Current rates of purchasing of antibiotics without a prescription across sub-Saharan Africa; rationale and potential programmes to reduce inappropriate dispensing and resistance

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ABSTRACT

Introduction: Antimicrobial resistance (AMR) is a global concern. Currently, the greatest mortality due to AMR is in Africa. A key driver continues to be high levels of dispensing of antibiotics without a prescription.

Areas covered: A need to document current rates of dispensing, their rationale and potential ways forward including antimicrobial stewardship programmes (ASPs). A narrative review was undertaken. The highest rates of antibiotic purchasing were in Eritrea (up to 89.2% of antibiotics dispensed), Ethiopia (up to 87.9%), Nigeria (up to 86.5%), Tanzania (up to 92.3%) and Zambia (up to 100% of pharmacies dispensing antibiotics without a prescription). However, considerable variation was seen with no dispensing in a minority of countries and situations. Key drivers of self-purchasing included high co-payment levels for physician consultations and antibiotic costs, travel costs, convenience of pharmacies, patient requests, limited knowledge of antibiotics and AMR and weak enforcement. ASPs have been introduced in some African countries along with quality targets to reduce inappropriate dispensing, centering on educating pharmacists and patients.

Expert Opinion: ASP activities need accelerating among community pharmacies alongside quality targets, with greater monitoring of pharmacists' activities to reduce inappropriate dispensing. Such activities, alongside educating patients and healthcare professionals, should enhance appropriate dispensing of antibiotics and reduce AMR.

ARTICLE HISTORY

Received 28 April 2023 Accepted 7 September 2023

KEYWORDS

Africa; antibiotics; antimicrobial resistance; antimicrobial stewardship programmes; AWaRe classification; community pharmacies; over-thecounter purchasing; quality indicators; utilization patterns

Article highlights

- There is still considerable purchasing of antibiotics without a prescription across Africa, with 100% of community pharmacies in some African countries dispensing antibiotics without a prescription
- However, rates of dispensing vary considerably both within and across countries. It is important to address current high rates typically for selflimiting conditions to reduce AMR, which is a major issue across sub-Saharan Africa (currently the continent with the highest prevalence rate of AMR globally) and an important part of National Action Plan activities to reduce AMR
- High rates of purchasing of antibiotics without a prescription are
 exacerbated by issues of affordability (cost of medicines and physician
 costs as well as travel costs to facilities) among the population as well
 as possible loss of earnings with long waiting times to see
 a professional in healthcare facilities. Community pharmacists are
 more convenient
- Educating pharmacists and patients can reduce inappropriate dispensing of antibiotics. The instigation of quality indicators as part of antimicrobial stewardship programmes also helps reduce inappropriate dispensing
- With the publication of the AWaRe book, it is increasingly likely that future quality indicators will be based on its content. Alongside this, there will be an increasing use of information technology and mobile telephones to monitor future antibiotic dispensing patterns against agreed indicators
- The curricula in universities for healthcare professionals will also need to be upgraded to make sure they are fully competent to appropriately counsel patients on the optimal management of their infectious disease/those of their children post qualification, backed up by continuous professional development activities

1. Introduction

There are growing concerns globally regarding the increase in antimicrobial resistance (AMR), which has resulted in increased morbidity, mortality, and costs [1–5]. A recent study estimated that in 2019 there were up to 4.95 million (95% uncertainty intervals (UI) 3.62-6.57) deaths worldwide associated with bacterial AMR, with an estimated 1.27 million (95% UI 0.911-1.71) deaths directly attributable to bacterial AMR [2]. The costs associated with AMR are also considerable [3,6,7]. The World Bank estimated in 2017 that the loss of world output due to AMR could possibly be as high as US\$3.4 trillion annually if not addressed [8]. As a result, AMR is increasingly seen as the next global pandemic unless inappropriate practices are addressed [9]. Concerns regarding the costs and health impact of AMR have resulted in an appreciable number of international, regional and local activities to reduce inappropriate prescribing and dispensing of antibiotics due to the correlation with AMR. As a result, subsequently reduce the burden of AMR [10-12]. A crucial area of focus among key stakeholders is ambulatory care among humans as this currently accounts for approximately 90 to 95% of antibiotic utilization worldwide, with the highest rates seen in low- and middle-income countries (LMICs) [13,14].

A critical continent in the goal to reduce AMR globally is Africa, which currently has the highest prevalence of infectious diseases and associated prescribing of antimicrobials globally [15–19]. In addition, the greatest burden of AMR globally is currently in Western sub-Saharan Africa, where AMR rates continue to rise [2,20]. Recent initiatives across Africa to address concerns with rising AMR include the instigation of

National Action Plans (NAPs), building on the World Health Organisation's (WHO) initiative with their Global Action Plan to reduce AMR [21–24]. However, there are many challenges with implementing NAPs across Africa, with African countries at different stages of their development and implementation as well as surveillance and monitoring of agreed activities, which depends on available resources and personnel [19,22,25,26]. For instance in Ghana, there are still concerns due to the lack of available resources and commitment to fully progress their NAP [27], which is similar to other African countries with limited resources and technologies allocated to AMR mitigation [28].

A recognized concern across LMICs, especially among African countries, is the appreciable self-purchasing of antibiotics without a prescription, often for self-limiting viral infections including upper respiratory tract infections (URTIs) [29–39]. This activity, if left unchallenged, will continue to drive up AMR in Africa [36,38–41]. Such activities have been exacerbated by the COVID-19 pandemic with a resultant increase in antibiotic utilization, especially among LMICs, despite limited evidence of bacterial co-infections or bacterial secondary infections over time [40,42–48].

Overall, a number of systematic reviews have been undertaken to document the extent of dispensing of antibiotics without a prescription especially in LMICs despite local legislation banning this practice [38,49]. Ocan et al. (2015) documented that overall 38.8% of all antibiotics were dispensed without a prescription among a number of LMICs (95% CI: 29.5–48.1) [50]. Nepal et al. (2018) documented similar figures for the World Health Organisation (WHO) Southeast Asian Region, with an average prevalence of 42.64% (range: 7.3%) to 85.59%) of antibiotics dispensed [35]. Batista et al. (2020) in their global systematic review (with most studies coming from LMICs) documented that typically over 60% of antibiotics were dispensed without a prescription [51]. Torres et al. (2021) documented a higher rate of purchasing of antibiotics without a prescription among adults in LMICs, with a pooled prevalence rate of 78% (95% CI: 65-89%; range 50-93.8%) of antibiotics dispensed [29]. More recently, Li et al (2023) in their systematic review documented a pooled prevalence of 63.4% (95% CI 59·6–67·1) of antibiotics dispensed without a prescription, with the highest number of papers coming from sub-Saharan African countries [38]. Similar to other studies, Li et al. found the prevalence of dispensing of antibiotics without a prescription was significantly higher in lower income countries versus high-income countries [38,52].

In a recent systematic review involving children in LMICs, nearly half of the antibiotics given to them were without a prescription [53]. This was typically for acute respiratory tract infections (ARIs), including coughs and fever as well as acute diarrhea [53]. In this systematic review, higher rates of dispensing without a prescription were seen in studies that involved simulated children with infectious diseases at 56% (95%CI: 49–62%) as opposed to the rates seen with other methodologies [53].

With respect to systematic reviews just involving African countries, Yeika et al. (2021) documented a median prevalence of 55.7% (IQR 41–75%); range 12.1% to 93.9% [36], which is

similar to Li et al (2023) [38]. The highest reported rate of antibiotics being dispensed without a prescription was seen in Western Africa at 70.1% (IQR 48.3-82.1%) followed by Northern Africa at 48.1% (IQR 41.1-64.3%) [36]. Belachew et al. (2021) documented higher rates in sub-Saharan Africa, with a pooled rate of 69% (95% CI 58-80) [37], which is again similar to Li. et al (2023) with a pooled rate of 70.7% among included sub-Saharan African countries [38]. URTIs as well as acute diarrhea were among the most frequent conditions among patients purchasing antibiotics for themselves or their children in both studies [37,38]. In their study involving six LMICs, 3 in Africa and 3 in Asia, Do et al. (2021) also found appreciable variation in the extent of purchasing of antibiotics without a prescription in the 3 African countries contained in their review. Prevalence rates ranged from 36.1% of occasions in Ghana to just 8.0% in Mozambique and 1.2% in South Africa [33]. These differences reflected differences in public healthcare facilities with medicines provided free-of-charge in Mozambique and South Africa as well as greater monitoring of the regulations surrounding antibiotic dispensing in South Africa [33]. In addition, higher co-payments as well as convenience of pharmacies in Ghana especially among patients without insurance [33,54].

Typically, among African countries, the purchasing of antibiotics without a prescription is illegal (Supplementary Table S1), which is similar to other continents [35,38,49,55–63]. Whilst the purchasing of antibiotics without a prescription may possibly occur in Botswana, this is believed to be very limited due to current regulations issued by the Botswana Medicines Regulatory Authority (BOMRA), which are enforced. Access to free healthcare, including medicines as part of Universal Health Coverage, also helps negate the need and expense of purchasing of antibiotics without a prescription in Botswana. Alongside this, at all levels of the public healthcare system, which covers over 85% of the population in Botswana [64, 65], only prescribed medicines can be dispensed. The strict regulations in Botswana through BOMRA, which are followed up, coupled with medicines being provided free-ofcharge in the public healthcare sector as part of UHC, has severely limited the dispensing of antibiotics without a prescription in the country.

Similarly in Namibia, there was no evidence of the purchasing of antibiotics without a prescription in two recent studies for respiratory and other infections, aided by strict legal regulations in the country, the monitoring of pharmacies to help enforce the regulations as well as the training of pharmacists on antibiotics and AMR whilst attending University [66–68]. The strict regulations banning the purchasing of antibiotics without a prescription in South Africa also limited such activities in the studies of Do et al. (2021) and Anstey Watkins et al. (2019) in rural South Africa [33,69]. The findings from these two publications are in direct contrast to those of Mokwele et al. (2022). Mokwele et al. found that antibiotics were being sold without a prescription in a number of privately-owned pharmacies in specific rural pharmacies in one Province in South Africa; however, this was not seen in any corporate (franchised) pharmacies that mystery shoppers visited [70]. The findings in Botswana, Namibia and South Africa contrast markedly with the situation in Zambia, where at one stage 100% of community pharmacies dispensed antibiotics without a prescription [71].

Overall although the findings are heterogeneous, there currently appears to be appreciable purchasing of antibiotics without a prescription across sub-Saharan Africa [36–38,41]. There are a plethora of reasons for continuing high rates of dispensing of antibiotics without a prescription across Africa (Box 1).

Box1 – Documented reasons for the purchasing of antibiotics without a prescription in Africa (adapted from [33,41,54,63,72–88])

- · Patient demand and expectations
- Weak enforcement and monitoring of current regulations surrounding the dispensing of antibiotics without a prescription
- Economic factors among community pharmacists and medicine vendors
- Patient convenience and economics especially if there are extensive co-payments (both to see a physician and to subsequently purchase prescribed medicines) and appreciable distances and costs to travel to public healthcare clinics – alongside potential loss of pay with time of work
- Trust in community pharmacists alongside ease of access compared with sometimes long waiting times to see a healthcare professional in public ambulatory care clinics
- Pharmacists may be the only healthcare professional available to treat patients especially in more rural areas
- Lack of knowledge of antibiotics and AMR among dispensing staff including both pharmacists and patients
- Poor attitudes toward antibiotics especially among patients in terms of not conserving them for bacterial infections as opposed to requesting them for self-limiting viral infections including colds, coughs and sore throats

Lack of knowledge regarding antibiotics and AMR among pharmacy personnel in some of the African countries starts in the universities and continues post-qualification [79,80]. This needs to be addressed going forward. Encouragingly, educational, and other interventions, including dissemination of guidelines, have enhanced appropriate dispensing of antibiotics in the community among LMICs [31,57,63,89,90]. In Kenya, there was little or no purchasing of antibiotics without a prescription among community pharmacies linked with the University of Nairobi, which were superintended by pharmacists, including during the recent COVID-19 pandemic [91,92]. This is particularly important at this time when, as mentioned, there has been an appreciable increase in antibiotic utilization among LMICs to treat patients with COVID-19 despite limited prevalence of bacterial co-infections or secondary infections, which could lead to increasing AMR [40,43,48,93–97].

Given the priority to reduce AMR across sub-Saharan Africa, exacerbated by high rates of purchasing of antibiotics without a prescription, we believe there is a need to update the evidence base of current rates of the purchasing of antibiotics without a prescription across the continent coupled with their rationale and potential ways forward [36,37,41,98,99]. This is especially important if this involves considerable dispensing of 'Watch' antibiotics as their increasing use is likely to drive up resistance rates [60,100–102]. There should be limited prescribing and dispensing of antibiotics in the 'Watch' group

across countries as these antibiotics are considered to have greater resistance potential and toxicity than those in the 'Access' group [103–105]. Alongside this, there should be no prescribing or dispensing of antibiotics of 'Reserve' antibiotics in ambulatory care since these are considered antibiotics of last resort and should be reserved for hospital use only [103–105].

Various activities have been implemented across Africa and other LMICs to decrease inappropriate purchasing of antibiotics without a prescription [89]. Activities include the instigation of antimicrobial stewardship programmes (ASPs) [57,106]. The instigation of such activities to reduce inappropriate dispensing of antibiotics is important as it can be morally challenging to effectively ban the purchasing of antibiotics without a prescription especially in rural areas in Africa. This is because physician numbers are often limited in rural areas of Africa. There can also be considerable travel costs and time for patients in rural areas to see a healthcare professional (HCP) in a public healthcare clinic in urban settings potentially offset by trust in community pharmacists. Alongside this, there can be high co-payments to see a physician, which can be unaffordable on top of the cost of medicines [37,75,82,84,85]. For instance in their study, Khuluza and Heide (2017) found that the cost of 83.3% of common antibiotics and antimalarials exceeded the daily wage of a low-paid government worker in Malawi, and were thus considered as unaffordable for the majority of the population [107]. In addition, there have been situations where policies to reduce the purchasing of antibiotics without a prescription have failed to achieve the desired results [49,57]. There was only a modest impact in Columbia following the initial law banning the purchasing of antibiotics without a prescription [55,108]. However, lax monitoring of the law resulted in limited impact some five years later [55]. In Zimbabwe, strict enforcement of the regulations banning the purchasing of antibiotics in the early 2000s resulted in limited sales despite pressure from patients. However, considerable changes in the economic circumstances of patients have resulted in most patients in Zimbabwe now obtaining their antibiotics from the informal market despite current regulations [37,85,109-111]. A recent study in Vietnam also demonstrated the limited impact of current regulations banning the purchasing of antibiotics without a prescription with only limited sanctions for pharmacist who abuse the regulations [58].

Consequently, the aim of this paper is to consolidate the current evidence base regarding the extent of antibiotics being purchased without a prescription across Africa, building on the many systematic reviews in LMICs which include Africa as well as those focusing on Africa [29,36,38,39,50,51]. Alongside this, the rationale behind self-purchasing as well as potential ways forward, building on successful ASPs among LMICs to limit this practice as well as the learnings from unsuccessful ASPs including in Africa. This will be achieved by undertaking a narrative review of the literature with senior-level personnel throughout sub-Saharan Africa providing expert input. Expert input will also inform suggestions for potential ways forward. We believe the findings and suggestions can subsequently be used by all key stakeholders across Africa and beyond to guide future activities to reduce

inappropriate purchasing and dispensing of antibiotics without a prescription particularly focusing on 'Watch' antibiotics.

2. Body of the paper

2.1. Materials and methods

The principal approach was a narrative review of key areas building on the considerable knowledge of the coauthors.

Several systematic reviews and meta-analyses have been performed documenting the extent of purchasing of antibiotics without a prescription in recent years, including among children and specifically for Africa [29,34–37,51,53,78]. However, a number of these contained references going back several decades, and circumstances will have changed among the studied African countries since then. For instance, in Zimbabwe, recent changes in the economic circumstances have resulted in most patients now obtaining their antibiotics from the informal market [85]. This is very different from the situation in the early 2000's where there was strict monitoring of pharmacy practice coupled with appreciable consequences for pharmacists for abuse of the regulations [37,109,110]. In South Africa, the moves toward universal healthcare in recent years should negate any co-payments associated with the use of medicines. Consequently, reducing the need to purchase antibiotics without a prescription, although this does still happen [70,112].

As a result, we concentrated on published studies from 2016 onwards. 2016 was chosen as we believed this would still provide a rich source of published studies without including circumstances that may be outdated. In addition, this was the year the WHO Global Action Plan to reduce AMR was launched [23,113]. Where pertinent, a summary of the methodology was included in the Tables along with a summary of the key findings, in line with published reviews [29,35–37]. The publication year was also included given likely variation in prevalence rates over time in countries as circumstances change.

We are also aware that some local African publications would not necessarily be included in a systematic review, especially if the reviews only concentrated on papers published in Pub Med or Web of Science. For instance, data on the extent of purchasing of antibiotics without a prescription could be contained within papers discussing key stakeholders' attitudes and perceptions toward antibiotics and AMR [114-119]. Alongside this, we were aware that in some African countries there may not be any data on current prevalence rates for the purchasing of antibiotics without a prescription either because strictly enforced laws prevent this; consequently, this is not studied, e.g. as seen in Botswana. Alternatively, no specific prevalence data appears to exist, e.g. from Benin and Burkina Faso. These countries would have been missed in systematic reviews just documenting current prevalence rates for the purchasing of antibiotics without a prescription if we only examined published papers.

However, we acknowledge that this approach may lead to bias. To minimize bias, and maximize relevant information and the implications included in the narrative review, the coauthors included in this narrative review have considerable experience among African countries and beyond researching and dealing with key issues surrounding the purchasing of antibiotics without a prescription. Alongside this, experience with implementing policies to improve appropriate dispensing of antibiotics. Experiences include the development of pertinent quality indicators as well as researching and implementing ASPs. Finally, the principal aim of the paper is to suggest potential ways forward for all key stakeholder groups across Africa to reduce inappropriate dispensing of antibiotics given its current extent, building on knowledge of key drivers, quality targets and ASPs. In view of this, data on current purchasing rates and legislation is included in Supplementary material rather than being included as a critical component of the paper.

Our chosen approach mirrors similar studies undertaken by the coauthors across a number of African countries and beyond when providing future guidance regarding the management of both infectious and noninfectious diseases, as well as more general approaches, and is in line with institutional guidance [19,31,42,120–130].

In most situations, the African countries have been broken down by income levels based on the World Bank classification included in the publication of Adekoya et al (2021) when reviewing antibiotics based on the AWaRe (Access, Watch and Reserve) classification among 138 countries [131]. This is because the provision of universal healthcare with its free-ofcharge healthcare, including medicines, combined with improved functioning of healthcare systems, can reduce the purchasing of medicines without a prescription [132,133]. The only exception concerns ASPs. In this situation, we were looking to document examples across LMICs to provide future quidance as were unaware of many examples in Africa. In addition, we wanted to document examples where ASPs had failed to reach their desired objective of limiting the purchasing of antibiotics without a prescription, and the possible reasons for this, to also provide future direction.

Where pertinent, the antibiotics dispensed were broken down by their AWaRe classification of 'Access', 'Watch' or 'Reserve'. As discussed, the 'Access' group of antibiotics are considered as first- or second-line antibiotics for up to 26 common or severe clinical syndromes, typically with a narrow spectrum and a low resistance potential. The 'Watch' group of antibiotics have a higher resistance potential and side-effects; consequently, community pharmacists and others should carefully consider their dispensing especially when an 'Access' antibiotic maybe more suitable for the condition if an antibiotic is needed. This is in line with the recommendations in the AWaRe book [13,104,105]. The 'Reserve' group should rarely, if ever, be dispensed in the community and only prescribed as last resort antibiotics in hospitals [13,103,105,134].

As mentioned, potential future activities to reduce inappropriate dispensing of antibiotics across Africa were based on the considerable experience of the coauthors across a range of African countries and beyond. This approach using senior-level coauthors has been successfully used by us when recommending future activities to reduce inappropriate use of antibiotics across sectors in Africa and other LMICs as well as improve the management of non-communicable diseases [19,31,57,120,123,126,129,130].

2.2. Principal findings

It is imperative that African countries seek to reduce inappropriate dispensing of antibiotics without a prescription given that ambulatory care accounts for up to 95% of human use in LMICs, and up to 100% of pharmacies in some African countries currently dispense antibiotics without a prescription [13,14,71]. The key issues to discourage inappropriate dispensing of antibiotics without a prescription start with a thorough knowledge of current prevalence rates, and the principal drivers of such activities, before moving to debate potential ways forward among all key stakeholder groups. Potential activities should be part of general activities across Africa and beyond to enhance the appropriate use of antibiotics in humans as part of NAPs, thereby helping to reduce AMR [19,21]. This has already started in Africa regarding their use in hospitals, building on the progress of NAPs across Africa [19,130].

The initial steps involving any proposed changes start with collecting evidence regarding current prevalence rates for the purchasing of antibiotics without a prescription across sub-Saharan Africa from 2016 onwards. Activities include identifying principal disease areas where antibiotics are being dispensed without a prescription and key factors that contribute to this practice. Subsequently, documenting activities and programs that have been initiated by health authorities and other organizations across Africa and beyond to combat inappropriate dispensing of antibiotics without a prescription as well as their impact. This section will also include activities that have been instigated by governments and others to reduce the purchasing of antibiotics without a prescription but failed to achieve the desired result, and the possible rationale for this failure. Documentation of the potential reasons for failure can offer considerable guidance to health authorities and others as they plan their future initiatives. Possible quality measures to reduce inappropriate dispensing and their effectiveness will also be documented and analyzed.

The collective findings can subsequently be used, along the coauthors' considerable knowledge, to provide guidance to all key stakeholders across Africa and beyond on potential approaches to reduce future inappropriate dispensing of antibiotics without a prescription. The guidance will be divided into macro, meso and micro levels in line with recent studies [135, 136].

2.2.1. Current extent of purchasing of antibiotics without a prescription across Africa

Table 2S in Supplementary Material documents current rates of the purchasing of antibiotics without a prescription among a range of sub-Saharan African countries. This builds on recent systematic reviews involving LMICs including African countries [29,34,36–38,50,51]. One problem is that these studies typically included published studies earlier than 2016, with the earliest being 1989. Overall, the lowest pooled rate among the systematic reviews was in 2015, at 38.8% of all antibiotics dispensed (95% CI: 29.5–48.1) [50]. Cameroon, Ethiopia, Nigeria, Sudan and the West African countries were included in the review [50]. A higher pooled rate was seen in another systematic review published in 2021, which included Nigeria,

with a pooled prevalence rate of 78% (95% Cl: 65–89%; range 50–93.8%) of antibiotics dispensed without a prescription [29].

As seen (Table S2 Supplementary Material), there was also appreciable variation in the extent of the purchasing of antibiotics without a prescription among and within African countries. The variation in the rates of purchasing seen among the various African countries appeared to be largely independent of income levels. Some of the highest rates seen were in Eritrea (up to 89.2%), Ethiopia (up to 87.9%), Mozambique (93.75%), Nigeria (up to 86.5%), Tanzania (up to 92.3%) and Zambia (up to 100% of pharmacies dispensing antibiotics without a prescription). Some of the lowest rates were seen in Kenya (as low as 0%), Mozambique (as low as 1.4%), Namibia (as low as 0%), South Africa (as low as 0%) and Zimbabwe (very little initially although changing in recent years).

Appreciable variation in the prevalence rates for the purchasing of antibiotics without a prescription seen within African countries (Supplementary Table S2) include Eritrea (9.8% to 89.2%), Kenya, (0% to 52%) Mozambique (1.4% to 93.75), South Africa (0% to 47%) and Zimbabwe (very little to patients typically obtaining their antibiotics from the informal market place). These differences may be due to differences in the stakeholders approached, their location and circumstances including economic circumstances, the methodology involved as well as the timing of the study. However, it is difficult to say this with any certainty. In any event, there was appreciable purchasing of antibiotics without a prescription among a number of African countries, which needs to be urgently addressed to reduce AMR in Africa in the future.

In their systematic review involving 10 African countries (Cameroon, Ethiopia, Eritrea, Kenya, Malawi, Sudan, Tanzania, Uganda, Zambia and Zimbabwe), Belachew et al. (2021) found that upper respiratory tract infections (URTIs) and/or acute diarrhea were the most common reasons for the purchasing of antibiotics without a prescription, with amoxicillin ('Access') and co-trimoxazole ('Access') the most frequently dispensed antibiotics [37]. Another study found that the most common indications for the dispensing of antibiotics without a prescription were URTIs, gastrointestinal (GI) symptoms including diarrhea and fever or febrile illnesses [36]. Batista et al. (2020) in their worldwide review also found that the indications for which antibiotics were most purchased without a prescription were RTIs (100.0%), diarrhea (40.0%) and urinary tract infections (UTIs) (30.8%), with the most purchased antibiotics being amoxicillin (86.9%) ('Access'), azithromycin (39.3%) ('Watch'), ciprofloxacin (39.3%) ('Watch') and coamoxiclav (39.3%) ('Access') [51].

Overall, within an appreciable number of African countries, many antibiotics were purchased without a prescription for RTIs, acute diarrhea and UTIs, with 'Access' antibiotics (penicillins, cotrimoxazole and metronidazole) being the most commonly dispensed. This was followed by the macrolides, including azithromycin ('Watch') and the quinolones ('Watch') (Table S2).

Table S3 documents the African countries where currently there does not appear to be any published data regarding the

extent of purchasing of antibiotics without a prescription. However, this occurs in some but not all of these countries.

2.2.2. Key factors driving self-purchasing of antibiotics across Africa

Table 1 documents key factors driving the purchasing of antibiotics among the various African countries and their incomelevels building on Box 1, with Table 2 documenting the overall knowledge of antibiotics and AMR, or lack of it, including concerns, among key stakeholder groups across Africa. This includes dispensers and patients.

Key factors driving the purchasing of antibiotics without a prescription across Africa, especially sub-Saharan Africa, include issues of convenience with community pharmacies, especially among working personnel, enhanced by the length of time to see a HCP in public facilities and the travel costs involved, exacerbated if this leads to loss of income especially among informal workers. Alongside this, the additional copayments to see HCPs in their clinics alongside the costs of any medicine dispensed. These combined costs can have catastrophic consequences for some patients [180,181], with issues of poverty negatively impacting on antibiotic misuse [86,182].

Table 2 shows there is currently variable knowledge regarding antibiotics and AMR among key stakeholder groups across Africa. Overall, there are considerable concerns regarding the wide-spread beliefs across Africa that antibiotics are effective in treating viral infections as well as the general lack of knowledge regarding AMR and its implications among key stakeholder groups. However, this is not universal. Alongside this, acceptance of self-medication with antibiotics among key stakeholders. Consequently, there is an urgent need to address the lack of knowledge among all key stakeholder groups to reduce inappropriate dispensing of antibiotics and associated AMR across Africa.

2.2.3. Activities across Africa and beyond to reduce inappropriate purchasing of antibiotics without a prescription

Suggested activities to enhance appropriate dispensing of antibiotics, including without a prescription, incorporate the development and implementation of indicators. The agreed indicators can subsequently be used to determine improvements in appropriate dispensing of antibiotics without a prescription across Africa. The agreed and chosen indicators can also subsequently be incorporated into ASPs to determine their effectiveness in reducing inappropriate antibiotic use.

There are three principal types of quality indicators that can be developed as part of activities to improve medicine utilization (Supplementary Table S4). There must always be a clear purpose for their development as well as their use in practice to improve appropriate dispensing, especially when this is without a prescription. While different indicators have been used, for instance, to improve antimicrobial prescribing in hospitals across Africa [130,183–186], any indicator that is being considered in ambulatory care among community pharmacists must have clarity and be feasible to implement. This is

Table 1. Key factors driving the purchasing of antibiotics without a prescription across Africa.

Countries	Author and year	Key factors and drivers increasing the purchasing of antibiotics without a prescription	
Multiple African countries			
Multiple African Countries	Belachew et al., 2021 [74]	 Systematic review and meta-analysis involving multiple Africa countries among LMICs The African countries involved in the review included: Cameroon, Ethiopia, Eritrea, Kenya, Malawi, Sudan, Tanzania, Uganda, Zambia and Zimbabwe Four key drivers regarding the purchasing of antibiotics were identified. These included: Business model – resulting in tensions between professionalism and commercial necessity Pressures due to customers' demand and their expectations based on previous practices and outcomes Absence of, or a limited enforcement, of any regulations banning the self-purchasing of antibiotics Limited knowledge and/or poor attitudes regarding antibiotics among staff in community outlets 	
	Yieka et al., 2021 [36]	 Systematic review and meta-analysis involving countries among 19 African countries (including sub-Saharan African countries): Algeria, Cameroon, DR Congo, Egypt, Eritrea, Ethiopia, Ghana, Ivory Coast, Kenya, Libya, Malawi, Mozambique, Namibia, Nigeria, Rwanda, Senegal, Sudan, Tanzania, and Uganda Common reasons for purchasing included: No education or limited education among patients Low income or currently unemployed Remoteness of healthcare facilities and perceived long waiting times at healthcare facilities to see a healthcare professional versus the convenience of medicine outlets including community pharmacies 	
	Li et al., 2023 [38]	 Mixed-method systematic review including 40 papers (25% of the total) from sub-Saharan African countries Common reasons for purchasing included: Strong customer demand for non-prescription antibiotics Lack of relevant knowledge among patients regarding antibiotics and AMR Pharmacy/drug seller staff motivated by financial reasons or personal viewpoints Alternative health-care services are expensive especially where high co-payments are involved or they are inconvenient especially if this involves time of work/considerable queues to see a healthcare professional Irregular prescribing practices/lack of consistency Weak social, industry, and legal regulations 	
3 East African Countries: Kenya, Uganda and Tanzania	Green et al, 2023 [86]	 Mixed method approach including a questionnaire among 6827 patients with UTIs and in-depth interviews among 82 patients Reasons for purchasing antibiotics without a prescription included: Long travel distances, long queues to see a HCP, and perennial antibiotic stock – outs in public health facilities Lack of curtesy and disrespectful clinical staff in public health facilities Preference to work rather than losing a day's wages to see a HCP coupled with affordability issues (travel costs, costs of HCP visit and medicine costs) Cash-flow issues Familiarity with antibiotics Ease of unregulated access to antibiotics 	

Table 1. (Continued).

Countries	Author and year	Key factors and drivers increasing the purchasing of antibiotics without a prescription
3 African countries (Ghana, Mozambique, South Africa)	Do et al., 2021 [33]	 Quantitative and qualitative assessments of antibiotic access and use across 3 African countries involving exit interviews and interviews with households Common reasons for purchasing included: Less time consuming and cheaper Overall, more convenient than accessing treatment including antibiotics through health-care facilities Disease severity and whether the antibiotic was intended for a child
Low-Income Single African Count	ries*	
Eritrea	Bahta et al., 2021 [137]	 Focus group discussions and key informant interviews among 36 pharmacists and assistants Key reasons for dispensing without a prescription included: Economic reasons (pharmacists and patients) Inadequacy and inaccessibility of healthcare services Prescribers ordering patients to take antibiotics without a prescription Long queues to see healthcare professionals in healthcare facilities when available as well as scarcity of available medicines in healthcare facilities Previous successful experiences with antibiotics Weak regulations
	Russom et al., 2021 [118]	 2477 interviews with adults using a structured questionnaire Principal reasons for self-medication with antibiotics included: The non-seriousness nature of the disease (39.0%) The need for quick relief (33.9%) Pevious successful experiences with antibiotics (16.1%) No time to visit a health facility (15.0%) and typically long queues at health facilities (14.0%)
Ethiopia	Gebretekle et al., 2016 [138]	 Qualitative interviews among personnel in 5 community pharmacies in Adia Ababa Common reasons for purchasing included: Limited resources among patients and lower education of patients Patient pressure Pharmacists looking to maximize revenue (vs. professional role) and weak regulatory systems
	Erku et al., 2018 [139]	 2-phased mixed-method study including 100 simulated patient visits to drug retail outlets Key drivers for dispensing without a prescription included: Perceived financial benefits, high expectations and/or demand from patients Competition among pharmacies for patients
	Bogale et al., 2019 [140]	 Cross sectional study involving 595 household respondents Key factors for purchasing without a prescription included: Age of the patient Knowledge/educational status Income/affordability to see a healthcare professional/purchase medicines
	Demissie et al., 2022 [141]	 Community-based cross-sectional design study involving 826 respondents using a pre-tested questionnaire Key drivers for purchasing included: being male, having no health insurance scheme and the availability of antibiotics in drug outlets
	Edessa et al., 2022 [142]	 Community-based cross-sectional study involving 100 simulated cases Insufficient knowledge of retailers regarding AMR was significantly associated with inappropriate dispensing of antibiotics without a prescription

Countries	Author and year	Key factors and drivers increasing the purchasing of antibiotics without a prescription
Malawi	Sambakunsi et al., 2019 [143]	 Cross sectional study, mixed-methods study design involving 2 focus groups and a structured questionnaire among a total of 120 respondents Key reasons for purchasing without a prescription included: Concerns with the availability of medicines in public healthcare facilities Personnel in the public system (with patients sometimes advised to obtain their medicines from retail pharmacies) Long distances to travel to healthcare facilities These multiple factors make patients lose confidence in the public system and resort to self-medication
	Machongo et a l , 2022 [144]	 Interviews with 16 caregivers of children Patients frequently use antibiotics inappropriately believing they are effective in treating coughs and colds in children
Mozambique	Mate et al., 2019 [115]	 Cross-sectional study among 1091 adults using a semi-structured questionnaire Principal reasons for purchasing included: Perception that there is no need to attend a health facility for e.g. an ARI (26.8%), someone else's advice (7.7%) and symptoms were similar to a previous episode (6.2%) General poor quality of care in health facilities (6.7%) and long waiting times in public facilities (4.3%)
	Torres et al., 2020 [145]	 Cross-sectional study involving both individual and group interviews among 32 pharmacy clients and 17 pharmacists Principal reasons for purchasing included: Patients' demands and expectations, and their beliefs in the healing power of antibiotics Physician prescribing practices Pressure on profits and fragile law enforcement/absence of accountability mechanisms
Rwanda	Tuyishimire et al., 2019 [146]	 Structured questionnaire among 570 undergraduate students The principal reason for purchasing was that the illness was not considered serious enough to have a consultation (50.72%)
Tanzania	Mboya et al., 2018 [147]	 Cross-sectional descriptive study involving 152 adults Participants with poor knowledge of antibiotics had appreciably higher odds of using antibiotics irrationally, including purchasing without a prescription, versus those with good knowledge Participants without health insurance had higher odds of using antibiotics irrationally compared to those with health insurance
	Emgård et al., 2022 [148]	 Eight focus group discussions with mothers of children <5 years Principal reasons for purchasing of antibiotics without a prescription included: Antibiotics are perceived as universal treatments for common diseases Often a long wait at facilities and disrespectful treatment at healthcare facilities Transport costs with often husbands not providing the necessary financial support Often healthcare facilities do not stock the suggested medicines and patients have to pay for them at community pharmacies Pharmacies and pharmacy staff seen as more trustworthy and convenient
	Mabilika et al., 2022 [149]	 Cross-sectional study involving 430 respondents using a digital questionnaire Key reasons for purchasing included: Being single Having health insurance Distances to a health facility (reduced distances reduces self-purchasing)
Uganda	Kibuule et al, 2016 [150]	 Cross-sectional survey among 200 households treating children <5 years with ARIs using a developed questionnaire Key factors for purchasing included: Level of education of the guardian/parents; confidence of parents/guardians to self-diagnose ARIs, prior ability to treat ARIs appropriately Source and access to antibiotics, e.g. community pharmacy or drug store
Low-Middle Income Single	e African Countries*	
Cameroon	Amin et a l. , 2019 [151]	 Cross-sectional survey using a structured questionnaire among 329 patients attending for outpatients in 2 hospitals The principal reasons for self-medication were: Cost cutting (40.9%) Past experience from similar symptoms (29.3%)

9

Table 1. (Continued).

Countries	Author and year	Key factors and drivers increasing the purchasing of antibiotics without a prescription
Congo	Shembo et al., 2022 [152]	 Semi-structured in-depth interviews with 18 participants in households Key reasons for purchasing without a prescription included: Relying on previous experiences with antibiotics Financial reasons – difficult to afford to see physicians every time feel unwell Attract a 'spirit of sickness' if go to healthcare facilities every time feel unwell
Ghana	Afari-Asiedu et al., 2018 [72]	 32 in-depth interviews with Licensed Chemical Sellers (LCS) as well as focus group discussions with 40 community members Key factors for purchasing included: Patient demand with previous knowledge of effectiveness of some antibiotics Delays in seeking care at health facilities and distance/cost to health facilities Financial constraints among patients and poor implementation of current regulations
	Ahiabu et al., 2018 [153]	 Recall visits among 12 households Key factors for purchasing included: Lack of controls, community knowledge and poverty Perceived barriers to formal healthcare
	Mensah et al., 2019 [154]	 Questionnaire among 361 participants Key factors for purchasing without a prescription included: Influence from others – friends and relations (32.7%) Bureaucracy of health/hospital system (23.0%) Cost savings (22.2%) and mild severity of the illness (17.7%)
	Afari-Asiedu et al., 2020 [155]	 15 in-depth interviews among healthcare professionals and eight focus group discussions among 55 community members Inappropriate antibiotic use/purchasing of antibiotics without a prescription were influenced by a number of factors including a general lack of knowledge regarding antibiotics, e.g. tetracyclines and metronidazole were poured into 'akpeteshia' (a local gin) to treat hernia and perceived stomach sores
	Kretchy et al., 2021 [156]	 Community-based cross-sectional survey using a semi-structured questionnaire among 350 adults in a rural area Key reasons for purchasing without a prescription included: Past successful experience (47% of those surveyed) Ease of purchasing of antibiotics from medicine outlets Convenience of community pharmacies (36%) Patients living in a rural area were also more likely to purchase antibiotics without a prescription due to more limited education
	Amponsah et al., 2022 [157]	 Interviews among 337 students (163 pharmacy and 174 nonpharmacy) An increase in the study level of students reduced the likelihood of both pharmacy and non-pharmacy students purchasing antibiotics without a prescription
Ghana	Nyarko et al., 2023 [158]	 Interviewer-administered questionnaire among 200 staff members in medicines outlets Stronger preference among interviewees for not dispensing antibiotics and referring patients to a doctor if they have certain symptoms including a high fever, fatigue or sinusitis Interviewees were also less likely to dispense antimicrobials without a prescription for children or the elderly with severe infections and refer them
Nigeria	Khakid et al., 2019 [159]	 217 pharmacy students participated in an online survey with a validated questionnaire The principal reasons for purchasing antibiotics were previous knowledge (40.4%) and convenience with no time to see a doctor or pharmacist (27.5%)
	Abubakar et al., 2020 [160]	 Cross-sectional study involving 98 community pharmacists using a validated self-administered questionnaire Pharmacists with <5 years of working experience (66.7%) were significantly more likely to dispense antibiotics without a prescription 5 times or more in a day compared to those with >5 years community pharmacy experience
Sudan	Hussain et al., 2023 [161]	 Cross-sectional study design involving 1492 patients The key reasons for purchasing antibiotics without a prescription were: Convenience (63.3%) Cost-saving (34.8%)

NB: AMR: Antimicrobial resistance; ARIs: Acute Respiratory Illness; *World Bank classification based on Adekoya et al 131].

Table 2. Knowledge of key stakeholder groups regarding antibiotics and AMR across a range of African countries and income levels.

Country	Author and year	Key findings
Multiple Countries		
3 East African countries (Kenya, Tanzania and Uganda)	Lubwama et al., 2021 [80]	 Self-administered questionnaire among 328 final year medical and pharmacy students There were concerns regarding the knowledge of antibiotics and AMR among final year students including Pharmacy students among these three African countries In general, students had low scores regarding their knowledge of AMR and antibiotic use in clinical scenarios, exposing gaps in their training. This needs to be addressed going forward
3 East African countries – Kenya, Tanzania and Uganda	Green et al., 2023 [86]	 Mixed method approach including a questionnaire among 6827 patients with UTIs and in-depth interviews among 82 patients Individuals who were more familiar with antibiotics were more confident and most likely to engag in self-medication
ow Income Single African Count	ries*	
Eritrea		 Face-to-face interviews with 577 participants (99.5% response rate) using a structured questionnaire 29.3% of interviewees believed that self-medication with antibiotics is acceptable practice 84.7% of interviewees had inadequate knowledge regarding antibiotics, with only 15.3% found to b knowledgeable
	Bahta et a l ., 2021 [137]	 Focus group discussions and key informant (KI) interviews among 36 pharmacists and assistants Some KIs believed some dispensers were not knowledgeable regarding new clinical Knowledge and did not have adequate knowledge regarding their contribution to fighting AMR
	Russom et al., 2021 [118]	 2477 interviews with adults (97.4% response rate) using a structured questionnaire 73.3% and 39.0% of the study population respectively were aware of the term 'antibiotic' and antibiotic resistance, with 78.2% correctly reporting that antibiotic resistance is an issue that could affect them and their family However, less than half of the study population correctly reported indications of antibiotics for common illnesses with 63.4% believing that antibiotics can be used to treat viral infections, 61.89 that antibiotics can be used to treat watery diarrhea, 58.9% for a common cold and 54.2% for a drough
Ethiopia	Seid et al., 2018 [163]	 Self-reported structured questionnaire among 323 graduates paramedical students Despite the majority of students viewing antimicrobial resistance as a preventable public problem appropriate strategies are introduced, among the students, including pharmacy students, there wer concerns with poor knowledge regarding AMR
	Bogale et al., 2019 [140]	 Cross sectional study involving a questionnaire among 595 household respondents in Ethiopia (98.3% response rate) Household respondents generally had inadequate knowledge and inappropriate practices toward the rational use of antibiotics
	Belachew et al., 2022 [83]	 Cross-sectional survey among 276 staff in 270 drug outlets using a validated self-administered questionnaire The majority of the 276 participants in drug outlets demonstrated good levels of knowledge about antibiotics use (77.9%) and AMR (76%) in a cross-sectional survey Participants who did not perceive they were competent to supply non-prescribed antibiotics were less likely to report they dispensed antibiotics without a prescription
	Demissie et al., 2022 [141]	 Community-based cross-sectional design involving 826 respondents using a pre-tested questionnaire The most common sources of information for self-medication were self-decisions without any information (46.81%), promotion about medicines (24.45%) and relatives (18.75%)
	Edessa et al., 2022 [142]	 Community-based cross-sectional study among 100 simulated cases regarding childhood diarrhea among drug retail outlets A considerable proportion of retailers in community drug outlets had insufficient knowledge regarding antibiotics as well the emergence and spread of AMR Insufficient knowledge of retailers regarding antibiotics and AMR was significantly associated with inappropriate dispensing of antibiotics
Malawi	Sambakunsi et al., 2019 [143]	 Cross sectional study involving 2 focus groups and a structured questionnaire among 105 respondents Discussion group respondents had limited knowledge of antimicrobials, their use or AMR 74% of participants were unable to differentiate antimicrobials from other categories of medicine 92.4% felt antimicrobials could be used to stop a fever, 54% wrongly believed that antimicrobials ar effective in treating common colds and 53% would use antimicrobials to treat URTIs
	Machongo et a l ., 2022 [144]	 Interviews with 16 caregivers of children Overall, caregivers of children had limited knowledge regarding antibiotics and their use as well a AMR Most caregivers were currently using antibiotics inappropriately through self-modication to treat
		Most caregivers were currently using antibiotics inappropriately through self-medication to treat viral infections including URTIs

Country	Author and year	Key findings
Mozambique	Mate et al, 2019 [115]	 Cross-sectional study among 1091 adults using a semi-structured questionnaire 52.4% of adults surveyed had poor knowledge regarding antibiotics, with only 46.4% having reasonable knowledge about the use of antibiotics
	Cambaco et a l. , 2020 [32]	 Most patients had never heard of the term AMR; however, they were familiar with the phenomenon Surveyed patients often understood the term 'resistance' as treatment failure and likened this to noncompliance, ineffective treatment, disease resistance or an inability of the physical body to respond to the infection
	Torres et al., 2020 [164]	 Qualitative interviews among 17 pharmacists Patients' behavior and beliefs on the curative power of antibiotics, e.g. many patients believe 'antibiotics cure everything', enhances requests for antibiotics without a prescription from commity pharmacists
Rwanda	Nisabwe et a l. , 2020 [114]	 Descriptive cross-sectional study conducted among 282 medical, dental and pharmacy students Concerns among healthcare students including pharmacy students included: 83% (n = 191) were unfamiliar with the concept of AMS – with 49% not yet discussing AMR as p of their education 38% did not believe that antibiotics were overused in Rwanda 23% did not agree that inappropriate antimicrobial use contributed to AMR
Tanzania	Mboya et al., 2020 [165]	 Cross-sectional descriptive study involving 152 adults visiting pharmacies or accredited drug store Among these adults, only 25% had adequate knowledge about the use of antibiotics Higher levels of education and having health insurance were associated with better levels of knowledge concerning antibiotics and their use in various illnesses Overall, 50.7% of respondents thought it acceptable to share antibiotics with others Sore throat and influenza were felt by 62.5% and 46.1% of the respondents respectively as disease that can be treated with antibiotics
	Simon et al., 2020 [84]	 Cross-sectional study among 730 parents/caregivers of children <5 years of age using a structure interview guide Overall, there was low level of knowledge regarding antibiotics among parents/caregivers of children <5 years of age
	Sindato et al., 2020 [166]	 Semi-structured questionnaire among 828 participants Among the 828 participants, there was moderate knowledge, attitude and practices regarding the use of antibiotics and AMR Participant's age and their level of education were significantly associated with knowledge of antibiotics and AMR
	Gabriel et al., 2021 [167]	 Cross-sectional study assessing knowledge regarding the rational use of antibiotics among 960 patients/consumers 50.7% of patients who purchased antibiotics without a prescription from pharmacies believed influenza could be treated with regarding antibiotic, 61.4% a sore throat and 60.5% a urinary trainfection 42.3% of patients were willing to use the same antibiotic if a friend or family member used the antibiotic previously to treat similar signs and symptoms
	Emgård et al., 2022 [148]	 Eight focus group discussions with mothers of children <5 years Overall, considerable belief that antibiotics are a universal treatment, used to prevent or treat mosymptoms or diseases among children Antibiotics were also perceived as protecting the child's body or strengthening the children's immune system – further helping to combat infectious diseases
	Nkinda et al., 2022 [168]	 Simulated clients among 672 accredited drug outlets and community pharmacies Among prescribers and dispensers there was adequate knowledge regarding antibiotics Encouragingly among prescribers: Only 14.8% agreed and strongly agreed that prescribing antibiotics which a patient does not ne does not contribute to resistance Only 17% agreed and strongly agreed that antibiotics can treat viral infections Only 7% agreed and strongly agreed antibiotics can be stopped when symptoms resolve
Low-Middle Income Sin Cameroon	gle Countries* Amin et al., 2019 [151]	 Cross-sectional survey using a structured questionnaire among 329 patients attending hospital outpatients Out of the 225 patients who resorted to self-medication with antibiotics in order to treat their hea problems – 43.1% (95% CI 36.5–49.9) sought no advice while 38.2% (95% CI 31.8–44.9) obtained their advice from non-medical personnel
	Elong Ekambi et al., 2019 [169]	 Interviews among 1,192 customers in community pharmacies using a structured questionnaire The vast majority of interviewees (88.3%) believed that all microbes can be treated with antibiot (88.3%) In addition, the belief that antibiotics were appropriate for bacterial infections was more common among those with a higher level education (OR = 4.03, 95% CI:1.89–8.57, p < 0.0001) and among public/private servants (OR = 2.47, 95%CI:1.21–5.08, p = 0.013)

Country	Author and year	Key findings
Congo	Shembo et al., 2022 [152]	 Semi-structured in-depth interviews with 18 participants in households Household participants were familiar with the term 'antibiotics;' however, limited knowledge of the indications and risks of antibiotics including AMR Inappropriate use of antibiotics was common reflecting limited knowledge of key areas
Ghana	Abbey et al. (2016) [170]	 Structured interviews (N = 501) and eight focus group discussions including 56 caregivers of children <5 years and e8 community key informants Typically, low awareness and inadequate recognition of pneumonia among studied participants in a rural setting in Ghana
	Afari-Asiedu et al., 2021 [171]	 10 in-depth interviews among staff of Ghana health services, pharmacy council and the association of over-the-counter medicine sellers (OTCMS) at district and regional levels There were concerns with the knowledge of OTCMS in Ghana, who are permitted to sell cotrimox azole without a prescription, regarding antibiotics and AMR Currently as well, OTCMS dispense a greater range of antibiotics than the current regulations enhanced by a lack of monitoring of practices, which increases AMR It is suggested that the Ghana Health Service and MoH appreciably extend approved health facilities especially to rural communities to enhance appropriate access as well as use of antibiotics to reduce reliance on OTCMS and the current abuse of the system to improve patient care. This is seen as more productive with improving antimicrobial use in Ghana than spending considerable resources training OTCMS personnel
	Sefah et al., 2022 [79]	 Cross-sectional survey among 160 fifth-year pharmacy, medical students and fourth (final)-year nursing and physician assistantship students Variable knowledge of antibiotic use, AMR, and AMS among surveyed healthcare students Good knowledge was associated with the study course and years of study (p < 0.001), with differences seen in the level of knowledge among the different healthcare students and their years of study Efforts must be made to enhance the curricula in these important areas
Kenya	Omulo et al., 2017 [172]	 Two-hundred households were interviewed at entry into the study of which 149 were also interviewed at exit. 80% of household personnel surveyed felt antibiotics should not be shared or discontinued following alleviation of symptoms However, 66% and 74% of respondents respectively considered antibiotics effective for treating colds and flu Clinicians and community pharmacists were highly trusted source of information regarding the management of diseases including infectious diseases
	Muloi et al., 2019 [173]	 Cross-sectional study among 40 personnel, principally pharmacy technicians, in drug stores More than 2/3rds of community pharmacy personnel were aware of the terms 'antibiotic resistance and 'drug resistance' However, fewer than 50% had heard of the terms 'AMR' and 'super bugs' and > 80% believed AMR occurs when their body becomes resistant to antibiotics rather than the bacteria themselves developing resistance
Nigeria	Badger-Emeka et al., 2018 [174]	 Cross-sectional study among 400 adults using a semi-structured self-administered questionnaire Patients typically lacked knowledge and awareness regarding the hazards associated with self-purchasing of antibiotics
	Ajibola et al., 2018 [175]	 Structured questionnaire administered among 1230 undergraduate students and community members Concerns with the knolwedge of both undergraduate students and community members Only 53% and 42.4% of undergraduate and community members respectively felt that antibiotics cannot cure all infections, 57.5% and 55.3% respectively that antibiotics cannot be used for colds and 68.4% and 62.9% respectively that the unnecessary use of antibiotics could make them ineffective In addition, only 32.6% of undergraduate students and 42.2% of community members felt that self-medication with antibiotics could lead to AMR
	Chukwu et al., 2020 [116]	 Cross-sectional study using a validated questionnaire among 482 respondents from across Nigeria Overall poor understanding of AMR and/or proper use of antibiotics among 482 members of the public Essential that more holistic public programs are undertaken to increase awareness of appropriate antibiotic use and AMR in order to lower resistance in Nigeria rates
	Akande-Sholabi et al., 2021 [176]	 Cross-sectional study among 866 healthcare students including pharmacy students Among the surveyed healthcare students who completed the questionnaire, there was only moderate knowledge of AMR This confirms the need to enhance the teaching of antibiotics and AMR among students and subsequently ensure there are strict policies in Nigeria to regulate their subsequent use
	Abdu-Aguye et al., 2022 [177]	 Descriptive cross-sectional study using a paper-based questionnaire among 164 final year pharmacy students Among the surveyed students: Most had some knowledge of antibiotics and AMR – however several misconceptions were identified Only 48.8% indicated that they knew what AMS was Less than half of the respondents agreed their current knowledge of antibiotics, AMR or AMS was adequate for their future careers Over 90% agreed they would like more education on these key areas prior to qualification

13

Table 2. (Continued).

Country	Author and year	Key findings
Sudan	Hussain et al., 2023 [161]	 Cross-sectional study design involving 1492 patients More than half of the surveyed patients (55.1%) stopped taking the antibiotics when their symptoms disappeared due to lack of knowledge Only about 10% of surveyed patient consulted either a physician or the pharmacist before stopping their antibiotics
Zambia	Mudenda et al., 2021 [119]	 Structure questionnaire among 144 community pharmacists Whilst there was good knowledge among the 144 community pharmacists surveyed (93.8%), with 67% of those surveyed having positive attitudes regarding AMR and AMS, there were appreciable concerns 75% demonstrated poor practices toward AMR and AMS, with high rates of dispensing of antibiotics without a prescription
	Mudenda et al., 2022 [178]	 Structured self-administered questionnaire among 172 pharmacy students Among the 172 pharmacy students surveyed, most had good knowledge and positive attitudes toward antibiotics (90% and 84% average scores respectively); however, suboptimal practices (64% average score) about the use of antibiotics and AMR However, the prevalence of self-medication with antibiotics was 41% Despite some encouraging scores, there is a need to improve the pharmacy curriculum regarding antibiotics, AMR and ASPs
High-Middle Income Si South Africa	ingle African Countries* Mokoena et al., 2021	A survey among 83 minibus drivers revealed the following:
	[179]	 A common misconception was that antibiotics can be used to treated cold/influenza and fever 75% believed AMR occurred in the human body and 64% believed it was OK to share antibiotics

NB: AMS = Antimicrobial stewardship, AMR = Antimicrobial Resistance; ASPs = Antimicrobial Stewardship Programmes; *World Bank classification based on Adekoya et al [131].

especially important for community pharmacies located in rural areas across Africa.

Alongside this, easy-to-use and reliable tools must be introduced for valid data collection and management. These tools are important to enhance the implementation of potential quality indicators and their subsequent use across Africa and beyond [130,187–189] (See Supplementary Table S4 for more details including explanations). Without easy-to-use tools, continually monitoring the appropriateness of dispensing will be challenging and likely to fail in the long-term. In addition, any indicators that will be used in practice must be developed and agreed upon among all key stakeholder groups so they all have a sense of ownership. Otherwise, a lack of ownership will compromise their use in practice.

Table 3 describes the limited number of indicators that have been used to date among LMICs, including African countries, to assess the appropriateness of dispensing of antimicrobials among community pharmacies and drug sellers across LMICs, providing future direction. These indicators include the extent of dispensing without a prescription as well as their appropriateness.

Table 4 documents a number of indicators that can potentially be discussed among key stakeholder groups across Africa before implementation. These potential indicators are based on current indicators being used in practice (Table 3)

combined with those contained within the WHO AWaRe Book and the Drive-AB suggested list [13,195]. These possible indicators are in addition to the potential instigation of strict regulations regarding which antibiotics, if any, can be sold without a prescription especially in rural areas of Africa where there are currently high patient co-payments. Alternatively, in more urban areas where there are currently long waiting times to see a physician alongside appreciable costs. Costs, in addition to the costs of any medicines, include pertinent travel costs, co-payment costs where there is no universal healthcare, as well as loss of income (indirect costs) from taking time off work. Alongside this, ambulatory healthcare clinics are often out-of-stock of medicines requiring patients to visit pharmacies and other medicine sellers anyway for any prescribed antibiotics causing frustration. This is beginning to change in countries such as South Africa with new systems in place to better manage medicine stocks [196].

Potential indicators are in addition to enforcing existing regulations across Africa regarding the dispensing of antibiotics without a prescription (Supplementary Table S1) where pertinent and not appreciably detrimental to patients. These include a number of structure as well as process measures including % of antibiotics including Access antibiotics dispensed based on AWaRe guidance (Table 4).

Table 3. Indicators used to assess the appropriate dispensing of antibiotics without a prescription including among African countries.

Indicator	Reference
Overall antibiotic consumption in DIDs (DDDs per one thousand inhabitants per day)/total units before and after ASP interventions	[56, 190–192]
ATC groups of antibiotics dispensed, e.g. % Penicillins versus total antibiotics dispensed; % cephalosporins versus total antibiotics dispensed; % fluoroquinolones versus all antibiotics dispensed	[92]
Number of clients dispensed an antibiotic without a prescription and %s	Table S2
% adherence to current agreed guidelines	[193]
% of children receiving appropriate treatment for uncomplicated ARIs, malaria, and non-bloody diarrhoea	[193]

Table 4. Possible quality indicators that could be used to date to improve the appropriateness of dispensing of antibiotics without a prescription across Africa.

Indicator	Reference
Structure	
% of antibiotics dispensed correctly labeled, e.g. dose, length of course, etc.	[195]
% of antibiotics dispensed correctly recorded	[195]
% of antibiotics dispensed chosen from an essential medicines list	[195]
% of antibiotics dispensed from an agreed list of antibiotics for the setting vs. all antibiotics dispensed	[13]
% of antibiotics purchased/dispensed broken down by agreed 'Access' vs. 'Watch' and 'Reserve' antibiotics (pack/unit based)	[103,105]
% of injectable antibiotics purchased without a prescription vs all injectables dispensed (packs) where injectable antibiotics are being dispensed in community pharmacies	[13]
% of antibiotics dispensed without a prescription vs. all antibiotics dispensed (packs)	Tab l e S2
% adherence to antibiotics dispensed based on the AWaRe guidance for common infections seen in community pharmacies across Africa, e.g. URTIs, UTIs and STIs	, [13,105]
Process	
% of dispensing where patients are asked about key issues including allergies and any renal impairment	[13]
% of community pharmacies/drugs stores with point-of-care facilities or guidelines readily available to assist patients with diagnosis and appropriate treatment	[13, 63]
% of antibiotics dispensed based on the AWaRe guidance for common infections seen in community pharmacies across Africa such as URTIs, UTIs and STIs, e.g. is the condition self-limiting or not and are there more suitable alternatives?	[13,105]

NB: STIs = Sexually Transmitted Infections; URTIs = Upper Respiratory Tract Infections; UTIs = Urinary Tract Infections; AWaRe Guidance - [104].

Alongside this, as mentioned, there needs to be regular monitoring regarding the extent of antibiotics dispensed per day or week through mobile and other technologies [82,127,197]. Such activities are important alongside the instigation of any quality indicators to be able to constantly monitor the situation and give 'real time' feedback.

The instigation of indicators is important since, as mentioned, limited access to prescribers and associated costs such as travel costs, especially in rural areas where there are also high co-payments, can be seen by some as morally challenging if strict regulations banning the dispensing of antibiotics without a prescription are enforced [37,82,198,199]. Community pharmacists can play a key role in this situation as a trusted source for information and potential treatment suggestions, which builds on their activities during the recent COVID-19 pandemic [63,66,75,92,200–203]. The increasing recognition of the potential role of community pharmacists is one of the reasons behind changes in the UK, which will allow pharmacists to prescribe antibiotics in clearly designated conditions [204].

A number of ASPs and other activities have been undertaken across Africa and beyond to improve the appropriate management of infectious diseases in ambulatory care, including reducing inappropriate purchasing of antibiotics for self-limiting conditions such as ARIs. Community pharmacists and medicine vendors are key targets for ASPs to reduce inappropriate dispensing of antibiotics without a prescription [52,63,203,205]. Examples of ASPs that have been instigated in Africa and in other LMICs to reduce inappropriate dispensing are documented in Table 5. African and non-African countries have been combined in Table 5 to increase the number of documented exemplars since all LMICs typically share similar challenges regarding the instigation of ASPs [214].

Examples among African countries include educational activities linked to the Pharmacy Undergraduate Programme in Kenya, which resulted in low levels of dispensing of antibiotics without a prescription [92]. The low levels seen in the study of Mukokinya et al. (2018) contrast with appreciably higher rates in the study of Muloi et al. (2019) among

pharmacies not allied to the university [173]. A similar situation was seen during the recent COVID-19 pandemic regarding the dispensing of antibiotics without a prescription for patients with actual or suspected COVID-19 [91,208]. In Uganda, multiple interventions including educational programmes, enhanced the appropriate management of children with uncomplicated malaria, pneumonia and non-bloody diarrhea [193].

In their study, Lubogo et al. (2021) found that training and workshop activities among drug sellers in rural Uganda, including the provision of information, education and communication, was cost-effective at US\$6/trained drug seller to improve the quality of treatment, complimenting similar activities among healthcare workers [90]. This is important in Uganda given current high resistance rates to recommended and prescribed antibiotics for the treatment of common infections [215].

We are aware, as mentioned, that there have been situations among LMICs where Government or health insurance company interventions have failed to produce the desired result. These are discussed in Table 6 to give guidance of possible pitfalls for key stakeholders across Africa and beyond to avoid in the future if they wish to reduce inappropriate purchasing of antibiotics without a prescription.

We are also aware that there are several online pharmacies globally including across Africa. There needs to be additional regulations surrounding this activity especially given increasing concerns about substandard and falsified (SF) medicines across Africa and the implications for AMR [216–218], coupled with the lack of advice to patients with online pharmacies. The implications of these activities will be explored in a follow-up paper as this is outside the scope of this paper.

2.2.4. Potential future activities to reduce inappropriate purchasing of antibiotics without a prescription

Community pharmacists and their assistants are a key stakeholder group to reduce inappropriate dispensing of antibiotics. Ideally, community pharmacists and their assistants can provide information about the medicines dispensed as well as give therapeutic advice. These activities build on their

Table 5 Summary of ASPs and other	r activities to reduce inappropriate disp	ensing of antihiotics without a n	rescription across Africa and beyond
Table 3. Sullillary of ASES and Othe	i activities to reduce mappropriate disp	ensing of antibiotics without a p	rescription across Arrica and Deyond.

Country and reference	Intervention and Aims	Impact of the Intervention
-	 Drug sellers in Dhaka participated in 6 standardized role-playing scenarios A guidline for acute respiratory infections (ARIs) guideline was developed following the role-play alongside a one-day educational course concerning appropriate management of ARIs The guidelines only recommended antibiotics for children with complicated ARIs 	 Mixed results were seen: In children, the dispensing of antibiotics for uncomplicated ARIs decreased (30% baseline vs. 21% post-intervention; p = 0.04) However, drug sellers were equally likely to dispense antibiotics for complicated ARIs and referrals to physicians for complicated ARIs decreased (70% baseline vs. 58% post-intervention p = 0.03) For adults, dispensing of antibiotics without a prescription remained similar for uncomplicated ARIs (48% baseline vs. 40% post-intervention; p = 0.1) but increased among those with complicated ARIs (44% baseline vs. 78% post-intervention; p < 0.001)
	 In public pharmacies in Brazil, there have always been restrictions on the dispensing of antibiotics without a prescription and generally impossible for pharmacists to sell antibiotics without a prescription In 2010, the law was applied to private pharmacies 	 Moura et al. (2015) found no difference in antibiotic utilization among public pharmacies between 2008 and 2012 However in private pharmacists, Moura et al. (2015) documented a decrease in antibiotic use of 1.87 DDD/TID (p < 0.001) immediately after restrictions banning the sales of antibiotics without a prescription (from 2008 to 2012). The authors also found a greater decrease in the more developed regions as well as in the State Capitals Lopes-Junior et al. (2015) also found that sales of amoxicillin among private pharmacies fell by approximately 30% post legislation despite a general growth in the pharmaceutical market. The authors also found decreased sales of other popular antibiotics including tetracyclines (30.5% decrease), sulfonamides (28.5% decrease) and macrolides (25.0% decrease) Mattos et al. (2017) observed an increase in antibiotic utilization from 2008 to 2011 (cephalosporins –216.8%, quinolones – 170.9% and aminopenicillins – 140.9%), followed by a decrease in 2012 (cephalosporins – minus 19.4%, quinolones – minus 12.7% and aminopenicillins – minus 11.1%)
China [207]	 Multiple initiatives were introduced in Shaanxi Province in China to reduce the purchasing of antibiotics without a prescription given rising concerns. These included: Stricter regulations for dispensing antibiotics, and improving pharmacists' education Stipulating there must be a qualified pharmacist's present to dispense antibiotics Increased frequency of unannounced pharmacy inspections and punishments for abuse 	 These multiple measures resulted in decreased antibiotic sales between 2011 and 2017 There was decreased dispensing of antibiotics without a prescription for a 5-year-old child with diarrhea between 2011 and 2017 - from 72.3% to 50.2% (p < 0.0001) - simulated patients There was similar reduction for simulated patients with URTIs - down from 95.8% to 69.5% (p < 0.0001)
Kenya [19,91,92,173,208,209]	 Activities included: Education among pharmacists linked to the Pharmacy Undergraduate programme at the University of Nairobi (UoN) Regular interaction with University staff and students regarding key issues surrounding antibiotics and AMR The University recently launching and implementing an AMS curriculum for undergraduate pharmacy students as part of its NAP to reduce AMR 	 There was a low level of dispensing of antibiotics without a prescription (94.1% of antibiotics dispensed with a valid prescription) in the study of Mukokinya et al. (2018) among pharmacies allied to the UoN These contrasts with pharmacies not allied to the university and not superintended by pharmacists. In the study of Muloi et al (2019), 52% of surveyed pharmacists not allied to the University had sold antibiotics without a prescription In the study of Opanga et al. (2021) at the start of the COVID-19 pandemic, there was no purchasing of antimicrobials without a prescription among patients with actual or suspected COVID-19 among community pharmacies allied to the UoN. These community pharmacists typically recommended alternative treatments This compares with the study of Kimathi et al. (2022) who found that 23.4% of respondents had self-medicated with antibiotics during the pandemic, 60.6% at the onset of COVID-19 symptoms before confirmatory tests, with 51.5% self-medicating more than once
	 The government implemented a number policies in 2010 to enforce existing laws whereby antibiotics could only be dispensed to patients presenting with a prescription As part of the policies, antibiotic prescriptions had to be retained and registered in pharmacies, with fines imposed for noncompliance 	 Antibiotic utilization decreased by 22.9% (10.5 to 7.5 DDD/TID) between 2007 and 2012, with the trend accelerating after greater enforcement of the legislation There were significant changes in the dispensing of penicillins and sulfonamides: -0.86 DDD/TID (p < 0.00) and -0.17 DDD/TID (p = 0.07) respectively There was also an appreciable seasonal reduction in the use of penicillins in Mexico after greater enforcement of the legislation

Table 5. (Continued).

Country and reference	Intervention and Aims	Impact of the Intervention
Namibia [42,66,67,122]	 Key activities included: Education among pharmacists starting in universities and continuing post qualification Implementation of regulations banning the purchasing of antibiotics without a prescription Activities of community pharmacies regularly monitored 	 In a survey among 100 households in Namibia, typically cold/flu medication, paracetamol, and decongestants were used to treat adults or their children with ARIs including for common colds and influenza. There was no purchasing of antibiotics without a prescription There was a similar situation during the COVID-19 pandemic with no change in antibiotic utilization patterns early in the pandemic among 55 community pharmacies surveyed compared with other African countries including Nigeria
Nigeria [211]	 Randomised trial to assess if access to C-reactive protein (CRP) test kits coupled with staff training on how to use these RTI management In private community pharmacies, pharmacists can reduce non-prescription antibiotic dispensing for RTIs 	Antibiotic dispensing decreased by 15.66% (209/300 [intervention] vs 256/300 [control]) in the adjusted analysis
Republic of Srpska [63, 212]	 Activities included: Education of pharmacists regarding the appropriate management of diseases including ARIs together with the production of guidelines for the 42 most frequent diseases and conditions seen in everyday practice in community pharmacies in the Republic Greater enforcement of the regulations banning the dispensing of antibiotics without a prescription together with possible fines for violation of laws (Euro500–1500 for pharmacy directors and Euro500–750 for pharmacy technicians) Special attention given to the importance of adequate communication and skills among pharmacists starting in University and continuing post qualification 	 The dispensing of antibiotics without a prescription decreased from 58% to 18.5% of pharmacies of pharmacies surveyed (simulated patients) OTC therapy to alleviate symptoms was offered in 72.3% of pharmacies in 2015 up from 67.2% in 2010 OTC medication dispensed included throat and nasal sprays, decongestants, oral expectorants, analgesics and antihistamines Significantly fewer pharmacies dispensed an antibiotic without a prescription where OTC medicines were offered Encouragingly, the most common reason for not dispensing to simulated clients was that antibiotics cannot be dispensed without a prescription
Thailand, 2015 [213]	 Activities included: Principally education involving a multidisciplinary intervention among grocery stores in a rural province in Thailand Trained community leaders were used to reduce the extent of antibiotic availability in village grocery stores 	 There were 87% fewer antibiotics available post-intervention compared with pre-intervention Grocery stores in the control group saw only an 8% reduction in antibiotic availability between the two time periods
Uganda [193],	Four-part intervention to improve the management of pediatric febrile illness among drug sellers: Training and work activities Provision of information, education, information and communication Supply activities including diagnostics and medicines Monthly support supervision via supervisors trained in either pharmacy or clinical medicine	 The intervention increased the appropriate treatment of children with uncomplicated malaria, pneumonia symptoms and non-bloody diarrhea by 80.2% (95% CI 53.2–107.2), 65.5% (95% CI 51.6–79.4) and 31.4% (95% CI 1.6–61.2) respectively versus the pre-intervention period Adherence to guidelines during the intervention phase was high without causing excessive prescribing of antimicrobial medicines

Table 6. Summary of activities that have been unsuccessful to appreciably reduce inappropriate dispensing of antibiotics without a prescription.

and references	Intervention and Aim	Impact of the Intervention
Chile [55]	 Regulations limiting self-purchasing of antibiotics in Chile were implemented in 1999 These regulations were reinforced with an educational campaign and the involvement of community pharmacists. 	 Initially the policies were effective in reducing antibiotic consumption with antimicrobial consumption decreasing from 12.3 DID before the intervention to 8.5 DID just after the enforcement (in 2000) However, these activities were not sustained and possibly because of this antibiotic consumption increased from 2002 onwards
Columbia [55,108]	Introduction of a law in 2005 banning the self-purchasing of antibiotics combined with initial enforcement	 The initial enforcement of the law had a modest impact on overall antibiotic sales in the first three years (-1.00 DDDs/1000 inhabitants per day) A follow-up study five years after implementation found that a high number of pharmacies (80.3%) were still not complying with the law as a result of lax monitoring This prompted calls for a greater enforcement of the law to reduce the purchasing of antibiotics without a prescription
Venezue l a [55]	 The government implemented policies to try and limit the dispensing of three antibiotic groups without a prescription However, there were no public awareness campaigns and the 'enforcement' was only via government publications with no formal follow up of the regulations 	 As a consequence, there was no decrease in antibiotic utilization levels in the country In fact, the opposite happened and there was an increase in antibiotic utilisation in the country despite the policies
Vietnam [58]	 Strict regulations banning the dispensing of antibiotics without a prescription along with constant supervision from the pharmaceutical regulatory authorities However, limited sanctions for community pharmacists in Vietnam when dispensing antibiotics without a prescription, with a fine of only US\$15–25 per documented violation In addition, potential for extensive co-payments for medical services for patients besides the cost of medicines – which could end up costing the patient considerably more than purchasing medicines directly from community pharmacies Going straight to pharmacists is seen as typically more convenient and does not waste time waiting to see a physician, which may decrease daily wages 	 487 out of 1,626 participants taking part in the study involving community pharmacies and drug sellers were able purchasing antibiotics without a prescription 81.7% were able to purchase antibiotics without a prescription involving 29 different antibiotics In 86.4% of occasions, participants were prescribed antibiotics by drug sellers Most antibiotics were sold to treat RTIs (61.4%)

 $\label{eq:NB:ARIs} \textbf{NB:ARIs} = \textbf{Acute Respiratory Tract Infections}; \ \textbf{RTIs} = \textbf{Respiratory Tract Infections}.$

considerable role helping patients during the recent COVID-19 pandemic, as well as wider role in countries such as the UK [66,200,201,204,219]. Pharmacists' activities can include advice on alternative treatments to antibiotics for self-limiting infections including URTIs or acute diarrhea. Activities can also include advice on dosing and storage requirements when antibiotics are deemed necessary based on the balance of risk, as well as discussions on allergies and potential sideeffects [92,203]. Alongside this, we have seen antimicrobial stewardship as a key identified Continuous Professional Development (CPD) need among community pharmacists as recently seen in Zambia. Alongside this, the need for regulatory compliance and a culture for monitoring of pharmacy practices must become mainstream among Universities in Africa training pharmacists. Such activities should safeguard future patient safety away from a philosophy of commercial gain [220].

As part of this, community pharmacy personnel must acknowledge unique patient considerations when speaking with them. Considerations includes the education and literacy levels of patients, their cultural beliefs and their native language as well as their physical and mental capacity. An

important consideration is also the ethnic diversity within a country [221]. If a country is ethnically diverse, this requires additional skills from the pharmacist or assistant in mitigating risk factors associated with antibiotic use including AMR. Such considerations are important as sub-Saharan Africa is one of the most ethnically diverse continents [222]. As a result, as mentioned, community pharmacy personnel need to acknowledge unique patient considerations when speaking with them. In addition, be cognizant of their potential education and literacy levels, their cultural beliefs and their native language, and where possible their physical and mental capacity. Good listening and questioning skills are also essential to help with a diagnosis as well as ascertain any potential drug-drug interactions with any current medicines. This also includes any herbal medicines to guide possible alternative treatments for their infectious disease [179,223]. Generally, when patients have good guidance of how to use the medicines dispensed, they tend to use them correctly.

Community pharmacists can also track trends in the dispensing of antibiotics, as well as trends in local resistance patterns, through information provided by the Ministry of Health or local hospitals. Community pharmacists can

Table 7. Suggested activities in the short to medium term to reduce inappropriate dispensing of antibiotics without a prescription.

Key Group Suggested activities

Health authorities (operating more at a macro level)

A) Patients

- Improve existing communication with patients to improve their knowledge of antibiotics and antimicrobial resistance (AMR). This includes knowledge regarding the lack of effectiveness of antibiotics for essentially viral infections coupled with concerns with their over use including adverse reactions enhancing AMR
- Potential channels for effective communication with patients include physicians, pharmacists/drug stores, schools, billboards and social
 media outlets
- In the case of social media outlets need to address current misinformation as this can be counter productive as seen with COVID-19 and misinformation regarding possible treatments including hydroxychloroguine and ivermectin as well as vaccines [224–227]
- Longer term seek to introduce universal healthcare building on the agreed Sustainable Development Goals as recent activities have been compromised by the COVID-19 pandemic [228–230]

B) Pharmacists/health authorities

- Work with universities to ensure the curriculum is adequately covered surrounding the management of infectious diseases, AMR and ASPs and continued post-qualification through Continuous Professional Development (CPD) activities [220]. This includes the clear obligation of all HCP groups to reduce inappropriate purchasing and dispensing of antibiotics without a prescription
- Instigate potential ASPs surrounding key advice and guidelines to share with patients. This includes suggested treatments for common
 presented infections included within the WHO AWaRe book [13,105], as well as potential enforcement of regulations severely limiting
 inappropriate dispensing of antibiotics especially those in the 'Watch' and 'Reserve' groups among community pharmacies and other
 medicine outlets
- Work with community pharmacists when developing and implementing agreed indicators, including structure and process indicators, to enhance their acceptance and subsequent use. Agreed indicators can incorporate agreed OTC medicines and certain antibiotics, with the consultation of local health authorities, especially surrounding certain 'Access' antibiotics that may be dispensed by community pharmacist without a prescription where pertinent/expedient and when the risk and benefits to patients have been fully evaluated. This builds on recent activities for instance in the UK [204]
- Make sure in time that appropriate systems are in place, including appropriate IT systems, to monitor the availability of antibiotics in
 pharmacies and reduce shortages, especially in public healthcare facilities dispensing medicines, as shortages can be counterproductive if they increase the purchasing of antibiotics in drug stores/shops
- Monitor current antibiotic dispensing practices, especially for 'Watch' and 'Reserve' antibiotics vs. agreed 'Access' antibiotics as part of agreed indicators/restrictions especially given concerns with the rising utilisation of 'Watch' antibiotics among LMICs in recent years [101]. We have seen in Tanzania that the mass distribution of azithromycin increases resistance rates [102]
- Alongside this, local and regional health authorities must ensure that comprehensive awareness campaigns are instigated among
 patients to reduce requests for antibiotics for essentially self-limiting conditions. This along with capacity building activities among
 community pharmacy and medicine outlet personnel to improve the management of clients or their children presenting with
 infectious diseases espeically for self-limiting infectious diseases
- In addition, where pertinent health authorities need to provide details of registered medical practitioners currently practicing to enable pharmacists to rapidly verify the validity of the prescriptions through contacts where pertinent. In this way, help improve antibiotic dispensing generally

C) Universities

- Make sure HCPs including future community pharmacists are fully aware of the current regulations surrounding the dispensing of
 antibiotics without a prescription in their country during their training, as well as core concepts including AMS and ASPs, by critically
 examining current curricula especially given concerns with the training of pharmacy students during the pandemic [125]
- Work with key personnel in the Pharmacy departments of universities to research and monitor dispensing activities among community pharmacies
- Following this, work with universities and community pharmacists to develop potential interventions (ASPs) including agreed indicators. Subsequently introduce these and monitor their impact. Following this, refine the ASPs if needed, i.e. not achieving the desired impact (Table 6)

Key Group	Suggested activities
· ·	 Work with health authorities and universities to design optimal communication strategies to limit patients' expectations that they will be dispensed an antibiotic for a self-limiting condition; however, they will be offered effective alternatives Use this opportunity to cement the role of pharmacists and their assistants in the community as the preferred first contact HCP for a number of ailments including URTIs and UTIs – this builds on their expanding role as part of the COVID-19 pandemic with proactivity across LMICs [66, 200, 201, 203] As part of this, take part in ongoing CPD activities including surrounding the 'AWaRe' book [13,105], and its implications, to optimize the care of patients with infectious diseases in the community and reduce subsequent AMR Seek to introduce systems that can better monitor the flow of antibiotics through shops and stores including mobile technologies – imperative as part of the development of appropriate quality indicators Work with health authorities and others to reduce potential shortages of medicines, especially if this means necessarily dispensing 'Watch' vs. 'Access' antibiotics Work with health authorities to introduce pertinent indicators to improve the appropriate dispensing of antibiotics – even without a prescription. As part of this, Pharmacy Councils across Africa need to work closely with health authorities regarding the introduction of pertinent IT systems to monitor antibiotic use – this can increasingly be mobile technologies in Africa given their networks and current problems with landlines Leverage the needs and opportunities to provide relevant CPD, AMR education and antibiotic guidelines to community pharmacists and medicines seller. Mobile Apps can increasingly be used to provide high-impact (and cost-effective) advice and guidance [231, 232]
Universities (typically operating at the macro and meso level)	 Refine the curriculum to make sure it covers all essential aspects of antibiotics, AMR and the AWaRe classification of antibiotics/ AWaRe book of conditions Alongside this, refine CPD activities to help improve the appropriate dispensing of antibiotics in the future Work with key stakeholder groups regarding the messaging and channels to patients to lower their expectations for an antibiotic to treat self-limiting conditions Work with key stakeholder groups to develop and refine possible indicators to improve the dispensing of antibiotics, especially without a prescription
Regulatory authorities and policy makers (typically operating at the macro level)	 Develop capacity to help enforce appropriate legislation for public protection Strengthen the medicine policy and regulatory frameworks that enhance the rational use of antibiotics including appropriate dispensing Progress One-Health approaches and strategies to further mitigate AMR risks Ensure coordinated multisectoral collaboration, including private sector participation, in reducing inappropriate dispensing of antibiotics without a prescription
Patients and Patient Associations (Patients typically operating at the micro level)	 Work with all key stakeholder groups to ensure that any messaging to patients is understandable given the extent of misconceptions currently regarding antibiotics and their use as well as AMR. This includes animations for children and patient engagement to reduce unnecessary requests [233] Work with health authorities and others to use social media to rapidly spread key messages regarding antibiotics and their use as well as AMR Work with health authorities and others to address key misconceptions circulating with respect to antibiotics and their uses as well as AMR – especially for essentially self-limiting conditions Work with key groups including university personnel to enhance the communication skills of future pharmacists and assistants especially surrounding infectious diseases likely to be seen in ambulatory care as well as misconceptions surrounding antibiotics and AMR Work with health authorities and others regarding the development of pertinent future dispensing/quality indicators
Pharmaceutical companies and the private sector (typically operating at the macro and meso level)	 Promote a responsible behaviour through the different key stakeholder groups, i.e. producers, distributors and pharmacies in the value chain delivering antibiotics to the population through awareness activities Involve key groups, e.g. biotech firms, laboratories and clinics that have legitimate commercial interests into promoting antibiogram tests to improve future empiric prescribing of antibiotics Employ good manufacturing practice (GMP) and good distribution practice (GDP) to ensure that marketed antibiotics in Africa are of quality, including deploying robust post-marketing surveillance of their marketed antibiotics

subsequently use this information along with local health authority personnel to develop additional communication and other campaigns to reduce inappropriate dispensing of antibiotics and subsequently AMR. Overall, education and training of HCPs, including community pharmacists and licensed drug sellers, as well as patients or their guardians, is critical to reduce inappropriate dispensing of antibiotics and with it AMR.

Table 7 provides suggestions for all key stakeholder groups in the short to medium term to improve appropriate dispensing of antimicrobials given rising concerns across Africa and the implications for continuing AMR.

Tribal authorities can also assist with meetings to educate their community where pertinent, and social media can be a powerful tool of passing information to the public. However, care is needed to address possible misinformation. For instance, there was considerable misinformation regarding the prevention and treatment of patients with COVID-19 including vaccines during the early waves of the pandemic which was a concern [224,225,227,234,235].

Underpinning future activities is the obligation and the responsibility of the competent institutions, e.g. the Ministry of Health and Governments, for enacting precise, clear and strict regulations regarding prescription only medicines, including antibiotics, with appropriate penalties and fines. There is also a clearly defined obligation of every HCP in this process, and the obligation of continuous monitoring and inspections by official institutions. HCPs should be aware of their obligations starting in university and continuing post qualification. As part of this, patients and public/media must be aware of the current regulations surrounding prescriptiononly medicines, the rationale for this classification and how they can help community pharmacists in their activities. However, there also needs to be some flexibility especially in more rural areas where there are greater distances and costs to visit HCPs in healthcare centers, and where community pharmacists and their assistants may be the only HCP available. In addition, where the costs of medicines combined with co-payment costs of visiting HCPs in clinics is clearly unaffordable for most workers and their families [107]. Trained community pharmacists can guide patients on appropriate management choices building on the examples in Kenya and Namibia (Table 7). Such activities build on their role in the NAPs to reduce AMR across Africa as well as their increasing role in countries such as the UK [19, 204].

2.3. Discussion of the findings and the implications

Reducing the burden of AMR is a high priority across Africa in view of its impact on lives lost across the continent, the increasing burden on the healthcare system especially post-COVID-19 as well as associated costs [2,3,10,236]. Rising AMR rates have been enhanced by the growing use of 'Watch' antibiotics across LMICs including among African countries [101].

As mentioned, a critical area to address to reduce AMR is the inappropriate use of antibiotics in ambulatory care. This is

because ambulatory care currently accounts for approximately 90% or more of overall antibiotic utilization globally especially in LMICs, which includes among African countries [13,14]. Within total ambulatory care utilization, the purchasing and dispensing of antibiotics without a prescription, often for selflimiting conditions such as URTIs, contributes an appreciable proportion of overall antibiotic use across Africa (Table S2) [29,31,36,37]. Consequently, there was an identified need to comprehensively document current practices across Africa and the rationale behind the purchasing of antibiotics without prescription among both patients and dispensers. Alongside this, potential ways forward to limit inappropriate dispensing behavior. Possible activities to reduce inappropriate dispensing of antibiotics include the introduction of quality indicators (Tables 4 and 5) that can be used in practice along with accompanying ASPs. As a result, help to reduce AMR. Documenting potential activities, including possible quality indicators and ASPs, was the rationale behind this study, culminating in suggested ways forward for all key stakeholder groups across Africa to reduce AMR (Table 7). Suggested activities build on the considerable experiences of the senior-level coauthors.

The findings from this narrative review shows that there is still considerable purchasing of antibiotics a prescription across a number of African countries despite government legislation banning the sales of antibiotics without a prescription (Tables S1 to S3). Countries with the highest rates of purchasing without a prescription include Eritrea Ethiopia, Nigeria, Mozambique, Tanzania and Zambia, and build on earlier systematic reviews including those of Belachew et al. (2021) [37]. and Yeika et al. (2021) [36], as well as systematic reviews among LMICs including African countries [29,38,41,50,51,53]. However, there are some African countries, as well as some situations within African countries, where there is little of no purchasing of antibiotics without a prescription. African countries include Botswana and Namibia where the introduction strict regulations, coupled with regular monitoring of pharmacists, limits the dispensing of antibiotics without a prescription. In addition, in certain circumstances including Kenya among pharmacists linked to the University of Nairobi and among rural settings in South Africa [33,92]. These countries and situations provide exemplars for the future.

Encouragingly, the penicillins (typically in the Access group), metronidazole (Access), cotrimoxazole (Access) and tetracyclines (Access) were among the most dispensed antibiotics without a prescription across Africa where this data was available (Table S2), with more limited dispensing of macrolides, quinolones and cephalosporins. Alongside this, limited if any dispensing of 'Reserve' antibiotics without a prescription among the studied African countries. The antibiotic dispensing patterns seen across Africa (Supplementary Table S2) are perhaps not surprising with ARIs, UTIs and acute diarrhea among the most common complaints when antibiotics were dispensed without a prescription. Alongside this, the 'Reserve' group of antibiotics are typically very expensive compared with other antibiotics. Consequently, may well be unaffordable to the majority of patients who pay 'out of pocket' for their healthcare.

The reasons for high rates of purchasing of antibiotics without a prescription seen in recent years across Africa (Tables 1 and 2) include patient demand, economic factors including high patient co-payments for healthcare as well as medicines, travel costs to see HCPs in healthcare facilities as well as time away from work, i.e. opportunity costs, exacerbated by long waiting times to see an HCP in a public healthcare facility. In addition, previous experiences of patients with similar infectious diseases as well as limited knowledge about antibiotics and AMR among all key stakeholder groups, including patients and pharmacists. Alongside this, weak monitoring and enforcement of current regulations.

Addressing inappropriate dispensing of antibiotics is critical as part of NAPs across Africa to reduce increasing rates of AMR [19]. We have seen several indicators used across Africa as part of ASPs to reduce inappropriate dispensing of antibiotics, with more suggested (Tables 3 and 4). There have also been a number of ASPs introduced among African countries and beyond to reduce inappropriate dispensing of antibiotics, especially for ARIs (Table 5). This is encouraging as there have been concerns with the introduction of ASPs among LMICs including African countries due to resource and other issues [214]. However, this has changed recently in Africa especially in hospitals [237–241]. Such activities are important to help to reduce AMR across Africa as part of agreed NAPs [19]. Potential ASP activities include educational initiatives among all key stakeholder groups as well as greater enforcement of current legislation. Greater education among all key stakeholder groups includes patients. The introduction of legislation, and/or greater enforcement of current legislation combined with possible fines, should potentially emphasize 'Watch' antibiotics along with agreed indicators. We have seen in a number of South American countries, as well as Malawi (Tables 1 and 2) and Vietnam (Table 6), that enforcement of any regulation, alongside potential fines, needs to be followed through. Otherwise, these initiatives and activities will fail to achieve the desired results. These combined findings resulted in a number of suggestions for all key stakeholder groups in Africa going forward to reduce future inappropriate dispensing of antibiotics without a prescription (Table 7).

The suggested activities recognize the increasing role of community pharmacists post COVID-19 as key players in the healthcare system managing self-limiting conditions including ARIs, UTIs and acute diarrhea [66,75,200–202]. Community pharmacists also had an increasing role combating false information and its consequences during the recent pandemic, which resulted in requests for ineffective antimicrobials causing side-effects as witnessed with hydroxychloroquine and ivermectin [42,202,227,242]. Alongside this, providing advice on preventative measures including PPE and hand washing to limit the spread of the virus [66,200,201].

Education of key stakeholder groups, alongside the development of appropriate indicators associated with ASPs, can be based on the recent AWaRe guidance, which encourages the appropriate use of antibiotics based on risk assessments. Educational activities can include encouraging

the appropriate dispensing of 'Access' antibiotics where these are indicated [13,105]. This is especially important in rural areas of Africa where, as mentioned, there can be limited access to prescribers with community pharmacists often the principal HCP in the area. Totally banning the dispensing of antibiotics without a prescription in urban areas can also be potentially morally challenging where there are high co-payments to see a physician or nurse and purchase medicines coupled with long waiting times them and the resultant implications [37,82,107,198,199]. We will continue to monitor activities across Africa, including the development of potential indicators surrounding the AWaRe book, building on developments in information technology. This includes the use of mobile telephones to track and monitor dispensing patterns [197]. In addition, interventions that have recently been implemented but too early to assess their impact.

We are aware of a number of limitations with this paper. These include the fact that we did not undertake full systematic reviews for each area for the reasons given. However, we have documented an appreciable number of papers discussing the current situation regarding the purchasing of antibiotics without a prescription across Africa, the rationale and potential ways to address this. The latter has been achieved with the considerable knowledge and input from senior level coauthors from across Africa and beyond. Despite these limitations, we believe our findings and suggestions for the future with all key stakeholder groups are robust given the number of exemplars and suggestions going forward.

3. Conclusions

In conclusion, there is still extensive purchasing of antibiotics without a prescription across Africa. This is a concern given rising AMR across Africa, with the implications for increased morbidity, mortality and costs. A number of ASPs have been undertaken across Africa and beyond to reduce inappropriate dispensing of antibiotics acting as exemplars. Successful activities typically involve comprehensive activities among all key stakeholder groups with education a key component. We will continue to monitor the situation given its current urgency and the need to reduce AMR across Africa as part of ongoing NAPs.

4. Expert opinion

In order to appreciably reduce AMR globally and the associated implications, it is essential to reduce inappropriate dispensing of antibiotics without a prescription across Africa. This is because the highest consumption of antibiotics globally, as well as mortality due to AMR, is in sub-Saharan Africa. Alongside this, over 90 to 95% of antibiotic utilization across Africa is currently in ambulatory care as opposed to hospital in-patients, with the purchasing of antibiotics for essentially self-limiting conditions such as ARIs and acute diarrhea currently constituting an appreciable proportion of overall antibiotic utilization among humans. Typically across Africa, the purchasing of antibiotics without a prescription is banned. However, there is weak enforcement among many African

countries. Such legislation is also counter-productive in rural areas where community pharmacists maybe the only healthcare professional available. Alongside this, in many African countries, there can be high prohibitive costs to see an HCP in a healthcare facility. This is in addition to any travel costs alongside potential loss of income from seeing physicians within working hours, especially with long waiting times. The cost of any antimicrobial can also be a concern. Consequently, the way forward in these situations is to enhance the appropriateness of any antibiotics dispensed in community pharmacies and drug stores. This can be achieved through offering suitable alternatives for essentially self-limiting conditions. In addition, reducing the extent of any dispensing of 'Watch' antibiotics through legislation as well as subsequent close monitoring of antibiotics dispensed among community pharmacists through mobile technologies and other approaches.

Any antibiotic dispensed should subsequently be based on a thorough risk assessment of the patient. This can be through implementing treatment suggestions and agreed quality targets based on the indications listed in the recently published AWaRe book and classification of antibiotics. The AWaRe book guidance has been endorsed by the WHO. As such, providing a universally globally accepted guideline source in place of multiple local, national and international guidelines, which can be contradictory. As a result, reducing the potential for different guidelines being used within and among the different African countries, which only causes confusion.

Alongside these activities, there also needs to be improved education of all key stakeholder groups regarding antibiotics and AMR to reduce inappropriate requests. The need for additional education reflects identified concerns concerning the current knowledge of antibiotics and AMR among key stakeholder groups across Africa. Key stakeholder groups include students, practicing physicians, nurses in healthcare facilities and pharmacists as well as patients. Improving knowledge of these HCPs starts in universities and continues post qualification. Educated pharmacists, especially those allied to universities in Kenya and Namibia, limited the purchasing of antibiotics without a prescription. As a result, providing exemplars to other countries. Patients are also a key target for educational activities as they drive requests for antibiotics. However, to be successful with patients, community pharmacists and their assistants need to acknowledge the education and literacy level of patients in their communication with them alongside any cultural beliefs of presenting patients. In addition, where possible, speak to patients in their native language to improve any communication between community pharmacists and assistants with patients. Such considerations are important because there can be considerable misinformation and misunderstanding surrounding terms such as AMR and the implications. Such activities are especially important in sub-Saharan Africa as this is one of the most ethnically diverse continents globally. Good listening and questioning skills can also help ascertain any current medicines patients are taking, including any herbal medicines, in case of potential drug-drug interactions. Finally, community pharmacists should also increasingly be able to keep track of local resistance patterns with the help of local health authorities. Improved knowledge base of local resistance patterns is

essential when pharmacists or their assistants are discussing possible treatment alternatives with client customers regarding their infectious diseases.

Future research should be centered on possible ASPs among community pharmacists and drug sellers to improve appropriate dispensing of antibiotics given limited examples to date across Africa. This includes the development and monitoring of robust processes and quality indicators based around the AWaRe book. A necessary pre-requisite is robust systems in place to monitor the dispensing of antibiotics in community pharmacists and drug stores, increasingly linked to a diagnosis. In addition, researching cost-effective ways of communicating with patients to reduce unnecessary requests for antibiotics especially potential social media avenues. These are likely developments in the next five to ten years across Africa to meet the goals within each country's NAPs as well as global action plan goals to reduce AMR, and we will continue to monitor the situation.

Funding

This paper was not funded.

Declaration of interest

A Cook and C Moore are funded by the Welcome Trust (222051/Z/20/Z) for the ADILA project. E Yeika, SA. Opanga, ZU Mustafa, V Marković-Peković, A Kurdi, BD Anand Paramadhas, E Wesangula, E Hango, N Schellack, S Mudenda, I Hoxha and JC Meyer have either worked for national or regional government agenices or are advisers to them on key issues surrounding AMR including the development and monitoring of NAPs. In addition, S Opanga received a grant from Kenya AIDS Vaccine Institute Institute of Clinical Research and Institut Merieux for tackling AMR in Kenya and GM Rwegerera also works for Destiny Medical and Research Solutions Proprietary Limited, Gaborone, Botswana. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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