: The laboratory analysis data indicates adherence to USP tolerance limits for bioavailability, but there are discrepancies in content of amoxicillin and SP measured in the formulations. No difference was observed between innovative and traditional independent pharmacies. These findings underscore the critical need for comprehensive and regular quality control checks throughout the entire pharmaceutical supply chain. This should include upstream activities, such as the acquisition of active pharmaceutical ingredients (raw materials) and manufacturing processes, wholesaling, and retail distribution.

Keywords; Falsified medicines, Substandard medicine, Innovative pharmacies, Traditional independent pharmacies, Medicine quality, Zambia

Introduction

Access to good quality medicines is fundamental for effective disease management and achieving the United Nations' goals for universal health coverage (UHC), as outlined by the Sustainable Development Goals (SDGs), specifically SDG 3, which emphasises ensuring healthy lives and promoting well-being for all, and has several targets [1–3]. Target 3.8 stipulates "achieving universal health coverage, including financial protection, access to quality essential healthcare services, and access to safe, effective, quality, and affordable essential medicines and vaccines" by 2030.

Quality-assured medicines not only strengthen health systems but also build trust among the populace. Conversely, substandard and falsified (SF) medicines endanger patient health, compromise treatment effectiveness, and erode public confidence in health systems [1,4]. The World Health Assembly has standardised the definitions of medicine quality [5]. Substandard medicines refer to products that do not meet the required quality standards or specifications. Unregistered medicines are those that have not undergone evaluation or approval by the relevant national or regional regulatory authority before being marketed, distributed, or used. However, falsified medicines intentionally and fraudulently misrepresent their identity, composition, or source.

Low- and middle-income countries (LMICs) such as Zambia often face disruptions in their pharmaceutical supply chains, a situation worsened by global crises such as the COVID-19 pandemic [6,7]. These disruptions may create a thriving market for the proliferation of SF medicines, especially when demand surpasses supply [8,9]. Significant mortality rates may be linked to the consumption of poor-quality medicines namely antimalarials and antibiotics [5,10]. Furthermore, antimicrobial resistance (AMR) may arise when patients ingest poor-quality medicines, which can complicate treatment in both developed and developing nations [11,12].

Malaria and infectious diseases, such as pneumonia, remain significant public health challenges in Zambia, and as such, private pharmacies play a pivotal role in the provision of medicines. Especially during times when public health facilities face stockouts, many individuals are compelled to purchase from private establishments [9,13,14]. Within the retail sector, the most readily accessed medicines are antibiotics and antimalarials, which are often purchased without prescriptions [15–17].

Zambia's pharmaceutical distribution (predominantly in the private sector) is structured in a tiered manner, starting from importers, moving through wholesalers and sub-wholesalers, to finally reaching pharmacies, health shops, and drug stores [18,19]. This tiered distribution model poses several challenges, which include difficulty navigating non-traditional supply channels with multiple storage points and may increase the risk of SF medicines infiltrating legitimate supply chains. Despite these hurdles, the pharmaceutical sector is undergoing transformative changes driven by innovative technologies.

Entrepreneurs are leveraging modern technologies through implementing advanced inventory systems and establishing retail partnerships to ensure access to quality-assured medicines [20,21]. Zambia is similarly experiencing the rise of innovative pharmacies that adopt these innovations and expand services into e-pharmacy and telepharmacy.

Previous studies offer glimpses into the presence of SF medicines in Zambia; however, a comprehensive understanding of this problem remains elusive [22,23]. This study aimed to examine the quality of medicines available in both innovative and traditional independent pharmacies in Lusaka, Zambia.

Methods

Study Setting and Design

A cross-sectional survey using an overt sampling approach was conducted between August and September 2022 to examine the quality of amoxicillin, and SP purchased in two types of pharmacies: innovative and traditional independent pharmacies. This study was supplemented by insights obtained from surveys conducted with pharmacy personnel in Lusaka, Zambia's capital, and the largest city, with an estimated population of three million people [24] (Figure 1). It serves as a pivotal centre for economic, political, and healthcare activities. Lusaka's diverse healthcare infrastructure provided a comprehensive platform for sampling independent pharmacies. In designing the study and determining the sampling methodology, we referred to the MEDQUARG guidelines [25] and the published checklist for medicine quality studies [26].

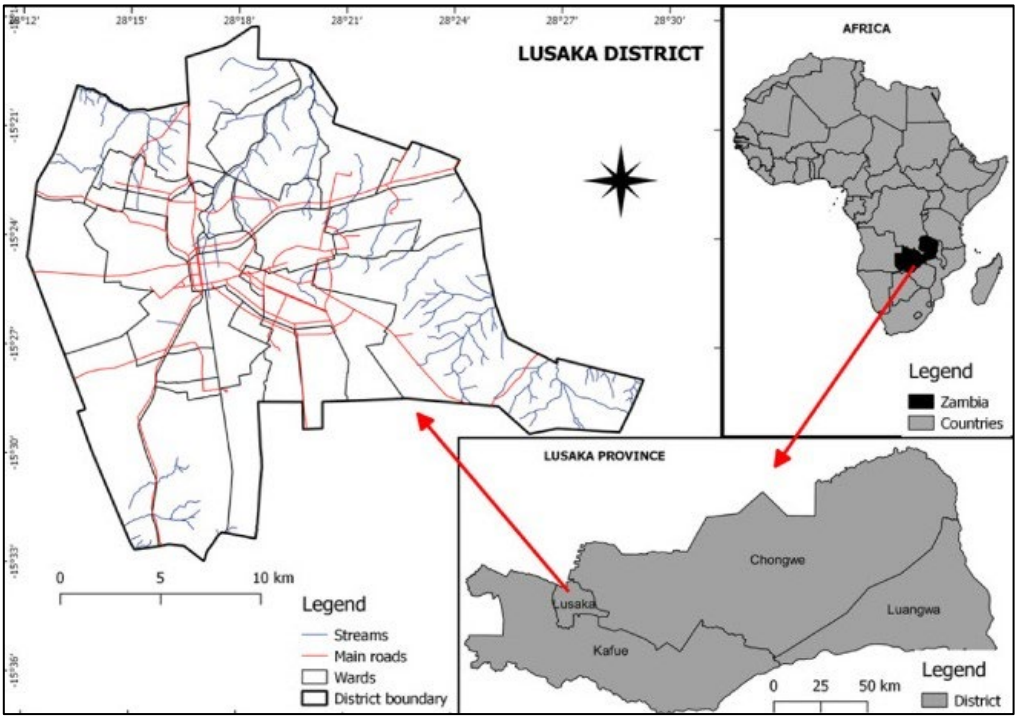

Figure 1: Location of the study area, Lusaka District, Zambia. *Source*; permission to use this figure was obtained from Mutukwa et al [27]

Study Population and Pharmacy Sampling Collection

The sampling process started with acquiring a list of all licensed pharmacies in Lusaka (n=333) from the Zambia Medicines Regulatory Authority (ZAMRA) [19]. Chain outlets, drugstores and health shops were excluded from this study and the list was refined to focus solely on innovative and traditional independent pharmacies. .

Inclusion Criteria: Retail pharmacies were identified based on their registration from ZAMRA's latest master list retrieved from their website in January 2022. These pharmacies were then stratified based on their alignment with innovative pharmacy distribution channels or traditional supply chains. Identification of innovative pharmacies was aided by Medsearch Zambia and key informants within the pharmaceutical sector, followed by verification for the characteristics outlined in the Salient Advisory Reports [20].

All 26 pharmacies classified as innovative were selected for this study and a random sample of 26 traditional independent pharmacies were included whilst four of them refused to participate. For each refusal, an alternative pharmacy was selected in close geographical proximity to ensure integrity and representation of the original stratification.

The choice of medicine samples

Zambian treatment guidelines are aligned with WHO recommendations, to prescribe SP for Intermittent Preventive Treatment against malaria in pregnant women (IPTp). SP is widely available in pharmacies and is commonly acquired over the counter for uncomplicated malaria because of its affordability and need for fewer pills [28]. Amoxicillin, a widely used antibiotic, is typically used to treat upper respiratory tract infections (UTIs). Given the potential for AMR stemming from its misuse or overconsumption, monitoring the quality of these medicines in the retail sector is crucial to ensure their safety, efficacy, and regulatory compliance.

Sample Size Calculation

The hypothesis guiding the sample size calculation posited that medicines in innovative pharmacies would be of better quality than those in traditional independent pharmacies. The proportion of substandard medicines in independent pharmacies (p1) was estimated at 17.6% based on Zambian analyses conducted by ZAMRA as part of the medicine quality surveillance [29]. Conversely, innovative pharmacies (p2) are assumed to house only 5% of these medicines. Ideally, this proportion should be 0%; any figure above 10% is alarming [25]. To achieve 80% power to detect a difference of at least 12.6% in proportion of substandard medicines in innovative vs traditional independent pharmacies using statistical tests at the 5% level of significance, a minimum sample size of 96 samples per group was deduced using the formula: $n = (Z_{\alpha}/2+Z_{\beta})^2 * (p_1(1-p_1) +p_2(1-p_2)) / (p_1-p_2)^2$

Where $Z_{\alpha}/2$ is the critical value of the normal distribution at $\alpha/2$ (for a level of significance of 5%, α = 0.05, and the critical value is 1.96). Z_{β} is the critical value of the normal distribution at β (for a power of 80%, β is 0.2, and the critical value is 0.84), and p_1 and p_2 are the expected sample proportions of the two groups [30,31]. Preliminary discussions with pharmaceutical experts and retailers led to the expectation that each pharmacy would stock approximately five brands of amoxicillin and SP, estimating 130 medicine samples per group for each medicine. To ensure an unbiased representation, samples from all available amoxicillin and SP brands were purchased from each pharmacy.

Pharmacy Outlet Participants and Questionnaire Survey

The participants in the survey supplementing medicine quality analysis consisted of pharmacy-qualified personnel, including pharmacists and pharmacy technologists, who were present in the outlet on the day of the survey. In cases where no pharmacy personnel were present, the available personnel, which included pharmacy managers or shop assistants, were interviewed.

A structured questionnaire recording the outlet characteristics, pharmacy environment, and specific details of the medicine (amoxicillin and SP) samples was administered in each outlet, and it was digitised using the ODK platform. Written informed consent was obtained from all participants prior to commencement. Prior to using the final questionnaire, a pilot test was conducted at two Lusaka-based retail pharmacies to enhance clarity and relevance. Pilot participants were excluded from the final investigation outlined here. Observational assessments of the pharmacy outlets were also conducted. All interviews were conducted by the lead investigator (SKM).

Sample Collection and Storage

The study focused solely on adult solid dosage forms, encompassing capsules and tablets, deliberately omitting syrups and injectables. The purchasing process included recording pertinent data points, such as the outlet type (innovative or traditional independent pharmacy), transaction date, amount disbursed, brand name, formulation, batch number, manufacturing entity, expiry date, and total quantities of the procured medicines. For amoxicillin, the average purchase comprised 30 capsules (three blisters;10 capsules per pack). In contrast, for SP, the purchase consisted of 3 tablets, which is the total number in a packet.

Details of the medicine samples were recorded on an Excel spreadsheet, including the sample number, brand name, medicine type (originator, branded generic, or generic), lot or batch number, manufacturing date, expiry date, manufacturer name, manufacturing country, international non-proprietary names (INN) of the SAPIs, dosage form, strength, and price per dosage form. Comprehensive digital images of the tablets or capsules, including primary and secondary packaging, the leaflet, and the sample number, were captured using the mobile phone camera stored in a

dedicated file. The medicine samples were kept in their primary and secondary packaging wherever feasible. In instances where the original packaging was absent, the samples were placed in light-protective paper envelopes to shield them from possible exposure to direct sunlight. Each sample was encased in a zip-lock bag with its data form and housed in a temperature-controlled room at approximately 20°C. An export licence was secured from ZAMRA to ensure compliance with regulatory requirements before shipping the samples to the London School of Hygiene and Tropical Medicine (LSHTM) in London, UK, for laboratory analysis.

Assessing the quality of medicines

Visual Inspection

Prior to the analytical analysis, each sample's packaging underwent a visual assessment and photos were recorded. For this visual inspection phase, we referred to a simplified checklist from Schiavetti et al.,[32] focusing on key aspects such as packaging, identity, traceability, and physical appearance of the samples. Each sample was weighed prior to quantitative content analysis and dissolution testing, measuring the SAPI released utilising high performance liquid chromatography–diode array detection (HPLC-DAD) following authorised United States Pharmacopoeia (USP24) monographs for compliance to tolerance limits corresponding to each medicine's dosage form.

High-Performance Liquid Chromatography - Diode Array Detection Conditions

Reference standards of the SAPIs were sourced from Sigma-Aldrich, based in Dorset, United Kingdom. All essential equipment and solvents were procured from Thermofisher Scientific in Hemel Hempstead, UK. Quantitative analyses were carried out using Thermo Scientific™ Dionex™ Ultimate™ 3000 HPLC-DAD system (Thermofisher, Hemel Hempstead, UK) and separation of each SAPI was achieved using an AcclaimC_{18} 120 Å (250 X 4.6 mm, Thermofisher, Hemel Hempstead, UK) column, using eluent composition, flow rate and wavelength on DAD as shown in table 1 The authenticity of the detected peaks was determined by comparison of retention time and spiking the sample with commercially available reference standard of the SAPI. A calibration curve for each SAPI was generated by Chromeleon (Thermo Scientific™ Dionex™ Chromeleon™ 6.8 Chromatography Data System) using known amounts of the reference standard injected into the column.

Table 1: SAPI and eluent composition, flow rate, and DAD settings.

SAPI	Eluent	Flow rate	DAD set at -nm
Sulfadoxine / Pyrimethamine	Ammonium formate (10 mM, pH of 2.7) with 40% (v/v) acetonitrile	1.5 ml/min for 2.7 mins.	275
Amoxicillin	Ammonium formate (10 mM, pH of 2.7) with 10% (v/v) acetonitrile	1.2 ml/min for 2.7 mins	235

Content Analysis

Quantitative analysis was performed by dissolving each tablet or capsule in the appropriate solvent, subjected to sonication, and subsequently centrifuged. The supernatant, containing the soluble ingredients, were then injected into the HPLC column. The assay quantified the SAPI present in each tablet or capsule. Results from the content analysis were presented as a percentage, comparing the detected SAPI in each sample to the dose indicated on the packaging and multiplying by one hundred. Laboratory analysis involved running triplicates for each sample, with comparisons made against known good and poor quality samples and controls sourced from UK pharmacies.

Dissolution Testing

Dissolution testing was performed using the Pharma Test PT 017 dissolution apparatus (Pharma Test Group, Pharma Test, Hainburg, Germany). The bioavailability of individual medicines was carried out according to the authorised monographs outlined in the United States Pharmacopeia (USP 24) following conditions listed in the table 2 below;

Table 2: Monographs followed for the dissolution testing of SP and amoxicillin.

Medicine	Dosage form	Speed (RPMs)	Medium	Volume (mL)	Tolerance
Sulfadoxine / Pyrimethamine	Tablet	75	pH 6.8 phosphate buffer 0.05M	1000	60% at 30 mins
Amoxicillin	Tablet	100 for 250 mg	Water	900	75% at 30mins
	Capsule	75 for 500mg	Water	900	80% at 60mins

The amount of SAPI released over a set period of time was measured using the column and conditions outlined above. Data achieved was used to determine the samples adherence or not to the USP-defined tolerance limits.

Definitions for Substandard and Falsified Medicines

The pharmacopoeial limits were referred to for classifying medicines with a SAPI content to not be less than or more than but is between 90%-110% for SP and between 90%-120% for amoxicillin as of good quality. Any medication falling outside these bounds was categorised as substandard. The table above encapsulates these criteria, drawn from USP 24 monographs for dissolution whereby SP tablets and amoxicillin (both capsules and tablets) must meet the specified API dissolution criteria, that is, more than 60% of SP must dissolve at 30 mins of start of the dissolution process. Following similar specifications, more than 80% SAPI of amoxicillin must be detected at 60 mins in the dissolution process for the capsules and 75% SAPI of amoxicillin for tablets (see Box 1). Samples that met the specified tolerance limits were classified as good quality, and conversely, any sample that did not meet the specified tolerance limits were labelled substandard, in accordance with WHO's definitions.

Box1: Classification for quality analysis by dissolution and content range for SP and amoxicillin

Parameter	Sulfadoxine/pyrimethamine (SP) Tablets	Amoxicillin Capsules	Amoxicillin Tablets
SAPI Content Range (%)	≤90 – ≥110%	≤90 – ≥120%	≤90 – ≥120%
Dissolution at 30 minutes	≥ 60% of the SAPI	-	≥ 75% of the SAPI
Dissolution at 60 minutes	-	≥ 80% of the SAPI	-

Note: ≤ = not less than; ≥ not more than

Data Entry and Statistical Analysis

Data were entered into Microsoft Excel and rigorously checked for coding errors and inconsistencies. Descriptive and analytical methods were employed in our analysis. Categorical variables were expressed as frequencies (%). The association of explanatory variables with the quality of amoxicillin (defined by SAPI≤90% or ≥120%) was ascertained using the Pearson Chi-square test or Fisher's exact test, based on their appropriateness. A binary logistic regression model was applied to determine the crude odds ratios and 95% confidence intervals, with amoxicillin quality as the outcome variable (good = 1, poor = 0). The model considered pharmacy type as the main explanatory variable and medicine characteristics as covariates. The variables were initially grouped into clinically or operationally meaningful categories based on their relevance to the study objectives. Each variable was then individually assessed for its association with medicine quality using bivariate logistic regression. A *p*-value threshold of ≤ 0.25 was employed at this stage to identify potentially relevant variables, aiming to be inclusive in the exploratory phase of the analysis. Subsequently, variables that met this criterion were evaluated for collinearity and included in the multivariable logistic regression model. Non-significant predictors were introduced sequentially to identify potential confounders. The adequacy of the model was verified using the Hosmer-Lemeshow test. All analyses were performed using STATA version 14 (Stata Corp., College Station, Texas, USA).

Ethical Approval

Ethical approval for this study was obtained from the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022) in Zambia and the London School of Hygiene and Tropical Medicine Ethics Committee (Ref:28040) in the UK. Written Informed consent was obtained from all participants. Adherence to strict ethical and professional guidelines was ensured throughout the study to safeguard participants' confidentiality. The identities of the retail outlets and participants were kept anonymous.

Results

Operational and Infrastructure Characteristics of Pharmacies

A comparison of the operational and infrastructure characteristics between innovative and traditional independent pharmacies is shown in Table 3. Innovative pharmacies were frequently located in shopping malls 46.2% (12/26) compared with 23.1% (6/26) traditional ones. Whilst traditional independent pharmacies were located in peri-urban areas 50.0% (13/26) compared with innovative pharmacies, 38.5% (10/26). Innovative pharmacies had a higher proportion of pharmacists present at the time of the survey 69.2% (18/26), whereas traditional independent pharmacies had a similar proportion of pharmacy technologists, 38.5% (10/26) and pharmacists, 38.5% (10/26). Almost all innovative pharmacies were equipped with functional air conditioning 96.2% (25/26). A significantly larger proportion of innovative pharmacies 76.9% (20/26), had a backup power source than traditional independent pharmacies 6.9% (7/26) with (p = 0.0008). The mean temperature recorded in innovative pharmacies was 21.23°C (SD=1.728), which was lower than that recorded in traditional independent pharmacies at 22.69°C (SD=2.328). However, both types were within the recommended ambient temperature range of 20-25°C. All innovative pharmacies 100% (26/26) followed the first expiry, first out (FEFO) system, in contrast to only 61.5% (16/26) of traditional pharmacies (p < 0.001) following this practice.

Table 3: Operational and Infrastructure Characteristics of Pharmacies (Lusaka, 2022)

	Total N = 52	Innovative pharmacy N = 26	Traditional Independent pharmacy N = 26	*p*-value
Location of outlets				
City centre	2 (3.8%)	1 (3.8%)	1(3.8%)	0.301[b]
Commercial area	9 (17.3%)	3 (11.5%)	6 (23.1%)	
Shopping mall	18 (34.6%)	12 (46.2%)	6 (23.1%)	
Peri urban	23 (44.2%)	10 (38.5%)	13 (50.0%)	
Personnel present at time of survey				
Pharmacist	28 (53.8%)	18 (69.2%)	10 (38.5%)	**0.041[a]**
Pharmacy technologist	17 (32.7%)	7 (26.9%)	10 (38.5%)	
Others*	7 (13.5%)	1 (3.8%)	6 (23.1%)	
Highest qualifications				
GCSE	1 (1.9%)	0 (0.0%)	1 (3.8%)	**0.032[b]**
Certificate	2 (3.8%)	0 (0.0%)	2 (7.7%)	
Diploma	21 (40.4%)	8 (30.8%)	13 (50.0%)	
Degree	27 (51.9%)	18 (69.2%)	9 (34.6%)	
Masters	1 (1.9%)	0 (0.0%)	1 (3.8%)	
Years of work experience	Mean (SD)	4.19 (2.91)	3.96 (3.40)	0.794
Gender				
Male	31 (59.6%)	13 (50.0%)	18 (69.2%)	0.258[a]
Female	21 (40.4%)	13 (50.0%)	8 (30.8%)	
Training regarding substandard and falsified medicines				
Yes	16 (30.8%)	9 (34.6%)	7 (26.9%)	0.764[a]
No	36 (69.2%)	17 (65.4%)	19 (73.1%)	
Outlet has an air conditioner				
Yes	47 (90.4%)	25 (96.15%)	22 (84.62%)	0.075
Yes, but not functional	1 (1.9%)	1 (3.85%)	0 (0.00%)	
No	4 (7.7%)	0 (0.00%)	4 (15.38%)	

Experience power cut in the last 6 months				
Yes	23 (44.2%)	9 (34.62%)	14 (53.85%)	0.352
No	25 (48.1%)	15 (57.69%)	10 (38.46%)	
I don't know	4 (7.7%)	2 (7.69%)	2 (7.69%)	
Backup power source available				
Yes	27 (51.9%)	20 (76.92%)	7 (26.92%)	**0.0008**
No	25 (48.1%)	6 (23.08%)	19 (73.08%)	
Ambient temperature of location	Mean (SD)	21.23 (1.73)	22.69 (2.33)	**0.013**[a]
Storage had adequate storage**				
Yes	42 (80.8%)	26 (100.0%)	16 (61.5%)	**<0.001**[a]
No	10 (19.2%)	0 (0.0%)	10 (38.5%)	
Outlet is in good condition				
Yes	45 (86.5%)	26 (100.0%)	19 (73.1%)	**0.051**[a]
No	7 (13.5%)	0 (0.0%)	7 (26.9%)	
Medicines stored according to FEFO				
Yes	42 (80.8%)	26 (100.0%)	16 (61.5%)	**<0.001**[a]
No	10 (19.2%)	0 (0.0%)	10 (38.5%)	

[a]Pearson Chi-square test, [b]Fishers exact test. * others included registered nurse (1), laboratory technician (1), cosmetician (1), shop assistant (1), pharmacy managers (2), and pharmacy student (1) ** Storage conditions complied to ZAMRA recommendations. Bold *p*-values indicate statistically significant differences. FEFO = first expiry, first out.

Comparison of Attributes of Amoxicillin and Sulfadoxine/pyrimethamine available in Innovative and Traditional Independent Pharmacies

The attributes of the sampled medicines, amoxicillin and SP, are summarised in Table 4. All the medicines collected were stated as being of generic brands. The stated country of manufacture for samples of amoxicillin was Kenya, accounting for 44.7% (51/114) of the total. Furthermore, 43.1% (25/58) of amoxicillin samples purchased from innovative pharmacies were stated Kenya as their country of manufacture, compared to 46.4% (26/56) in traditional independent pharmacies. China was the second stated country of origin, accounting for 21% (25/114) of the samples. Among the innovative pharmacies, 27.6% (16/58) of the amoxicillin samples were stated to be from China, whilst in traditional pharmacies, the figure was 16.1% (9/56). The difference in the stated country of origin between innovative and traditional pharmacies was statistically significant (p = 0.010), of which 7% (8/114) of the samples were found to be repackaged in plastic pill packs. All repackaged samples were obtained exclusively from traditional independent pharmacies 14.3% (8/56). Examples of repackaging are shown in Figure 2. A small fraction, 1.8% (2/114) of the samples, showed visual defects, all of which were from traditional independent pharmacies (Figure 3). The mean days to expiry were 694.41 (SD = 236.67) days in innovative pharmacies and 783.33 (SD = 214.98) days in traditional independent pharmacies. The mean unit price of amoxicillin was K 49.50 (SD = 52.71) in innovative pharmacies, compared to K 29.25 (SD = 9.19) in traditional independent pharmacies (p = 0.005).

The majority of the SP samples, 81.1% (43/53), were stated to be manufactured in India and a higher proportion of such samples were found in traditional independent pharmacies, 88.9% (24/27), than in innovative pharmacies 73.1% (19/26). Furthermore, 3.8% (2/53) samples of SP were repackaged in

medicine packs and 11.1% (2/27) were purchased from traditional independent pharmacies. None of these SP samples exhibited visual defects (discolouration, wrong spelling or disintegrated tablets). The mean days to expiry were 529.92 (SD = 165.13) days for samples from innovative pharmacies and 525.46 (SD = 281.53) days in traditional independent pharmacies. The mean unit price of SP was K 11.81 (SD = 2.73) in innovative pharmacies, compared to K 12.19 (SD = 5.04) in traditional independent pharmacies.

Table 4: Medicine sample attributes of amoxicillin and sulfadoxine/pyrimethamine (Lusaka,2022)

Medicine	Attributes	Total samples collected	Innovative pharmacy	Traditional Independent pharmacy	*p*-value
		N = 114	**N = 58**	**N = 56**	
Amoxicillin	**Stated country of manufacture**				
	Kenya	51 (44.7%)	25 (43.1%)	26 (46.4%)	
	China	25 (21.9%)	16 (27.6%)	9 (16.1%)	**0.010**
	India	21 (18.4%)	9 (15.5%)	12(21.4%)	
	Germany	5 (4.4%)	5 (8.6%)	0 (0.0%)	
	United Kingdom	3 (2.6%)	2 (3.4%)	1 (1.8%)	
	South Africa	1 (0.9%)	1 (1.7%)	0 (0.0%	
	Unknown	8 (7.0%)	0 (0.0%)	8 (14.3%)	
	Repackaged in plastic pill packs				
	Yes	8 (7.0%)	0 (0.0%)	8 (14.3%)	**0.009**
	No	106 (93%)	58 (100.0%)	48 (85.7%)	
	Visual defects present				
	Yes	2 (1.8%)	0 (0.0%)	2 (3.6%)	0.461
	No	112 (98.2%)	58 (100.0%)	54 (96.4%)	
	Days to Expiry	Mean (SD)	694.41 (236.67)	783.33 (214.98)	0.412
	Price/unit(Kwacha)	Mean (SD)	49.50 (52.71)	29.25 (9.19)	**0.005**
		N = 53	**N = 26**	**N = 27**	
Sulfadoxine/ pyrimethamine(SP)	**Stated country of manufacture**				
	India	43 (81.1%)	19 (73.08%)	24 (88.9%)	**0.005**
	Tanzania	7 (13.2%)	7 (26.92%)	0 (0.0%)	
	Unknown	3 (5.6%)	0 (0%)	3 (11.1%)	
	Repackaged in plastic pill packs				
	Yes	2 (3.8%)	0 (0.0%)	2 (11.1%)	0.235
	No	51 (96.2%)	27 (100.0%)	24 (88.9%)	
	Visual defects present				
	No	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	Days to Expiry	Mean (SD)	529.92 (165.13)	525.46 (281.53)	0.427
	Price/unit (Kwacha)	Mean (SD)	11.81 (2.73)	12.19 (5.04)	0.745

K = Kwacha. 1 Kwacha (K) = 0.052 US dollars. Bold *p*-values indicate statistically significant differences.

Medicine repackaging

Figure 2 depicts an example of typical packaging of repackaged amoxicillin and sulfadoxine/pyrimethamine. Some packages are not properly labelled and lack expiration date information.

Visual defects

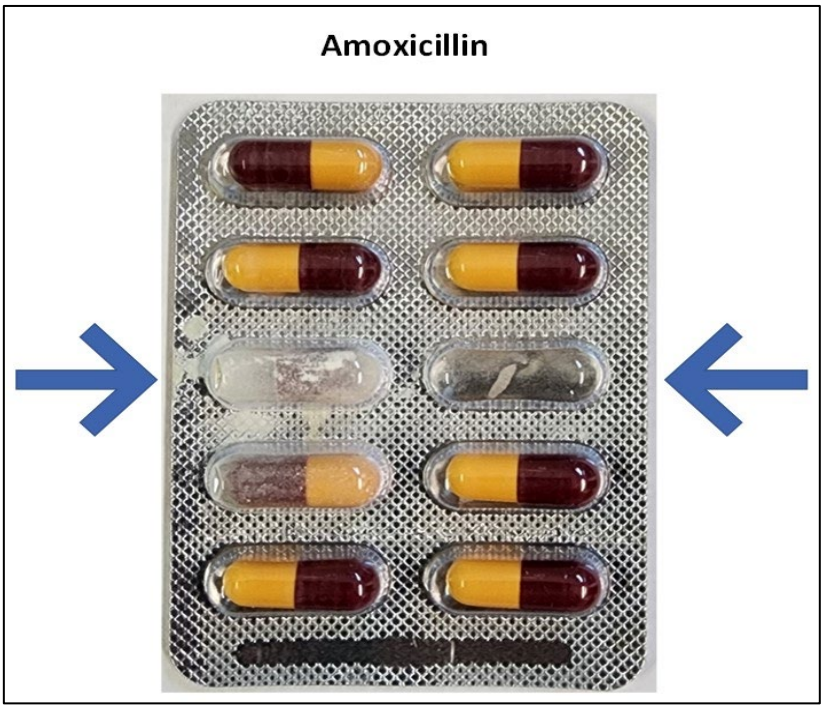

Figure 3: Image depicting a defective amoxicillin sample. Blue arrows indicate the absence of capsules in the blister.

Medicine Information and results of laboratory analysis

Amoxicillin

A total of 114 amoxicillin samples were purchased and analysed in the laboratory: 58 from innovative pharmacies and 56 from Traditional Independent pharmacies. The content and dissolution testing results are outlined Table 5 in terms of compliance with USP tolerance limits, (related to the batch number, stated manufacturer, expiry date, and dosage of the formulation.

Table 5: Amoxicillin information and quality results obtained by high-performance liquid chromatography and dissolution (Lusaka, 2022).

Brand name	Batch No	Expiry date (month /year)	Dosage form/ Strength (mg)	Stated country of manufacture	Content analyses - number compliant with USP tolerance limits/ total number	Dissolution tests number compliance with USP tolerance limits / total number
Amoxi Denk	23911	02/23	Tablet/500	Germany	0/2	2/2
Amoxi Denk	24418	11/23	Tablet/500	Germany	2/2	2/2
Amoxi Denk	25989	10/24	Tablet/500	Germany	1/1	2/2
Kemoxyl - 250	79575	07/24	Capsule/250	Kenya	3/4	4/4
Kemoxyl - 250	79746	08/24	Capsule/250	Kenya	1/2	2/2
Kemoxyl - 250	80693	01/25	Capsule/250	Kenya	3/15	15/15
Kemoxyl - 250	80695	01/25	Capsule/250	Kenya	4/12	12/12
Kemoxyl - 250	81293	04/25	Capsule/250	Kenya	1/2	2/2
Amoxicillin	980429	07/22	Capsule/500	UK	1/1	1/1
Medomox	2254001	01/25	Capsule/250	India	0/1	1/1
Elymox	1D37	03/24	Capsule/250	Kenya	0/1	1/1
Elymox	1D87	03/24	Capsule/250	Kenya	2/6	6/6
Elymox	1E18	04/24	Capsule/250	Kenya	3/6	6/6
Elymox	1E19	04/24	Capsule/250	Kenya	1/1	1/1
Elymox	1F71	05/24	Capsule/250	Kenya	0/2	2/2
Amoxicillin	AXABV0012	05/23	Capsule/250	UK	0/2	2/2
Galmox 250	GLXC210024	05/24	Capsule/250	India	1/1	1/1
Galmox 250	GLXC21002A	05/24	Capsule/250	India	2/2	2/2
Galmox 250	GLXC21003A	05/24	Capsule/250	India	0/2	2/2
Galmox 250	GLXC21004A	05/24	Capsule/250	India	0/1	1/1
Galmox 250	GLXC21005A	05/24	Capsule/250	India	1/2	2/2
Amoxy - 250	P1C02	04/24	Capsule/250	China	0/1	1/1
Amoxy - 250	P1C03	08/24	Capsule/250	China	1/2	2/2
Amoxy 250	P2C01	02/25	Capsule/250	China	0/1	1/1
Amoxy - 250	P2C02	02/25	Capsule/250	China	11/21	21/21
Moxileb - 250	PC171	07/23	Capsule/250	India	1/1	1/1
Moxileb - 250	PC181	07/23	Capsule/250	India	1/1	1/1
Moxileb - 250	PC211	08/23	Capsule/250	India	0/2	2/2
Moxileb - 250	PC261	08/23	Capsule/250	India	1/1	1/1
Amyn - 250	S364190242	10/22	Capsule/250	India	0/2	2/2
Amyn - 250	S3642201	01/25	Capsule/250	India	1/1	1/1
Amyn - 250	S364220131	01/25	Capsule/250	India	0/2	2/2
Spamox	XD081	11/25	Tablet/250	India	0/1	1/1
Spamox	XD0B1	11/23	Tablet/250	India	0/1	1/1
Zoxil	ZCAHV0007	07/24	Capsule/250	South Africa	1/1	1/1
Kemoxyl - 250	N/S	01/25	Capsule/250	N/S	0/1	1/1
Kemoxyl - 250	N/S	N/S	Capsule/250	N/S	0/1	1/1
Moxacil - 250	N/S	N/S	Capsule/250	N/S	0/2	2/2
Amoxi	N/S	N/S	Capsule/250	N/S	0/1	1/1
Amoxy	N/S	N/S	Capsule/250	N/S	0/1	1/1
Amoxy - 250	N/S	N/S	Capsule/250	N/S	0/2	2/2
Complaint with USP tolerance limits					**43/114 (37.7%)**	**114/114 (100%)**
Noncompliant with USP tolerance limits					**71/114 (62.3%)**	**0/114 (0%)**

USP = US Pharmacopeia. N/S =not stated.

Sulfadoxine/pyrimethamine

A total of 53 SP samples were purchased and analysed in the laboratory: 27 from innovative pharmacies and 26 from traditional independent pharmacies. The content and dissolution testing results are outlined Table 6 in terms of compliance with USP tolerance limits, (related to the batch number, stated manufacturer, expiry date, and dosage of the formulation.

Table 6: Sulfadoxine/pyrimethamine information and results of quality testing by high-performance liquid chromatography and dissolution (Lusaka,2022).

Brand name	Batch No	Expiry date (month /year)	Dosage form/Strength (mg)	Stated country of manufacture	Content analyses - number compliant with USP tolerance limits/ total number	Dissolution tests number compliance with USP tolerance limits / total number
Maladox	0371879	07/23	Tablet/500/25	India	0/1	1/1
Maladox	0373379	11/23	Tablet500/25	India	0/4	4/4
Maladox	0371880	08/23	Tablet/500/25	India	0/4	4/4
Maladox	0371881	08/23	Tablet/500/25	India	0/1	1/1
Maladox	1372774	05/24	Tablet/500/25	India	0/7	7/7
Maladox	1372775	05/24	Tablet/500/25	India	0/8	8/8
Maladox	2371767	02/25	Tablet/500/25	India	0/2	2/2
Paludoxin	KPL002	01/24	Tablet/500/25	India	0/2	2/2
Pharmadar	PDR -2101	04/24	Tablet/500/25	India	0/7	7/7
Sulphadar	2008246	07/24	Tablet/500/25	Tanzania	0/7	7/7
Stalfin	Z41	11/22	Tablet/500/25	India	0/6	6/6
Stalfin	Z42	11/22	Tablet/500/25	India	0/1	1/1
N/S	N/S	N/S	Tablet/500/25	N/S	0/3	3/3
Complaint with USP tolerance limits					**0/53 (0%)**	**53/53 (100%)**
Non complaint with USP tolerance limits					**53/53 (100%)**	**0/53 (0%)**

USP = US Pharmacopeia. N/S = not stated

Dissolution and SAPI Content Analysis

A total of 114 amoxicillin and 53 samples SP samples were analysed using HPLC-DAD (Tables 5 and 6) for content analysis and dissolution testing. All the samples confirmed the presence of SAPIs, indicating that none were falsified. However, only 37.7% (43/114) of the amoxicillin samples were found to be of good quality in that they contained between 90% and 120% of the SAPI. And 62.3% (71/114) did not meet the authorised tolerance limits, rendering them to be substandard. Comparison between the pharmacy types revealed that 43.1% of samples from innovative pharmacies and 32.1% from traditional pharmacies met the threshold of good quality, although this difference was not statistically significant (p=0.312). For sulfadoxine in the SP samples, none met the criterion of containing between 90% and 110% of the SAPI. Moreover, only 35.9% (19/53) of the samples contained the stated amount of pyrimethamine with the rest having more than USP specified limits.

Notably, all the samples of amoxicillin and SP adhered to the USP tolerance limits for dissolution, hence they are bioavailable and will treat the infection. However, 5.3% (5/114) of amoxicillin and 13.2% (6/53) of SP samples were found to be expired at the time of content analysis.

Predictors associated with Amoxicillin Quality

Logistic regression analysis was conducted to determine potential predictors associated with the quality of amoxicillin, dichotomised as 'good' or 'poor', with poor quality amoxicillin, defined by SAPI ≤ 90% or ≥ 120%. Table 7 presents the findings of bivariate and multivariate analyses.

In the bivariate analysis, the largest differences in the quality of amoxicillin were associated with the following attributes: type of outlet, whether the medicine was repackaged in plastic pill packs, and its expiry status at the time of analysis. Among these, only repackaging in plastic pill packs was statistically significant. The proportion of poor-quality amoxicillin samples found in traditional independent pharmacies was slightly higher (67.9%) than that in innovative pharmacies (56.9 %). Despite this difference, the association was not statistically significant (Odds Ratio 0.63, 95% CI 0.29-1.34; *p*=0.251). All repackaged samples in plastic pill packs were of poor quality, and this was statistically significant (*p*= 0.023). Furthermore, samples that expired by the time of analysis also had a higher proportion of poor quality (83.3%) than the ones that had not expired (61.1%). However, this difference was not statistically significant (Odds Ratio 0.31, 95% CI 0.14-0.67; *p*=0.407). Negligible difference was found in the quality of amoxicillin sold according to the location, in terms of being in a commercial area or otherwise, the presence of either pharmacist or other personnel, or the sample's price.

In the multivariable regression analysis, the outlet type did not indicate an association with medicine quality (Odds ratio 0.83, 95% CI 0.38 - 1.82, *p*=0.734). This implies that outlet type may not be a substantial driver of medicine quality when controlling for other factors. Notably, medicines repackaged in medicine packs experienced perfect statistical separation, and all such samples were of poor quality.

Table 7: Bivariate (crude) and multivariate (adjusted) models of the association between poor-quality amoxicillin (as defined by API ≤ 90% or ≥120%) and attributes of outlets and medicines purchased.

Attributes of outlets and purchased medicines	Total number of samples	Number (%) of poor-quality samples (API ≤ 90% or ≥120%)						
	N = 114	N = 71 (%)	Crude OR (95% CI)		*p*-value	Adjusted OR (95% CI)		*p*-value
Outlet type (Pharmacies)								
Traditional Independent	56	38 (67.9%)	1.00					
Innovative	58	33 (56.9%)	0.63	(0.29,1.34)	0.251**	0.83	(0.38,1.82)	0.734
Location								
Commercial area	51	31 (60.7%)	1.00					
Others	63	40 (63.4%)	0.89	(0.41,1.91)	0.847	-	-	-
Personnel present								
Pharmacist	61	38 (62.3%)	1.00					
Others	53	33 (62.3%)	0.99	(0.47,2.13)	1.000	-	-	-
Air conditioner available								
Yes	88	53 (60.2%)	1.00					

No	26	18 (69.2%)	1.48	(0.69,3.18)	0.492	-	-	-
Backup power								
Yes	68	40 (58.8%)	1.00					
No	46	31 (67.4%)	1.44	(0.67,3.09)	0.432	-	-	-
Adequate storage space								
Yes	94	57 (60.6%)	1.00					
No	20	14 (70.0%)	0.61	(0.71,3.24)	0.412	-	-	-
Kept medicines according to FEFO								
Yes	95	58 (61.1%)	1.00					
No	19	13 (68.4%)	1.38	(0.65,2.95)	0.612	-	-	-
Price (K)								
> 35	10	5 (50.0%)	1.00					
< 35	104	66 (63.5%)	1.74	(0.81,3.72)	0.499	-	-	-
Stated country of manufacture								
Kenya	51	33 (64.7%)	1.00					
Others	63	38 (60.3%)	0.83	(0.38,177)	0.699	-	-	-
Days to expiry								
> 876	53	33 (62.3%)	1.00					
< 876	61	38 (62.3%)	1.00	(0.46,2.14)	1.000	-	-	-
Days from procurement								
> 14	24	17 (70.8%)	1.00					
< 14	90	54 (60.0%)	1.51	(0.29,1.32)	0.356	-	-	-
Repackaged in medicine packs (Perfect Separation)[a]								
Yes	8	8 (100.0%)	1.00					
No	108	63 (59.4%)	0	-	**0.023****	0	-	0.99
Expired by time of analysis								
Yes	8	5 (83.3%)	1.00					
No	108	65 (61.1%)	0.31	(0.14,0.67)	0.407	-	-	-
Visual defects								
Yes	2	1 (50.0%)	1.00					
No	112	70 (62.5%)	1.67	(0.78,3.57)	1.000	-	-	-

[a] The variable "Repackaged in medicine packs" experienced perfect statistical separation, where one category had a 100% occurrence rate of the event and the other had 0%. ** indicates variables included in the multivariable analysis. K = Zambia Kwacha. 1 Kwacha = 0.052 US dollars. Bold *p*-values indicate significant statistical differences.

Discussion

It is reassuring that no falsified medicines (absence of SAPIs) were detected among the samples of amoxicillin (n=114) and SP (n=53) purchased in Lusaka in 2022. However, the content analysis revealed deviations in the declared API content for all SP samples, and 62.3% of the amoxicillin samples. Notably, these deviations were primarily in excess of the specified USP tolerance limits. Furthermore, all these samples complied with the USP dissolution tolerance limits. Our study's emphasis on dual assessment is substantiated by empirical findings from Afghanistan[33]. The SP tablets in Afghanistan intended for malaria treatment, while meeting content analysis standards, were subsequently found to be substandard due to their failure in dissolution testing. This led to the tablets being ineffective in treating the illness. This case exemplifies the critical necessity for medicines to fulfil both content and dissolution criteria to ensure therapeutic efficacy. Our study's adherence to this rigorous dual-criteria methodology offers a more comprehensive evaluation of medicine quality. Our findings suggest that while many samples may comply with the USP dissolution tolerance limits, their failure in content testing poses a cause for serious concern. Deviations in API content pose substantial risks to treatment efficacy and public health outcomes. Excess levels in API content could lead to overdosing, potentially

resulting in adverse drug reactions and elevated healthcare burdens. On the other hand, lower levels in API content might result in underdosing, rendering treatments ineffective and possibly contributing to the emergence of antimicrobial resistance. These deviations, whether in excess or deficit, underscore the importance of stringent quality control in pharmaceutical manufacturing and distribution to ensure both the safety and effectiveness of medicines.

Comparative assessments of regional data from medicine quality studies revealed that 28% of amoxicillin in the DRC [34] and 19.2% in Malawi [35] were reported as out of specification based on HPLC analysis. Similarly, studies employing both HPLC content analysis and dissolution testing have documented inconsistencies in compliance for amoxicillin samples [36,37]. Quality concerns regarding substandard SP using both HPLC analysis and dissolution testing were also apparent in various countries, for example, 13.7% (8/58) of samples in Tanzania [38], 35.7% (10/28) in Malawi [35], and all (9/9) in Afghanistan [39].

The content analysis in the present investigation highlights a concern; although the samples contained the SAPIs, a significant portion (all SP samples and 62.3% of amoxicillin) failed to comply with the USP tolerance limits for amount. Storage and transportation conditions, along with exposure to heat and humidity, can affect medicine quality [40,41]. Recent global supply chain disruptions, exemplified by the COVID-19 pandemic, have accentuated these challenges [7,45]. A key factor to consider is the purity of the SAPI used in the formulation [42]; for instance, almost all manufacturing sites (5 out of 7) for 6-Aminopenicillanic acid (6-APA), a key intermediate for the production of antibiotics such as amoxicillin, are located in China, with just one in Europe and another in Mexico [43]. Moreover, all the 6-APA used in the manufacturing of amoxicillin APIs in India are sourced from China [44]. The 2020 supply chain disturbances, especially impacting pivotal pharmaceutical centres such as China, precipitated the shutdown of factories producing essential SAPIs for medicines such as amoxicillin [7]. Any entry of substandard SAPIs into the supply chain during this period may have cascaded into the production of poor-quality medicines, a pattern that resonates with the findings of this study. Hence, this reported study conducted in 2022, may have been influenced by these challenges and investigation is warranted to determine the persistence of these occurrences. These observations highlight the need for a multifaceted approach to quality control in the pharmaceutical sector, which should extend beyond the retail level and cover upstream activities such as the origin of the pure APIs used in the formulation and manufacturing processes. Quality checks are equally crucial during the intermediate steps, including wholesaling and retail distribution. Considering that suspect medicines (substandard and falsified) can enter the supply chain at multiple points, a comprehensive and ongoing quality control strategy is imperative to ensure the safety and efficacy of medicines [5].

Dissolution testing is an indicator of the bioefficacy of a medicine because it is an indicator of the release of SAPI in the body [33]. Hence, the dissolution test is not just a procedural step but also a robust measure to assess the bioavailability of a formulation. It aids in streamlining batch releases, ensuring consistent quality of drugs throughout their shelf life, and acts as a marker to identify substandard batches while passing those that maintain the required standards [46]. However, it is important to note that not all medicines have authorised pharmacopoeia monographs to guide their dissolution profiles [47] .In this study, despite the discrepancies in results of content analysis, all samples complied with tolerance limits for dissolution analysis, indicating that they yielded therapeutic levels of the active ingredient upon administration. This emphasises the need to perform both content analysis and dissolution tests, since the former may reveal a contaminant which was not found here. The bioefficacy of a drug may be compromised over time as the SAPI levels diminish. In such cases, the dissolution rates could also deteriorate, ultimately undermining the therapeutic potential of the drug [37]

Both innovative and traditional independent pharmacies often sourced their amoxicillin from the same manufacturers. This commonality in sourcing could explain why there were no significant statistical differences in the quality of amoxicillin between these two types of outlets. However, failings in the quality of amoxicillin were found to be associated with repackaging of medicines in plastic pill packets a practice which was primarily found in some traditional independent pharmacies, though the number of instances of this were few. In multivariable analysis, a notable phenomenon known as 'perfect separation' was observed, specifically in relation to amoxicillin that had been repackaged in plastic pill packets. In statistical terms, 'perfect separation' refers to an independent variable, in this case, the repackaging into plastic pill packets flawlessly predicting a specific outcome. In this study, all repackaged amoxicillin did not contain the stated amount of API. This may stem from repackaging amoxicillin from tins into plastic pill packets, possibly undertaken under suboptimal conditions or without rigorous quality control, thus potentially exposing the medicines to elements such as moisture. The samples of repackaged pills were sourced from individual shops that were contained in different tins, negating the possibility of homogenous substandard quality originating from a single batch, and underlining the significance of the observed quality issues. This observation of the sale of loose capsules in plastic pill packets aligns with findings of other studies [48]. Moreover, selling loose capsules hampers regulatory scrutiny. Such products often lack essential identifiers, including the manufacturer's name, batch number, expiry dates, and stated country of manufacture which was also found in this investigation. Whilst there has not been any specific commentary emanating from ZAMRA on this matter, the observed issues align with guidelines regarding good distribution practices, emphasizing the need for proper labeling and packaging. Similar quality

concerns have been noted in regional studies conducted in Malawi and Tanzania, highlighting the broader relevance of this study's findings in the regional context.

The visual inspection conducted during this study highlighted certain aspects of pharmaceutical manufacturing that warrant closer examination. Although no classic red flags associated with falsified medicines were found, there were unmistakable signs of manufacturing lapses. An example that stands out is the amoxicillin blister pack, which was intact and sealed, yet missing two capsules; furthermore, the remaining capsules were found to contain only powder instead of the expected SAPI. While this case alone cannot be used to make broad generalisations, it highlights potential concerns about the rigour of the manufacturing process and the importance of meticulous quality control in the pharmaceutical supply chain. Some differences were observed when comparing innovative and traditional independent pharmacies. Innovative pharmacies were frequently found to sell medicines in their original blister packaging, a practice that enhanced traceability and tracking. However, manufacturing defects were also observed in blistered products from traditional independent pharmacies. These findings highlight the need for increased regulatory oversight to ensure the provision of good quality-assured medicines.

Although there were notable differences in storage practices between innovative and traditional independent pharmacies, these did not translate into differences in the quality of medicine. This observation further emphasises the need of upstream surveillance of products in supply chains. Nevertheless, adherence to good storage practices should be encouraged in both types of pharmacies.

Limitations

This study aimed to shed light on the quality of medicines available in Zambia; however, certain limitations influenced its scope and findings. A key constraint was that the anticipated sample size based on preliminary consultations with pharmaceutical stakeholders did not match actual data collection. It was expected that multiple brands of amoxicillin and SP would be available in each pharmacy, projecting approximately 130 medicine samples per group of each medicine. However, most retailers stocked a single SP brand and, on average, two brands of amoxicillin. Although we procured samples of all the available brands, the range was limited. Anecdotally, a few retailers cited supply chain disruptions due to the COVID-19 pandemic and Zambia's economic challenges as reasons for their limited stock. Given these constraints, future research should examine a broader range of products, perhaps across multiple regions, to better understand the impact of these disruptions on medicine quality and availability.

Furthermore, in our study, the use of an overt sampling approach allowed for transparent and straightforward data collection; however, it may have introduced bias, as participants were aware of the study's purpose, possibly influencing their responses or behaviour.

The cross-sectional design of this study has both strengths and limitations. It provides a snapshot of conditions during a specific timeframe but cannot illustrate the dynamic nature of medicine quality over a prolonged period. Furthermore, the exclusive focus on amoxicillin and SP potentially overlooks the quality of other essential medicines in the Zambian landscape.

Conclusion

This study offers crucial insights into the challenges of ensuring medicine quality in Zambia's pharmaceutical sector, highlighting the imperative for regular, rigorous surveillance across the entire pharmaceutical supply chain. Such surveillance should encompass not only downstream activities, such as retail distribution, but also upstream processes, including the acquisition of pure APIs (raw material) and products from WHO prequalified manufacturers. Our findings indicate that innovative pharmacies with good storage practices and selling medicines in their original blister packaging may ensure medicine quality. However, the full impact of these innovative practices will require further investigation through well-designed studies. Overall, the data generated from here provides a foundation for crafting targeted strategies to ensure consistent availability of good-quality medicines to the public.

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Chapter 6: Research Paper 5 - Stakeholder Perceptions (Qualitative Study)

Chapter Introduction

This chapter provides a qualitative study examining Zambian stakeholder perceptions towards innovative private pharmacy distribution channels, including pharmaceutical professionals, innovators, wholesalers, and retailers. These channels represent alternative, privately led methods of dispensing medicines, such as telepharmacy, delivery, and e-pharmacies. Despite their recent introduction in Zambia, there remains a significant gap in the scholarly literature regarding their functionality and consequences, especially regarding the quality of the medicines provided. This research aimed to shed light on this underexplored area and contribute valuable knowledge to the field, potentially guiding future improvements in pharmacy distribution systems and thus impacting patient outcomes.

This study addresses the fifth objective of overarching PhD research, focusing on identifying the perceived shortcomings of the innovative pharmacy approach's and necessary enhancements to ensure that patients receive good-quality medicine. A qualitative methodology involving in-depth interviews with 15 stakeholders was adopted to gather insights into the challenges, potential benefits, and suggestions for improvement of these novel pharmacy channels. This chapter builds upon previous chapters that examined the characteristics of innovative and traditional independent pharmacies in Lusaka, Zambia and Chapter 5's investigation of the prevalence of substandard medicines (namely amoxicillin and sulfadoxine/Pyrimethamine) in both types of pharmacies.

This chapter explores a variety of interconnected factors, including the availability, affordability, and transportation of medicines, examining their potential impact on and relevance to overall medicine quality. The study is intended for submission to BMC Public Health.

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Student ID Number	1403479	**Title**	Mr
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Surname/Family Name	Matafwali		
Thesis Title	Innovative Private Pharmacy Distribution Channels: Implications on Medicine Quality in Zambia		
Primary Supervisor	Dr Harparkash Kaur		

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Stage of publication	**Not yet submitted**

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conceptualised the study and developed the protocol with methodological guidance from my supervisors and advisory team. Additionally, I conducted the fieldwork, analysed the data, and wrote the first drafts of the manuscript. I also revised the manuscript based on feedback from co-authors.

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Stakeholder Perceptions on Innovative Private Pharmacy Distribution Channels and Implications for Medicine Quality in Zambia

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Abstract

Introduction: Innovative private pharmacy distribution channels, including delivery services, telepharmacy, and e-pharmacies, have the potential to improve access to good quality medicine in Zambia. Despite their introduction, the innovative characteristics of these systems and their wider implications, particularly regarding the quality of the medicines provided, have not been thoroughly explored. Additionally, stakeholders' perspectives on and experiences with these channels remain largely uncharted. This qualitative study sought to examine stakeholders' perceptions and experiences regarding innovative private pharmacy distribution channels and their implications for the quality of medicines in Zambia.

Methods: A purposive sample of 15 stakeholders participated in the study, comprising pharmacists, pharmacy managers, regulatory authorities, and representatives from pharmaceutical companies and professional organisations. In-depth interviews were conducted using a semi-structured interview guide for each stakeholder. Interviews were recorded and transcribed, and data analysis employed grounded theory.

Results: Four primary themes emerged from the analysis: current challenges in the pharmaceutical supply chain, potential benefits of the innovative pharmacy approach, the limitations and shortcomings of the innovative pharmacy approach, and recommendations for improvement. Participants identified current challenges concerning affordability, transportation, and availability of medicines as well as substandard medicines and regulatory issues. The potential benefits of the innovative pharmacy approach, such as increased product availability and enhanced traceability, were acknowledged. Nevertheless, limitations and shortcomings, including behavioural, financial, regulatory, and technical challenges, were also recognised.

Conclusion: Stakeholder perspectives, as revealed in this study, highlight the challenges and limitations of the innovative pharmacy distribution channels in Zambia. These perspectives also offer essential insights into how improvements, such as digitisation, education, government intervention, and enhanced regulation, can be realised to optimise this innovative approach. Importantly, these stakeholders' views contribute to a more nuanced understanding of the unique needs in Zambia's context. This understanding can inform more effective policy interventions, thus enriching the broader narrative of medicine distribution in the country.

Keywords: Innovative pharmacy distribution channels, Medicines quality, Stakeholder perceptions, Qualitative study, Zambia, Pharmaceutical supply chain, Policy interventions

Introduction

Innovative pharmacy distribution channels represent novel and alternative methods of delivering medicines to patients, to enhance the accessibility, affordability, and quality of medical products [1–3]. These channels often employ technology with the potential to optimise the supply chain and increase the efficiency and transparency of the distribution process. Examples include mobile health (mHealth) solutions that enable patients to order and receive medicines directly to their homes through mobile devices, e-commerce platforms connecting pharmacies and medicine manufacturers to consumers online, and last-mile delivery services using drones or other means to transport medicines to remote or difficult-to-access areas [1,4–6]. As in many other low- and middle-income countries (LMICs) in Zambia, the adoption and implementation of innovative pharmacy distribution channels could prove particularly transformative. The unique challenges and opportunities within Zambia's healthcare landscape, coupled with growing adoption, provide fertile ground for these innovative approaches.

In addition to innovations in delivery technology, other solutions at the pharmacy retail level include services such as inventory management systems and innovative retail pharmacy partnerships such as franchising and counterfeit medicine detection systems. By offering innovative services and system efficiencies, entrepreneurs aim to reduce healthcare product costs and improve product availability [2].Other examples of innovative approaches include social enterprise pharmacies, which reinvest profits from the sale of pharmaceutical products to enhance healthcare infrastructure and services in underserved communities, and community-based pharmacies employing local healthcare workers to provide patient education and counselling alongside dispensing medicines [7,8]. These companies operate in various geographies and countries, including Kenya, Nigeria, Ghana, and Zambia [1,2,9].

Nevertheless, concerns exist regarding the quality and safety of medicines sold through these different channels, particularly as proper regulatory oversight may be lacking [1,2,10]. Miller et al.[10] highlighted the challenge of the absence of regulatory frameworks specific to e-pharmacies in LMICs including Kenya, Nigeria, and India. The absence of such regulatory frameworks makes pharmaceutical supply chains vulnerable to substandard and falsified (SF) medicines, compromising patient safety. Online purchase of medicines has become a global phenomenon with significant economic, social, and health impacts [11]. The COVID-19 pandemic has increased the number of online purchases of prescription medicines [12,13]. However, this has led to the sale of SF medicines by illegal and inappropriate online vendors, resulting in untold effects on morbidity and mortality worldwide. Reports of increased unregulated medicine sales on social media platforms, such as WhatsApp and Facebook, have also emerged [11,13].

Distribution in the private sector in Zambia is carried out through a network of importers, wholesalers, sub-wholesalers, pharmacies, health shops and drug stores [14]. Pharmaceutical importers and

wholesalers form links with manufacturers, retail pharmacies, and hospitals. Pharmaceutical manufacturers are mainly located outside the country, with only five leading local manufacturers of pharmaceutical products [15,16], who are projected to fulfil only 10-15% of the demand for pharmaceuticals. Zambia, like several other LMICs, largely depends on imports from other countries, particularly India, for 80% of essential medicines [17,18].

Pharmaceutical wholesalers provide distribution and stockholding functions. This enables retail pharmacies to be supplied in sufficient quantities to meet their daily needs, while ensuring that pharmacies do not have to maintain large stocks, mainly because of a lack of storage space. There are approximately 30 licenced major wholesalers in Zambia, and approximately six account for a large part of the volume [14,19]. Wholesalers and sub-wholesalers rely mainly on three primary distribution methods: delivery by wholesaler vehicles, private couriers, and customer pick-up. Although distribution by wholesaler vehicles is typically concentrated in the capital city and a few principal towns, some wholesalers use smaller vans to distribute beyond the main roads and into rural areas. Some wholesalers also use public transport, such as minibuses, to send their products to customers farther away.

Understanding the range of stakeholder perceptions of the potential impact of these innovative pharmacy distribution channels on medicine quality is crucial. Using in-depth interviews with a range of key stakeholders, this qualitative study aimed to explore stakeholder perceptions, including wholesalers, retailers, innovators, and regulatory authorities, of innovative private pharmacy distribution channels that are currently operational in Zambia. Specifically, this study sought to identify the perceived advantages and disadvantages of these channels in relation to the quality and safety of the medicines sold through them. By understanding stakeholder perceptions, this study aimed to provide valuable insights of key stakeholders into how these innovative pharmacy distribution channels can be regulated and monitored to ensure public access to quality medicines.

Methods

Study Design

This qualitative study was undertaken as part of a PhD research that aimed to compare the quality of medicines (antimalarials and antibiotics) available in innovative pharmacies with those available in independent pharmacies using traditional supply chains, from October to November 2022. In-depth interviews aimed to provide a comprehensive understanding of participants' perspectives, in their own words, on the issues under study [20–22]. This method is suitable for collecting information and contextual details regarding complex problems in qualitative research. Key informants, such as the stakeholders

in this study, can offer a wealth of information and insight from an expert's perspective on the reality of the situation they observe daily. The interviews were conducted in Lusaka, Zambia.

Study Setting

The study was conducted in Zambia, with in-depth interviews conducted primarily in Lusaka, the capital city. Some stakeholders were interviewed in other locations (one international location) to capture a diverse range of perspectives and experiences relating to innovative private pharmacy distribution channels and the quality of medicines in Zambia. Lusaka, with its central location and significant economic and administrative importance, was selected as the key study location. It is home to approximately three million people [23]. Lusaka's population has an increased average household income, education levels and access to healthcare services compared to other provinces [24]. The city has a mix of public and private healthcare facilities including hospitals, clinics, and pharmacies. Independent pharmacies, which are privately owned and not affiliated with a hospital or clinic, are a significant source of medicine for many residents of Lusaka [25]. The city provides a rich context for exploring stakeholders' perceptions and experiences with innovative private pharmacy distribution channels in Zambia.

Sampling and Participants

Purposive sampling was used to select 15 participants, who represented the range of stakeholders involved in innovative private pharmacy distribution channels in Zambia. The inclusion of participants from different sectors and management levels allowed for a comprehensive exploration of the potential benefits and challenges of innovative private pharmacy distribution channels in Zambia. One participant, representing an innovative organisation, declined to participate because the individual was busy.

Data Collection

The in-depth interviews were conducted in English and ranged in duration from 20 to 60 minutes. The interviews were typically conducted at the interviewee's workplace in a private office, with only the participant and researcher present. However, due to logistical constraints, three interviews were conducted over Zoom and three were conducted at a nearby quiet cafeteria. Written informed consent was obtained from each participant prior to the interviews. The interviews were conducted by SKM, the first author, and a Zambian pharmacist. The semi-structured interview guide asked about stakeholder perceptions and experiences with innovative private pharmacy distribution channels, their views on the quality and safety of medicines sold through these channels, and their suggestions for improving the quality of medicines in Zambia. Two distinct interview guides were designed to

address the different roles and experiences of participants. One guide was tailored for wholesalers, retailers, and innovators who had direct contact with the medicines. The other was developed for regulatory and professional bodies, whose interactions with medicines are indirect, thereby necessitating a different set of questions.

An inductive approach was adopted throughout the study to allow themes to emerge from the data. The interviews were recorded and transcribed with the participants' consent. However, in three cases, notes were taken instead of recordings because the participants were uncomfortable with the recording. The interview recordings and notes were transcribed with the assistance of a fellow PhD student with qualitative research experience. After each interview, the transcriptions were reviewed by SKM to ensure accuracy. The final transcripts were then cross-checked against the original notes and recordings.

Data Analysis

Interview data were managed using NVivo version 12 (QSR International Pty Ltd.). Transcripts were initially coded independently by SKM and a fellow social science PhD student with extensive experience in qualitative research. Following this independent coding process, SKM then reviewed and made final adjustments to the codes to ensure consistency and accuracy. The qualitative data collected from the in-depth interviews were analysed using a thematic analysis approach, as outlined by Braun and Clarke [26,27]. Thematic analysis is a flexible and widely used approach for analysing qualitative data that allows the identification of patterns and themes that emerge from the data itself. This is particularly useful in exploring complex phenomena. The analysis began with familiarisation with the data by reading and re-reading the transcripts. The initial codes were then generated from the data and grouped into themes based on the identified patterns. A constant comparison was used to ensure that the themes accurately represented the data and that they were distinct from one another. The themes were then refined, reviewed, and defined to produce a clear narrative relevant to the research questions. As the analysis progressed, the researchers engaged in reflective discussions to ensure that the themes were grounded in the data and aligned with research objectives. To provide an external check on the data and analysis process, the themes and sub-themes were critiqued and validated by an experienced qualitative researcher (VB).

Ethical Considerations

This study was conducted with the necessary ethical approval from the London School of Hygiene and Tropical Medicine Ethics Committee (Ref:28040) in the UK, as well as the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022) in Zambia. Written Informed consent was obtained from all participants who participated in

this study. In some cases, approval was first sought from corporate CEOs or other high-ranking officials to ensure the participation of the relevant representatives.

In this research, particular ethical considerations were paramount due to the first author's (SKM) role as a Zambian pharmacist responsible for data collection. These considerations included maintaining participant anonymity and managing power dynamics. The issue of participant anonymity was addressed by offering consistent reassurance regarding the confidential nature of the study, particularly when participants expressed concerns about identity disclosure. These considerations underscore the importance of a rigorous ethical framework in this study.

The professional background of the first author as a pharmacist may have influenced the interview dynamics. Participants may have viewed the researcher as a knowledgeable insider, potentially affecting their responses. This professional lens could also introduce biases into the study, influencing both the questions posed and interpretation of the data. A reflexivity process was employed throughout the study to counteract these potential biases. This involved a continuous reflection on how the researcher's perspectives might influence the study. Efforts were also made to maintain a neutral stance during the interviews to accurately capture participants' thoughts and experiences.

Results

A total of 15 participants, representing a diverse array of key stakeholders, were interviewed. As shown in Table 1, participants had varying levels of work experience, with the majority falling within the 5-9 years and greater than 14 years categories. Over 50% of the participants held at least a master's degree. The sample was composed of individuals from a variety of sectors in the pharmaceutical industry, including wholesalers (n=3), innovators (n=5), retailers (n=3), national medicine supply agencies (n=1), national medicine regulators (n=1), professional pharmacy bodies (n=1), and supply chain experts (n=1)

Table 1: Table of participant characteristics (Lusaka,2022)

Participant	Role	Sector	Education level	Years of experience
Participant 1	Senior management	Wholesale	Bachelors	5 - 9
Participant 2	Senior management	Innovator	Bachelors	5 - 9
Participant 3	Supply chain	Innovator	Masters	5 - 9
Participant 4	Manager	Retailer	Masters	5 - 9
Participant 5	Manager	Retailer	Bachelors	> 14
Participant 6	Senior management	Nationals Medicines Supply Agency	Masters	10 - 14
Participant 7	Manager	Innovator	Masters	> 14

Participant 8	Director	Wholesale	Masters	5 - 9
Participant 9	Senior management	National Medicines Regulator	Masters	> 14
Participant 10	Director	Retailer	Masters	> 14
Participant 11	Senior leadership	Pharmacy Professional Body	Bachelors	> 14
Participant 12	Supply chain	Innovator	Bachelors	5 - 9
Participant 13	Senior management	Innovator	Bachelors	> 14
Participant 14	Manager	Wholesale	Masters	> 14
Participant 15	Supply chain	Supply chain	PhD	> 14

Four main analysis categories emerged: current challenges in the pharmaceutical supply chain, potential benefits of the innovative pharmacy approach, limitations and shortcomings of the innovative pharmacy approach, and recommendations for improvement (Table 2). Participants from the innovator, wholesaler, and retailer categories provided insights primarily based on their direct experiences with different innovative approaches. Conversely, regulatory and professional bodies largely shared their perceptions of these innovations, often drawn from an oversight or regulatory perspective rather than direct use or implementation. However, a few from this group also discussed their perceptions of innovative approaches, informed by either direct encounters or second-hand information.

Table2: Summary of themes and category content

Category	Themes	Sub-themes
Challenges in the pharmaceutical supply chain	Affordability of medicines	Medicines are expensive Stockouts of medicines Monopolies are barriers to access
	Poor transportation	
	Presence of poor-quality medicines	
	Regulatory challenges	Practice and regulation mismatch Regulation impacts access and affordability Rigid licensing guidelines Availability of medicines Slow regulatory process
Potential benefits of the innovative pharmacy approach	Improved availability of products	Fast track product registration Improve access and distribution Improve economy Improve procurement efficiency Improve supply chains bottlenecks
	Improved quality assurance	Authentication of products Improved monitoring of products
	Improved traceability	Improved trace and track
Limitations and Shortcomings of the Innovative Pharmacy approach	Behavioural challenges	Lack of awareness People are slow to change Reluctant acceptance of technology Resistance to change
	Financial challenges	High cost of innovation Lack of financial support
	Lack of government interest	Lack of involvement by the ministry of health

		No government support
	Quality assurance challenges	Lack of authentication technologies
	Regulatory challenges	Lack of specific regulations Rigid pharmaceutical regulations
	Technical challenges	Electricity and internet as barriers Innovation is not inclusive Last point delivery confusion Lead time challenges
Recommendations for improvement	Digitisation	Digitise patient records Increased digitisation of the country
	Education	Increase training for regulators Increase awareness
	Government lead	Introduce more technology Investment into technology
	Quality assurance	Leverage technology Need innovation for authentication
	Regulation	Need for a new regulatory framework Need for localised regulations Need for regulation to enforce medicine quality
	Research	

Challenges in the Pharmaceutical Supply Chain

The participants underscored several key challenges within the current pharmaceutical supply chain in Zambia that impede access to good quality medicines. These barriers broadly encompass issues of affordability, inadequate transportation systems, prevalence of poor-quality medicines, and regulatory hurdles. These included the affordability of medicines, with several participants noting that "medicines are expensive" (Participant 7). Frequent "stockouts of medicines" (Participant 4) were also highlighted, which indirectly relates to affordability because when medicines are out of stock, patients may be compelled to buy the same drugs at higher prices elsewhere or resort to less effective but more affordable alternatives. Participants, mostly wholesalers, identified several regulatory challenges that impacted the pharmaceutical supply chain. Participants identified regulations that favour monopolies, creating a barrier to access, stating that "the regulation requires that one particular pharmaceutical company brings a particular brand of a drug" (Participant 4). Other participants mentioned a "mismatch between practice and regulation" (Participant 7), where regulations were not aligned with the needs of patients and healthcare providers. For instance, one participant noted the requirement for a pharmacist to be present in each physical pharmacy location, which could pose a challenge in areas with pharmacist shortage and limit the accessibility of medicines in these regions. "Strict licensing guidelines" (Participant 7) and "slow regulatory processes" (Participant 4) were also cited as additional challenges impacting the access and affordability of medicines. Additionally, poor transportation infrastructure was also cited as a challenge, particularly in rural areas. One participant noted that "we also need to think about how to cater to people outside

Lusaka, especially with the bad roads… and at the same time, maintaining the quality of those medicines. Because they are not common goods" (Participant 14).

Finally, the presence of poor-quality medicines was also identified as a major challenge. Several participants mentioned that "counterfeit products, especially with the distribution process that is not very well regulated, is resulting in a lot of counterfeit products around" (Participant 2). Another participant pointed out that "our economy is always about the cheapest, but the problem is that it being cheap, most of the time, what we are finding counterfeit medication" (Participant 13).

Potential Benefits of the Innovative Pharmacy Approach

Participants recognised some potential benefits of the innovative pharmacy approach. Such an approach, particularly one that innovatively removes intermediaries and middlemen in the supply chain or delivers medicines directly to patients, could enhance product affordability and availability. As one participant expressed, these approaches could "...improve accessibility to medical products, through improving the distribution process..." (Participant 2). Participants also underscored the role the innovative pharmacy approach could play in overcoming numerous supply chain bottlenecks, such as the presence of many intermediaries and challenges in medicine transportation. Enhanced quality assurance, particularly product authentication and monitoring, has emerged as another potential benefit. It was pointed out that the introduction of technology could be instrumental in improving the quality of medicines by enabling checks at several points.

Furthermore, the notion of fast-tracking product registration using innovative technologies was raised. This was viewed as a potential means to increase access and distribution, bolster the economy, and enhance procurement efficiency. It was articulated that fast-tracked product registration could stimulate multiple manufacturers to register products within a country, thereby increasing the variety and availability of medicines. Additionally, improved traceability was identified as a key benefit of the innovative pharmacy approach. Participants envisaged a system in which an application could enable the real-time tracking of medicine delivery from the pickup point to the final delivery destination. This could facilitate a seamless ordering and delivery process for retail pharmacies, leading to an efficient, real-time delivery of orders.

Limitations and Shortcomings of the Innovative Pharmacy Approach

The participants also highlighted several limitations and shortcomings of this innovative pharmacy approach. One major challenge identified was behavioural, which included a lack of awareness and slow adoption of technology among regulators, government, and some sectors of the pharmaceutical business. While some participants did not explicitly discuss resistance to change, the slow adoption of

technology can be seen as an implicit form of resistance due to reluctance or unfamiliarity with new systems. However, it is important to note that other participants expressed positive views about embracing change in the sector, with one saying, "innovation is never kept, because you cannot put a cap on ideas and the mind. It's always encouraged that people should think through better ways of doing business" (Participant 8). Financial challenges were also noted as significant barriers, particularly the high cost of innovation and the lack of financial support. One participant commented on these barriers, saying, "the major challenge is just no support whatsoever, lack of capital, lack of financial support, lack of structural support" (Participant 2).The lack of government interest and involvement in the innovative pharmacy approach was a concern for participants. As one participant stated, "it's a lonely world out there, because there's basically no support" (Participant 2).

Regulatory challenges emerged as a key theme, with participants identifying issues at both ends of the spectrum. Some participants expressed concerns regarding the lack of specific regulations, particularly in emerging areas such as online and telepharmacy services. One participant stated, "we need robust systems to help regulators enforce the law, especially regarding online and tele pharmacy services" (Participant 1). However, the existing pharmaceutical regulations are perceived as too rigid, potentially hindering innovative practices. This juxtaposition suggests a need for balanced, flexible regulations that can accommodate both traditional and innovative pharmacy practices, while ensuring the safety and efficacy of services.

Quality assurance challenges were identified, including a lack of authentication technologies. Authentication technologies in the pharmaceutical sector typically refer to the systems or methods that screen the legitimacy and quality of medicines. These technologies could include barcode scanners or radio-frequency identification (RFID), which allows the tracking of pharmaceutical products throughout the supply chain. They provide assurance that the product is genuine, properly stored, and has not expired, thus enhancing the overall quality of medicines available to patients. One participant noted that "there are no systems to monitor the products at the end user, the patient, especially in rural areas and among the dense areas" (Participant 1).

Participants also noted several technical challenges, including access to basic services, such as electricity and the Internet. For example, one participant pointed out that certain technologies, such as barcodes, can be limited in their usefulness because they require smartphones and electricity to function (Participant 13). Participants also pointed out that not all innovations are inclusive, meaning they may not be suitable or available to everyone. Some innovative approaches might be out of reach for stakeholders or customer groups that lack the necessary technology. Additionally, the 'lead time', or the time from the start of an innovative project to when it starts showing results, was identified as

a challenge. It can take a long time to develop, test, and implement new ways of doing things, which can discourage people from adopting innovative approaches, particularly smaller operations with limited resources.

Finally, participants highlighted that each pharmacy has its own unique set of circumstances, or 'setup'. This refers to the specific conditions or context in which a pharmacy operates. For example, a rural pharmacy might not have reliable Internet access, which would make certain technologies less useful. One participant noted, "Sometimes technologies aren't suited to the needs of an organisation and its people because each setup is unique. They have to be flexible enough to be adaptable" (Participant 6).

Recommendations for Improvement

Based on participants' experiences, recommendations for improving the innovative pharmacy approach and potentially improving medicine quality were provided. The participants suggested several digitisation initiatives, such as digitising patient records and increasing the digitisation of the country, to enhance efficiency and effectiveness in the supply chain. Improvements to logistics management have also been proposed. Specifically, one recommendation was to introduce an 'electronic logistics management information system.' This system would enhance visibility and transparency, making what each facility has issued and dispensed easily visible and trackable.

Education and awareness among stakeholders were also considered necessary improvements. Several participants recommended increasing training for regulators and stakeholders, highlighting the need to train more people to use technologies and have expertise in the processing of waivers and dossiers.

Several areas were identified by the participants for potential improvements in encouraging the innovative pharmacy approach. Government leadership was underscored as key to the advancement of this approach. Participants advocated for a proactive role for the government, especially in the implementation of more technology and investing in technological advancements within the pharmaceutical supply chain.

An urgent call for regulatory adaptation is another critical point highlighted by the participants. They recommended the establishment of a new regulatory framework that is accommodative and promotes innovative pharmacy practices. The need for localised regulations that consider regional peculiarities and needs is also underlined. Moreover, stringent regulatory measures were deemed necessary to enforce the quality of medicines, emphasising that regulations play a pivotal role in curbing the availability of substandard or counterfeit drugs in the market. One suggestion is to provide regulatory allowances for innovative companies to import medicines in bulk. This bypasses the

limitation of reliance on only a few wholesalers and aligns the supply more closely with the perceived needs of pharmacies (Participant 7). Finally, participants urged an increase in research in the field of pharmaceutical supply chains. This research should focus on understanding how innovation can impact systems, and ultimately, the quality of medicines.

Discussion

This qualitative study engaged a diverse set of stakeholders, including regulators, pharmaceutical professionals, and healthcare providers, to understand their perceptions of innovative private pharmacy distribution channels in Zambia. Stakeholders reported both direct and indirect experiences with these channels, acknowledging a range of benefits and challenges. Key advantages, as identified by respondents, include greater accessibility to medications, more efficient distribution and supply chain mechanisms, improved product traceability, and the ability to alleviate various supply chain bottlenecks. However, challenges such as the high cost of medicines, frequent stockouts, complex regulatory frameworks, transportation difficulties, and the presence of substandard medications were also raised. To address these issues, stakeholders have suggested the adoption of digitisation efforts, comprehensive training programs for regulators, proactive government involvement in technology implementation, enhancements in logistics management, regulatory reforms, and further research into pharmaceutical supply chain optimisation.

In this study, stakeholder recommendations offer new perspectives that are particularly relevant for pharmaceutical supply chains in LMICs. These insights align with existing research that underscores the transformative impact of digitisation in streamlining supply chain efficiencies. For example, Peltoniemi et al. [28] have pointed out that digitisation has led to more efficient, predictable, and technologically advanced dispensing processes at the pharmacy level. Digitisation is widely acknowledged as a vital mechanism for increasing transparency, traceability, and accountability in the supply chain [29–31]. Our study findings add to this discourse by emphasising the need for customised digital solutions that consider local contexts and unique challenges, a dimension often absent in the current literature.

The potential advantages of innovative private pharmacy distribution channels, as highlighted by our study, include improved accessibility, affordability, and quality assurance of pharmaceuticals. These findings resonate with existing research that underlines the transformative role of technology in enhancing access to medicine in LMICs. For example, studies by Yadav and Glassman [2] indicate that technological innovations can significantly improve various aspects of the pharmaceutical sector. Notably, the use of mobile health (mHealth) solutions allows patients to easily order and have medications delivered directly to their homes. Moreover, e-commerce platforms serve as digital

bridges connecting pharmacies and medicine manufacturers to consumers. Strategies such as last-mile delivery services, which use drones or other transport methods to reach remote areas, have been shown to break down access barriers and improve supply chain efficiency in LMICs [1,4–6].

The issue of medicine affordability, highlighted by participants in our study, is consistent with the existing literature that reports elevated drug prices as a persistent challenge in LMICs [32–35]. This finding adds further context-specific evidence from Zambia, emphasising that affordability continues to be a significant barrier to access to medicines. High costs not only limit the availability of medicines but also impact their utilisation, negatively influencing patient health outcomes. These elevated out-of-pocket expenses may compel patients to rely more on private healthcare providers, further exacerbating healthcare inequalities. Moreover, the financial burden often drives individuals to seek cheaper, yet potentially substandard alternatives from unlicensed outlets, thereby raising public health concerns.

Our study, along with the findings of Miller et al. [10], highlights a conspicuous absence of specific regulatory frameworks for innovative private pharmacy channels in Zambia. This regulatory gap has serious implications for public health as it opens the door to the sale of substandard or falsified medicines, thereby compromising both drug quality and patient safety. The urgency to address this issue is further underscored by the surge in online medicine purchases, a trend exacerbated by the COVID-19 pandemic [11–13]. Lack of regulation not only jeopardises the integrity of pharmaceuticals but also has cascading effects on public health outcomes, including increased rates of treatment failure, morbidity, and mortality. Nonetheless, technological solutions such as GS1 standards and blockchain offer innovative pathways for enhancing medicine quality and are considered promising. These technologies have shown potential for securing data and mitigating the risks of medicine counterfeiting [43–46]. However, the effective adoption and implementation of such technologies hinge on robust regulatory frameworks. Therefore, there are essential lessons to be learned from international regulatory bodies, such as the FDA and EMA. The establishment of the African Medicines Agency [49] also signifies a positive step toward developing a 21st-century regulatory framework that could guide Zambia and other member states to ensure medicine quality.

Our study emphasises the critical role of education and training for both the public and regulators. The technological and regulatory advancements discussed are meaningful only if they are adequately implemented and utilised. This calls for capacity building among regulators, a point echoed in research by Baber [47] and Tirivangani et al. [48] . The proactive role of government leadership is imperative for orchestrating these multifaceted improvements in the pharmaceutical supply chain. Only through a harmonised approach, encompassing technological advancements, regulatory reforms, and human

capital development, can we hope to tackle the pressing challenges in medicine quality and distribution.

Strengths of the study

This qualitative investigation is original in its context and contribution as it marks it first in Zambia. It provides a myriad of valuable insights into the perceptions and experiences of a diverse range of stakeholders concerning innovative private pharmacy distribution channels and their implications for medicine quality. Given the dearth of similar studies in Zambia, our research fills a significant knowledge gap and provides an initial framework for further investigation in this area. The rich insights provided into the complexities, potential advantages, and challenges tied to these channels underscore the value of qualitative enquiry in less-explored areas. This is particularly useful, given that a comprehensive understanding of the status quo is crucial for designing effective interventions.

The application of thematic analysis in our study facilitated the systematic identification, organisation, and elucidation of patterns and themes within the collected data, enhancing the credibility of the study and ensuring that the findings were grounded in participants' perspectives and experiences. Moreover, another strength of this study lies in the use of individual interviews. The interview data revealed tangible examples, detailed practices, and insightful perspectives on the regulation of an innovative pharmacy approach, which added depth of understanding to our broader enquiry. The range of stakeholders offered a diversity of viewpoints, enriching the dataset and potentially leading to a more comprehensive understanding of the topic.

This study's findings shed light on the potential benefits of innovative pharmacy approaches, including improved product availability, traceability, and procurement efficiency. These insights provide robust evidence to support the advocacy of innovative pharmacy strategies and to guide their implementation. Additionally, the study recognises the complexities associated with the innovative pharmacy approach, including behavioural, financial, regulatory, and technical challenges. These insights are particularly valuable for policymakers and regulators, as they can inform the development of policies and regulations that address these issues.

Limitations

Our study is constrained by the small sample size, which may limit the generalisability of the findings. Although the participants were purposively selected to represent diverse stakeholders, their views may not completely represent the wider population involved in innovative private pharmacy distribution channels in Zambia. Second, reliance on self-reported data inherently carries the risk of bias and errors. Participants might have skewed their responses towards what they perceived as

socially desirable or could have been influenced by their unique personal experiences and perspectives, which may not be representative of the wider stakeholder population.

A methodological consideration that may also affect the results is the potential for researcher bias or interpretation. Despite the rigorous application of thematic analysis for the systematic identification, organisation, and interpretation of patterns and themes within the data, the researcher's lens could shape the final outcomes. Moreover, the positionality of SKM, the first author as a pharmacist, may have shaped the process and outcomes of this research. Having background knowledge and professional experience in the field may have unconsciously influenced how the interviews were navigated, interpreted participants' responses, and identified emerging themes. Throughout the study, SKM endeavoured to maintain reflexivity and continually examined biases, assumptions, and interpretations.

Despite these limitations, this study offers valuable insights into stakeholder perspectives on innovative private pharmacy channels and their implications for medicine quality in Zambia, marking an important step in an underexplored research area. Future studies could expand this work by involving a broader and more diverse range of stakeholders and employing diverse data collection methods to improve the validity and reliability of the results.

Conclusion

This qualitative study offers an in-depth analysis of stakeholders' perceptions of innovative private pharmacy distribution channels in Zambia. This underscores a myriad of challenges, ranging from affordability and transportation to regulatory hurdles that currently plague the country's pharmaceutical supply chain. These obstacles not only impair the quality of medicines but also detrimentally affect patient outcomes. Despite these challenges, our research identified promising avenues for improvement. This highlights the transformative potential of digitisation, education, government involvement, and comprehensive regulations to elevate the pharmaceutical sector. Importantly, this study emphasises the ability of innovative pharmacy channels to improve product availability, quality assurance, and traceability of medicines. These findings have actionable implications for policymakers and serve as a foundational guide for enacting changes that can ensure the safe and effective operation of innovative pharmacy channels. Beyond Zambia, our findings have a broader relevance to other LMICs facing similar challenges in pharmaceutical supply chain management. They contribute to the wider discourse on health equity and access to quality medicines, advocating the adoption of some innovative technologies and practices as a pathway toward global health improvement.

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Chapter 7: General Discussion

7.1 Introduction

Ensuring access to good-quality medicines is essential for effective healthcare, which is pivotal for achieving the United Nations Sustainable Development Goals (SDGs). Specifically, SDG 3 underscores the importance of ensuring healthy lives and promoting overall well-being, with access to quality medicine central to this mission [1–3]. While good quality-assured medicines bolster health systems, poor quality, that is, substandard and falsified (SF) medicines, pose serious threats to patient health, hinder treatment effectiveness, and can erode trust in health systems [1,4]. Such consequences are especially pronounced in low- and middle-income countries (LMICs) such as Zambia. Compounding this issue, global events, such as the COVID-19 pandemic, have placed unprecedented strains on supply chains, rendering LMICs vulnerable to the proliferation of SF medicines [5,6]. The repercussions of this are manifold; not only do SF medicines result in avoidable morbidity and mortality, but their use also paves the way for antimicrobial resistance (AMR), a burgeoning global health threat [7,8].

In light of these challenges, private pharmacies in Zambia and other LMICs have become vital primary points of access to healthcare by patients hence, the onus of these entities to dispense quality-assured medicines is immense [9–11]. The evolving landscape of the pharmaceutical sector, characterised by the adoption of technologies such as inventory management systems and franchising systems, brings with it both opportunities and challenges [12,13]. Whilst these innovations herald efficiencies and improved medicine quality assurance, they also necessitate the adept navigation of evolving supply channels. The Zambian pharmaceutical landscape resonates with this change, with a nascent emergence of innovative pharmacies that integrate technology-driven solutions from inventory systems to telepharmacy.

Although anecdotal evidence highlights the concern related with SF medicines in Zambia, a preliminary investigation and understanding of this challenge is lacking [14,15]. This thesis aimed to investigate this knowledge gap by comparing the quality of medicines (antimalarials and antibiotics) available in innovative pharmacies with ones available in independent pharmacies which use traditional supply chains. This research also aimed to examine factors pertinent to maintaining quality across supply chains. To achieve these aims, my research focused on five objectives, addressed across the chapters of this thesis: (i) Assess and compare the medicine procurement practices in innovative and independent pharmacies (Chapter 3); (ii)Assess and compare medicine storage and transport practices in innovative and independent pharmacies (Chapter 3); (iii) Assess and compare the knowledge, availability, and usability of screening technologies for medicine quality in innovative and independent pharmacies (Chapter 4); (iv) Determine and compare the prevalence of poor-quality antimalarials and

antibiotics sold in innovative and independent pharmacies (Chapter 5); and (v)Determine the shortcomings of the innovative pharmacy approach and the improvements needed to ensure that the patient receives quality assured medicine (Chapter 6).

7.2 Main Findings

Chapter 2 - Characteristics of Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: A Descriptive Comparison

This chapter aimed to provide a comparison of the characteristics and practices of innovative and traditional independent pharmacies in Lusaka. In terms of structural aesthetics, innovative pharmacies exhibit a contemporary and organised setup, with a keen focus on modern service offerings such as internet pharmacy and telepharmacy. Conversely, traditional independent pharmacies uphold a classic design, aligning with what the community is familiar with and prioritising brick-and-mortar service delivery. An observation although not statistically significant is the difference in the preferred location of innovative pharmacies, which are predominantly found inside shopping malls, and this positioning possibly caters to an affluent clientele. In contrast, traditional independent pharmacies are more commonly located in peri-urban areas, indicating a focus on serving a localised residential community.

Regarding staffing, innovative pharmacies had more pharmacists present on site at the time of the survey. In contrast, pharmacy staff in traditional independent pharmacies have a mix of pharmacists, pharmacy technologists, and non-pharmacy personnel. Whilst there are variances in service offerings and staffing, both pharmacy types generally adhere to the Zambia Medicines Regulatory Authority (ZAMRA) guidelines, particularly regarding storage conditions. The majority of both pharmacy types met ZAMRA's storage/space recommendations, maintaining their outlets and shelves in commendable conditions. Chapter 2's exploration of the differences in innovative and traditional independent pharmacies in Lusaka not only reveals varied structural and operational contrasts but also sets a foundational understanding of the diverse pharmaceutical landscape, a theme that is further examined in subsequent chapters.

Chapter 3 - Assessment of Medicine Procurement, Transportation, and Storage Practices in Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: Implications on Medicine Quality

Building on the characterisations in Chapter 2, Chapter 3 delves into the specific practices of medicine procurement, transportation, and storage, highlighting critical differences in supply chain management that directly influence the medicine quality themes discussed in Chapter 5. Notably, innovative pharmacies primarily sourced medicines from affiliated parent companies, resulting in a streamlined supply chain and shorter times of procurement for the tracer medicines - amoxicillin and

sulfadoxine/pyrimethamine (SP). In contrast, traditional independent pharmacies frequently procured from wholesalers or sub-wholesalers, resulting in delayed delivery.

A difference was in the transportation of the medicines, as the innovative pharmacies most often received direct deliveries which used air-conditioned vehicles, ensuring optimal conditions. Meanwhile, traditional independent pharmacies often used personal vehicles to pick up medicines from suppliers. However, neither pharmacy type employing tracking or temperature monitoring systems during transport. The absence of this can introduce vulnerabilities, as medicines should ideally be moved using air-conditioned custom-built vehicles that can be programmed to have clinically controlled conditions.

Within the outlets, the majority of both pharmacy types had functional air conditioning units that are desirable for medicine storage. However, while almost half faced regular power disruptions, innovative pharmacies were notably better equipped with backup power solutions. Storage practices varied, as innovative pharmacies predominantly adhered to the "First Expiry, First Out" (FEFO) principle, which is occasionally facilitated by utilising advanced computerised inventory management systems. This digital approach potentially enhances efficiency, helping to monitor expiry dates and maintain accurate records. However, several traditional independent pharmacies did not follow the FEFO principle and also tended to use manual inventory methods, which may increase the likelihood of errors. A shared challenge for both pharmacy types was the lack of specialised training, especially concerning medicine quality, emphasising the need for continuous professional development. There is a pressing need for short courses focusing on best practices in procurement, transportation, and storage to be available to staff.

Chapter 4 - Comparative Analysis of Medicine Quality Surveillance between Innovative and Traditional Independent Pharmacies in Lusaka, Zambia

Chapter 4 extends the discussion from the operational aspects in Chapters 2 and 3 to the aspects of medicine quality surveillance, uncovering technology adoption disparities and their implications for pharmacovigilance, as later echoed in the stakeholder perspectives of Chapter 6. Both pharmacy types expressed concerns about encountering suspected poor-quality medicines within their supply chains, which suggests realised concerns regarding the quality of medicines available to consumers. Nonetheless, only a fraction, 32.7% (17/52) of those who suspected receiving poor-quality medicines took steps to report their apprehensions. Among those who did, the majority informed distributors, 76.5% (13/17), while a subset notified the National Medicines Regulatory Authority (NMRA), 35.3% (6/17).

Differences in the adoption of technology were also evident as innovative pharmacies utilised computerised recording systems and proprietary inventory management software to record information and track products. In contrast, traditional independent pharmacies mainly used manual recording methods, a pattern also observed in findings reported in Chapter 3, emphasising a difference in the implications for medicine traceability.

One notable observation was the lack of awareness regarding screening technologies designed to detect poor-quality medicines. Despite the critical role of these technologies in pharmacovigilance, particularly in regions without fully equipped national medicine quality laboratories, the awareness gap was noteworthy. These findings emphasise the importance of targeted educational initiatives to enhance pharmacy personnel's capabilities in detecting and countering the spread of poor-quality medicines. Chapter 4 highlighted not only the potential for improving pharmacovigilance in Zambia's pharmaceutical sector but also emphasised a significant challenge posed by the absence of trace and tracking technologies among the surveyed pharmacies.

Chapter 5 - Medicine Quality in Innovative and Traditional Independent Pharmacies in Lusaka, Zambia: Factors Influencing the Quality of Amoxicillin and Sulfadoxine/Pyrimethamine

In Chapter 5, the focus shifts to the direct analysis of medicine quality, specifically, amoxicillin and Sulfadoxine/Pyrimethamine (SP), building upon the procurement and storage practices discussed in Chapter 3. This sets the stage for the in-depth stakeholder insights to be presented in Chapter 6. A significant finding in this chapter is the absence of suspected falsified medicines within the retail environments studied. However, it was observed that some amoxicillin samples, and all samples of SP, failed in content analysis. Despite this, all samples met the US Pharmacopeia (USP) tolerance limits for bioavailability. This finding raises concerns, as the bioefficacy of a drug can be compromised over time if the levels of the active pharmaceutical ingredient (API) diminish due to degradation, which can occur under suboptimal storage conditions, such as exposure to direct sunlight. Degradation under such conditions can lead to reduced dissolution rates, potentially undermining the therapeutic effectiveness of the drug.

The findings further indicated no difference in the quality of amoxicillin between types of pharmacies, innovative and traditional independent pharmacies. Both amoxicillin and SP are frequently sourced from the same manufacturers by both innovative and traditional independent pharmacies. This shared sourcing practice may account for the absence of notable statistical differences in the quality of medicines between the two types of outlets. Repackaging medicines into plastic pill packs emerged as a potential issue, as none of the repackaged amoxicillin samples contained the stated amount of API upon content analysis, highlighting the potential risks associated with this practice. Innovative

pharmacies primarily sold medicines in their original packaging, whereas some traditional independent pharmacies sold amoxicillin, which was repackaged in plastic pill packs. In summary, these findings confirmed that both types of pharmacies face challenges concerning medicine quality, emphasising the need for comprehensive strategies to ensure consistent medicine quality.

Chapter 6 - Stakeholder Perceptions and Experiences Concerning Innovative Private Pharmacy Distribution Channels in Zambia: Implications for Medicine Quality.

Chapter 6 complements the earlier chapters by providing qualitative insights from stakeholders, illuminating the real-world implications of the practices and challenges identified in Chapters 2 through 5, and underscoring the urgent need for regulatory and technological advancements in the pharmaceutical sector. By engaging a diverse group within the pharmaceutical sector, this study aimed to explore the advantages, drawbacks, and implications of these systems for medicine quality. This highlighted key challenges within the current pharmaceutical supply chain affecting both types of pharmacies. The challenges relayed by stakeholders included supply chain challenges, such as the cost of medicines, transportation difficulties, and the potential existence of substandard medicines. These transportation concerns echo the findings in Chapter 3.

There were also discrepancies between the regulatory intentions and guidelines set by regulators and the actual practices in the field. The pronounced lack of specific regulations for newer pharmacy models, such as e-pharmacies coupled with protracted regulatory processes, was flagged as a significant concern. These regulatory gaps amplify the risk of substandard or falsified medicines entering the market. Furthermore, technical challenges realised, such as intermittent access to electricity and the Internet, impeding the adoption of novel technologies in the pharmacy space. There was a discernible resistance to change and a prevailing lack of awareness, which will further curtail the potential benefits of innovative approaches. In terms of financial concerns, the substantial costs associated with pioneering these innovations, paired with a paucity of financial backing, are seen as threats to the viability and scalability of such models.

However, stakeholders acknowledged the inherent benefits of these innovative strategies, such as the deployment of computerised systems, to bolster quality assurance and improve medicine traceability, which is fundamental to delivering good-quality medicines to patients. The recommendations that emanated from these insights were multifaceted. Stakeholders highlighted the urgency of digital transformation, especially regarding health records, to enhance efficiency and transparency in the supply chain. They supported educational and training initiatives tailored for regulators and key industry players to adeptly navigate the innovative pharmacy terrain. There was a consensus on the pivotal role of government-led interventions and investments in fostering these innovative channels.

A Key theme of this research was the emphasis on medicine quality assurance. Stakeholders suggested the swift integration of digital technologies, citing the urgent need for authentication methods such as barcoding. Concurrently, there were calls for formulating regulatory frameworks specifically designed for innovative pharmacy models, underscoring their criticality in ensuring quality-assured medicines and safeguarding patient health.

7.3 Recognised Limitations

This thesis provides insights into pharmaceutical distribution and medicine quality in Zambia, but it is not without its limitations. These constraints are integral to understanding the context of the findings and extrapolating them to broader scenarios. The following section describes the limitations of this research.

Geographical Scope

The confinement of this research to Lusaka, Zambia's capital, introduces a salient limitation concerning its geographical breadth. While Lusaka, an urban city, presents a microcosm of innovative pharmaceutical practices and possibly more structured healthcare systems, it will not wholly reflect the realities of peripheral or rural regions. In multiple global health studies, urban-rural disparities in health outcomes and access to medical resources have been highlighted. For instance, research conducted in India showed a more robust penetration of formal pharmaceutical distribution networks compared with rural regions [16]. Studies in LMICs have demonstrated disparities between urban centres and rural outskirts regarding the transportation of health products, including medicines [17,18]. Such differences can affect medicine quality if these products are exposed to heat or humidity en route. Similarly, Lusaka's pharmaceutical landscape may be considerably different from that of Zambia's rural areas, which often face logistical challenges and have limited healthcare facilities. Hence, findings derived from an urban centre such as Lusaka will not necessarily mirror the complexities, challenges, and dynamics of pharmaceutical distribution in Zambia's more remote regions.

Furthermore, although Lusaka offers insights into Zambia's urban pharmaceutical dynamics, extrapolating these findings to other countries, even within the same continent, can be precarious. Each country, or even distinct regions within them, may exhibit unique pharmaceutical infrastructure, regulatory frameworks, cultural beliefs about medicines, and economic factors influencing drug distribution and usage [19]. In many countries, private pharmacies play a pivotal role in primary healthcare delivery [9,10]. Thus, while this research offers an in-depth examination of Lusaka, its findings should be interpreted and generalised with caution, recognising the uniqueness of each geographical context, as the balance between public and private entities can vary across countries.

Research Design

The predominant use of a cross-sectional survey study design in this research presents inherent strengths and limitations. By nature, cross-sectional designs capture data at a single point in time, making them particularly adept at presenting a "snapshot" of the situation. However, this can also be a limitation, especially when examining dynamic systems such as pharmaceutical distribution and quality control. First, capturing data at a single time point restricts our understanding of temporal variations and evolution. Similar to other sectors, the pharmaceutical industry is in a constant state of flux and is influenced by many factors, including regulatory changes, technological advancements, economic shifts, and public health crises. A longitudinal study, in comparison, may offer insights into the progression or regression of specific practices over time. For instance, a study in South Korea highlighted how the pharmaceutical sector has evolved in response to regulatory changes over thirty years [20]. Additionally, cross-sectional designs inherently limit the establishment of causality. Although correlations can be identified, determining the directionality of the cause-and-effect relationships is challenging. This is especially pertinent in situations in which multiple factors interact. For example, research in South Africa noted that, while there was an apparent correlation between the location of pharmacies and patient outcomes, deeper scrutiny of findings suggested that this was confounded by other socio-economic variables [21]. Another limitation of the cross-sectional approach is its susceptibility to certain biases, notably the recall bias. Since participants are often required to recount past experiences or practices, there is a potential for misremembering or selectively recalling events, especially if there was a lapse in time. To mitigate this risk, specific time frames were included in the survey questions, encouraging participants to think within a recent and thereby, responses are provided within an accurate time window. In addition, the study may be subject to desirability bias, in which participants are inclined to provide socially desirable responses. Compliance bias may also affect the results, as participants might claim to adhere strictly to the guidelines than they actually do. To minimise these biases, the survey was designed to ensure anonymity and to emphasise the importance of honest responses for the integrity of the research.

In the context of this research, the cross-sectional design, primarily seen in Chapters 3, 4, and 5, provides valuable but static insights into the pharmaceutical landscape of Lusaka. Hence, the observed trends indicate "current" but do not shed light on the "how" or "why". This also means that certain exogenous factors, such as economic shifts, regulatory changes, and technological disruptions, may not be completely accounted for, as they could emerge after the data collection period and significantly impact the pharmaceutical domain. While the chosen research design provided a comprehensive overview of the current scenario, acknowledging its limitations is important for the holistic interpretation and utilisation of the findings. Future studies should consider integrating

dynamic research designs or supplementing cross-sectional data with qualitative longitudinal insights to create a richer and a nuanced understanding of the field.

Sample Size and Focus

The sample size and specificity of focus are vital considerations in research, playing a pivotal role in the breadth and depth of the findings and their external validity inherent limitations. Primarily, the modest sample size employed across various chapters, especially Chapter 5, may have limited the statistical power of the findings. Secondly, a limited sample size may not adequately capture the diversity and variability inherent in larger populations. Specific to this research, the limited number of innovative pharmacies in Lusaka further constrained the sample size. Although all available innovative pharmacies were sampled, the fact that the number was limited poses concerns about the generalisability of the findings to other contexts or larger urban landscapes. Furthermore, the decision to focus on only two types of medicines, as seen in Chapter 5, while offering specificity and depth, inadvertently sidelines other essential medicines. This narrow lens might omit distinct challenges, distribution dynamics, and quality assurance measures pertinent to medicines outside the chosen two. Moreover, the study's focus on a limited range of available brands might not adequately represent the broader brand landscape. This limitation was particularly pronounced given that the research was conducted shortly after supply chain disruptions resulting from COVID-19. Reported findings from other studies have also observed differences in quality between various types of antibiotics and antimalarials, emphasising variability across medicine types [22–24]. Different brands may have distinct supply chain dynamics, quality assurance mechanisms, and regulatory challenges. Fewer brands than anticipated were found, which may stem from external supply chain disruptions, a challenge highlighted but not investigated fully due to the time constraint of this research.

Overall, although the chosen sample size and focus provide detailed insights into select facets of the pharmaceutical sector in Lusaka, they also emphasise the importance of a wider scope in future research endeavours. Expanding the range, both in terms of the number of pharmacies and medicines and across brands, should offer a more holistic and representative understanding of the field. This breadth, paired with the depth of this research, can set the stage for effective interventions and policy decisions.

Exogenous Challenges

The nature of exogenous challenges is that they often exist beyond the immediate control of the researchers or entities being investigated. In this research, a myriad of external challenges, ranging from global health crises to economic challenges, have influenced the findings and added layers of complexity to the interpretation of results. The emergence and persistence of the COVID-19 pandemic

has cast a long shadow on global supply chains, and the pharmaceutical sector is no exception. Studies have indicated that several countries faced disruptions in the pharmaceutical supply chain owing to lockdown measures and redirection of resources to manage the pandemic [6,25]. In the Zambian context, these disruptions could have resulted in the limited availability of brands and restricted the assortment of medicines in the market. This constrained supply persisted for some time after the acute phase of the pandemic, impacting the period under investigation in this PhD research.

Supply chain disruptions, even outside the implications of COVID-19, profoundly affect the availability of medicine. According to United States Pharmacopoeia (USP) [26], these disruptions provide an opportunity for SF medicines to penetrate legitimate supply chains and endanger the safety of medicines. Any disturbance in sourcing the API, which could be due to supplier complications or geopolitical tensions, can severely hinder the local production and availability of certain medicines [26]. In conclusion, the pharmaceutical sector, like any other, does not operate in a vacuum. External- and macro-level challenges profoundly influence micro-level dynamics, leading to issues such as supply chain disruptions and increased costs. Recognising and understanding these exogenous challenges helps to contextualise the findings of this research. This insight could serve as a valuable resource for those interested in enhancing the resilience and responsiveness of pharmaceutical systems for the future.

7.4 Novel Contributions to Knowledge

The landscape of innovative private pharmacy distribution channels in LMICs has remained largely unexplored. Whilst existing literature has often emphasised the financial and accessibility aspects of these channels [12,13], there has been a notable absence of enquiries specifically focused on their implications for medicine quality. To my knowledge, this thesis presents the first results of innovative private pharmacy distribution channels focusing on medicine quality. Previous studies have chiefly explored medicine quality in traditional pharmacies across various regions [22,23,27]. By comparing these models, this research provides an understanding of how different models operate and how medicine quality may be affected. The exploration was comprehensive, delving into operational intricacies, procurement strategies, transportation and storage standards, and their overarching implications for medicine quality. This nuanced exploration distinguishes the research by adding a novel dimension to the existing knowledge.

There is a lack of knowledge on the prevalence of poor-quality medicines in Zambia, and a handful of studies [14,28,29] investigating medicine quality found varied proportions of poor-quality medicines. This current research was focused on widely used medicines, amoxicillin and SP, as well as considering additional contextual and supporting factors such as outlet type, storage, procurement and medicine

characteristics. Notably, the use of confirmatory tests using content analysis by the 'gold standard' technique of high-performance liquid chromatography with diode array detection (HPLC-DAD) and dissolution testing distinguishes this research, offering a more thorough perspective compared to previous Zambian research that predominantly relied on screening tools, such as Minilab®.

The qualitative component of this research centred on stakeholder perceptions, which accentuates the current regulatory shortcomings intrinsic to the innovative pharmacy distribution channels. While Miller et al.[30] have alluded to regulatory challenges presented by emerging technologies, such as ePharmacies in LMICs, studies specifically highlighting these challenges in the operational context of the innovative pharmacy approach and its impact on medicine quality are, to date, lacking. This research not only brings these challenges to the forefront but also elucidates the perceived potential benefits of the innovative pharmacy model, suggesting viable solutions tailored to the Zambian context.

Finally, this research strives to extend beyond traditional academic exploration to provide practical insights for stakeholders in the pharmaceutical industry. For example, highlighting important aspects that may affect the quality of medicines at the pharmacy outlet level, such as inventory management and reporting systems. By merging scholarly analysis with actionable recommendations, this research enhances its broader applicability and relevance for policymakers. In summary, examining both traditional and innovative pharmacy models and their implications for medicine quality in Zambia brings a novel perspective to the drug quality debates. These insights not only enrich the academic discourse but have also immediate and practical implications for policy formulation and healthcare practices within Zambia and in similar LMIC contexts.

7.5 Implications for Policy and Practice

In navigating the complex landscape of pharmacy practices and their policy implications, particularly in LMICs like Zambia, the necessity to triangulate data from diverse sub-studies and methodologies is crucial. This comprehensive approach allows me to discern the interconnectedness of my findings, providing a holistic understanding. Drawing upon both quantitative data and qualitative insights, I am now positioned to present an integrated set of recommendations that reflect the cumulative insights of my multifaceted research.

A key observation in this evolving pharmaceutical landscape is the emergence of innovative pharmacies. While they represent a significant advancement in pharmaceutical services, they also raise important questions about social equity. These pharmacies, often situated in settings that suggest they may cater to more affluent consumers. While direct data on the socio-economic status of their clientele was not collected, this positioning of pharmacies in affluent areas could potentially

contribute to widening the healthcare gap. This impact extends beyond consumer demographics to implications for pharmacist employment. To mitigate this, policy interventions are needed to ensure that the benefits of innovation in pharmaceutical services are accessible across all socio-economic strata.

Reflecting the situation in many LMICs, Zambia's pharmacy sector stands at a pivotal point in the broader healthcare paradigm. Focused on Lusaka, my research highlighted the distinct operational dynamics between innovative and traditional independent pharmacies. Despite these operational differences, no significant differences were found in the quality of medicines offered by both outlet types. In this section, I articulate policy implications relevant to both policy formulation and practical applications, with a particular emphasis on medicine quality.

The insights gained from this research not only broaden our understanding but also prompt profound reflections on the potential implications for Zambia's pharmaceutical sector. By addressing the observed disparities and aligning with international standards and guidelines, my findings are poised to guide stakeholders toward a more refined and effective pharmaceutical landscape in Zambia. This section will focus on key areas: enhancing pharmaceutical standards, strengthening medicine quality surveillance systems, enhancing education and pharmacy practices, and promoting the adoption of technology and appropriate regulations. Table 1 represents a summary of the findings and potential policy recommendations.

7.5.1. Enhancing Pharmaceutical Standards: The Cases of Sulfadoxine/Pyrimethamine and Amoxicillin

Ensuring the quality standards of essential medicines is a critical aspect of public health, especially in the context of Zambia. This section delves into the specific challenges encountered with two such medicines: Sulfadoxine/Pyrimethamine (SP) and amoxicillin. The experiences with these drugs not only shed light on specific issues but also illuminate broader systemic concerns in pharmaceutical quality control that necessitate attention and action.

Sulfadoxine/Pyrimethamine

The case of SP is particularly concerning. It was observed that none of the SP samples met quality standards, a situation requiring urgent action. This can be partly attributed to SP's current status in therapeutic guidelines. Although no longer recommended as the first-line treatment for malaria, but for intermittent preventive treatment in pregnancy (IPTp), it is still widely used in private pharmacies, primarily due to its affordability. This disconnect between guidelines and actual usage indicates a gap in market-driven quality assurance mechanisms, such as WHO pre-qualification. The WHO Prequalification program is a service provided by the WHO to assess the quality, safety, and efficacy

of medical products, with the aim of ensuring that medicines, vaccines, and diagnostics used in resource-limited settings meet global standards for public health [31]. This situation presents a clear link between availability, affordability, rational use, and quality – crucial considerations for policymakers in Zambia. It underscores the need for a re-evaluation of SP's role in therapeutic practices and regulatory oversight.

In addition to its recommendation of use of SP in IPTp, the WHO has recently introduced guidelines recommending SP for perennial malaria chemoprevention (PMC) in high-transmission areas [32]. Recognising SP's importance, Medicines for Malaria Venture (MMV) with support from UNITAID and in collaboration with Universal Corporation Ltd (UCL), has worked to produce WHO prequalified SP for IPTp and SP with amodiaquine (SPAQ) for Seasonal Malaria Chemoprevention (SMC) [33,34]. UCL's achievement as the first African manufacturer to receive WHO prequalification for these purposes marks a significant step in improving SP's quality and exemplifies the impact of collaborative efforts in enhancing drug standards in resource-limited settings.

Amoxicillin

Amoxicillin, a widely used antibiotic, also faces significant quality surveillance challenges, particularly as poor quality antibiotics may contribute to antimicrobial resistance (AMR) [7]. Concerns about storage practices and potential degradation highlight the need for strict quality control and proper storage protocols. Suggestions for pooled procurement of antibiotics, including amoxicillin, aim to ensure the distribution of quality-assured products [35,36]. A pooled procurement mechanism is a strategy where multiple entities collaborate to collectively negotiate and purchase medical supplies, aiming to achieve lower prices and ensure higher quality and supply reliability by leveraging their combined purchasing power [37]. Key supply-chain considerations, such as pooled procurement networks, could help achieve consistent pricing and availability of quality-assured antimicrobials.

Overarching Regulatory Considerations

The cases of SP and amoxicillin not only highlight the complexities in maintaining medicine quality but also the crucial role of international bodies in this endeavour. Organisations like the Global Fund, MMV, and UNITAID are instrumental in facilitating the procurement of quality-assured medicines. Their involvement is particularly vital in settings where local regulatory systems face challenges in ensuring consistent drug quality. The Global Fund, with its extensive resources and global reach, can play a pivotal role in procurement processes, ensuring that only medicines meeting stringent quality standards are distributed. Similarly, MMV's and UNITAID's collaborative efforts with manufacturers, as seen in the case of SP, demonstrate how international partnerships can elevate the quality of essential medicines, making them safer and more effective for public use.

These examples underscore the need for comprehensive strategies that integrate the efforts of both local and global entities. Such collaboration can address the regulatory and practical aspects of medicine quality in countries like Zambia. A synergistic approach, combining the expertise and resources of local regulatory bodies and international organisations, is essential for ensuring the procurement and distribution of quality-assured medicines. This approach not only aligns with international quality standards but also takes into account the affordability and accessibility challenges faced in LMICs, thereby ensuring the safe and effective use of essential medicines for all segments of the population.

7.5.2. Strengthening Medicine Quality Surveillance Systems

The urgency of strengthening surveillance systems for medicine quality is highlighted in Chapters 4 and 5, particularly in light of the challenges posed by supply chain traceability and the risks inherent in the repackaging of medicines practices**.** Such concerns resonate with findings from elsewhere in sub-Saharan Africa, such as Equatorial Guinea, Malawi, and Tanzania [22,23,38]. Zambia's medicine regulatory body, ZAMRA, is faced with the challenge of curtailing poor-quality medicines. Addressing this concern requires several actions, including conducting routine pharmacovigilance, improving reporting mechanisms, utilising screening tools, and raising awareness of poor-quality (SF) medicines. It is essential to clarify two critical concepts in this context: Pharmacovigilance and Post-Marketing Surveillance. Pharmacovigilance involves the science and activities related to detecting, assessing, understanding, and preventing adverse effects or any other medication-related issues [39]. Post Marketing Surveillance, in contrast, includes all activities aimed at monitoring the safety of a pharmaceutical product after it has entered the market [40]. Both are integral to ensuring the efficacy and safety of pharmaceuticals in Zambia and play a pivotal role in safeguarding public health.

Analytical chemistry techniques

ZAMRA's establishment of the national medicines quality laboratory (NMQL), with support from the European Union Commission, launched in 2023, marks a significant stride in bolstering pharmaceutical quality assurance. Ideally, regular quality surveillance needs to involve randomised sampling of medicines followed by sample analysis using the 'gold standard' confirmatory tests such as HPLC. However, strengthening this approach further through the integration of screening technologies such as GPHF-Minilab®, Near-Infrared Spectroscopy (NIR), Paper Analytical Devices (PADs/aPADs), and Raman spectroscopy presents a multi-layered challenge, especially given their limited availability in Zambia at present. A phased integration could start with PADs/aPADs at the point of importation and initial distribution due to their cost-effectiveness and ease of use [41,42]. Over time, more accurate technologies such as the NIR and Raman spectroscopy could be introduced [43,44]. This tiered approach would span from the importation stage, where portable technologies such as GPHF-Minilab® might be

deployed by customs, to national laboratories for confirmatory tests such as HPLC. While studies in Kenya [41,42] have emphasised the high return on investment for some of these technologies, such findings may not directly translate to the Zambian context due to constraints posed from availability and cost variations. Therefore, a tailored approach involving stakeholders from both the public and private sectors is crucial to effectively utilise these technologies for pharmaceutical surveillance in Zambia.

Reporting systems

The findings from Chapter 4 further indicate that there is a pressing need to improve and expand the current reporting systems to regulators. Comprehensive efforts should be undertaken to streamline and encourage the reporting of suspicious or poor-quality medicines to national regulators, ensuring swift action, such as removing suspect products from shelves in response to potential threats. Furthermore, the underutilisation of tools such as 'Adverse Drug Reaction Application (ADRA), the pharmacovigilance app reflects the existing gaps in implementation that need to be addressed. Policymakers and practitioners should work in tandem to ensure that such tools are not only available but also effectively integrated into the daily operations of pharmacies. In addition, considering that most pharmacy personnel receive alerts about poor-quality medicines from the NMRA via social media, there is an opportunity to build upon this communication channel. Policies could involve amplifying the dedicated and verified accounts of NMRA social media handles or platforms to circulate essential information to professionals more effectively. Nevertheless, as Chapter 6 delineates, technology is not the only possible solution. A carefully crafted regulatory framework encompassing both traditional pharmacies and novel models such as e-pharmacies remains pivotal.

World Health Organisation's Global Benchmarking Tool (GBT)

Regulatory systems dictate the safety, efficacy, and quality of medical products, with ramifications for health outcomes and innovation. The WHO's GBT is a novel tool that facilitates rigorous assessment of these systems [45]. By leveraging the GBT, ZAMRA can strengthen its regulatory system, receiving technical support and advice in quality assurance aspects, such as surveillance, which could, in turn, lead to safer and more effective medical products for the population. Tanzania's commendable achievement as the first African nation to attain maturity level 3 status for its regulatory system exemplifies the transformative capacity of the GBT [45]. Zambia can significantly benefit from emulating Tanzania's trajectory and by tapping into the WHO's vast expertise.

Envisioning Regional Collaboration and Integration

Regional collaboration needs to be commended, as initiatives such as ZANZIBONA have paved the way for Zambia to pool resources and expertise with other nations such as Zimbabwe, Botswana, and

Namibia. Furthermore, efforts by the New Partnership for Africa's Development (NEPAD) through the African Medicines Regulatory Harmonization (AMRH) cater to challenges unique to Africa [46]. The imminent launch of the African Medicines Agency marks a milestone in pan-African regulatory collaboration [47]. Although Zambia is not a signatory to the Treaty for the Establishment of the African Medicines Agency at the present moment, but it is actively engaging with such frameworks, which could position it at the forefront of regulatory innovations and equip it to navigate Africa's multifaceted health challenges.

7.5.3. Pharmacy Practice: Integrating Quality Assurance and Continuous Education

The insights from Chapters 3, 4, and 5 highlight the differences in medicine procurement, transportation, and storage practices between innovative and traditional pharmacies in Zambia. Innovative pharmacies have adopted digital technologies, such as inventory management systems and computerised processes, whereas traditional independent pharmacies rely on manual methods.

In pursuing harmonising standards within the pharmaceutical sector, emphasis should not be placed exclusively on hierarchical, top-down directives. Instead, there is a pressing need for an integrated approach that emphasises fostering a culture firmly anchored in education and heightened awareness, resulting in continuous improvement. Within this sectoral landscape, the mandate of regulatory bodies extends beyond the traditional enforcement constraints. A more holistic perspective on regulation recognises its dual role: it is not just about instituting control but also facilitating education or capacity-building. This empowers stakeholders by enabling them to understand, appreciate, and navigate the complexities inherent in pharmaceutical practice. Consistent alignment with evolving benchmarks and adherence to best practices is non-negotiable. For stakeholders to stay abreast of these shifting practices, a robust educational framework is required. Initiatives, such as training sessions, seminars, and workshops, play a crucial role in this regard. Guidance from globally recognised entities, such as the International Pharmaceutical Federation (FIP) through its Global Competency Framework, combined with localised expertise from institutions, such as the Pharmaceutical Society of Zambia (PSZ), can offer a well-rounded foundation. Drawing on these resources can ensure that the knowledge imparted is both globally relevant and locally contextualised, thereby setting the stage for an enriched pharmaceutical ecosystem in Zambia. The FIP emphasises that the linchpin of a resilient and effective pharmaceutical service lies in the capacity of professionals adept at discerning, mitigating, and rectifying disparities in quality [48]. Through anticipatory and proactive measures, the assurance of medicinal products that meet both safety and efficacy parameters can be realised.

In light of the challenges identified in this PhD research, it is crucial for Zambia's policy agenda to focus on Continuous Professional Development (CPD) within the pharmacy sector. This PhD research found

general shortcomings in areas such as repackaging medicines into plastic pill packs and reporting practices. For instance, the study noted that a significant proportion of pharmacies had inadequate conditions for drug storage, compromising the safety and efficacy of medicinal products. Likewise, many pharmacists acknowledged a lack of formal training in repackaging procedures and reporting protocols, suggesting areas where CPD could be particularly impactful. Such gaps in the current system underscore the need for a structured approach to CPD, which should involve systematic and progressive training sessions tailored to these specific challenges within the pharmacy sector [49]. This focus becomes even more important as the sector advances with new technologies and innovative methods. The overarching objectives should encompass two core facets: a perpetual commitment to enriching the pharmaceutical workforce with the latest insights and expertise and a rigorous alignment of these training frameworks with global standards and practices. Furthermore, these efforts should be collaborative among pharmacy associations, educational institutions, and health agencies to create standardised training curricula for professionals. With these efforts, Zambia's pharmaceutical sector can improve patient care and set standards that are recognised both locally and internationally.

7.5.4. Technology in Pharmacy Distribution: The Need for Adaptive Regulation in Zambia

The rise of innovative private pharmacy distribution channels, most notably e-pharmacies and telepharmacy, has the potential to reshape Zambia's pharmaceutical landscape. However, it is crucial to ensure that these advancements do not exacerbate existing healthcare inequalities, particularly between urban and rural areas. Considering the urban-centric focus of many innovative pharmacies, attention must be directed towards underserved rural communities and low-income urban residents. Telepharmacies and enhanced delivery systems are especially relevant in this context. They represent not just technological advancements but also opportunities for social equity in healthcare. By leveraging these models, healthcare divides maybe bridged, ensuring that the progress in pharmaceutical services benefits not only urban areas but reaches the remotest corners of the country. This approach is essential for providing equitable healthcare access to all, regardless of geographic location.

These channels promise to improve access to medicine, for example, in regions where transportation challenges persist. This shift was accentuated during the COVID-19 pandemic, which emphasises the importance of online platforms for medicine procurement [50]. Chapter 6 highlights a dichotomy: While e-pharmacies and telepharmacy offer a promising avenue for increasing accessibility, they fall short of addressing broader issues such as quality assurance and regulatory compliance within Zambia's pharmaceutical sector.

The rise of e-pharmacies, particularly in LMICs such as Zambia, presents various challenges. A primary concern is the unauthorised sale of prescription-only medications, which pose significant public health

risks [51]. The potential for an influx of SF medicines and data privacy breaches further amplifies these risks. Within the context of this research, stakeholders identified several barriers, such as reluctance to change in the sector, intermittent electricity and Internet access, and financial burdens associated with technological innovations. One emerging challenge that remains overlooked is the absence of a dedicated regulatory framework for innovative pharmacy channels like e-pharmacies. This gap not only increases the risk of delivering SF medicines to patients but also reflects broader regulatory struggles in the private sector, particularly in LMICs. While e-pharmacies introduce unique dimensions that are currently not covered by existing regulations, similar challenges in oversight exist across different sectors. The issue is not confined to Zambia; countries such as Kenya, Nigeria, and India are also grappling with comparable regulatory voids concerning e-pharmacies [30].

There could be benefits to consider with the emergence of innovative pharmacy platforms. Traditional pharmaceutical supply chains have long struggled with transportation challenges, as detailed in Chapter 3. Innovative solutions have emerged to address these challenges. For instance, in Rwanda, drones are employed to deliver medicines to remote and hard-to-reach areas [52]. E-pharmacies, in particular, promise to enhance access to medicine in remote or traditionally underserved areas. As emphasised by stakeholders, the shift towards digitalisation in the pharmacy sector has the potential to significantly bolster quality assurance and medicine traceability. However, it is crucial to note that the success of these computerised systems is contingent on the availability of a reliable power supply. In regions with frequent power outages or electricity supply instability, these systems could suffer interruptions, potentially compromising patient safety and medicine traceability. Backup generators or uninterruptible power supply (UPS) systems may be necessary to ensure continuous operation. Additionally, advancements in low-power computing and energy-efficient technologies could offer more sustainable solutions in such environments. Nevertheless, the utilisation of computerised systems plays a pivotal role in ensuring patient safety when implemented effectively. The inherent digital framework of these platforms offers an enhanced mechanism for medicine regulation, promotes traceability and transparency, and enables sophisticated data analytics.

There is a pressing need for adaptive regulation that recognises the promise and challenges of these digital platforms. Chapter 6 advocates a multifaceted approach: digital transformation, especially inpatient records; targeted training for regulators and industry players; and robust government endorsement and financial support for these channels. The overarching theme here is clear: regulatory frameworks tailored for innovative pharmacy models and balancing technological advancements with quality assurance are imperative. Embracing the digital transformation, rather than hesitancy and reluctance, represents the path forward. Therefore, it is imperative for the way forward to develop comprehensive and adaptive regulatory mechanisms to accommodate both traditional and digital

pharmacies. The evolving landscape of pharmacy necessitates innovative national regulatory strategies, collaboration with compliant businesses, and ongoing engagement with global regulatory bodies, drawing guidance from frameworks such as the WHO's Global Strategy on Digital Health 2020-2025 [53]. This adaptation needs to be led by ZAMRA, the national authority with the requisite knowledge and technical expertise, and to signal government endorsement for these changes within the sector. By bridging the technological potential with rigorous oversight, Zambia can then fully harness the advantages of e-pharmacies while ensuring the safety and well-being of its citizens and reaching the SDG's target 3.8 by 2030.

Table 1: Policy Recommendation Framework

Theme	**Findings**	**Policy Recommendation**
Medicine Quality	Both innovative and traditional independent pharmacies face challenges in maintaining medicine quality.	• Strengthen regulatory oversight and quality control mechanisms across all pharmacy types. • Strengthen post-marketing surveillance. • Encourage pharmacies to adopt quality assurance systems.
Pharmacovigilance	Gaps in pharmacovigilance practices were noted, potentially impacting medicine safety.	• Enhance pharmacovigilance systems, possibly through digital tools, to improve medicine tracking reporting.
WHO prequalification	MMV helped secure WHO prequalification for SP in Africa, improving its quality.	• Collaborate and encourage partnerships with organisations like MMV to enhance the quality of essential medicines.
WHO's Global Benchmarking Tool (GBT)	The WHO's GBT provides a framework for assessing and strengthening national regulatory systems, crucial for medicine quality and safety.	• Utilise the WHO's GBT to assess and enhance Zambia's regulatory system, aligning it with international standards and improving the quality of medical products.
Regional Collaboration and Integration	Initiatives like ZANZIBONA, NEPAD, AMRH, and the African Medicines Agency exemplify the benefits of regional collaboration in addressing unique pharmaceutical challenges in Africa.	• Actively engage in and contribute to regional collaborative efforts such as ZANZIBONA and the African Medicines Agency to pool resources, share expertise, and harmonise regulatory practices across Africa.
Education in Pharmacy Practice	Education plays a crucial role in enhancing pharmacy practice, with a focus on quality and safety standards.	• Incorporate modern pharmacy practices and digital literacy into pharmacy education curricula.
Innovative Pharmacies	Located mostly in urban shopping malls	• Implement policies to ensure innovative pharmacy benefits are accessible to all socio-economic groups.
Innovative pharmacy approaches potential in Rural Areas	Challenges of transportation and access to quality pharmaceutical services in rural areas.	• Support the development of telepharmacy and delivery services to enhance medicine accessibility in remote regions.
Adoption of Innovative Models and Regulation	Need for the measured adoption of innovative models in pharmacy practice, which requires updated regulatory frameworks.	• Facilitate the adoption of innovative models in pharmacy practice through supportive and specific regulation, ensuring alignment with evolving technological advancements.
Regulatory Frameworks	Existing regulations may not fully encompass innovative pharmacy practices.	• Update and expand regulatory frameworks to include innovative pharmacy models, ensuring comprehensive coverage of quality and safety standards.

7.6 Directions for Future Research

The implications of this research highlight critical areas that can be probed further to deepen our understanding of the pharmaceutical landscape in Zambia. These areas offer pathways to both validate and build on the findings presented here. First, continuing medicine quality surveillance in both innovative and traditional independent pharmacies is essential. Through comparative analyses, the detailed factors behind these differences can be explored, from procurement practices to storage conditions and technology use. While the characteristics of pharmacy practice recorded in Lusaka provide valuable insights, broadening the scope to other regions in Zambia offers a more comprehensive view. Other regions may have their differing pharmaceutical practices and challenges, making a nationwide study invaluable.

Given the crucial role of medicine quality, an in-depth examination of the pharmaceutical manufacturing processes in Zambia is warranted. Such scrutiny might uncover intricacies within supply chains, identifying potential weak points or inefficiencies that inadvertently compromise the quality of medicine.

Although this research primarily focused on the operational aspects of pharmacies, delving deeper into the overarching economic, political, and regulatory dynamics would be invaluable. Such an endeavour would provide a more comprehensive understanding of both the internal and external factors influencing the trajectory of Zambia's pharmaceutical landscape. Adopting a longitudinal design would offer an opportunity to understand the evolving nature of pharmacy practices in Zambia. By tracing the trajectory of these practices over time, deeper insights can be extracted into the long-term implications of policy shifts, interventions, and prevailing trends. The evaluative metrics of such studies could span a spectrum of parameters, from medicine quality to patient health outcomes.

Another essential avenue for exploration centres on barriers impeding the adoption of advanced technologies in the pharmaceutical sector. Utilising a qualitative approach to gather insights from diverse stakeholders, including pharmacists, technicians, and policymakers, could shed light on the structural and perceptual challenges.

Furthermore, as emerging technologies such as GS1 standards herald potential shifts in pharmaceutical quality assurance, it is imperative to undertake empirical studies to gauge their practical impact. Such investigations could document the challenges tied to their adoption, measure their direct effects on supply chain transparency, and outline their significance in ensuring quality.

In summary, while this research illuminates some key aspects of Zambia's pharmaceutical domain, the avenues for subsequent research are expansive. By navigating these uncharted territories, both the

academic and professional sectors can enhance their understanding and design transformative strategies, guiding Zambia towards a new pinnacle of pharmaceutical care.

7.7 Concluding Remarks

Pharmacies, whether traditional or innovative, currently form the backbone of Zambia's pharmaceutical landscape, ensuring that the population has access to medicines and healthcare advice. The dual nature of this sector, contrasting tradition with innovation, raises intricate questions concerning medicine quality, accessibility, and the interplay of regulatory and technological dynamics. This research provides an analytical lens for the evolution of Zambia's pharmacy landscape, revealing its potential strengths and challenges. This PhD research highlighted the balance between new innovative pharmacy approaches and traditional approaches in the Zambian pharmaceutical landscape. While innovative pharmacies offer opportunities for improvement in terms of efficiencies and quality control of medicines through the use of computerised systems and adapted inventory management technologies, the trust and cultural significance of traditional independent pharmacies cannot be overlooked.

New practices, especially the incorporation of technology, may hold promise for enhancing Zambia's pharmaceutical care. Nevertheless, despite their potential, these innovations are still nascent, with concerns such as insufficient regulatory frameworks posing challenges. This research emphasises that the future does not solely depend on adopting innovative methods; it is about blending the best of both traditional and innovative practices. Achieving this balanced vision requires not only changes within the sector but also strong and adaptive regulatory guidance. Without robust regulation and commitment to quality, persisting issues related to medicine quality could continue. In summary, this thesis advocates a balanced approach to improve Zambia's pharmaceutical industry. As Zambia navigates this complex interplay of tradition and innovation, it is clear that a harmonised strategy, fortified by robust regulatory measures, is imperative to ensure optimal health outcomes.

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Appendix 1 – Ethics approval; London School of Hygiene and Tropical Medicine Research Ethics Committee

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Mr Scott Matafwali
LSHTM

16 September 2022

Dear Mr Scott Matafwali

Study Title: Innovative Private Pharmacy Distribution Channels: Implications for Medicine Quality in Zambia

LSHTM Ethics Ref: 28040

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Protocol / Proposal	Scott Protocal_version 1_10-06-2022	10/06/2022	1
Protocol / Proposal	Scott Information and consent forms _version 1_10-06-2022	10/06/2022	1
Protocol / Proposal	Scott Interview guides_version 1_10-06-2022	10/06/2022	1
Protocol / Proposal	Scott Questionnaire_version 1_10-06-2022	10/06/2022	1
Protocol / Proposal	Scott Data collection tool _version 1_10-06-2022	10/06/2022	1
Investigator CV	Scott CV May22	10/06/2022	1
Other	Research_Ethics_online_training_certificate	10/06/2022	1
Information Sheet	Scott Information and consent forms _version 1_10-06-2022	10/06/2022	1
Local Approval	NHRA Response Mr Matafwali	10/07/2022	ver_1
Protocol / Proposal	Scott Information and consent forms _version 2_02-09-2022	02/09/2022	Version_2
Information Sheet	Scott Information and consent forms _version 2_02-09-2022	02/09/2022	Version_2
Covering Letter	Scott LSHTM ethics - Cover Letter_responses_0922	02/09/2022	Version_1
Local Approval	Mr. Scott Matafwali - Final approval	10/09/2022	ver_1

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

Page 1 of 2

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

Professor David Leon and Professor Clare Gilbert
Co-Chairs

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

Appendix 2 – Ethics Approval ; University of Zambia Biomedical Research Ethics Committee

UNIVERSITY OF ZAMBIA
BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: +260 977925304
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia
E-mail: unzarec@unza.zm
Federal Assurance No. FWA00000338 IRB00001131 of IORG0000774 NHRAR-REC No 2021-05-0002

11th July, 2022

Your REF. No 2926-2022

Mr. Scott Matafwali,
London School of Hygiene and Tropical Medicine,
Infectious and Tropical Diseases,
United Kingdom.

Dear Mr. Matafwali,

RE: INNOVATIVE PRIVATE PHARMACY DISTRIBUTION CHANNELS: IMPLICATIONS FOR MEDICINE QUALITY IN ZAMBIA (REF. NO. 2926-2022)

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 9th July, 2022. The proposal is **approved**. The approval is based on the following documents that were submitted for review:

a) **Study proposal**
b) **Questionnaires**
c) **Participant Consent Form**

APPROVAL NUMBER : REF. 2926-2022
This number should be used on all correspondence, consent forms and documents as appropriate.

i. **APPROVAL DATE : 11th July 2022**
ii. **TYPE OF APPROVAL : Standard**
iii. **EXPIRATION DATE OF APPROVAL : 10th July 2023**
iv. After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the UNZABREC Offices should be submitted one month before the expiration date for continuing review.
v. **SERIOUS ADVERSE EVENT REPORTING**: All SAEs and any other serious challenges/problems having to do with participant welfare, participant safety and study integrity must be reported to UNZABREC within 3 working days using standard forms obtainable from UNZABREC.
vi. **MODIFICATIONS**: Prior UNZABREC approval using standard forms obtainable from the UNZABREC Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
vii. **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the UNZABREC using standard forms obtainable from the UNZABREC Offices.

viii. **NHRA:** You are advised to obtain final study clearance and approval to conduct research in Zambia from the National Health Research Authority (NHRA) before commencing the research project.

ix. **QUESTIONS**: Please contact the UNZABREC on Telephone No. +260977925304 or by e-mail on unzarec@unza.zm.

x. **OTHER**: Please be reminded to send in copies of your research findings/results for our records. You are also required to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study. Use the online portal: unza.rhinno.net for further submissions.

Yours sincerely,

[redacted]

Sody Mweetwa Munsaka, BSc., MSc., PhD
CHAIRPERSON
Tel: +260977925304
E-mail: s.munsaka@unza.zm

Appendix 3 – Ethics Approval; National Health Research Authority Zambia

NATIONAL HEALTH RESEARCH AUTHORITY
Paediatric Centre of Excellence, University Teaching Hospital, P.O. Box 30075, LUSAKA
Chalala Office Lot No. 18961/M, Off Kasama Road, P.O. Box 30075, LUSAKA
Tell: +260211 250309 | Email: znhrasec@nhra.org.zm | www.nhra.org.zm

Ref No: NHRA000010/10/07/2022 **Date: 10th July , 2022**

The Principal Investigator,
Mr. Scott Matafwali,
London School of Hygiene and Tropical Medicine,
Infectious and Tropical Diseases,
United Kingdom.

Dear Mr. Matafwali,

Re: Request for Authority to Conduct Research

The National Health Research Authority is in receipt of your request for ethical clearance and authority to conduct research titled **"Innovative Private Pharmacy Distribution Channels: Implications for Medicine Quality in Zambia."**

I wish to inform you that following submission of your request to the Authority, our review of the same and in view of the ethical clearance, this study has been **approved** on condition that:

1. The relevant Provincial and District Medical Officers where the study is being conducted are fully appraised;
2. Progress updates are provided to NHRA quarterly from the date of commencement of the study;
3. The final study report is cleared by the NHRA before any publication or dissemination within or outside the country;
4. After clearance for publication or dissemination by the NHRA, the final study report is shared with all relevant Provincial and District Directors of Health where the study was being conducted, University leadership, and all key respondents.

Yours sincerely,

[redacted]

Prof. Godfrey Biemba,
Director/CEO
National Health Research Authority

Appendix 4 : Participant Information Sheet (Pharmacists, Pharmacy Technologists and Pharmacy Managers)

Study title: Innovative private pharmacy distribution channels: Implications for medicines quality in Zambia

Researchers

Principal Investigator: Mr Scott Kaba Matafwali

Supervisors: Dr Harparkash Kaur, Prof Sian Clarke

Introduction

I am Scott Matafwali, a PhD student from the London School of Hygiene and Tropical Medicine (LSHTM). I would like to invite you to take part in this research study. Joining the study is entirely up to you. Before you decide, you must understand why this research is being conducted and what it would involve. I will go through this information sheet with you and answer any questions you may have. Ask questions if anything you read is unclear, or if you would like more information. Please feel free to talk to others about the study if you wish. Take time to decide whether to participate.

What is the purpose of the study?

We are currently conducting surveys of retail pharmacies in Lusaka, Zambia. The surveys aim to assess the quality of medicine and contributory factors in pharmacies supplied by innovative distribution channels in Zambia and compare them to pharmacies that use traditional supply chains. We intend to purchase antimalarials and antibiotics that we will analyse in the laboratory to determine whether they have the correct amounts of active ingredients. We would also like to understand the contributory factors, such as the storage and purchasing practices of medicines in your pharmacy. The research will begin by administering a structured questionnaire, followed by the purchase of medicines. The research will also use a pharmacy audit tool that the investigator will use to observe the storage of medicines, the arrangement of medicines on shelves, and the pharmacy's outlook.

Why have I been asked to participate?

You have been invited because we believe you are the right person with relevant knowledge of pharmacy operations. With your permission, we will ask questions about the procurement and storage of these medicines. We will also ask questions about screening technologies that can detect poor-quality medicines and available reporting systems. All the interviews we collect also contribute to research articles and papers.

How long will the interview take?

The interview with you should take approximately 45 minutes

What are the possible risks?

We do not think you will have any significant problems participating in the study. However, if you feel some of the questions asked during the interview are sensitive, you are free to ask the interviewer to skip them.

What are the possible benefits?

There are no personal benefits to participating, but by answering our questions, you will help us improve our understanding of how to improve the availability of good quality antimalarials and antibiotics for the benefit of everyone living in Zambia.

Who will have access to the information I provide?

The information will be used for research purposes only, and no one other than the research team will be allowed to see the interview transcript. We will not disclose your identity or use your name in any reports of this work, and we will also not use the outlet name in our reports.

The study data will be archived at the London School of Hygiene and Tropical Medicine at the end of the project. The data will be made available to other researchers worldwide to research and improve medical knowledge and patient care. Your personal information will not be included, and there is no way that you can be identified.

Sharing the Results

Once we have completed this study, we will share the results through presentations at conferences or in publications in medical journals. We will not include your name or personal information in any presentation about this research.

What will happen if I refuse to participate?

Participation in this study is voluntary. You are free to decide whether you want to participate or not. If you agree, you can change your mind at any time. You can refuse to answer specific questions or stop the interview at any time. If you choose not to answer a question, stop the interview, or even not participate in the study, there will not be any adverse consequences for you or your organisation.

Who is organising and funding this study?

I am a PhD student at the London School of Hygiene & Tropical Medicine, and the commonwealth scholarship commission sponsors this PhD research.

Who has reviewed this study?

All research involving human participants is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given approval by London School of Hygiene and Tropical Medicine ethics committee (Ref: 28040) in the UK, as well as the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022).

What if I have questions?

If you have any questions, you can ask them now or later. If you wish to ask questions later, you may contact any of the following:

Principal Investigator Scott Matafwali PhD student +260975013637 +44(0)7415312086 Scott.Matafwali@lshtm.ac.uk	**Research Supervisor:** Dr Harparkash Kaur London School of Hygiene and Tropical Medicine Assistant Professor +44(0)20 7299 4629 Harparkash.Kaur@lshtm.ac.uk
The Chairperson National Health Research Ethics Board Paediatric Centre of Excellence, University Teaching Hospital Private Bag RW1X Ridgeway Lusaka, Zambia Tel/Fax: +260211 250309	Dr Sody Munsaka University of Zambia Biomedical Ethics Committee (UNZABREC) Ridgeway Main Campus, Nationalist Road, P.O. Box 50110 Lusaka Zambia. Tel: 260-1-256067 Email: unzarec@unza.zm

Appendix 5: Consent Form (Pharmacists, Pharmacy Technologists and Pharmacy Managers)

Study Title: Innovative private pharmacy distribution channels: Implications for medicines quality in Zambia

statement	(Tick or cross)
I confirm that I have read and understood the information sheet dated (version) for the above-named study. I have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
I understand that my consent is voluntary and that I am free to withdraw this consent at any time without giving any reason and without my/the participant's medical care or legal rights being affected.	
I understand that data about/from me/the participant may be shared via a public data repository or by sharing directly with other researchers and that I will not be identifiable from this information	
I agree with me/the participant taking part in the above-named study.	
I agree to an outlet audit	
the interviewee agrees to be interviewed	

□ *please tick* the interviewee agrees to be interviewed.

Signature of Interviewer: _____ **Date:** _____

Interviewer's name: _____ **Time:** _____

(Please print name)

(THE PROVIDER SHOULD NOW BE GIVEN AN INFORMATION SHEET TO KEEP)

Appendix 6: Information Sheet for Key Informants

Study Title: Innovative private pharmacy distribution channels: Implications for medicines quality in Zambia

Researchers

Principal Investigator: Mr Scott Kaba Matafwali

Supervisors: Dr Harparkash Kaur, Prof Sian Clarke

Introduction

I am Scott Matafwali, a PhD student from the London School of Hygiene and Tropical Medicine (LSHTM). I would like to invite you to take part in a research study. Joining the study is entirely up to you. Before you decide, you need to understand why the research is being done and what it would involve. I will go through this information sheet with you and answer any questions you may have. Ask questions if anything you read is unclear, or if you would like more information. Please feel free to talk to others about the study if you wish. Take time to decide whether to participate.

What is the purpose of the study?

We are currently conducting surveys of retail pharmacies in Lusaka, Zambia. The surveys aim to assess the quality of medicine and contributory factors in pharmacies supplied by innovative distribution channels in Zambia and compare them to pharmacies that use traditional supply chains. Additionally, we would like to get the key informant's point of view through an interview. We also intend to determine the shortcomings of the innovative pharmacy approach and the improvements needed to ensure that the patient receives good quality medicine, and we believe your insights will be important to the study.

Why have I been asked to participate?

You have been invited because we believe you are a key informant with a wealth of knowledge and insight into pharmacy supply chains and medicine quality. We intend to explore the experiences and perspectives on the overall theme's implications of innovative pharmacies on medicine quality, current regulations, and screening technologies.

How long will the interview take?

The interview with you should take approximately 45 minutes.

What are the possible risks?

We do not think you will have any significant problems participating in the study. However, if you feel some of the questions asked during the interview are sensitive, you are free to ask the interviewer to skip them.

What are the possible benefits?

There are no individual benefits to participating, but by answering our questions, you will help us improve our understanding of how to improve the availability of good quality antimalarials and antibiotics for the benefit of everyone living in Zambia.

Who will have access to the information I provide?

The information will be used for research purposes only, and no one other than the research team will be allowed to see the interview transcript. We will not disclose your identity or use your name in any reports of this work, and we will also not use the outlet name in our reports.

At the end of the project, the study data will be archived at the London School of Hygiene and Tropical Medicine. The data will be made available to other researchers worldwide for research and to improve medical knowledge and patient care. Your personal information will not be included, and there is no way that you can be identified.

Sharing the Results

Once we have completed this study, we will share the results through presentations at conferences or in publications in medical journals. We will not include your name or personal information in any presentation about this research.

What will happen if I refuse to participate?

Participation in this study is voluntary. You are free to decide whether you want to participate or not. If you agree, you can change your mind at any time. You can refuse to answer specific questions or stop the interview at any time. If you choose not to answer a question, stop the interview, or even not participate at all in the study, there will not be any adverse consequences for you or your organisation.

Who is organising and funding this study?

I am a PhD student at the London School of Hygiene & Tropical Medicine, and the commonwealth scholarship commission sponsors this PhD research.

Who has reviewed this study?

All research involving human participants is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by London School of Hygiene and Tropical Medicine ethics committee (Ref: 28040) in the UK, as well as the Biomedical Research Ethics Committee (REF. No 2926-2022) and the National Health Research Authority (NHRA000010/10/07/2022).

What if I have questions?

If you have any questions, you can ask them now or later. If you wish to ask questions later, you may contact any of the following:

Principal Investigator Scott Matafwali PhD student +260975013637 +44(0)7415312086 Scott.Matafwali@lshtm.ac.uk	**Research supervisor:** Dr Harparkash Kaur London School of Hygiene and Tropical Medicine Assistant Professor +44(0)20 7299 4629 Harparkash.Kaur@lshtm.ac.uk
The Chairperson National Health Research Ethics Board Paediatric Centre of Excellence, University Teaching Hospital Private Bag RW1X Ridgeway Lusaka, Zambia Tel/Fax: +260211 250309	Dr S Munsaka University of Zambia Biomedical Ethics Committee (UNZABREC) Ridgeway Main Campus, Nationalist Road, P.O. Box 50110 Lusaka Zambia. Tel: 260-1-256067 Email: unzarec@unza.zm

Appendix 7: Consent form Key Informants

Study Title: Innovative private pharmacy distribution channels: Implications for medicines quality in Zambia

Statement	Tick or cross
I confirm that I have read and understood the information sheet for the above-named study. I have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
I understand that my consent is voluntary and that I am free to withdraw this consent at any time without giving any reason and without my/the participant's medical care or legal rights being affected.	
I understand that data about/from me/the participant may be shared via a public data repository or by sharing directly with other researchers and that I will not be identifiable from this information	
I consent to the interview being audio recorded as part of the project. However please add this to the participant information sheet stating that the audio recording will be deleted as soon as the transcript/analysis has been completed.	
I agree with me/the participant taking part in the above-named study.	
The interviewee agrees to be interviewed.	

□ *please tick* The interviewee agrees to be interviewed.

Signature of Interviewee: _____ **Date:** _____

Interviewee's name: _____ **Time:** _____

Department/authority: _____

Appendix 8: Questionnaires

Structured Survey with Pharmacists, Pharmacy Technologists and Pharmacy Managers

Instructions to the interviewer: *This interview should be conducted with all willing participants at each pharmacy found in the study area. This interview should only occur once the participant has read the information sheet and completed the signed consent form.*

SECTION A: BACKGROUND INFORMATION		
A1	**Outlet ID Number**	[_____]
A2	**Type of outlet**	1. Traditional Independent Pharmacy [___] 2. Innovative Pharmacy [___] 77. Other If other specify [_____]
A3	**Geographical location**	1. City centre 2. Commercial area 3. Shopping mall 4. Peri-urban [___]
A4	**Date of visit** (dd/mm/yy)	[___|___]/[___|___]/[___|___]
A5	**Time of visit**	[___|___]
A6	**Name of interviewer** [_____]	

The interviewer says: *I would like to start by asking you some questions about yourself and the pharmacy where you work (interviewer instructions: Explain the different sections in the questionnaire and ask if someone else person will answer section D relating to procurement).*

SECTION B: CHARACTERISTICS OF RESPONDENT

B1	**Sex**	1. Male 2. Female [___]
B2	**Pharmacy-in-charge at the time of the interview**	1. Pharmacist 2. Pharmacy technologist 3. Pharmacy Manager 77. Other Answer code [___] If others specify: [_____]
B3	**Type of qualification?**	1. Masters 2. Degree 3. Diploma 4. Certificate 77 Other Answer code [___|___] If others specify: [_____]
B4	**How many years of professional experience do you have in total?**	[___|___] Years *If less than 1 year, specify* [___|___] months 88 Do not know Answer Code: [___|___]
B5	**How long have you been working in this pharmacy?**	[___|___] Years *If less than 1 year, specify* [___|___] months 88 Do not know Answer Code: [___|___]

B6	**What type of training have you received?**	0. None completed 1. Procurement training 2. Pharmacovigilance training 3. Storage practises 77. Others 88 Do not know Answer Code: [___|___]
B7	**When did you last receive training?** 1. Procurement training 2. Pharmacovigilance training 3. Storage practises	Training Date: _____
B8	**Type of services offered** *(Tick all that applies)*	0. Fixed bricks and mortar [___] 1. Delivery services [___] 2. Internet and ePharmacy [___] 3. Telepharmacy [___] 77. Others If other specify [_____]

SECTION C: STORAGE AND TRANSPORTATION		
C1	**What storage data is recorded?** *(Tick all that applies)*	0. None [___] 1. Lot/Batch number [___] 2. Expiry date [___] 4. Order number [___] 77. Others If other: [_____]

C2	**How often are stock records updated?**	0. None 1. Weekly 2. Monthly 4. Periodically 5. When going to purchase stock Answer Code: [___|___]
C3	**What kind of recording system does your pharmacy use for stock management?** *(Tick all that applies)*	0. None 1. Manual 2. Computerised 4. Both Answer Code: [___|___]
C4	**What kind of software does your pharmacy use to manage pharmaceutical products?**	0 None 1. Microsoft excel 2. Other proprietary software Answer Code: [___|___] If other: [_____]
C5	**What is the ambient temperature?**	1. Below 20 ° C 2. 20-25°c 3. 26-30°c 4. Above 30 ° C Answer Code: [___|___]
C6.	**The temperature of the pharmacy** *(Check the temperature)*	[___|___]
C7.	**Are the daily temperature logs filled in the last 3months?**	0. No 1. Yes, completely 2. Partially filled Answer Code: [___|___]

C8	**Time of day when the log is filled?**	0. None 1. Mornings 2. Afternoon 3. Evenings Answer Code: [___|___]
C9	**Is the pharmacy equipped with a functional refrigerator?**	0. No 1. Yes 2. Yes, but not functional Answer Code: [___|___]
C10	**Is the pharmacy equipped with a functional air conditioner?**	0. No 1. Yes 2. Yes, but not functional Answer Code: [___|___]
C11	**When did you last experience a power cut of more than 6 hours?**	0. None 1. In the last six (6) months 2. In the last year 3. In the last two (2) years 88. I don't Know Answer Code: [___|___]
C12	**Do you have a backup power source?**	a. No b. Yes Answer Code: [___|___]

C13	**If you answer yes to the above question, what backup system do you have?**	1. Genset 2. Inventor 3. Solar systems 4. Others: Answer Code: [___|___] If other: [_____]
C14	**How are medicines transported to your pharmacy?**	1. We always pick up from the distributor ourselves 2. The distributor always delivers 3. Both 4. Others: Answer Code: [___|___] If other: [_____]
C15	**Does the mode of transport have a/c?**	1. No 2. Yes 88. I Don't know Answer Code: [___|___]
C16	**Does the transportation have temperature tracking sensors?**	1. No 2. Yes 88 I Don't know Answer Code: [___|___]

I would now like to ask you specifically about the procurement and supply chain of the medicines you procure. This information is only for the researchers and will not be shared with anyone outside the study team. (Interviewer instruction: the person to answer this section may be different from the person who answers the other sections)

SECTION D: PROCUREMENT AND PRODUCT SUPPLY CHAIN

D1	**Who oversees the purchase of medicines in your pharmacy?**	1. Pharmacist 2. Manager 3. Director/CEO 77. Others: Answer Code: [___|___] If other: [_____]
D2	**Sex**	1. Female 2. Male Answer Code: [___|___]
D3	**Type of qualification**	1. Masters 2. Degree 3. Diploma 4. Certificate 77. Other (specify) [___|___] If other: [_____]
D4	**How is the procurement of medicines funded in the pharmacy?**	1. Business sales [____] 2. Government funded [____] 3. NGO funded [____] 4. Others [____] If other: [_____]
D5	**From how many suppliers do you purchase your medicines?**	Number of suppliers: [____] 88 - Do not know Answer Code: [___|___]

D6	**What type of pharmaceutical company do you get your medicines from?** *(tick all that applies)*	1. Other retailers [___] 2. Sub wholesaler [___] 3. Wholesaler/Importer [___] 4. Local manufacturer [___] 5. International manufacturer [___]
D7	**Do you procure medicines directly from a manufacturer?**	0 - No 1 - Yes 88 - Do not know Answer Code: [___|___]
D8	**What evidence of medicines quality do you demand before procurement?** *(tick all that apply)*	1. ZAMRA registration [____] 2. WHO prequalification certificate [____] 3. ISO certification [____] 77. Others [____] If other: [_____]
D9	**Do you have an information system (computerised/technology) to track the movement of medicines throughout the supply chain?**	0 - No 1 - Yes 88 - Do not know Answer Code: [___|___]
D10	**If yes to D9 above, what information technology system do you use?** *Tick all that applies*	1. Blockchain technology [____] 2. GS1 systems [____] 3. other barcode systems [____] 77. Others [____] If other: [_____]

D11	**What are the main reasons that assist with your decision to purchase medicines?** *(Tick all that applies and rank according to importance)*	1. Price [____] 2. High demand [____] 3. Quality [____] 4. Others [____] If other: [_____]
D12	**Do you agree with these statements?** *(1) Strongly disagree; (2) Disagree; (3) Neither agree nor disagree; (4) Agree; (5) Strongly agree.*	disagree agree Medicines with higher prices have better quality 1 2 3 4 5 Generics are usually poor quality 1 2 3 4 5 Brand products have better quality 1 2 3 4 5

I would now like to ask you specifically about medicine quality and screening techniques

SECTION E: MEDICINE QUALITY AND SCREENING TECHNIQUES

E1	**How concerned are you about medicine quality?** *(1) Strongly disagree; (2) Disagree; (3) Neither agree nor disagree; (4) Agree; (5) Strongly agree.*	very Disagree Maintain the quality of medicines 1 2 3 4 5 Risk of degradation during transportation 1 2 3 4 5 Risk of degradation during storage 1 2 3 4 5 Counterfeits 1 2 3 4 5
E2	**Have you received any kind of training to identify substandard or falsified?**	0 - No 1 - Yes 88 - Do not know

		Answer Code: [___|___]
E3	**If yes to E2 above, what kind of training have you received?** **Tick all that applies**	1. Course during the undergraduate degree [____] 2. Course during the post-graduate degree [____] 3. Specific post-graduate course [____] 4. CPD course [____] 77. Others Answer Code: [___|___] If other: [_____]
E4	**What source of information have you accessed concerning substandard and falsified information?**	1. Pamphlets [____] 2. Posters [____] 3. Memos [____] 77. Others Answer Code: [___|___] If other: [_____]
E5	**How would you know that the medicine is registered in Zambia?**	1. Registration number 2. It is on the ZAMRA website 3. Others Answer Code: [___|___] If other: [_____]
E6	**Which of the following distinguishing features of a good quality medicine?** *Tick all that applies*	1. Label [____] 2. Packaging material [____] 3. Expiry date [____] 4. Country of origin [____] 5. Brand name [____]

		6. ISO certification [____] 88 - I do not know Answer Code: [___|___]
E7	**How confident are you that your products are of good quality (i.e., contain the correct medicine in the right amount)?**	1 - Not Confident 2 - Somewhat Confident 3 - Neutral 4 - Confident 5 - Very Confident 88 - I do not know 99 - Refuses to answer Answer Code: [___|___]
E8	**What portable screening devices are you aware of?** *Tick all that applies* *(To add photo sheet prompts)*	1. Colourimetry (for example PADs) [____] 2. Thin-layer chromatography (eg,Minilab) [____] 3. Near-Infrared (NIR) [____] 4. Mid-infrared (MIR) [____] 5. Fourier transform infrared (FT-IR) [____] 6. Raman spectroscopy [____] 88 - I do not know Answer Code: [___|___]
E9	**Have you used any of the screening devices before?**	0 - No 1 - Yes 88 - Do not know Answer Code: [___|___]

E10	**If yes to E7 above, which ones?** *Tick all that applies*	1. Colourimetry (for example PADs) [____] 2. Thin-layer chromatography (eg, Minilab) [____] 3. Near-Infrared (NIR) [____] 4. Mid-infrared (MIR) [____] 5. Fourier transform infrared (FT-IR) [____] 6. Raman spectroscopy [____] 88 - I do not know Answer Code: [___|___]
E11	**What medicine authentication technology companies do you collaborate with?** *(Insert photo sheet with logos)*	1. Sproxil 2. PharmaSecure 3. mPedigree 77. Others Answer Code: [___|___] If other: [_____]
E12	**Have you experienced receiving poor-quality medicine from a distributor?**	0 - No 1 - Yes 88 - Do not know 99 - Refuses to answer Answer Code: [___|___]
E13	**What concern did you have regarding the medicine?**	1. Expired medicines 2. Discoloured medicines 3. Smelly medicines 77. Others 99 - Refuses to answer Answer Code: [___|___]
E14	**Have you ever reported a suspected poor-quality medicine**	0. No 1. Yes

		88. Do not know Answer Code: [___|___]
E15	**Who did you report the suspected medicines to?**	1. ZAMRA 2. Ministry of Health 3. Police 77. Others Answer Code: [___|___]
E16	**If yes to E14 above, what technology platform did you use?**	1. Email 2. Phone call 3. App (e.g. WEBRADR) 4. Website 0. Others Answer Code: [___|___] If other: [_____]
E17	**How many times have you reported poor-quality medicines in the last year?**	1 - One time 2 - Two times 3 - Three times 4 - Four times 5 - Five or more times 88 - Do not know 99 - Refuses to answer Answer Code: [___|___]
E18	**Do you receive ZAMRA warning alerts of poor-quality medicines?**	0 - No 1 - Yes 88 - Do not know Answer Code: [___|___]

E19	**If yes to E18 above, what technology platform did you receive the ZAMRA alert notification on?**	1. Email 2. Phone call 3. App 4. Social media 77. Others 88. Do not know Answer Code: [___|___] If other: [_____]
E20	**How do you dispose of expired drugs?**	1. Throw in the bin 2. Call ZAMRA 3. Call ZEMA 77. Others 88. Do not know Answer Code: [___|___] If other: [_____]

The interview is now over. Thank you for your time

(At this point, purchase the antimalarials and antibiotics)

Appendix 9: Medicine (Antimalarials and Antibiotics) Information Collection Tool

<table>
<tr><td colspan="2">1. Product Number

[__|__|__|__|__|__|__]</td><td colspan="2">2. Generic Name:</td></tr>
<tr><td>3. Strength
[__|__|__].[__]mg

[__|__|__].[__]mg

[__|__|__].[__]mg</td><td>4. Dosage form:
1 == Tablet
2 == Capsule

[__]</td><td colspan="2">5. Brand name:</td></tr>
<tr><td>6. Manufacturer:</td><td>7. Country of manufacture:</td><td>8. Package size:
There is a total of [__|__|__|__] tablets / capsules packs in each (select package type):
1 == Blister pack
2 == Pot/tin
[__]</td><td>9. Is this product a fixed-dose combination (FDC)?
1 == Yes
0 == No</td></tr>
<tr><td colspan="2">10. Batch/Lot number

_____</td><td colspan="2">11. Manufacture date (dd/mm/yyyy)

[___|___ /___|___/ _____]</td></tr>
<tr><td colspan="2">12. Expiry date (dd/mm/yyyy)

[___|___ /___|___/ _____]</td><td colspan="2">13. Number of tablets/capsules purchased

[___|___]</td></tr>
</table>

Appendix 10 : Checklist and Medicine Audit

		Comments
Storage		
Medicine boxes were raised off the floor	Yes No	
Exposure of medicines to sunlight	Yes No	
Shelves are free of moisture	Yes No	
Shelves are clean	Yes No	
The storeroom has adequate space	Yes No	
The storeroom was in good condition	Yes No	
Storeroom was tidy	Yes No	
Expiry and shelf life		
Medicines arranged according to FEFO	Yes No	
Days to expiry		
Days from procurement date		
Medicine samples		
Number of antimalarial brands usually stocked		
Number of antibiotics brands usually stocked		

Appendix 11: Stakeholders Interview Guide (with Authorities and Agencies)

Interviews with authorities and agencies – ZAMMSA, ZAMRA, PSZ

(Ensure that they have signed the consent form and have been provided with an information sheet)

Organisation:

Highest qualification:

Years of experience:

Job title:

A. Roles and Responsibilities
1. What are your primary responsibilities within the organisation? 2. How long have you been in this role? (years) 3. What is your organisation's role within the health structure of the country? 4. What is the role of your organisation in the medicine quality? 5. Please briefly describe the roles and responsibilities you perceive are important in other key organisations regarding medicine quality.
B. Pharmaceutical supply chains
1. How do you coordinate and collaborate with other authorities? (e.g. with ZAMRA, Police, Zambia Revenue Authority (ZRA), MoH) 2. What challenges, if any, are faced when coordinating with these other authorities? 3. Describe the challenges with medicine supply chains in the private and public sectors?

4. What improvements and solutions can be made to solve the challenges described?

C. Innovative pharmacy distribution channels and medicine quality

1. What innovative pharmacy distribution companies are you aware of?

2. Which innovative pharmacy distribution companies do you work with? *(Describe the relationship and collaboration)*

3. Describe how you think innovative pharmacy distribution channels may benefit the pharmaceutical supply chain related to medicine quality?

4. Describe what you think are the limitations of innovative pharmacy distribution channels in the pharmaceutical supply chain as it relates to medicines quality?

5. What improvements are needed to ensure that the patient receives good quality medicine? *(Probes: access to medicine? Rural reach? Pricing? Costs)*

D. Medicine regulation

1. What do you think is the impact of innovative pharmacy distribution companies on access to medicines and medicines quality? *(For example, mPharma).*

2. What do you think is the impact of internet/online pharmacies on access to medicines and medicines quality?

3. What do you think is the impact of social media advertising and the sale of medicines on social media on access to medicines and medicine quality?

4. Are there specific regulations and guidelines for internet/online pharmacies?

5. Do you have any suggestions on how we should regulate this sector?

E. General considerations

What are your final thoughts on this topic?

Appendix 12 : Stakeholders Interview Guide (Wholesalers, Retailers, and Innovative Pharmacy Distribution Companies)

Interviews with – Wholesalers, Retailers, and Innovative Pharmacy Distribution Companies

(Ensure that they have signed the consent form and have been provided with an information sheet)

Organisation:

Highest qualification:

Years of experience:

Job title:

A. Roles and Responsibilities
1. What are your primary responsibilities within the organisation? 2. How long have you been in this role? (years) 3. What is your organisation's role within the health structure of the country? 4. Please briefly describe the roles and responsibilities you perceive are important in other key organisations regarding medicine quality.
B. Pharmaceutical supply chains
1. How do you ensure that the medicines you supply and distribute are of acceptable quality? 2. How do you coordinate and collaborate with other authorities? (e.g. with ZAMRA, Police, Zambia Revenue Authority (ZRA), MoH) 3. What challenges, if any, are faced when coordinating with these other authorities? 4. Describe the challenges with medicine supply chains in the private sector?

5. What improvements and solutions can be made to solve the challenges described?

C. Innovative pharmacy distribution channels and medicine quality

1. What innovative pharmacy distribution companies are you aware of? *(Innovative pharmacy companies can still answer and name 'competitors' in the space)*

2. Which innovative pharmacy distribution companies do you work with? *(Describe the relationship and collaboration)*

3. Do you provide internet/online pharmacy services? How does this impact your business?

4. How are you using innovative technologies to improve purchasing of medicines? Storage and distribution of medicines and authenticating medicines?

5. Describe how you think innovative pharmacy distribution channels may benefit the pharmaceutical supply chain related to medicine quality?

6. Describe what you think are the limitations of innovative pharmacy distribution channels in the pharmaceutical supply chain as it relates to medicines quality?

7. What improvements do you think are needed to ensure that the patient receives good quality medicine? *(Probes: access to medicine? Rural reach? Pricing? Costs)*

D. Medicine regulation

1. What do you think is the impact of innovation in the pharmaceutical sector on access to medicines and medicines quality?

2. Are there specific regulations and guidelines for internet/online pharmacies that you are aware of?

3. Do you have any suggestions on how we should regulate this sector?

E. General considerations

What are your final thoughts on this topic?

Appendix 13 : Medicine Export Approval

Permit No: ZAMRA-WEB22/XPER/P/EXP/0003

ZAMBIA MEDICINES REGULATORY AUTHORITY

The Medicines and Allied Substances
(Importation and Exportation) Regulations, 2017

EXPORTATION PERMIT

This is to certify the (Name of permit holder) **SCOTT MATAFWALI** of (Physical Address) **1011, NEW AVONDALE, LUSAKA, 1011 NEW AVONDALE, LUSAKA PROVINCE, ZAMBIA** is authorised to :

No.	Export the following *medicines(s) allied substance(s).	Quantity
1	AMOXICILIN CAPSULES 0	3,500 Tabets/Capsules
2	SULFADOXINE + PYRIMETHAMINE TABLET 500 MG + 25MG	500 Tabets/Capsules
3		
4		
5		
6		
7		
8		

Port of exit from KENNETH KAUNDA INTERNATIONAL AIRPORT

This permit is valid until 30-08-2023

Terms and conditions imporsed by the Zambia Medicines Regulatory Authority (refer to notes overleaf)

[redacted]

Acting Director-General

31-08-2022

Date of Issue

Plot 2350/M ,Off KKIA Road,Lusaka-Zambia ,Tel:+260 211 432350, E-mail.pharmacy@zamra.co.zm. Website: www.zamra.co.zm,
Branches:Ndola, Chipata, Livingstone, Chirundu, Nakonde, Solwezi, Kasama, Kenneth Kaunda International Airport(KKIA)

TERMS AND CONDITIONS OF IMPORTATION/EXPORTATION PERMIT.

1. This permit is not transferable or renewable.

2. The holder of the permit shall produce the permit together with other approved or endorsed documents to an inspector and customers officer at the time of importation or exportation.
3. Theholder of the permit shall keep records relating to the importation or exportation of medicines or allied substances and avail the records to an inspector for inspection.
4. Non-complaince with any of the terms and conditions of the permit shall result in suspension or revocation of the permit.

Appendix 14 : Letter for Medicine Dispatch

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

(University of London)
Keppel St, London WC1E 7HT

Tel: (Direct) +44 (020) - 7299 4629 (Switchboard) +44 (020) - 7636 8636
E-mail: harparkash.kaur@lshtm.ac.uk

To whom it may concern

25/08/2022

The tablets in this consignment will be analysed for medicine quality at the London School of Hygiene and Tropical Medicine and will not be used in humans or animals. These samples have no retail value and are to be used purely for research. They are not of any commercial value.

Please address questions to:

Harparkash Kaur, BSc, PhD, CSci, CChem FRSC
Director of the Bioanalytical Facility
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT

Tel: (Direct) +44 (020) - 7299 4629
E-mail: harparkash.kaur@lshtm.ac.uk

Yours faithfully

[redacted]

Harparkash Kaur

London School of Hygiene and Tropical Medicine is the:

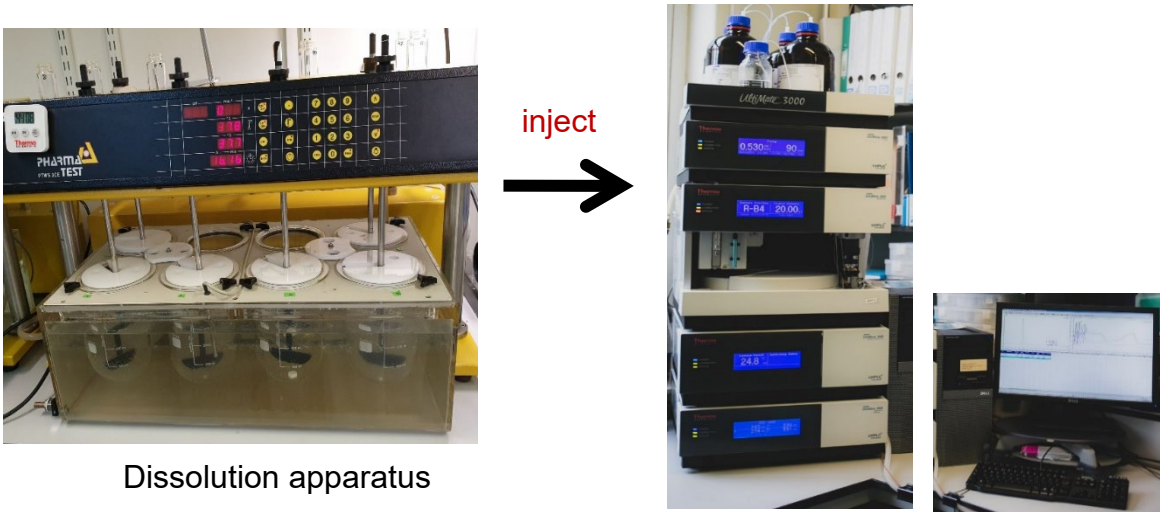
THE AWARDS 2016 | WINNER UNIVERSITY OF THE YEAR

Appendix 15: Images of Bioanalytical Laboratory equipment and Setup at London School of Hygiene and Tropical Medicine

(A)

Picture of HPLC -DAD setup at LSHTM

(B)



Dissolution apparatus

HPLC

Picture of the dissolution apparatus with HPLC-DAD set up at LSHTM.