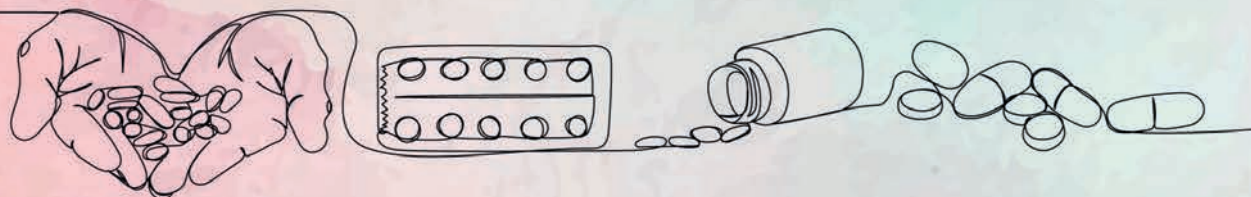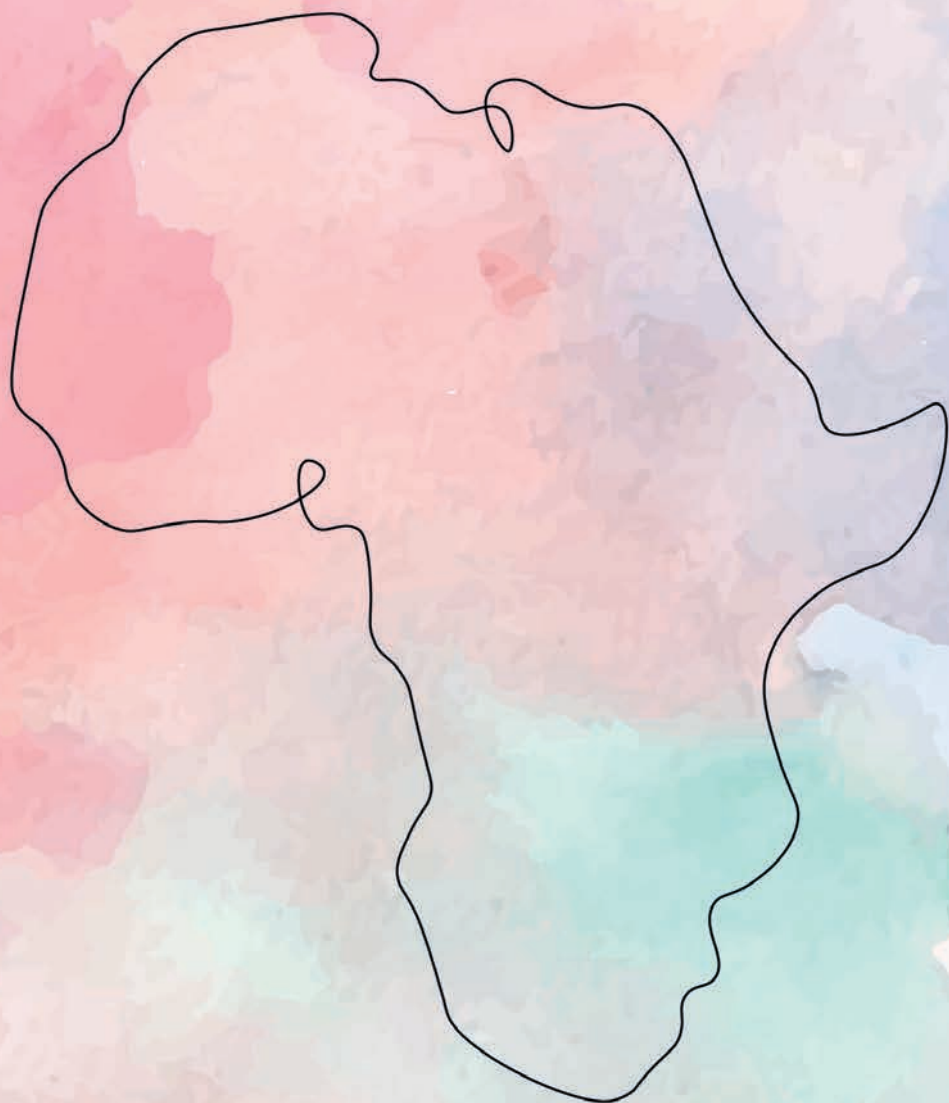# Contextualising access to essential medicines

lessons learned from East and Southern Africa

Gaby I. Ooms

CONTEXTUALISING ACCESS TO ESSENTIAL MEDICINES: LESSONS LEARNED FROM EAST AND SOUTHERN AFRICA

Gaby Isabelle Ooms

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TOEGANG TOT ESSENTIËLE GENEESMIDDELEN IN CONTEXT: LESSEN UIT OOST- EN ZUIDELIJK AFRIKA

(met een samenvatting in het Nederlands)

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GENERAL INTRODUCTION

"The essence of global health equity is the idea that something so precious as health might be viewed as a right."

– Paul Farmer

THE RIGHT TO HEALTH AS A FUNDAMENTAL HUMAN RIGHT

In 1945, in the aftermath of World War II, the United Nations (UN) was established to maintain international peace and security, facilitate good relations between nations, promote social and economic progress, and protect human rights (1). In its preamble, the UN Charter, for example, declared that the UN is determined to 'reaffirm faith in fundamental human rights, in the dignity and worth of the human person, in the equal rights of men and women, and of nations large and small' (2). In line with this fundamental goal, the UN published the Universal Declaration of Human Rights (UDHR) in 1948, which stated, amongst other things, that 'everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care' (3). This declaration, currently signed by all 193 Member States of the UN, was one of the first international documents to recognise the right to health of individuals (3).

Nearly two decades later, in 1966 the UDHR was followed by the International Covenant on Economic, Social and Cultural Rights (ICESCR), which further delineated the right to health (4). The ICESCR states that Member States should 'recognise the right of everyone to the enjoyment of the highest attainable standard of physical and mental health' (4). The ICESCR further declares that Member States should take multiple steps to ensure this right, which include the realisation of adequate maternal and child health, the prevention and treatment of diseases, and the assurance of adequate medical services and medical attention in case of sickness (4).

Many international and regional treaties addressing the right to health have followed in the years since, including the African Charter on Human and Peoples' Rights (ACHPR) (1981), and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa (2003), widely known as the Maputo Protocol (5,6). Along the lines of the ICESCR, Article 16 in the ACHPR states that every individual has the right to the highest attainable physical and mental health, and that signatories are mandated to take the necessary measures to protect the health of their people and ensure they receive proper medical attention when needed (5). The Maputo Protocol emphasises that signatories to the protocol shall ensure that the right to health of women, including sexual and reproductive health, is respected and promoted (6).

ACCESS TO MEDICINES AND THE ATTAINMENT OF HUMAN RIGHTS

The importance of access to essential medicines for the attainment of human rights has been recognised internationally. In 1978, for example, the International Conference on Primary Health Care was held, which resulted in the Declaration of Alma-Ata. This Declaration called on governments, health- and development workers, and the international community to promote and protect the health of all, and reaffirmed that health is a fundamental human

right (7). To realise a level of health that allows people to lead socially and economically productive lives, the Declaration underlines the critical importance of primary health care. Within the Declaration, provision of essential medicines is included as one of the key components of primary healthcare (7). Another example is that in 2009, during the twelfth session of the UN Human Rights Council, resolution 12/24 was adopted, which recognises that access to medicines is fundamental for achieving the full realisation of the right to the highest attainable standard of health for everyone, and that Member States are responsible for ensuring access to essential medicines for all (8). A year later, the Office of the United Nations High Commissioner for Human Rights (OHCHR) convened an expert consultation, during which it was again emphasised that access to medicines is fundamental for the realisation of the right to health, and that Member States need to ensure access to medicines through sustainable financing, strengthened health systems, and appropriate health legislation (9).

Most recently, access to medicines was included in the 2030 Agenda for Sustainable Development, better known as the Sustainable Development Goals (SDGs), under Goal 3: 'Ensure healthy lives and promote well-being for all at all ages' (10). The Agenda for Sustainable Development and its SDGs were developed to build on the Millennium Development Goals, and seek to sustainably improve the economic, social and environmental development of all Member States and its citizens. It aims to realize the human rights of all people, end poverty and hunger, achieve gender equality and empowerment of girls and women, foster peaceful, just and inclusive societies, and protect the planet. Target 3.8 'Achieve universal health coverage, including financial risk protection, access to quality essential healthcare services and access to safe, effective, quality and affordable essential medicines and vaccines for all' specifically, and to an extent target 3.7 'by 2030, ensure universal access to sexual and reproductive healthcare services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes', pertain to access medicines (10).

THE WHO MODEL LIST OF ESSENTIAL MEDICINES

Nevertheless, access to medicines remains problematic, with at least half of the world population still lacking access to even the most basic commodities (11). With the aim to tackle this problem, in 1977 the World Health Organisation (WHO) created the WHO Model List of Essential Medicines (model EML). According to the WHO, essential medicines are those that 'satisfy the priority healthcare needs of the population' (12). The model EML includes medicines that are selected because of their relevance to public health, their efficacy and safety, and their comparative cost-effectiveness (12). At all times, medicines included on the model EML should be available to all, with guaranteed quality, and at an affordable price. The list is updated every two years, and functions as a guide for countries to develop national essential medicines lists, specifically tailored to a country's needs and challenges (13).

The current model EML includes almost 500 essential medicines, including those which are the subject of this thesis: sexual and reproductive health commodities, medicines for the management of snakebites, and controlled medicines: medicines which are subjected to additional regulation internationally due to their potential risk for non-medical use and dependence, or because they are a precursor for illicit drugs (12).

ACCESS TO ESSENTIAL MEDICINES

In many countries around the world, access to adequate health services, including medicines, is still lacking. In 2017, only 33%-49% of the world population was covered by essential health services, with coverage in low-income countries being as low as 12%-27% (14). Further, two billion people are facing catastrophic or impoverishing health spending (14).

Sub-Saharan Africa is the region with the most pressing issues with regards to access to medicines and health services. **Table 1** provides an overview of some health-related indicators for Sub-Saharan Africa and the European Union (EU), as comparison (15). As can be seen, much still needs to be done to improve access to medicines and health services for people to attain a healthy life, especially in this region.

ACCESS TO MEDICINES FROM A HEALTH SYSTEM PERSPECTIVE

Previous research has led to the identification of multiple factors that influence access to essential medicines (18–21). One of the ways these factors have been organised is by levels, as first formulated by Hanson et al. (2003), and adapted by Bigdeli et al. (2013) (19,22). The original five-level framework by Hanson et al. classifies constraints to improving access to

Table 1. Health-related indicators, for Sub-Saharan Africa and the European Union (16,17).

Indicator	Sub-Saharan Africa	European Union
UHC service coverage (%)	44	81
Contraceptive prevalence, any method *(% of married women ages 15-49)*	33	73
Adolescent fertility rate *(births per 1,000 women ages 15-19)*	102	9
Infant mortality rate *(per 1,000 live births)*	50	3
Maternal mortality rate *(per 100,000 live births)*	534	6
Cause of death, by communicable diseases and maternal, prenatal and nutrition conditions *(% of total)*	54	6
Pharmacists *(per 10,000 population)*	0.6	8.3
Nurses and midwives *(per 1,000 population)*	1.3	9.5
Physicians *(per 1,000 population)*	0.2	3.9
Specialist surgical workforce *(per 100,000 population)*	2	92
Total population pushed below or further below the $3.65 a day poverty line by household health expenditure (%)	29.3	0.6

health interventions by the level at which a constraint operates. Constraints work at different levels of organisation, ranging from household- and community level to environmental and contextual characteristics (22). Bigdeli et al. (2013) adapted the framework into the 'Access to Medicines from a Health System Perspective Framework' to make it more applicable to the constraints related to access to medicines (see **Figure 1**) (19). In this framework, dynamic relationships are believed to be essential for a well-functioning health system and better health outcomes. The building blocks of a health system were therefore rearranged to better illustrate the two specific determinants necessary for better health outcomes: health resources and service delivery.

The level of individuals, households, and the community is the first level at which constraints can work. At this 'demand' level, the constraints are experienced at, and a consequence of, a more personal nature. Factors influencing access to medicines at this level include perceived quality of medicines and health services, ability of individuals or households to pay for medicines and services, ability of individuals to reach health services, and social and cultural characteristics, including stigma (19). Level II are constraints related to the delivery of health services, also referred to as the 'supply' side. Here, the interplay between service delivery and the health resources is shown. Health resources is composed of five interconnected building blocks: medicines, relating to their availability, affordability, accessibility, acceptability and quality; health information; health financing; human
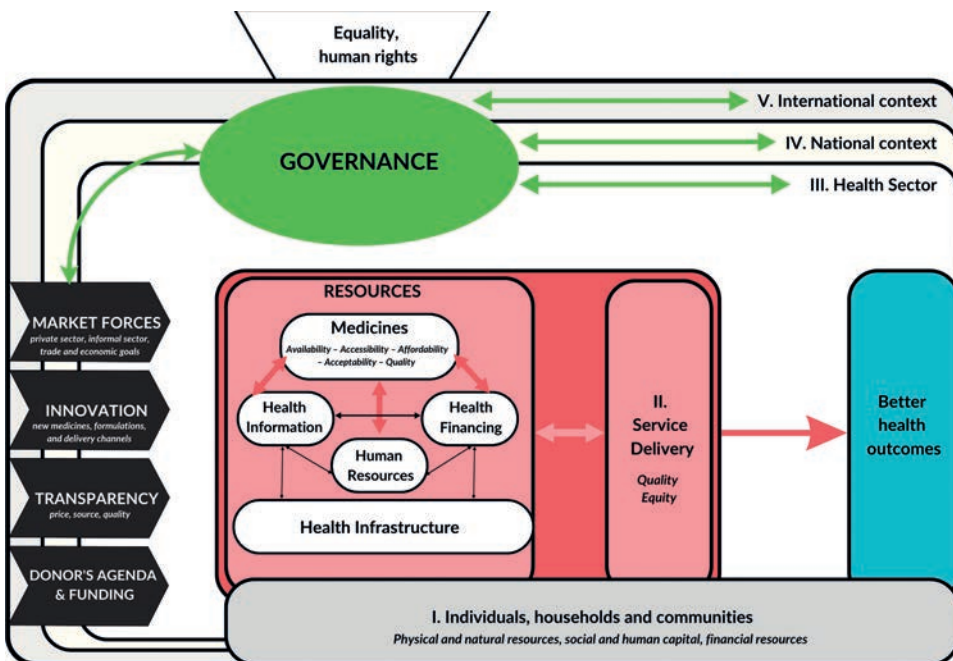
Figure 1. The Access to Medicines from a Health System Perspective Framework (19).

resources; and health infrastructure. Further, quality and equity are central to good service delivery (19). Services offered by different providers (public sector, private sector, private not-for-profit sector) also impact access, influencing availability, affordability and services provided. At the third level constraints operate at the health sector level; they are primarily related to governance. Important factors that play a role in access to medicines at this level are medicine procurement processes, including selection, registration, procurement and distribution of medicines, health sector financing, and health and pharmaceutical policies, including price control policies, national essential medicines lists and standard treatment guidelines (19). Level IV, the national context, concerns constraints operating at a national level and are related not only to legislative and organisational practices in the health sector but can also relate to other sectors influencing access to medicines. Level V, the international context, captures the constraints of access to medicines as a consequence of regional and international practices and regulations. At level IV and V, the framework breaks down governance at the national and international level in four determinants: market forces relating to medicine regulations; innovation of new medicines, formulations, and delivery channels; transparency, referring to transparency in information regarding the price, source, and quality of products; and donors' agenda and funding (19).

CONTEXTUALISING ACCESS TO ESSENTIAL MEDICINES

Since the beginning of 2000, access to medicines has been extensively studied using the WHO/Health Action International (HAI) methodology 'Measuring medicine prices, availability, affordability and price components' (23). The methodology was developed by the WHO in collaboration with HAI after a resolution was passed at the World Health Assembly in 2001, requesting the development of a standardised methodology to measure medicine prices (24). The original methodology measures the price, availability, affordability and price components of a basket of up to 50 essential medicines. It consists of a global core list of 14 medicines that are included in all surveys to enable international comparisons, a regional core list of 16 medicines covering medicines most relevant to the region, and a supplementary list of around 20 medicines chosen by the survey country, based on their local relevance (23). Since its development, the methodology has been used hundreds of times, with close to 1,000 studies published using this method of data collection (25).

While the original methodology focussed on essential medicines in general, in recent years the methodology has also been adapted to specific medicine groups or diseases. Examples are studies looking at medicines for cardiovascular diseases, epilepsy, non-communicable diseases, diabetes, cancer, and asthma (26–30). These studies have given us a broad understanding of the availability and affordability of essential medicines, especially in low- and middle-income countries. However, as can be deduced from the 'Access to Medicines from a Health System Perspective Framework', availability and affordability of medicines are not the only factors determining its access; access to essential medicines and health services

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is affected by a complex interplay of factors, and in Sub-Saharan Africa, the need to improve access is significant.

To better understand how constraints at the different levels of the health system influence access in this region, and what lessons might be learned, this thesis focusses on three distinct cases. Namely, internationally controlled essential medicines (ICEMs), the treatment of snakebite envenoming, and sexual and reproductive health (SRH). ICEMs are those listed on one of three international drug control conventions due to their potential for non-medical use or dependence, and are subject to stricter regulations compared to other essential medicines, which impact their accessibility (31). Snakebite envenoming, only recently recognised by the WHO as a Category A neglected tropical disease (NTD), has for a long time been a neglected issue. It has been underreported and under-researched, and is only now being universally recognised as a serious health issue (32). Conversely, SRH is prominently featured on the agenda of the international community and national governments, not least because of its critical importance to the health and wellbeing of people, especially women, which has been recognised by many (33). Nevertheless, SRH remains a controversial issue due to persistent socio-cultural beliefs surrounding the sexuality of women (34).

INTERNATIONALLY CONTROLLED ESSENTIAL MEDICINES

ICEMs are medicines that are included on the WHO EML, but that are also listed on one of three UN drug control conventions, namely, the UN Single Convention on Narcotic Drugs of 1961, the Convention of Psychotropic Substances of 1971, and the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988 (35–37). They are included in these conventions due to their potential risk for non-medical use and dependence, or because they are a precursor for illicit drugs (35–37). The purpose of the 1961 and 1971 Conventions was to regulate the use and availability of narcotic- and psychotropic medicines for scientific and medical purposes, while at the same time prevent illicit use for non-medical purposes (38). The 1988 Convention was a response to the increasing trafficking in narcotics and psychotropic substances, and its main purpose was to address their illicit use and trafficking (36).

Currently, fourteen medicines are ICEMs, and they are used for the management of pain and palliative care, epilepsy, anaesthesia, mental health, obstetric care, and opioid agonist treatment (OAT) (see **Table 2**). Medicines controlled under international drug conventions are subjected to tight regulation of manufacturing and licensing, and are classified according to the risk of non-medical use and dependence (see **Box 1**) (39,40).

As a consequence of these stricter regulations, the availability of ICEMs in LMICs is extremely poor and does not meet the medical needs of their populations. More than five billion people, around 80% of the world's population, have no or low access to opioids (41). The International

Table 2. Internationally controlled essential medicines and their therapeutic use.

International Drug Control Convention	Control Level	Medicine	Therapeutic Use
Single Convention on Narcotic Drugs of 1961	Schedule I	Fentanyl	Pain and palliative care, procedural sedation
		Hydromorphone	Pain and palliative care
		Methadone	Opioid agonist treatment, pain and palliative care
		Morphine	Anaesthesia, pain and palliative care
		Oxycodone	Pain and palliative care
	Schedule II	Codeine	Pain and palliative care
Convention of Psychotropic Substances of 1971	Schedule III	Buprenorphine	Opioid agonist treatment
		Diazepam	Anti-epileptic, anxiety disorders, pain and palliative care
		Lorazepam	Anaesthesia, anti-epileptic, anxiety disorders, procedural sedation
		Midazolam	Anaesthesia, anti-epileptic, anxiety disorders, pain and palliative care, procedural sedation
		Phenobarbital	Anti-epileptic
Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988	Table I	Ephedrine	Hypotension (anaesthesia)
		(Methyl)ergometrine	Uterotonic
	Table II	Potassium permanganate	Topical anti-infective

Narcotics Control Board (INCB), for example, estimated that 92% of morphine is consumed by only 17% of the world population, all living in high-income countries (42). While the United States is facing an opioid crisis, with more than 130 people dying of an opioid overdose every day, it is estimated that each year, more than 20 million people living in LMICs die while suffering extreme pain because of lack of access to opioids (43,44). Access to safe, affordable and timely surgical and anaesthesia care is also a major issue for almost five billion people worldwide, and an additional 143 million surgical procedures are needed in LMICs annually to avert preventable disability and deaths (45–47). Availability of psychotropic substances used for mental health and neurological disorders is also problematic; it is estimated that the prevalence of epilepsy is 9.39 per 1,000 population in SSA, while studies showed that 75% of people living with epilepsy (PLWE) and about 80% of people with mental disorders living in LMICs do not receive treatment (42,48). Phenobarbital is the cheapest treatment option available for epilepsy (49,50). The controlled status of some of these medicines might partly explain this treatment gap.

Many challenges with access thus exist in LMICs, including Sub-Saharan Africa, some of which are caused by barriers specific to ICEMs, while others relate to all essential medicines

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The Single Convention on Narcotic Drugs of 1961 and the Convention of Psychotropic Substances of 1971 both established four schedules for the categorisation of controlled medicines. In Schedule I of the 1961 Convention, Member States are required, *inter alia*, to estimate the national annual quantity necessary, to limit the use and distribution of controlled medicines to medical and scientific purposes only (35). Member States are required to document the total quantities of each medicine produced, manufactured, utilised, consumed, and imported or exported (35). The total quantities manufactured and imported by a Member State cannot exceed these reported quantities. Persons or enterprises engaged in the trade and distribution of controlled medicines also require special licenses for their legal handling, which are to be authorised by the Member State (35). Medicines controlled under Schedule II are subject to the same control measures as those in Schedule I, with the exception that Member States are not required to prevent accumulation of controlled medicines in the possession of retailers above those needed for the normal conduct of business (35).

The Convention of Psychotropic Substances of 1971 is aimed at the same regulatory outcomes as the 1961 Convention. Schedule I contains substances that are prohibited for use except for scientific and very limited medical use (37). In Schedules II-IV, Member States should limit the manufacture, export, import, distribution, stocks of, trade in and use of controlled medicines (37). Those involved in manufacturing, trading, distribution and possession of controlled medicines require special licenses, and medicines can only be supplied or dispensed to individuals on the basis of a medical prescription. Prescriptions can only be written by licensed personnel, and restrictions regarding refills and duration of prescription-validity are required (37). Moreover, manufacturers, wholesalers, exporters and importers need to keep records of all quantities manufactured and acquired (37). Import and export of psychotropic substances is only allowed when tightly regulated and authorised by both the import- and export Member State, and Member States are allowed to prohibit the import of any psychotropic substances listed in the 1971 Convention (37).

In the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988, targeted at preventing illicit trafficking of drugs, medicines are classified into two tables, with medicines included in Table II subjected to slightly stricter regulatory practices (36). Regulation is in line with the measures taken up in the 1961 and 1971 Conventions (35,37).

Box 1. The international drug control conventions explained.

and are inherent to weak health systems more broadly (44,51). Previous research has identified some overarching themes that hamper access, and relate to perceptions and attitudes of the public and healthcare workers, lack of healthcare worker training, stringent regulatory practices, fear of legal sanctions, inadequate supply chains, and costs (51–56). However, most of previous research has focussed only on single ICEM-related healthcare fields; the primary focus has been on access to opioids for pain and palliative care, and to a lesser extent on anaesthesia, while ICEMs for epilepsy care are primarily studied as part of the provision of epilepsy care as a whole. Not much research has focussed on all ICEMs or ICEM-related healthcare fields together, or the barriers that exist to accessing them in Sub-

Saharan Africa. Importantly, by treating ICEMs as one class of drugs, it might tease out new strategies that can inform governments' and stakeholders' plans of action to improve access to all ICEMs across the entire health system.

TREATMENT OF SNAKEBITE ENVENOMING

Snakebite envenoming is a major public health problem, especially affecting those living in rural regions in Africa, Asia, and Central and South America. Envenomation occurs following the bite of a venomous snake, when a mixture of toxins (venom) is injected (57). It is estimated that each year, about five million snakebites occur, of which 2.7 million are envenomings, leading to more than 138,000 deaths and 400,000 disabilities (57). In Sub-Saharan Africa, up to 32,000 snakebite deaths are reported every year, but the actual number of deaths is believed to be far higher given that up to 70% of snakebite cases remain unreported (58–61). However, snakebite has long been neglected by the global health community, including international aid organisations and donors, pharmaceutical companies, national governments, researchers, and civil society organisations (32). This while research in, for example, West Africa has estimated that the disability-adjusted life years (DALYs) caused by snakebites exceed those of many other NTDs which receive more attention globally (62).

Snakebite was first added to the WHO list of NTDs in 2009, but was removed from the list without explanation in 2013 (63). After years of advocacy, it was again added to the WHO list of NTDS in 2017 (63). Inclusion on the list of NTDs was deemed of critical importance to increase international attention, and subsequently more funding for research, and prevention and intervention strategies (63). A year later Member States passed a resolution at the World Health Assembly, and in 2019 the WHO launched a global snakebite strategy for prevention and control with the aim to reduce the morbidity and mortality as a consequence of snakebite envenoming by 50% by 2030 (64,65). To achieve this, four strategic aims were formulated: i. Empower and engage communities; ii. ensure safe, effective treatment; iii. strengthen health systems; and iv. increase partnerships, coordination and resources (64). As part of the strategy, WHO pledged to support countries in designing and implementing national action plans to integrate this strategy into their health agendas (64).

Despite these efforts, the health burden of snakebite envenoming, even though preventable, remains enormous, and it mainly affects the poor (66). Simple and effective treatment for snakebite envenoming has been around for decades. Good quality antivenoms, if adequately administered in a timely fashion, can effectively reverse the worst effects of envenoming. However, when treatment is inadequate, the consequences of snakebites can be death, permanent disability, including blindness, non-healing ulcers, extensive scarring, restricted mobility and amputation, as well as psychological distress and stigmatisation (58). Unfortunately, in many countries antivenom is not regularly available. Sub-Saharan Africa in particular has been facing an antivenom supply crisis for at least the last 20 years,

contributing to the high death and disability rates among snakebite victims (67,68). Multiple factors contribute to this crisis, including the limited financial resources available to sub-Saharan African countries for procurement and quality-assurance, antivenom market failure including a lack of appropriate antivenom for African snakes, and high dependency on antivenom imports (68–73).

In the past, however, there have been very little research efforts on snakebite in sub-Saharan Africa. Previous studies that involve primary data collection in East- and Southern Africa, for instance, are generally of limited scale and scope or outdated (74–78). Most studies on antivenom availability have estimated the availability compared to the needs; it is estimated that the number of effective treatments available in sub-Saharan Africa may be as low as 2.5% of what is needed (69). In very few countries in the region, however, has the availability and price of antivenoms in health facilities been studied (69,79). Further, few studies in Sub-Saharan Africa have focussed on community risk factors, health-seeking behaviour, snakebite victims' health outcomes, or the lived experience of snakebite victims.

SEXUAL AND REPRODUCTIVE HEALTH COMMODITIES

In 1994, the International Conference on Population and Development (ICPD) defined SRH as 'a state of complete physical, mental and social well-being and not merely the absence of disease and infirmity, in all matters relating to the reproductive system and to its functions and processes' (80). The human right that each individual has to sexual and reproductive health and rights (SRHR) means that people are entitled to appropriate information on SRH and access to safe, effective, affordable and appropriate family planning methods of their choice (80). If women decide to have children, they must have access to appropriate health services that enable them to have a healthy pregnancy and safe delivery, and the best chance of having a healthy infant (80). On top of that, men and women, including adolescents, must be informed and empowered to protect themselves against sexually transmitted infections (STIs) and HIV/AIDS, and must be properly and timely treated if infection occurs (80).

In 2019, 30 Organisation for Economic Co-operation and Development (OECD) Development Assistance Committee (DAC) donor countries spent on average 23% of their official development aid (ODA) for health on SRHR-related projects (33). Denmark, the United States and the Netherlands spent as much as 60%-85% of their ODA on SRHR-related projects, thus showing it is one of the donor countries' main areas of focus (33). However, SRH also remains a controversial issue due to persistent socio-cultural beliefs surrounding the sexuality of women and adolescents. Sub-Saharan Africa is a region where religion plays a significant role in society, as 63% of the population is Christian, and 30% Muslim (81). Consequently, dogma and ideology are important drivers of societal knowledge, attitudes, beliefs and practices. Sexuality education programmes, for example, emphasise sexual abstinence, rather than modern contraception, and topics such as gender inequality, abortion and homosexuality

are rarely discussed (34). Further, the Catholic Church, for instance, also teaches that modern contraceptives are sinful and that only abstinence or traditional forms of birth control should be used (82).

Notwithstanding the significant funding spent on SRH, access to SRH services remains an issue for people worldwide, especially for women and girls. In 2020, it was estimated that around 800 women died every day as a consequence of complications related to pregnancy and childbirth; 70% of these deaths occurred in Sub-Saharan Africa (83). In the same year, the lifetime risk of dying from a cause related to maternity was 400 times higher for a 15-year-old girl living in Sub-Saharan Africa than a 15-year-old girl living in Australia and New Zealand (1 in 40 versus 1 in 16,000, respectively) (83). In line with this, while the SDGs set the goal of lowering the maternal mortality rate to fewer than 70 deaths per 100,000 live births by 2030, currently, in Sub-Saharan Africa, the rate stands at 534 deaths per 100,000 live births (15,84). In 2021, while there was an unmet need for family planning of only 9% in Eastern and South-Eastern Asia, the unmet need in Sub-Saharan Africa stood at 37% (85). It is estimated that 43% of pregnancies in Sub-Saharan Africa are unintended, and that around 33 abortions per 1,000 women of reproductive age occur each year (85). Since in most of the countries in this region abortion is illegal, each year about 6.2 million unsafe abortions take place, resulting in 15,000 deaths (86). In 2016, there were also an estimated 376 million new cases of one of the four most common curable sexually transmitted infections (STIs), namely chlamydia, gonorrhoea, syphilis and trichomoniasis, with syphilis responsible for more than 200,000 stillborn and new-born deaths (87).

It is known that women and girls encounter numerous challenges in accessing SRH services in Sub-Saharan Africa. Previous research conducted in this region has identified barriers on both the supply and demand side. On the demand side, barriers include, amongst others, lack of knowledge on SRH, socio-cultural and religious beliefs and practices, poverty, stigmatisation, and healthcare workers' negative attitudes. On the supply side, barriers include unavailability and unaffordability of commodities and services, stockouts, distance to health facilities, staff shortages, and poorly trained HCWs (88–96). However, detailed research on availability and affordability of SRH commodities at the health system level is lacking. In Uganda one study did look at the availability and affordability of reproductive- and maternal health commodities, but the research included only six commodities (97). Further, in Sub-Saharan Africa, healthcare is provided by three distinct sectors: the public, private and mission sector. Research comparing SRH services across these three sectors is currently still limited. Previous research has studied only one sector (96,98,99), studied multiple sectors but did not stratify results per sector (100), or did not specify which sector(s) were studied (89,90), which does not allow for comparison across sectors. This while knowing more about the differences between sectors can help form targeted interventions to improve access: Among others, each sector often has their own supply system, methods of operation, and offering and pricing of services.

OBJECTIVE OF THIS THESIS

It is clear that the right to live a healthy life is a fundamental human right, which has been recognised by many international treaties (3–6). Within this, access to medicines has been recognised as a critical tool to attain this right to health (7–9). However, it is also clear that in many LMICs, including in Sub-Saharan Africa, this right has not been realised by many. Millions of people in the region lack access, and as a consequence suffer when in need of proper care (42,48,57,62,83,85,86). The problem of access to medicines, unfortunately, is complex. There is not just one cause of the lack of access, and subsequently there is not an easy fix. Access to medicines is influenced by an interplay of factors, found across the different levels of the health system. To improve access, barriers across the health system need to be tackled. In this thesis, three distinct cases, recognised for their controversy or neglect, are used to illustrate the complexity of access to essential medicines in Sub-Saharan Africa.

In all three cases, the corresponding medicines are on the WHO EML and should therefore be available at all times to those in need. However, this is too often not the case, especially in regions such as East- and Southern Africa. Given that ICEMs, snakebite envenoming and SRH cover three significantly different health topics: a strongly regulated field, a neglected tropical disease, and a mainstream but at the same time controversial topic, the questions that arise are: *What are the commonalities and differences in access to essential medicines and services between these cases?* And *what lessons might be learned in order to improve access to essential medicines, both case-specific and in general?* The aim is that, by contextualising access to medicines through interrogating such specific diseases, lessons can be learned to help improve access.

THESIS OUTLINE

This thesis consists of five chapters: an introductory chapter, which is followed by three chapters, each focussing on one case, and a concluding general discussion. **Chapter 2** focusses on internationally controlled essential medicines. In **Chapter 2.1** we review existing literature on barriers to accessing ICEMs in Sub-Saharan Africa. **Chapter 2.2** is a deep dive into the barriers to accessing ICEMs in Uganda, through the lens of key stakeholders. In **Chapter 2.3** we estimate what the impact would be of scheduling a currently non-controlled medicine, ketamine, as an internationally controlled substance on access for surgical and anaesthesia care in Sub-Saharan Africa. This is done through a case study on availability of ketamine and other general anaesthetics in Rwanda, as well as through key informant interviews with experts from the region.

In **Chapter 3** the focus is on snakebite envenoming. **Chapter 3.1** studies the burden of snakebite in rural Kenyan communities through a household survey. **Chapter 3.2** assesses the availability, affordability and stockouts of commodities used to treat snakebites in

health facilities in Kenya. In **Chapter 3.3** we investigate the capacity of health facilities and healthcare workers to treat snakebites in Kenya, Uganda and Zambia.

Chapter 4 has a main focus on access to sexual and reproductive health services and commodities. **Chapter 4.1** is a cross-country comparison of the availability, stockouts and affordability of SRH commodities in Kenya, Tanzania, Uganda and Zambia. In **Chapter 4.2** we focus on two key commodities for the treatment of post-partum haemorrhage, oxytocin and misoprostol, where we measure their availability, prices and affordability in Kenya, Uganda and Zambia. In **Chapter 4.3** we study healthcare workers' perspectives on access to SRH services in the public, private and private not-for-profit sectors in Kenya, Tanzania, Uganda and Zambia to gain insights into existing barriers.

Chapter 5 brings together the lessons learned from each of the chapters and identifies where commonalities and differences exist between the different cases. It also provides recommendations to improve access to essential medicines in East and Southern Africa, and identifies areas for future research.

CONTRIBUTION STATEMENT

GIO wrote the general introduction of this thesis. Her supervisors reviewed previous versions of the manuscript, and GIO implemented their feedback.

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2

INTERNATIONALLY CONTROLLED ESSENTIAL MEDICINES

"To leave [dying people in unbearable pain] that way when their pain could be relieved would be a breach of the most fundamental principles of human rights and a grave affront to respect for persons and their dignity."

– Margaret A. Somerville

2.1

BARRIERS TO ACCESSING INTERNATIONALLY CONTROLLED ESSENTIAL MEDICINES IN SUB-SAHARAN AFRICA: A SCOPING REVIEW

Gaby I Ooms, Janneke van Oirschot, Denise de Kant,
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ABSTRACT

Background

2.1

Access to internationally controlled essential medicines (ICEMs), medicines that are listed on both the World Health Organization's Essential Medicines List and one of three international drug control conventions, remains problematic in Sub-Saharan Africa (SSA). Previous reviews have focused only on specific ICEMs or ICEM-related healthcare fields, but none have focused on all ICEMs as a distinct class. This scoping review therefore aims to identify the barriers to accessing ICEMs across all relevant healthcare fields in SSA.

Methods

A scoping review was conducted across indexing platforms Embase, PubMed, Scopus and Web of Science of studies published between January 1 2012 and February 1 2022. Articles were eligible if they mentioned barriers to accessing ICEMs and/or ICEM-related healthcare fields, if studies were conducted in SSA, or included data on an SSA country within a multi-country study. The review was guided by the Access to Medicines from a Health System Perspective framework.

Results

The search identified 5519 articles, of which 97 met the inclusion criteria. Many barriers to access were reported and were common across the ICEMs drug class. Main barriers were: at the individual level, the lack of knowledge about ICEMs; at the health service delivery level, low availability, stockouts, affordability, long distances to health facilities, insufficient infrastructure to store and distribute ICEMs, and lack of ICEM knowledge and training among healthcare workers; at the health sector level, lack of prioritisation of ICEM-related healthcare fields by governments and subsequent insufficient budget allocation. Cross-cutting, governance-related barriers pertained to lack of proper quantification systems, cumbersome procurement processes, and strict national laws controlling ICEMs, leading to overly restrictive prescription practices.

Conclusion

This review showed that there are a multitude of barriers to accessing ICEMs in SSA across all health system levels. Many of the barriers identified are applicable to all ICEMs, highlighting the importance of tackling barriers for this entire class of drugs together.

INTRODUCTION

According to the World Health Organization (WHO), essential medicines are those that 'satisfy the priority healthcare needs of the population' (1). These medicines should therefore always be available with guaranteed quality and at an affordable price. In 1977, the WHO adopted the WHO Essential Medicines List (EML), which includes medicines that are selected because of their relevance to public health, efficacy and safety, and comparative cost-effectiveness (1). The most recent list is the 22nd edition, published in 2021 (2).

Some of the medicines listed on the WHO EML are also listed on one of three United Nations (UN) drug control conventions, namely the UN Single Convention on Narcotic Drugs of 1961, the Convention of Psychotropic Substances of 1971 and the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. This is due to their potential risk for non-medical use and dependence, or because they are a precursor for illicit drugs (3–5). Medicines listed on these conventions are 'controlled' and are consequently subject to strict regulations. When medicines are listed on the WHO EML and one of the three conventions, they are identified as internationally controlled essential medicines (ICEMs). Currently, fourteen medicines are ICEMs, and they are used for the management of pain and palliative care, epilepsy, anaesthesia, mental health, obstetric care, and opioid agonist treatment (OAT), for which methadone and buprenorphine are commonly used (see **Table 1**). The aim of the drug control conventions is to protect the health and wellbeing of people by ensuring availability of substances for medical and scientific purposes while at the same time preventing diversion and non-medical use (6). However, access to ICEMs remains problematic for many in need of medical treatment worldwide.

The availability of ICEMs in low- and middle-income countries (LMICs) is extremely poor and does not meet the medical needs of their populations. The International Narcotics Control Board (INCB) estimated that 92% of morphine is consumed by people living in high-income

Table 1. Internationally Controlled Essential Medicines and their therapeutic use.

Therapeutic use	Medicine
Anaesthesia	Lorazepam, midazolam, morphine
Anti-epileptic	Diazepam, lorazepam, midazolam, phenobarbital
Anxiety disorders	Diazepam, lorazepam, midazolam
Hypotension (anaesthesia)	Ephedrine
Opioid agonist treatment	Buprenorphine, methadone
Pain and palliative care	Codeine, diazepam, fentanyl, hydromorphone, methadone, midazolam, morphine, oxycodone
Procedural sedation	Fentanyl, lorazepam, midazolam
Topical anti-infective	Potassium permanganate
Uterotonic	(Methyl)ergometrine

2.1

countries, who represent only 17% of the world population (7). While the United States is facing a so-called opioid crisis, with more than 130 people dying of an opioid overdose every day, it is estimated that each year, more than 20 million people living in LMICs die while suffering extreme pain because of lack of access to opioids (8,9). International guidelines for pain management are currently lacking after the retraction of WHO guidelines in 2019 (10). Availability of psychotropic substances used for mental health and neurological disorders is also problematic; it is estimated that the prevalence of epilepsy is 9.39 per 1,000 population in Sub-Saharan Africa (SSA), while studies showed that 75% of people living with epilepsy (PLWE) and about 80% of people with mental disorders living in LMICs do not receive treatment (7,11). Phenobarbital is the cheapest treatment option available for epilepsy (12,13). The controlled status of some of these medicines might partly explain this situation.

Sub-Saharan Africa is one of the regions where many suffer needlessly because access to ICEMs is known to be inadequate (6,14). For example, Uganda and Nigeria have a reported unmet need for opioids for palliative care of 89.0% and 99.8%, respectively (9). Many challenges exist in the region, some of which are specific to ICEMs, but others relate to all essential medicines and are inherent to weak health systems more broadly (9,15). To enable targeted action to improve access to ICEMs in SSA, it is imperative to have a detailed overview of all the barriers faced by people when trying to access them. Previous reviews have focused only on single ICEM-related healthcare fields; mostly on pain and palliative care (16,17), and to a lesser extent on epilepsy (18,19) or anaesthesia (20). However, no reviews have focused on all ICEMs or ICEM-related healthcare fields together, or the barriers that exist to accessing them in SSA. Importantly, by treating ICEMs as one class of drugs, such a review might inform government and patient strategies to improve access to all ICEMs across the entire health system. This scoping review therefore aims to identify the barriers described in literature to access ICEMs across all related healthcare fields in SSA.

METHODS

Our study design was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) (21) checklist, and the methodological framework for scoping studies proposed by Arksey and O'Malley (22) and elaborated by Pollock et al. (23). Specifically, they guided the development of the research question, identification of relevant literature through electronic database searches and reference checking, inclusion and exclusion criteria, extraction of the data, and reporting of the results (22,23).

Search strategy and study selection

A search of literature indexing platforms Embase, PubMed, Scopus and Web of Science was conducted on February 1 2022. To ensure up-to-date information, only studies published from 1 January 2012 to the search date were included. Key search words included all

the countries of the Sub-Saharan region, terms related to barriers, such as: "treatment gap" OR "barriers" OR "challenges" OR "access" OR "availability" OR "accessibility" OR "affordability" OR "drug control" OR "drug policy", and the names of the ICEMs, the healthcare fields in which they are used, and related terms used to describe ICEMs, such as: "controlled drugs" OR "controlled medicines" OR "controlled substances". The full search syntax used across the literature indexing platforms can be found in Supplementary File 1. References of the selected studies were examined for additional literature.

Articles were deemed eligible if they mentioned any barriers to access to ICEMs and/or related healthcare fields. Study populations were limited to persons aged 18 year or older, as access to ICEMs for children encompasses additional barriers and dimensions. Only studies conducted in SSA, or multi-country studies with specific data on an SSA country, were selected for inclusion. Studies were restricted to the English language. All types of articles were included, with the exception of conference abstracts, historical reports and protocols. Articles were not excluded based on study design.

Data extraction and analysis

The search results of the literature indexing platforms were downloaded into a Reference Manager database (Mendeley). Duplicates were removed, after which all titles were screened for eligibility in a stepwise approach (see **Figure 1**). The screening and preselection of the studies, based on the title and abstract, was conducted by one author (GIO). To ensure the quality and reliability of the search protocol, full articles were then screened independently by two authors (GIO and JO) to determine their inclusion in the study. When the authors had different opinions about inclusion or exclusion of an article, the article was reviewed together to reach consensus. Data was analysed deductively using the Access to Medicines from a Health System Perspective Framework, in which the components of the framework functioned as categories for data extraction (24). To increase the quality and reliability of the analysis, a data extraction form was created based on Arksey and O'Malley's framework, comprising the following information: author, year of publication, study location, study design, study population and sample, healthcare field, and main findings related to access barriers (22). Included literature were not assessed for quality due to the range in scope and design of included studies.

The barriers to accessing ICEMs in SSA are presented per the five main levels of *the Access to Medicines from a Health System Perspective* framework: (I) individuals, households and community; (II) health service delivery; (III) health sector level; (IV) national level; (V) international level, as well as the cross-cutting category of governance (24).

2.1

RESULTS

Characteristics of included articles

2.1

The search generated a total of 5519 articles; 1463 citations from PubMed; 2809 from Embase; 717 from Web of Science and 530 from Scopus. Of the 5519 articles, 2339 were duplicates. After screening titles and abstracts based on inclusion criteria, 291 were included for full-text assessment. Full-text assessment led to the inclusion of 97 articles for data extraction (see **Figure 1**). Characteristics of the included articles are summarised in Supplementary File 2. No additional papers were found after screening the references of the included papers.

The articles consisted of quantitative studies (n=35), qualitative studies (n=20), mixed-methods studies (n=17), expert pieces (n=10), reviews (n=8) and other studies such as programme evaluations, simulated client visits or health system assessments (n=7).
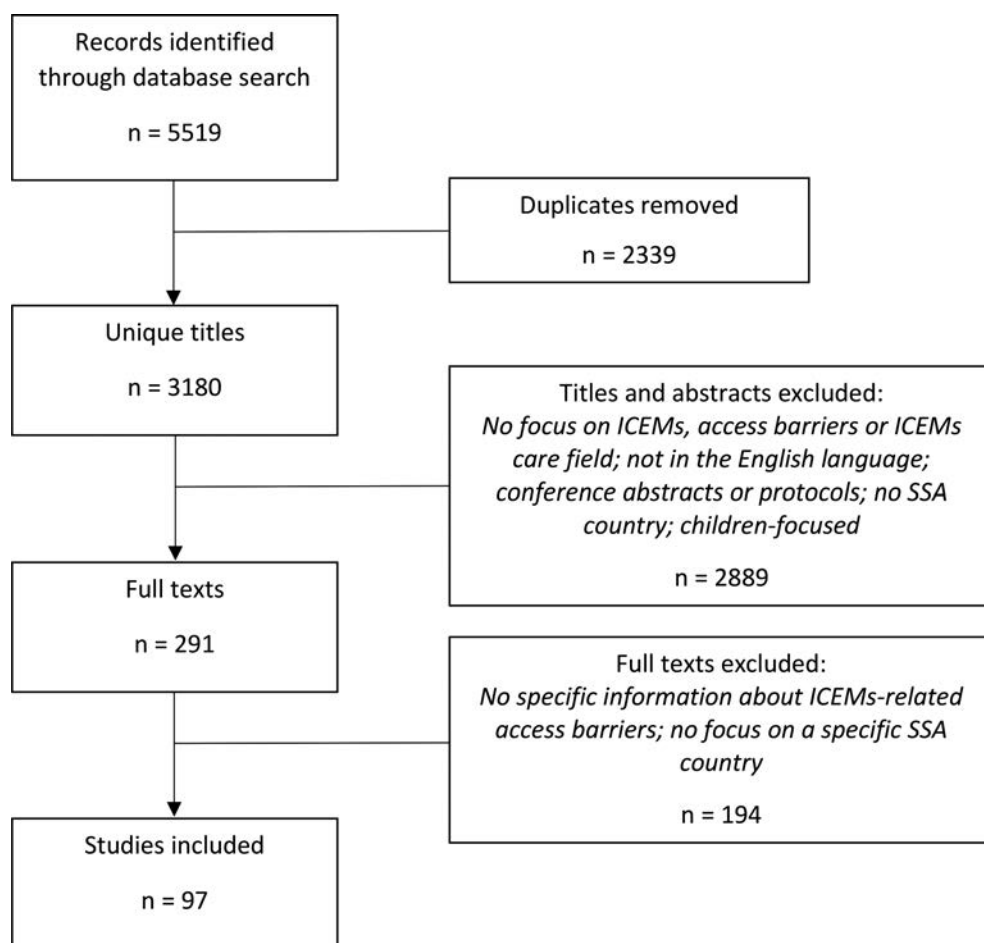
Figure 1. PRISMA-ScR article selection process.

Twenty-four studies were carried out in multiple countries, while 74 studies concerned country-specific research. These studies were carried out in Kenya (n=10), Ethiopia (n=9), Tanzania (n=8), Uganda (n=8), South Africa (n=6), Ghana (n=4), Madagascar (n=4), Nigeria (n=4), Liberia (n=3), Botswana (n=2), Mozambique (n=2), Rwanda (n=2), Sierra Leone (n=2), Zimbabwe (n=2), and single studies from the Democratic Republic of the Congo (DRC), Eritrea, Eswatini, Malawi, Senegal, Somalia and Zambia. Studies covered all healthcare fields, including pain and palliative care (n=45), anaesthesia (n=19), epilepsy (n=11), OAT (n=7), mental health (n=3), obstetric care (n=3), ICEMs in general or multiple healthcare fields (n=8), and non-medical use of ICEMs (n=1). An overview of the barriers to access to ICEMs in SSA is given in **Figure 2**.
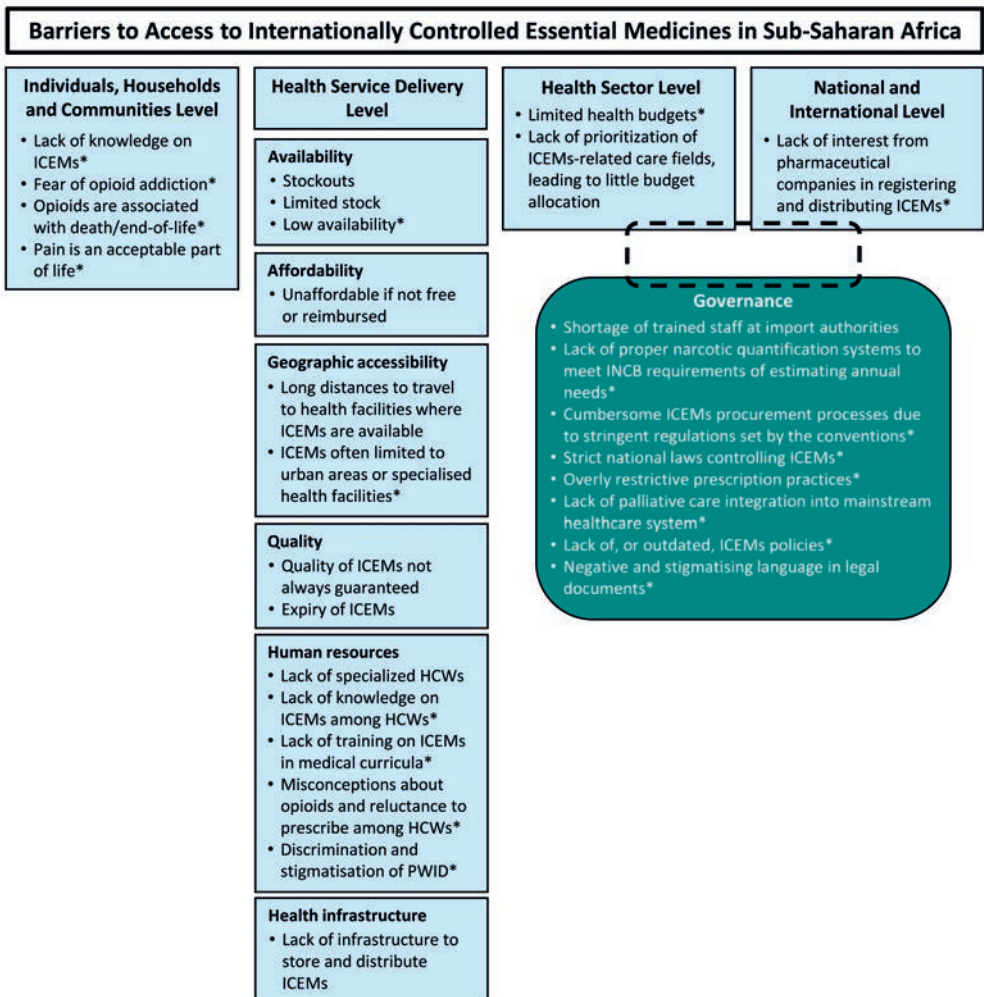
Figure 2. Barriers influencing access to internationally controlled essential medicines in Sub-Saharan Africa. *: ICEMs-specific barrier.

Individuals, households and community

Examination of included studies indicates that at the individuals, households and community level, access to ICEMs was influenced by multiple factors. Public knowledge about ICEMs and related healthcare fields was commonly reported to be lacking. For instance, knowledge about causes and treatment of epilepsy and mental disorders was often minimal, with people believing epilepsy to be incurable, contagious or caused by supernatural forces (12,25-28), and being sceptical about the efficacy of anti-epileptic medication such as phenobarbital (25). However, having positive experiences with anti-epileptic medication increased their acceptability, both at the individual (12,25) and community level (12). Similarly, lack of knowledge about palliative care was commonly reported (16,29). A number of studies also reported patients feared becoming addicted to opioids (28,30–32), and associated them with death because patients with end-stage diseases are the ones who commonly receive them (28,33). In Kenya, for example, 29% of surveyed religious leaders believed that use of opioids hastened death, and 8% believed the use of opioids to alleviate a patient's pain was morally the same as killing a patient (34). It was also reported that in some SSA countries it was discouraged to complain or talk about pain, as some level of pain is believed to be acceptable (32,35).

In the case of OAT, one paper that specifically looked at women in Tanzania found that enrolment for women was negatively influenced by being in a violent relationship and having a partner who was also using drugs; 83% of surveyed women who were injecting drugs who were not enrolled in an OAT programme, were in a relationship deemed to be violent (36). Conversely, studies indicated that in Kenya, for both men and women, the financial, emotional and psychosocial support of family facilitated continued OAT enrolment (37,38).

Health service delivery

At the health service delivery level, access to ICEMs was influenced by their availability, affordability, geographical accessibility, quality, human resources, and health infrastructure, including weak supply chains.

Availability

As shown in **Table 2**, a large number of studies reported that availability of ICEMs remains problematic in SSA as they were often unavailable or stocked out (14,16,40–49,17,50–59,18,60–65,26–28,30,32,39). In Zambia and Madagascar, for instance, phenobarbital was available at only 20% and 36% of surveyed pharmacies, respectively (18,58). In a survey among 109 physicians from across SSA, 49% indicated they did not have access to liquid opioids (66). In Eswatini, morphine was not available at health centres; patients had to be referred to a higher-level facility (55). Only one government facility in Nigeria and Cameroon stocked oral morphine in 2018 (35), and 50% of nurses in Eritrea indicated that lack of opioids was a barrier to access (67). Stockouts were a problem in Zambia, where 45% of

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Table 2. Availability of internationally controlled essential medicines, per country.

Country	Availability (%)										
	Codeine	Diazepam	Ephedrine	Ergometrine	Fentanyl	Lorazepam	Methadone	Midazolam	Morphine	Oxycodone	Phenobarbital
Ethiopia (101–103)		33, 82[a], 90[b]						90[b]	27, 63[a]		
Kenya (104)									25		
Liberia (105,106)		26[c], 92			12	26[c]		12	35		26[c]
Madagascar (107,108)		90	81					5	38		36
Malawi (109)		78							9		
Mozambique (110)		75						4			
Sierra Leone (111)		85		80	15			30	45		63
Tanzania (112)		91									
Uganda (113,114)		55		18					70[d]		
Zambia (115,116)	36				9		9			9	20

ICEMs: Internationally Controlled Essential Medicines.

[a]Availability of benzodiazepines in general.

[b]Availability of either diazepam or midazolam.

[c]Availability of psychotropic medicines in general.

[d]Availability of opioids in general.

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surveyed hospitals indicated that morphine had been stocked out for at least 90 days (68). In Zimbabwe 22% of surveyed healthcare workers (HCWs) indicated opioids had been stocked out in the last three months (69). Methadone for OAT was also unavailable in many countries (28,43,70). For instance, in Tanzania while a publicly-funded OAT program exists, access is very limited (43).

Studies reported that an inconsistent availability of ICEMs forced patients to switch to alternative medications, go without until a new supply arrived, or buy them from private suppliers (25,41,70). Further, even when ICEMs were available, stock was often limited. For instance, when phenobarbital was available in Madagascar, pharmacies only stocked one to two boxes of it, and the phenobarbital prescribed often covered only 7 days of treatment (58,71). The inconsistent availability of ICEMs impacted treatment adherence; patients were more likely to discontinue their treatment due to unavailability of their medications (26).

Numerous studies demonstrate that some countries did reach the WHO benchmark of at least 80% availability for some ICEMs, as can be seen in **Table 2** (61–65,72–75). However, often availability differed depending on health facility level. In Mozambique, for example, diazepam was available at 55% of surveyed rural facilities, and at 83% of more specialised rural facilities (64). In 2014, morphine was not available in any surveyed clinics or health centres in Kenya, but it was available in all surveyed secondary hospitals (47). In Malawi, opioids were available at 31% of all hospitals, but only 2% of lower level health facilities (those not defined as hospitals nor routinely providing in-patient care) (74).

Affordability

In some SSA countries ICEMs were provided free of charge in the public sector (28,29,31,40,41,51,76). In Ethiopia for instance, patients' medication fees were waived if they were in possession of a fee waiver card, which was available to the poorest in the population (12), and in Kenya, Malawi and Uganda, morphine was available free of charge to patients (29,31,77). In some countries insurance schemes are being rolled out, which cover healthcare costs such as medication purchases (12). However, reimbursement of health facilities through such insurance schemes is not without problems, resulting in stockouts, and patients still resorting to the private sector for their medicines, where affordability was an issue (14,16,76,78,79,25,26,28,32,41,48,58,70).

Phenobarbital is the cheapest treatment option available for epilepsy in SSA, and can cost as little as USD 10 per year (12,13). In Madagascar, a 30-day treatment of phenobarbital nevertheless can cost a patient more than 10% of their monthly salary, while a box of phenobarbital can cost more than USD 20 in the DRC (25,71). Further, research conducted by Mbuba et al. (2012) indicated that even when the ICEM itself was affordable, indirect costs such as those for transportation to the health facility could make it unaffordable. Unaffordability of

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ICEMs can lead to treatment discontinuation in the case of epilepsy (25,76): in Rwanda, 74% of patients indicated they discontinued treatment due to financial reasons (18). Similar problems were reported when seeking pain management (35). In Zimbabwe, 76% of surveyed HCWs indicated that most patients had to buy their opioids themselves (69).

In the case of OAT, methadone and buprenorphine are, as of 2020, not reimbursed in South Africa as they are not included on the national EML, meaning patients have to pay out-of-pocket (70,81). This makes it unaffordable to a significant part of the population, especially since OAT is almost 30 times more expensive in South Africa than other middle-income countries, such as Georgia and the Ukraine (82).

Geographical accessibility
Distance to health facilities or pharmacies where ICEMs were available was a repeatedly cited barrier (14,27,51). In Ethiopia and Nigeria about half of surveyed patients discontinued their treatment with phenobarbital within a year, with the most commonly given reason being difficulty travelling to the health facilities (27). Another study found that in 14 of 20 SSA countries, accessing a pharmacy that dispensed opioids was difficult (51), and a scoping review found that only about 20% of SSA countries provided palliative care in primary healthcare settings (16). In the DRC, Equatorial Guinea and Madagascar there was only one hospice or palliative care service, serving populations of more than 92 million, 1.4 million and 28 million, respectively (16,83). Research also showed that in many countries, accessing ICEMs in rural areas is even more problematic (84). In Ghana, accessing morphine outside a hospital is difficult (48), and in South Africa, Tanzania, Zambia and Zimbabwe, morphine availability was limited to the bigger cities (31,33).

In South Africa, for 32% of patients in one study who had successfully accessed OAT, it had been difficult to find a doctor who could provide the treatment (81). Forty-eight percent indicated they would have started OAT earlier if there had been better treatment availability and if more information about it was available (81). However, an evaluation of an OAT programme in Durban showed that once people who inject drugs (PWID) were enrolled in the programme, retention at 12 months was high (74%) (70). Multiple studies show that in Kenya, OAT clinics had fixed opening hours and clients had to visit the clinic each day for their methadone dose, which was a barrier to clients due to the distance, transportation costs, as well as the loss of income due to the daily visits (37,38). Fixed clinic hours were reported as a barrier to women engaged in sex work, who worked at night and therefore had difficulty accessing the clinics in the morning (38).

Quality
A number of studies indicated that ICEMs bought on both the licit and illicit market did not always meet quality standards (27,48). In Madagascar 18% of phenobarbital samples bought at

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a pharmacy did not meet quality standards, nor did the diazepam bought on the illicit market (71). All 15 ergometrine injections bought by researchers in Tanzania, and all 55 injections bought in Ghana, from both public and private pharmacies, did not meet quality standards (85,86). Further, some facilities faced expired ICEMs (41,87). In Ghana, HCWs explained expired medicines were a consequence of HCWs not prescribing psychotropic medicines, or medicines from donor agencies being near expiry when they were received (41).

Human resources

One cross-cutting issue for the ICEM-related healthcare fields reported in a large number of studies was the lack of appropriately trained HCWs (15,16,46,65,67,75,77,88–92,26,93–99,27–29,33,42,44,45). In Liberia for instance, the anaesthesiologist and nurse anaesthesiologist workforce densities are 0.02 and 1.56 per 100,000 population, respectively (62). The shortage of appropriately trained HCWs is especially common in rural areas, where there are few specialised doctors (14,27,28,42,46). In Mozambique, 77% of anaesthesiologists work in Maputo, where only 5% of Mozambique's population lives (46). In Kilifi County, Kenya, only mental health nurses, social workers and occupational therapists were available at mental health outpatient facilities, and were not allowed to prescribe psychotropic medicines (42). Indeed, a number of studies indicated that many HCWs across SSA lacked the knowledge and skills to properly treat patients. Instead, healthcare was provided by untrained or undertrained HCWs (26,27,100,32,35,45,50,89,91,94,95).

One study showed that in Botswana, nurses felt like they lacked the knowledge and training to be able to advocate for prescription of opioids in outpatient settings (97). In Eritrea, a knowledge-attitude survey found that almost 60% of nurses had answered less than 50% of the questions on opioids correctly (67). In Nigeria only 24% of surveyed physicians had received more than 2 hours of training on pain management at undergraduate level, 92% of surveyed HCWs had not received any formal training on pain management, and 51% indicated they only treated pain when patients complained (101,102).

Multiple studies indicated that the lack of appropriately trained HCWs was fuelled by the lack of training opportunities within countries (103,104). Uganda did not have a neurology specialty within their medicine curriculum, while Mozambique had no formal exposure to anaesthesiology within the curriculum (26,46). In 2017, a review of palliative care education in 13 African countries found that only Kenya, South Africa, Uganda and Tanzania provided postgraduate education in palliative care (17). In Ethiopia, HCWs and hospital officials indicated pain was neglected in undergraduate medical education, and 71% of surveyed health facilities also rarely or never provided HCWs with continuous professional development and medical education (32,65). Studies also indicated that some countries did include palliative care in educational curricula. In Botswana, palliative care is included in 90% of medical and nursing education (53). In Sierra Leone, 86% of surveyed nurse anaesthesiologists had attended training (92).

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Even when HCWs had received training on ICEMs, oftentimes the addictive qualities of the medicines were overemphasised (28). Relatedly, misconceptions about palliative care and a reluctance to prescribe opioids because of opiophobia, fear of addiction or side effects, and lack of knowledge how to handle it, existed in many countries (15,16,88,97,99,101,105–108,30–32,35,49,50,77,87). In Kenya, 96% of surveyed HCWs believed opioids cause addiction (106), and Kenyan nurses at a tertiary hospital admitted they adjusted opioid doses or substituted them for weaker analgesics (50). Among surveyed Ethiopian nurses in one study, 82% believed drug addiction to be a major problem in patients who use morphine long term (107), and 70% believed that elderly patients cannot tolerate opioids and that patients should be withheld opioids for as long as possible (100). In Nigeria, 70% of surveyed physicians who treat patients with moderate to severe pain reported having rarely or never prescribed opioids, with the most common reasons being fear of respiratory depression (87%) and fear of addiction (85%) (102). Interestingly, 85% of surveyed Nigerian pharmacists did not believe that long-term use of opioids often induced addiction in patients (109). Some HCWs in Kenya also believed that the use of opioids accelerated death (50,106). HCWs in Uganda also reported a reluctance to discuss end-of-life care (98).

Some research also indicated many HCWs did feel confident about their knowledge of opioids and their prescription. In Uganda for example, 100% of doctors interviewed at the Uganda cancer institute reported they felt confident prescribing opioids, and 80% reported they felt confident in symptom assessment and management (98). In South Africa, even though 91% of surveyed pharmacists indicated they had a lack of training about opioids, 81% reported they felt comfortable providing pain management to patients, and 71% and 62%, respectively, reported they had good knowledge and a positive attitude regarding palliative care and opioids (110). A scoping review of 47 African countries found that Kenya, Uganda and Zambia had a broad awareness of palliative care among HCWs (16).

Lastly, in the case of OAT, some studies indicated that PWID were often discriminated against by HCWs in general healthcare settings, making them distrustful of formal healthcare, and forming barriers to receiving OAT (36,43).

Health infrastructure

Examination of included studies indicates that many countries in SSA had a lack of infrastructure to properly store and distribute opioids (16,77,99). In Uganda for instance, health facilities must be accredited to provide morphine, with an accreditation requirement including the presence of an eligible prescriber and a safe storage location. Consequently, less than 50% of facilities are accredited to provide palliative care services (29). In some countries distribution of opioids is centrally controlled by the government, limiting non-medical use but also the availability for medical use (79).

Health sector level

Findings from multiple studies indicate that in many SSA countries, governments have limited budgets that cannot cover all the healthcare needs of their populations. Infectious diseases are often prioritised, resulting in little budgetary allocation and attention from policy makers to chronic non-communicable diseases, anaesthesia or palliative care (14,15,78,103,111,16,27–30,67,75,77). In Ghana, HCWs surveyed in one study believed lack of government funding was part of the reason why shortages of psychotropic medications occurred (41). In many SSA countries, palliative care is still largely funded by international aid, making it sensitive to fluctuations in donor priorities (17,87,111). Similarly, in South Africa, OAT is largely financed by donor agencies (82).

National and international level

A number of studies also indicated that in many SSA countries, the potential profits pharmaceutical companies and suppliers can make are low due to the low price of the medicine relative to the cumbersome process and high registration costs, making it unattractive to register their products (35,77,112). In Zimbabwe for example, ephedrine was not available due to this reason (112).

Governance

Analysis of included studies indicates that some of the main barriers to accessing ICEMs are related to governance, which cuts across the health sector level, national level and international level. How 'governance' impacts on access to ICEMs is explained in more detail below.

International conventions

Review of the literature indicates that many SSA countries struggled to meet the requirements set out in the international drug control conventions. As per the Single Convention on Narcotic Drugs, 1961, countries need to submit their annual needs for narcotics to the INCB (United Nations, 1972). However, many countries did not have a system to properly document the use of and need for narcotics, resulting in the quantifications being based on invalid estimates (14,28,77,113). In Kenya, for example, the average reported consumption from 2009-2011 was 26.7 kg, which would have provided morphine to 4300 patients, even though it was estimated that 92,000 patients were in need (29). Further, in 2018, only 11 of 24 countries in West and Central Africa submitted estimates (103). In Mozambique, mandatory reporting was a challenge as there had been no staff with technical expertise for at least five years (14). When a country exceeds its submitted estimates, a request can be made by the country to the INCB for additional narcotics. However, oftentimes this is not done, or only after a long period of time (113).

Relatedly, wholesalers and procurers reported that the international conventions functioned as a barrier due to the requirements that needed to be met before ICEMs could be procured

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(15,77,113). In a study from Ghana, for example, HCWs referred to the cumbersome procurement process for psychotropic medicines as a reason for shortages, stating they led to delays in medicine delivery of up to two years (41). Similarly, cumbersome requirements to import ICEMs in Uganda were said to deter some wholesalers from importing them (113). For phenobarbital, the border regulations due to its controlled status were also reported as a barrier to their import (18). Further, another study found that in 2019 the only available opioid in Nigeria was pentazocine due to the strict national laws controlling narcotic medicines (114). Similarly, another study reported healthcare and relief organisations tend to use non-controlled medicines instead of ICEMs due to the challenges faced with importing controlled substances (113).

A number of studies indicated that a shortage of staff at import authorities, and their lack of training on how to properly issue import authorisations also impeded access to ICEMs, resulting in long import times due to delayed or erroneous authorisations (28,103,113). Moreover, a recent study reported that generally, it took three to twelve months to obtain the export and import authorizations in LMICs in SSA (113).

Regulatory practices

A number of studies reported overly restrictive prescription practices were common in many SSA countries (14,15,53,56,67,99,108,17,28,30,31,35,42,51,52). In Botswana, Kenya, Malawi and Nigeria only doctors were allowed to prescribe psychotropic medicines (35,42,79). HCWs in Uganda reported difficulties prescribing opioids as they needed additional documentation books, special licenses to prescribe opioids, and feared losing their licenses if errors were found in their prescription behaviour (28). Similarly, Cleary et al. (2013) found that of 20 SSA countries studied, 18 had restrictive laws for opioid prescribing, which included special prescription forms (11 countries) or the need for duplicate or triplicate forms (13 countries), with these forms not being readily accessible in many countries (51). In Tanzania HCWs described difficulties in obtaining a license for opioid prescribing (30). In Senegal, only 5% of doctors had the prescription pad necessary to prescribe opioids (54). In eight of 20 studied countries opioids could be dispensed for only a few days at a time, ranging from 2 days in Ghana to 14 days in Malawi (51). Forty-eight percent of nurses in Eritrea indicated that the strict opioid regulations were a barrier (67). HCWs, even when permitted to do so, were also afraid to prescribe opioids due to the lack of legal protection or fear of legal sanctions within their country (15,32,87). In Eswatini, Mozambique, and Zimbabwe, stakeholders reported inclinations towards stringent storage and prescription regulations for ICEMs (14).

The literature shows that not all countries adhered to the stricter regulation of dispensing ICEMs. In Mozambique, diazepam could be prescribed by a community health worker, and phenobarbital by a medical technician (64). In Sierra Leone benzodiazepines were also provided by unauthorised HCWs (61). In Tanzania, 70% of surveyed pharmacies dispensed

diazepam without requesting to see a prescription, opening the door for non-medical use (72). In Uganda, 21% and 41% of surveyed pharmacies, respectively, sold phenobarbital and diazepam without a prescription, and 41% sold codeine without a prescription (115). Further, only 23% of these facilities complied to stock control requirements, such as having a controlled drugs prescription book to record sales; batch numbers of dispensed drugs and contact details of patients; dedicated files for archiving copies of opioid and psychotropic prescriptions (115). Similarly, a lack of up-to-date record keeping for psychotropic medicines was found in health facilities in Kenya (42).

Policies

A number of policy-related barriers to ICEMs access were found in the surveyed literature. In Somalia, only 29% and 7% of surveyed health facilities had guidelines for anaesthesia or pain relief available (91). In most SSA countries, palliative care was poorly integrated into the mainstream healthcare system (16,29,103). At the Uganda cancer institute, doctors reported that working together was more of a challenge than a benefit due to the challenges in coordinating care (98). Further, it was reported in multiple studies that many SSA countries had a lack of guidelines for pain assessment and management (32,55,67,103) and that often, policies and legislation were outdated (77). Similarly, two studies reported that policies on palliative care or pain management, including the use of pain rating scales, were often lacking or unknown to HCWs in Ethiopia and Eswatini (32,55). In 14 of 20 studied countries, laws regarding opioids contained negative or stigmatizing language (51). Moreover, some studies highlighted that often, coexisting goals of improving access to ICEMs for medical use and preventing illicit use were not balanced (14,15). For instance, in South Africa, methadone and buprenorphine were not listed as medicines for OAT on the country's EML (14,70).

DISCUSSION

This scoping review presents an overview of the barriers to accessing ICEMs in SSA. The literature showed that many barriers to access exist and are common across the ICEMs drug class. While some barriers were specific to ICEMs, others were observed for non-controlled medicines as well. ICEM-specific barriers observed at the individuals, households and community level were: the lack of public knowledge about ICEMs; fear of opioid addiction; the association of opioids with death; and cultural acceptability of some level of pain in life. Barriers influencing access to both ICEMs and other medicines observed at the health service delivery level included stockouts, unaffordability, long distances to reach health facilities, medicine quality, lack of specialised HCWs, and a lack of infrastructure to store and distribute medicines. Low availability, an issue also experienced across other medicine groups, was exacerbated by the controlled status of ICEMs. Other ICEM-specific barriers were lack of knowledge and training on ICEMs among HCWs, which caused misconceptions about the medicines, and discrimination and stigmatisation of PWID specifically. At the health sector level, there was a lack of prioritisation of ICEM-related healthcare fields, and due to

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the limited health budgets available in most of SSA, this led to low budget allocation to these healthcare fields. This is also an issue for other healthcare fields, and not limited to only ICEMs. At the national and international level, there was a lack of interest in ICEMs from pharmaceutical companies due to the cumbersome regulations and low profit margins for ICEMs in SSA markets. Cross-cutting governance-related barriers were mainly ICEMs-specific and pertained to: lack of proper quantification systems; cumbersome procurement processes due to the regulations set by international drug control conventions; strict national laws controlling ICEMs leading to overly restrictive prescription practices; and negative and stigmatising language in legal documents.

While many of the access barriers identified in this review were applicable across all ICEMs, the following were specific to opioids: the fear among HCWs and the community of the addictive quality of opioids; the requirement for national estimates of medical need for opioids as stipulated by the Single Convention on Narcotic Drugs, 1961 (United Nations, 1972). For the use of methadone and buprenorphine in OAT, a specific barrier is that PWID are discriminated against when seeking healthcare, which becomes a barrier to accessing ICEMs.

Based on this review, recommendations have been formulated to improve access to ICEMs in SSA, which are detailed below (see **Figure 3**). Misconceptions and lack of knowledge on ICEMs and the diseases they treat was found to be an important barrier at the individuals, households and community level. To assuage this, community-based sensitisation and public education programmes are needed. A pre- and post-intervention study in Japan, evaluating a community intervention programme providing educational materials such as flyers, posters, booklets and public lectures, showed for example, that overall perceptions of palliative care and opioids improved significantly among both the general public and family members of patients with cancer (116). In a similar study completed in Saudi Arabia on epilepsy, significant improvements were found in the attitudes of the general public towards epilepsy and PLWE after an educational awareness campaign (117).

Many of the barriers identified at the health service delivery level in this study are barriers that are not confined to ICEMs and should be viewed in the larger context of the weak health systems found in much of SSA. For instance, the unaffordability of medicines is a systems-wide problem, with many of the medicines found on the national EMLs unaffordable when they are not available in the public sector, or not reimbursed (118–121). Rolling out reimbursement programmes, such as national health insurance schemes, which include ICEMs in their coverage package, might be a way to tackle affordability issues if the schemes are properly functioning and managed (122,123).

Similarly, a lack of (specialised) HCWs is a region-wide problem: there are 0.2 physicians and 1.0 nurses and midwives per 1,000 people in SSA, which is below the WHO threshold of

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4.45 HCWs needed to achieve universal health coverage (124–126). The inadequate health workforce in the region is caused by a multitude of factors, including insufficient training capacity, migration of HCWs across continents, governance issues, poor health workforce retention, morbidity and mortality among HCWs, poor planning and limited funding, making it a complex issue (127). Further, as found in this review, there is an inequitable distribution of the health workforce, with the workforce skewed towards urban settings. This forces rural-dwelling patients to travel long distances to access medicines, especially those that are found only at more specialised health facilities. The WHO recommends a task-shifting approach as one of the tools to be used to tackle human resource issues. Task-shifting entails transferring tasks to other cadres of HCWs with less experience, or delegating certain tasks to HCWs who receive training to obtain specific skills (128). Since nurses are one of the main cadres of the health workforce, allowing nurses to prescribe ICEMs would potentially increase accessibility of ICEMs. Uganda, for example, was the first country to introduce nurse-prescribing laws, allowing nurses and clinical officers to prescribe opioids independently after completing a nine-month training course, increasing access especially in rural areas (29,87,129,130). By 2013, Kenya, Sierra Leone and Tanzania had also introduced nurse-prescribing with a special permit (51). Nurse-prescribing programmes for epilepsy and mental health, along the lines of the opioid nurse-prescribing programme, can be a successful strategy to also increase accessibility to services for PLWE and people living with a mental disorder. In the United Kingdom, an epilepsy nurse specialist programme, in which nurses were allowed to prescribe anti-epileptics, increased access to services and medications (131).

However, this review also showed that in the existing health workforce, a lack of knowledge about ICEMs, and subsequent negative misconceptions, were common and impeded access. This is in line with an INCB study, which found that, according to Member States, one of the most common impediments to accessing ICEMs was lack of HCW training and awareness about ICEMs (7). Therefore, in order to properly train and prepare both their existing and future health workforces on ICEMs and related healthcare fields, governments should focus their efforts on in-service training and medical education, and the better inclusion of ICEMs and related healthcare fields in medical curricula.

Essential medicines regularly do not reach the 80% WHO availability benchmark in many SSA countries (119–121,132). However, the controlled status of ICEMs generally leads to a significantly lower availability when compared to other essential medicines (58,62,63,65,74). In Sierra Leone for example, morphine and fentanyl were shown to have an availability of 45% and 15%, respectively, while ketamine (anaesthesia) and tramadol (pain management), both non-controlled medicines, were reported to have an availability of over 90% (61). Availability of ICEMs is also impacted by stockouts. Stockouts of medicines are a global issue, and shortages have been increasing over recent years in high-income countries and

Recommendations to Improve Access to ICEMs in Sub-Saharan Africa

Individuals, Households and Community Level
- Community-based sensitisation and public education programmes

Health Service Delivery Level
- Reimbursement programmes (e.g., national health insurance schemes)
- Task-shifting of prescribing of ICEMs to other cadres of HCWs
- In-services HCW training and continued medical training
- Supply chain strengthening

Health Sector Level
- Increase budgetary allocation to ICEMs-related care fields
- Improve integration of mental health, epilepsy and palliative care services into primary healthcare

National and International Level
- WHO and INCB, together with patients, civil society organisations and drug policy experts should develop new, international guidelines on the use of opioids for pain and palliative care

Governance
- Implement national systems to track populations' health needs to enable proper estimation of ICEMs needs
- Technical support from INCB to enable countries to comply to Conventions' requirements without having overly restrictive regulatory processes
- Review ICEMs policies to ensure a balance between protection from non-medical use, and access for medical use

Figure 3. Recommendations to improve access to internationally controlled essential medicines in Sub-Saharan Africa. HCW: healthcare worker; ICEMS: Internationally Controlled Essential Medicines; INCB: International Narcotics Control Board; SSA: WHO: World Health Organization.

LMICs (133). Again, shortages are both a systems-wide issue, as well as exacerbated by the controlled status of the medicines. So, while strengthening the supply chain in general might increase the availability of ICEMs, to significantly increase their availability, targeted action needs to be taken.

One of the ICEM-specific barriers exacerbating availability and stockout issues is related to the requirement that countries need to annually quantify and predict the amount of narcotic drugs their population will need, which many SSA countries are poorly equipped to do. Governments should put systems in place that track the needs of their population so sufficient estimates can be sent to the INCB. Further, this review also revealed that stringent import and procurement regulations hampered access to all ICEMs, as it demotivated manufacturers and wholesalers to import them. The INCB has an important role, and some would argue a responsibility, to support countries to meet the Single Convention on Narcotic Drugs, 1961 requirements (United Nations, 1972). In 2012, at the request of the Commission on Narcotic Drugs, and recognizing the additional workload of national competent authorities due to the regulations set by the international drug control conventions, the INCB developed an electronic management tool, the International Import and Export Authorization System (I2ES), which countries can use to monitor and manage the import and export of controlled

medicines more easily (134,135). Nevertheless, many SSA countries are still under-resourced, and more technical support from the INCB is needed to ensure better accessibility of ICEMs.

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In many SSA countries, HCWs fear legal sanctions due to the stringent laws on prescribing and handling of ICEMs, and subsequent disproportionately serious penalties for errors or mishandling. Similarly, a 2014 INCB report showed that in 81 countries, penalties for inadequate recordkeeping of ICEMs ranged from fines to license revocation and prison sentences (136). Governments should, guided by drug policy experts, civil society and HCWs, review their policies on ICEMs prescribing and handling, to ensure that while laws protect against diversion, they are not overly stringent and criminalise prescribers.

At the health sector level, mental health, epilepsy and palliative care are often underfunded and lack prioritisation. Governments should increase their budgetary allocation to the ICEMs-related healthcare fields. Better integration of mental health, epilepsy and palliative care services into primary healthcare is also recommended to decrease accessibility barriers, especially in rural locations where specialised health care is not easily accessed.

At the international level, clear guidance on the use of opioids is lacking. In 2011 the WHO published guidelines to this extent, titled "Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines". However, these were retracted in 2019, and until now, no new guidelines have been published to replace them (10). The WHO and INCB should, together with patients, civil society organisations and drug policy experts, develop new guidelines that can help governments and policy makers navigate the international regulations and safety concerns surrounding opioids so they can offer the best health care available to those in need.

Strengths and limitations

This is the first review that studied barriers to access to all ICEMs in SSA, and not only of one specific drug group or healthcare field. This review included both quantitative and qualitative studies, and due to the broad inclusion criteria, a large number of studies could be included, creating a detailed overview of the barriers found in SSA. However, some limitations of this study should also be noted. The majority of the articles found during the literature search pertained to palliative care and anaesthesia, while much less information was found on ICEMs used for epilepsy, mental health and OAT. This indicates a lack of research in these healthcare fields, implying future research ought to focus specifically on accessibility of ICEMs for these specific healthcare fields. Also, many SSA countries are not represented in this literature review as no literature was found about these countries. This gap in the literature is alarming since it may indicate an overall lack of attention to issues related to ICEMs accessibility in these countries. Further, since the literature search included articles over a 10-year period, some data might be outdated if recent studies had not been conducted in that location. Grey literature, such as reports from the WHO or INCB, were not included

in the search, which might have led to some information being missed. In this review only articles in the English language were included. Since this is a scoping review, and the high number of included studies included a broad range of study designs and methodologies (quantitative and qualitative studies, mixed-methods studies, expert pieces and reviews, as well as programme evaluations, simulated client visits and health system assessments), it was not possible to apply standardised quality assessment criteria across all studies. Last, literature was searched in four international databases, but not in Africa-specific databases. However, due to the range of included journals in the international databases, as well as snowball sampling that was used, we believe most of the relevant literature on access to ICEMs in SSA has been covered by this review.

CONCLUSION

This review showed that there are a multitude of barriers to accessing ICEMs in SSA across all health system levels. It further showed that while there are many barriers that are specific to ICEMs, access is also hampered by barriers that are generally encountered for all types of medicines. However, often the controlled status of the ICEMs exacerbates the situation. Further, many of the barriers identified in this review are applicable to all ICEMs, highlighting the importance of tackling barriers to access for this entire class of drugs together. Thus, to improve access to ICEMs in SSA, a multi-pronged strategy is needed for the entire class of ICEMs, consisting of community sensitisation and health system strengthening targeted at the health service delivery level, the health sector level, and governance at the national and international level.

CONTRIBUTION STATEMENT

GIO, HAvdH, AKM and TR designed the study. GIO and JvO collected and analysed the data, and GIO wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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2.1

SUPPLEMENTARY DATA

Supplementary File 1. Search strategy

1 Pubmed

2.1

(((("africa south of the sahara"[MeSH Terms] OR ("africa"[All Fields] AND "south"[All Fields] AND "sahara"[All Fields]) OR "africa south of the sahara"[All Fields] OR ("sub"[All Fields] AND "saharan"[All Fields] AND "africa"[All Fields]) OR "sub saharan africa"[All Fields])) OR ("sub Saharan Africa" OR "Africa" OR "Sudan" OR "Angola" OR "Benin" OR "Botswana" OR "Burundi" OR "Congo" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Guinea" OR "Guinea-Bissau" "Gabon" OR "Kenya" OR "Nigeria" OR "Rwanda" OR "Sao Tome" OR "Tanzania" OR "Uganda" OR "Djibouti" OR "Eritrea" OR "Equatorial Guinea" OR "Ethiopia" OR "Somalia" OR "Comoros" OR "Lesotho" OR "Madagascar" OR "Malawi" OR "Mauritius" OR "Mozambique" OR "Namibia" OR "Reunion" OR "Seychelles" OR "Swaziland" OR "Zambia" OR "Mali" OR "Burkina Faso" OR "Cape Verde" OR "ivory coast" OR "Gambia" OR "Ghana" OR "Zimbabwe" OR "Liberia" OR "Mauritania" OR "Niger" OR "Senegal" OR "Sierra Leone" OR "Togo" OR "South Africa" OR "Cote d'Ivoire" OR "Eswatini"))

AND

(("treatment gap" OR "barriers" OR "challenges" OR "access" OR "availability" OR "accessibility" OR "affordability" OR "price" OR "drug control" OR "drug policy" OR (("Drug and Narcotic Control"[Mesh]) OR "Health Services Accessibility"[Mesh])))

AND

(("controlled drugs" OR "controlled medicines" OR "controlled substances" OR "codeine" OR "diazepam" OR "fentanyl" OR "hydromorphone" OR "methadone" OR "midazolam" OR "morphine" OR "oxycodone" OR "buprenorphine" OR "lorazepam" OR "phenobarbital" OR "ephedrine" OR "ergometrine" OR "methylergometrine" OR "anesthesia" OR "anaesthesia" OR "anticonvulsant" OR "anxiety disorders" OR "management of cancer pain" OR "opioid agonist treatment" OR "opioid substitution therapy" OR "harm reduction" OR "opioids" OR "opioid" OR "oxytocic" OR "pain and palliative care" OR "pain care" OR "palliative care" OR "pain treatment" OR "psychotropic substances" OR ((((((("Pain Management"[Mesh]) OR "Analgesics, Opioid"[Mesh]) OR "Controlled Substances"[Mesh]) OR "Palliative Care"[Mesh]) OR "Psychotropic Drugs"[Mesh]) OR "Anticonvulsants"[Mesh]) OR "Analgesia"[Mesh]) OR "Benzodiazepines"[Mesh]) OR "psychotropic medicines" OR "analgesia" OR "epilepsy" OR "antiepileptic"))

AND

(("2012/01/01"[Date - Publication] : "3000"[Date - Publication]))

2 Embase

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"Comoros" OR "Lesotho" OR "Madagascar" OR "Malawi" OR "Mauritius" OR "Mozambique" OR "Namibia" OR "Reunion" OR "Seychelles" OR "Swaziland" OR "Zambia" OR "Mali" OR "Burkina Faso" OR "Cape Verde" OR "ivory coast" OR "Gambia" OR "Ghana" OR "Zimbabwe" OR "Liberia" OR "Mauritania" OR "Niger" OR "Senegal" OR "Sierra Leone" OR "Togo" OR "South Africa" OR "Cote d'Ivoire" OR "Eswatini")

AND

("treatment gap" OR "barriers" OR "challenges" OR "access" OR "availability" OR "accessibility" OR "affordability" OR "price" OR "drug control" OR "drug policy" OR "Drug and Narcotic Control" OR "Health Services Accessibility")

AND

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AND

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3 Web of Science

(ABSTRACT ("sub Saharan Africa" OR "Africa" OR "Sudan" OR "Angola" OR "Benin" OR "Botswana" OR "Burundi" OR "Congo" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Guinea" OR "Guinea-Bissau" "Gabon" OR "Kenya" OR "Nigeria" OR "Rwanda" OR "Sao Tome" OR "Tanzania" OR "Uganda" OR "Djibouti" OR "Eritrea" OR "Equatorial Guinea" OR "Ethiopia" OR "Somalia" OR "Comoros" OR "Lesotho" OR "Madagascar" OR "Malawi" OR "Mauritius" OR "Mozambique" OR "Namibia" OR "Reunion" OR "Seychelles" OR "Swaziland" OR "Zambia" OR "Mali" OR "Burkina Faso" OR "Cape Verde" OR "ivory coast" OR "Gambia" OR "Ghana" OR "Zimbabwe" OR "Liberia" OR "Mauritania" OR "Niger" OR "Senegal" OR "Sierra Leone" OR "Togo OR "South Africa" OR "Cote d'Ivoire" OR "Eswatini"")

AND

ABSTRACT ("treatment gap" OR "barriers" OR "challenges" OR "access" OR "availability" OR "accessibility" OR "affordability" OR "price" OR "drug control" OR "drug policy" OR "Drug and Narcotic Control" OR "Health Services Accessibility")

AND

ABSTRACT ("controlled drugs" OR "controlled medicines" OR "controlled substances" OR "codeine" OR "diazepam" OR "fentanyl" OR "hydromorphone" OR "methadone" OR "midazolam"

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OR "morphine" OR "oxycodone" OR "buprenorphine" OR "lorazepam" OR "phenobarbital" OR "ephedrine" OR "ergometrine" OR "methylergometrine" OR "anesthesia" OR "anaesthesia" OR "anticonvulsant" OR "anxiety disorders" OR "management of cancer pain" OR "opioid agonist treatment" OR "opioid substitution therapy" OR "harm reduction" OR "opioids" OR "opioid" OR "oxytocic" OR "pain and palliative care" OR "pain care" OR "palliative care" OR "pain treatment" OR "Pain Management" OR "Analgesics" OR "Psychotropic Drugs" OR "Benzodiazepines" OR "psychotropic medicines" OR "psychotropic substances" OR "analgesia" OR "epilepsy" OR "antiepileptic"))

AND

2012-01-01 to 2022-01-02 (Publication Date)

4 Scopus

(TITLE-ABS-KEY ("sub Saharan Africa" OR "Africa" OR "Sudan" OR "Angola" OR "Benin" OR "Botswana" OR "Burundi" OR "Congo" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Guinea" OR "Guinea-Bissau" "Gabon" OR "Kenya" OR "Nigeria" OR "Rwanda" OR "Sao Tome" OR "Tanzania" OR "Uganda" OR "Djibouti" OR "Eritrea" OR "Equatorial Guinea" OR "Ethiopia" OR "Somalia" OR "Comoros" OR "Lesotho" OR "Madagascar" OR "Malawi" OR "Mauritius" OR "Mozambique" OR "Namibia" OR "Reunion" OR "Seychelles" OR "Swaziland" OR "Zambia" OR "Mali" OR "Burkina Faso" OR "Cape Verde" OR "ivory coast" OR "Gambia" OR "Ghana" OR "Zimbabwe" OR "Liberia" OR "Mauritania" OR "Niger" OR "Senegal" OR "Sierra Leone" OR "Togo" OR "South Africa" OR "Cote d'Ivoire" OR "Eswatini")

AND

TITLE-ABS-KEY ("treatment gap" OR "barriers" OR "challenges" OR "access" OR "availability" OR "accessibility" OR "affordability" OR "price" OR "drug control" OR "drug policy" OR "Drug and Narcotic Control" OR "Health Services Accessibility")

AND

TITLE-ABS-KEY ("controlled drugs" OR "controlled medicines" OR "controlled substances" OR "codeine" OR "diazepam" OR "fentanyl" OR "hydromorphone" OR "methadone" OR "midazolam" OR "morphine" OR "oxycodone" OR "buprenorphine" OR "lorazepam" OR "phenobarbital" OR "ephedrine" OR "ergometrine" OR "methylergometrine" OR "anesthesia" OR "anaesthesia" OR "anticonvulsant" OR "anxiety disorders" OR "management of cancer pain" OR "opioid agonist treatment" OR "opioid substitution therapy" OR "harm reduction" OR "opioids" OR "opioid" OR "oxytocic" OR "pain and palliative care" OR "pain care" OR "palliative care" OR "pain treatment" OR "Pain Management" OR "Analgesics" OR "Psychotropic Drugs" OR "Benzodiazepines" OR "psychotropic medicines" OR "psychotropic substances" OR "analgesia" OR "epilepsy" OR "antiepileptic"))

AND

2012 to PRESENT

Supplementary File 2. Characteristics of the included articles

2.1

2.2

BARRIERS TO ACCESSING INTERNATIONALLY CONTROLLED ESSENTIAL MEDICINES IN UGANDA: A QUALITATIVE STUDY

Gaby I Ooms, Paul Klatser, Hendrika A van den Ham, Tim Reed

ABSTRACT

Context

Access to internationally controlled essential medicines is a problem worldwide. More than five billion people cannot access opioids for pain and palliative care or do not have access to surgical care or anaesthetics, 25 million people living with epilepsy do not have access to their medicines, and 120.000 women die annually due to post-partum haemorrhage. In Uganda, access to controlled medicines is also problematic, but a lack of data on factors that influence access exists.

Objectives

The objective of this study was to identify the social, cultural, and regulatory barriers that influence access to internationally controlled essential medicines in Uganda.

Methods

Semi-structured interviews with 15 key stakeholders with knowledge on controlled medicines from relevant institutions in Uganda. Interviews were transcribed verbatim and analysed using the *Access to Medicines from a Health System Perspective* framework.

Results

Barriers in accessing controlled medicines were experienced owing to lack of prioritisation, difficulties in finding the balance between access and control, deficiencies in the workings of the estimate- and distribution system, lack of knowledge, inadequate human resources, expenses related to use and access, and stigma. It was believed that some abuse of specific controlled medicines occurred.

Conclusion

The findings of this research indicate that to improve access to internationally controlled essential medicines in Uganda, health system strengthening is needed on multiple fronts. Active engagement and concerted efforts are needed from all stakeholders to ensure access and prevent abuse.

INTRODUCTION

The World Health Organization (WHO) Model List of Essential Medicines (EML) contains medicines that aim to satisfy the priority health care needs of the population, and they ought to be available at all times (1,2). The EML also includes medicines controlled by law through the Single Convention on Narcotic Drugs of 1961, the Convention on Psychotropic Substances of 1971, and the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988 (3–6). Controlled medicines are subjected to stricter regulatory practices than non-controlled medicines owing to their potential for abuse (4–6). On the 20th EML, fourteen medicines are controlled under one of the conventions (7). These internationally controlled essential medicines (ICEMs) are used as anaesthetics, anticonvulsants, topical anti-infective, oxytocic, anxiety disorder medicines, for opioid agonist treatment (OAT), and for pain and palliative care (see **Table 1**) (7).

Globally, five billion people are unable to access essential opioids or anaesthesia if needed, and more than six million people die in unbearable pain annually; more than 25 million people living with epilepsy do not receive the medicines they need; and 120,000 women die annually due to post-partum haemorrhage (8–11). Meanwhile, 92% of morphine is consumed by just 17% of the global population, all living in high-income countries (8,12).

Difficulties accessing ICEMs are partly because of the strict regulation surrounding these medicines (8,13). Legal restraints are further augmented by Article 39 of the Single Convention, which allows countries to adopt more severe measures than those provided in the Single Convention on Narcotic Drugs (4). In many countries this leads to a stronger focus on preventing illicit drug trafficking than on ensuring availability of these medicines (14).

Although Uganda is heralded as an example for other countries due to, among others, local manufacturing of oral morphine, availability of hospice and palliative care services, and nurse prescribing, access to controlled medicines remains problematic (15,16). A study on opioid availability in Africa showed that in Uganda methadone was unavailable, and only codeine and injectable or immediate-release oral morphine were occasionally available at facilities (17). Major problems for patients were also experienced in accessing pharmacies that prescribe these medicines, as only hospital pharmacies are allowed to handle opioids (17). Furthermore, other ICEMS have not received a similar level of attention as opioids; data is lacking on their day-to-day availability in Uganda, as well as on the factors that inhibit their accessibility. Consequently, action to improve access is difficult, highlighting the need for detailed data on access to controlled medicines in Uganda (18–21). The aim of this research is to identify the factors that influence access to ICEMs in Uganda, using semi-structured interviews.

2.2

2.2

Table 1. Controlled medicines listed on the WHO EML.

Medicine	Therapeutic use							
	Anaesthesia	Anti-convulsant	Anxiety disorders	Management of cancer pain	Opioid agonist treatment	Oxytocic	Pain and palliative care	Topical anti-infective
Buprenorphine					X			
Codeine							X	
Diazepam	X	X	X					
Ephedrine	X							
Ergometrine						X		
Fentanyl				X				
Hydromorphone							X	
Lorazepam		X	X					
Methadone					X		X	
Midazolam	X	X						
Morphine	X						X	
Oxycodone							X	
Phenobarbital		X						
Potassium permanganate								X

METHODS

Study design and population

This qualitative study consisted of semi-structured interviews with key experts. Mapping was done through document desk review, and in consultation with the Ministry of Health (MoH), the National Drug Authority (NDA) and a non-governmental organisation (NGO) to conceptualise the supply chain and service delivery of ICEMs. The process identified 11 relevant stakeholder groups, including MoH, NDA, the police, manufacturers, distributors, healthcare professionals, and NGOs and civil society organisations (CSOs). Stakeholders were selected based on the following criteria: 18 years or older; capacity to give informed consent; knowledge on access to ICEMs; ability to communicate in English.

2.2

Data collection

Interviews were conducted between August 2, 2016, and August 27, 2016. Fourteen were completed face-to-face and one used video-calling. Biases were believed minimal between the two methods as video-calling also allows face-to-face interaction and thus facilitates trust-building. The face-to-face interviews were conducted at a place chosen by the respondents to ensure they felt comfortable. Interviews were semi-structured, meaning questions were asked in a systematic and consistent order, but allowed for follow-up questions if relevant to the topic of study. This allows for flexibility that reflects awareness that respondents understand the research topic in various ways (22).

An interview guide was developed containing questions pertaining to respondents' knowledge and perceptions on the social, cultural, and regulatory factors that influence access to ICEMs in Uganda. Examples of questions are as follows: "What factors influence access to ICEMs?"; "Can you tell me about the enforcement of the regulatory practices concerning ICEMs?"; "What are the challenges surrounding the supply and distribution of ICEMs?"; and "What do you think are the main challenges experienced by patients in accessing ICEMs?" For more information, see Supplementary File 1. The interview guide was tested in a pilot interview with a healthcare professional. Consequently, minor modifications in phrasing were made to improve comprehensibility.

Respondents were provided with a participation information sheet and asked to sign an informed consent form. All interviews with the exception of one, due to the wishes of the respondent, were recorded. During the interviews field notes were collected, capturing mood and expressions of the respondents. Interviews lasted from 40 to 75 minutes.

Data management and analysis

Analysis of the interviews was done using the programme MAXQDA version 12. Data was entered manually. Textual data from interview transcripts and field notes were collected, organized, and cleaned. Transcripts were transcribed verbatim and coded deductively

and inductively into themes using the *Access to Medicines from a Health System Perspective* framework (23). This framework argues that access to medicines barriers function at the local, national, and international level, and that health system building blocks are not separate factors, but interactions exist between these blocks (23). The framework was adapted during the research to the contextualisation of the controlled medicines situation. The researchers (GIO and TR) coded the first transcript separately to generate code-categories independently. After, the researchers reviewed the separately coded transcripts together to reach consensus on the final code-categories to be used for the analysis of the transcripts.

Quality assurance

This research used the COREQ framework for reporting methods and findings (24). In this research, credibility and dependability were taken into consideration through the consensual coding, and peer-debriefing during the writing process as done by the coauthors (TR, PK, and HAH). Informant triangulation occurred through the inclusion of different stakeholders in the research. Transferability was considered through purposive sampling and thick descriptions of the data collection process, such as how and where the interviews were conducted. Confirmability was achieved by considering the aforementioned considerations and by ensuring the researchers' neutral, objective stances through reflectiveness on the manner of data collection (25). The study was approved by Makerere University School of Health Sciences Research and Ethics Committee, approval number 2016-29.

RESULTS

Fifteen of nineteen stakeholders contacted participated. Stakeholders interviewed are shown in **Table 2**. Topical saturation was reached; the last three interviews did not yield new concepts.

An account is given of the stakeholders' perceptions regarding the factors influencing access to ICEMs in Uganda. An overview of the findings is shown in **Figure 1**. The results are categorised according to the components of the adapted framework. Themes more often mentioned in interviews are shown as bigger boxes. Key themes were as follows: regulation – access vs excess, availability, and illicit use.

International Level

Multiple respondents stated international control bodies guide control at country level. Uganda has to justify the use of ICEMs to these bodies, and its legislation and control is also based on the bodies' principles. However, ability to meet the requirements of the control bodies is difficult, influencing availability of the ICEMs at the national level.

Table 2. Characteristics of interviewed stakeholders.

No.	Discipline	Profession	Gender
1	Healthcare provider	Specialist physician	Male
2	Healthcare provider	Specialist physician	Female
3	Healthcare provider	Senior pharmacist	Male
4	Healthcare provider	Senior pharmacist	Male
5	Local manufacturer	Senior advisor	Male
6	Local manufacturer	Senior advisor	Male
7	Distributor	Senior advisor	Male
8	Distributor	Senior advisor	Male
9	Civil Society Organization	Director	Male
10	Civil Society Organization	Senior advisor	Female
11	Non-Governmental Organization	Senior advisor	Male
12	Non-Governmental Organization	Director	Male
13	Ministry of Health	Senior advisor	Male
14	Ministry of Health	Senior advisor	Male
15	National Drug Authority	Senior advisor	Male

2.2
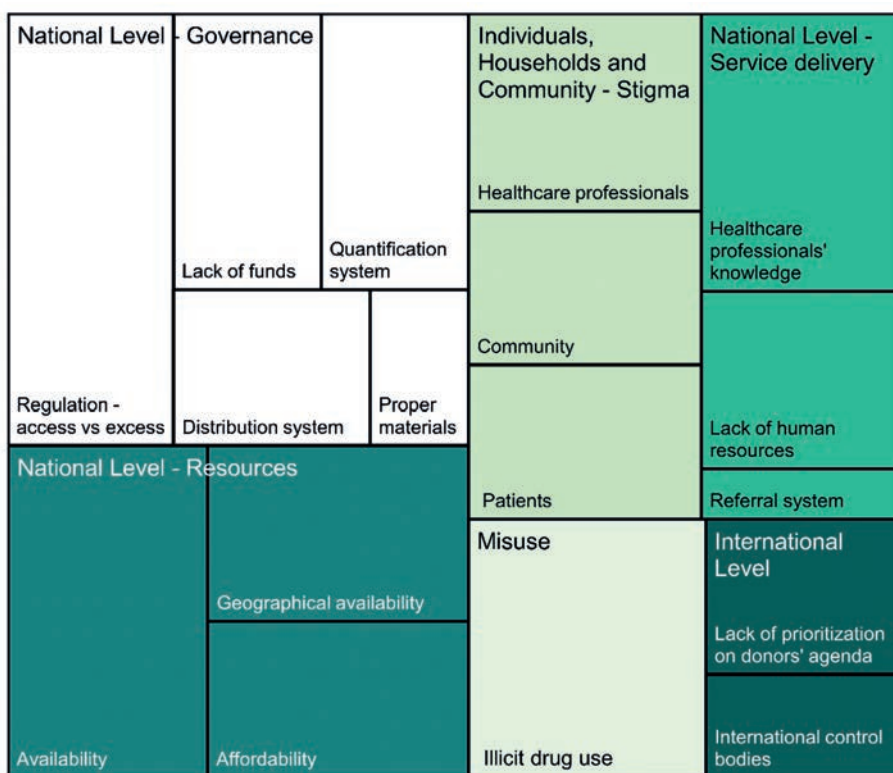
Figure 1. Treemap chart. Overview of the factors influencing access to ICEMs.

"… Countries tend to adopt global norms. If the control is right from the global level,
it is likely the countries are going to have control systems, that inevitably influences
access, inevitably." (R12)

2.2

Respondents believed that ICEMs were not a donor priority. They agreed that donor funding might help improve access but raised the question of sustainability of donor-supported programmes. Donor funding alone was thought to not be enough to meet the needs.

National Level

Governance

The MoH's budget was argued to be inadequate to meet the population's needs, resulting in prioritisation of certain health themes. The disease fields related to ICEMs were argued not to be prioritised in terms of budget allocation, causing the central procurement agency to be unable to guarantee supply of the medicines. This resulted in stock-outs and insufficient quantities at health centres.

Respondents often referred to the necessity of drug control. Even though some believed ICEMs regulations were in line with their potential for abuse, other respondents mentioned regulations were a barrier. It was stated that it caused extra work, such as the necessity of additional documentation books and special licenses for prescribing opioids. Furthermore, some prescribers fear the threat of legal sanctions, such as license revocation, influencing prescribing practices. However, participants also stated that some abuse of ICEMs occurred in Uganda. For instance, diazepam was argued to be available without a prescription and was used by parents to calm children so they could work uninterrupted. According to respondents, they were unaware of side-effects:

"Many parents tend to use it because it […] calms down the children and sedates
them. The children can then sleep, and then the parents go to do their work. But
the parents are not aware about the negative effects of the diazepam." (R15)

Respondents stated that for other ICEMs abuse was limited because the formulations available are not easily abused. Interestingly, some respondents mentioned abuse of pethidine, which is a controlled medicine but is not listed on the WHO EML. Linked to the fear of abuse, use of opioids for opioid agonist treatment (OAT) is illegal. The reasoning is that while it could be used for treatment, opioids are also injected by persons suffering from addiction.

The information system, specifically the estimates system, was also believed to hamper access. Quantities of ICEMs listed on the Single Convention allowed into a country are based on a country's annual requests to international control bodies. Respondents stated Uganda

has no system to document the use and need of ICEMs. Instead, quantification is based on estimates, leading to inadequate quantities and stock-outs:

> "There is no logistics management information system that can be used to […] document the cases that are being seen and then also to build in a forecast factor and say two years from now, this is what we need. So it is very difficult to do that type of quantification." (R6)

Another problem with the estimates system was related to human resources. Respondents argued that problems were exacerbated by healthcare providers' lack of knowledge on how to quantify the needs:

> "The other aspects would be the personnel at the health centres, are they available, who adequately quantify the need that they require […]? If you cannot quantify your need from the health centre, then how are you able to indicate to the person supplying you the medicines that this is what you need?" (R7)

The distribution system was also thought to be a barrier. Respondents said that when health centres order a certain quantity of ICEMs, they sometimes only receive a fraction of the order due to problems experienced by the distributor or due to practical delivery issues.

Service Delivery

Uganda has a special morphine prescribing policy, which allows nurses to prescribe morphine. This policy was a response to the shortage of doctors able to prescribe opioids. However, the number of prescribers was argued to still be insufficient to treat those in need. Moreover, respondents mentioned human resources are unequally distributed across Uganda as health care providers preferred to work where remuneration for their services was best; this is not in rural areas or the public sector. Besides, respondents argued that many health care providers allowed to prescribe ICEMs were in practice not adequately skilled to do so because they lacked training and knowledge. Related, even when they had received training on ICEMs, respondents mentioned that the addictive qualities and side effects were overemphasized, leading to fears:

> "The issue is […] the reluctance of prescribers to prescribe controlled medicines. But like morphine, people didn't want to prescribe it. They say no-no-no-no, people get addicted to these medicines." (R1)

Lastly, information sharing between health centres was thought inadequate. Referral of patients was argued to often not occur because lower-level centres were unaware of the availability of ICEMs at higher levels, hampering service delivery.

> "So you find at times, when they're in a health centre II, they don't want to refer you to a health centre III because I don't know whether they have it. So we just tell you that the medicine is not there. But if there is a strong referral system and I know that this health centre III has this, then it makes it easier."[1] (R5)

2.2 *Resources*

An important obstacle to accessing ICEMs was affordability. Many voiced that patients often have to travel far to access medicines, costing money. ICEMs were also not always available in the public sector, where all medicines are free to the patient, forcing patients to seek care from the private sector where costs are substantial. Patients might also have a chronic need for medicines, exacerbating financial hardships:

> "Well they can't afford it. I think you need to look at the poverty situation in this country. Sometimes critical medicines are not available in the system, and the patients have to buy. […] They have to sell their property, just to get some basic treatment." (R12)

Discrepancies in the availability of specific ICEMs were identified by respondents. Respondents also referred to the lack of availability of different formulations, and the substantial gap between need and actual availability:

> "When you look at our consumption on the global map, we're still very low compared to other countries in terms of consumption. So we need to do a lot in terms of improving this availability, and ensuring that these medications are available for those who need them." (R4)

Geographical availability also affected accessibility because it was believed that rural areas had more difficulties with access than urban areas owing to longer distances and lesser facilities.

Individuals, Households, and Communities

Respondents reported beliefs and attitudes of the community and patients negatively influenced use of ICEMs. They stated communities associated ICEMs with diseases that are "in bad faith", and patients known to be taking medicines for such diseases are socially excluded

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[1] Uganda's health system consists of seven levels of health service delivery: Health Centre I (village health teams); Health Centre II (first point of contact between patient and formal healthcare services); Health Centre III (first line health services. Provide basic care); Health Centre IV (secondary and emergency care); General Hospital (services offered at HC IV, and offers training and consultations); Regional Referral Hospital (services offered at general hospital, additionally specialized services); National Referral Hospital (regional referral hospital, additionally teaching and research hospital) (26).

and isolated, such as is the case for epilepsy. Owing to stigma, persons using anti-epileptics did not want to take them in public.

Not surprisingly, patients also held stigmatising views. Respondents argued patients feared addiction, and they associated some ICEMs with death because patients with end-stage diseases received palliative care, which sometimes includes opioids, to alleviate their pain.

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> "For the patients, what is happening is that you know most people who are having cancer and are near death, most of them are the ones taking morphine. So many of them are now associating the use of the narcotic to death, and not to the cancer." (R3)

DISCUSSION

This is the first study that provides qualitative insights into access to ICEMs in Uganda from a multiple-stakeholder perspective that not only focuses on access to opioids for palliative care. Barriers experienced were due to the controlled status of the medicines, while some were also barriers that were experienced by medicines in general. For instance, barriers that were experienced accessing ICEMs that also influence access to medicines in general were the use of an estimate system to quantify medicine needs, practical and logistical issues of supply, lack of human resources, expenses related to use and access, and physical and geographical availability. ICEM-specific barriers in Uganda were due to non-prioritisation of ICEMs, difficulties in finding a balance between control and access, lack of knowledge among health care providers and the population, and stigma. In addition, some abuse of specific controlled medicines was mentioned.

This research on access to ICEMs upholds findings of previous research in a specific country context – that of Uganda. The finding that a lack in budget provisions for ICEMs in Uganda was an impediment to access is supported by previous research. In India, no budget was allocated to palliative care, and in many African countries, where epilepsy is often also categorised as a mental health disorder, no specific health budget is allocated to mental health (27,28). The present research suggests lack of budget provisions plays a role in the availability of ICEMs and that international focus might contribute to more attention for these medicines.

The extra documentation books and special licenses necessary for opioid prescription in Uganda was thought to influence access negatively as health care providers were thought to be more reluctant to prescribe opioids. Similar problems hampered the prescription of opioids, as well as anti-epileptics, in other African countries (17,29). The research further showed that reluctance to prescribe ICEMs due to fear of potential legal sanctions existed among healthcare providers. These fears were found to impede access of ICEMs in other countries as well (12,30). Interestingly, legal sanctions were thought to not be overly

restrictive by Ugandan policy makers, raising the question whether the offenses are in truth not too restrictive, and what can be done to allay the fears of health care providers.

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Furthermore, respondents raised the issue that a lack of knowledge among health care providers might affect sufficient caregiving. Past research supports these findings, showing that many health care providers have little knowledge or understanding of controlled medicines (8,12-14,31). The finding that health care providers are at times reluctant to prescribe ICEMs because they fear the addictive qualities was also found in previous studies (8,30-33). Similar beliefs and stigmatization were thought to be present in communities and among patients in Uganda, which is supported by other research (8,12,30,33,34). These findings suggest that in Uganda, lack of proper knowledge on ICEMs among health care providers, communities, and patients might lead to beliefs and attitudes that adversely affect the use and prescribing of ICEMs.

The research also showed that needs for ICEMs in Uganda are based on estimates and not on actual need. These estimates might already have been inadequate, as was found in other research (8,13,30,31). One study showed that in Uganda, the actual availability of morphine covered only 2.3% of the population's needs (35). Two other studies found that ephedrine was never available to 28% of anaesthetists, and two-thirds of health centres IV had not been supplied with ergometrine for at least one-quarter of the year (21,36). The ICEMs treatment gap in Uganda thus remains substantial.

Previous research studies further found that indirect costs and out-of-pocket expenses for ICEMs are high in many low- and middle-income countries (12,13,34). This research found that in Uganda, most ICEMs are affordable in the public sector because they are subsidised by the government. Nevertheless, when they are unavailable there, patients need to visit the private sector where direct and indirect costs can be substantial.

Abuse of ICEMs was argued to not be a significant problem in Uganda. Nevertheless, some abuse was thought to occur, specifically of diazepam. Literature on this problem seems to be lacking, demonstrating a need for more research. Furthermore, an unexpected finding was that in Uganda pethidine, a medicine listed on the EMLU but not on the WHO EML, was mentioned to be abused by health care providers (7,37). Similar abuse was found in a study in Ghana (38). Pethidine was removed from the WHO EML because it was considered inferior to morphine due to its toxicity and costs (7,39). The WHO recommended it be removed from national lists and that countries focus on ensuring availability of morphine (39). This research thus highlights a point of contention between the WHO EML and the EMLU, and a need for review of pethidine on the EMLU.

Some limitations to this research should be noted. One interview was not recorded due to the respondent's wishes. Furthermore, the patient perspective was not included, while

this perspective would have provided valuable, experiential knowledge. This perspective would be interesting to research in a separate study to provide it the importance it deserves. The researchers were also unable to interview stakeholders from private sector facilities or the procurement agency. These perspectives would have been a valuable component to the knowledge base which we have lain now; comparing access to ICEMs barriers between the public and private sector might have yielded additional insights.

Based on this research, multiple recommendations were formulated to improve access to ICEMs in Uganda (see **Box 1**). Health system strengthening, and active engagement and concerted effort of the government, regulators, suppliers, educational institutions, patient organisations, advocacy groups, NGOs, and healthcare providers is needed. Health system strengthening is needed at the level of human resources, service delivery, policy, and the estimates- and distribution system. Affordability of ICEMs and community education are also crucial to ensure access.

CONCLUSION

Access to ICEMs in Uganda is hindered by multiple aspects, among which health system barriers are one of the most important. Barriers were experienced owing to lack of prioritization, difficulties in finding the balance between access and control, deficiencies in the workings of the estimate and distribution system, lack of knowledge, inadequate human resources, expenses related to use and access, and stigma. The findings of this research indicate that to improve access to ICEMs in Uganda, health system strengthening with active engagement from all stakeholders is needed.

Policy	Human resources
» Ensure compliance to regulation	» Include/ increase training on ICEMs in medical curricula
Estimates- and distribution system	**Affordability**
» Estimates system based on documentation » Strengthen distribution system	» Ensure ICEMs availability in the public sector
Service delivery	**Community**
» Increase ICEMs prescribing possibilities for healthcare providers based on the opioid nurse prescribing policy » Integrate ICEMs service delivery into existing programs to ensure prioritization	» Implement stigma-reduction programs » Develop information campaigns

Box 1. Recommendations to improve access to ICEMs in Uganda. ICEMs: Internationally Controlled Essential Medicines.

CONTRIBUTION STATEMENT

GIO and TR designed the study. GIO collected and analysed the data, and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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SUPPLEMENTARY DATA

Supplementary File 1. Interview guide

Introduction

1. As an introduction, could you tell me a bit about yourself and your position at ………………….…?

2. As I've explained, we are doing research on the availability and accessibility of essential controlled medicines. So what are your thoughts on the current situation in Uganda concerning availability and accessibility of controlled medicines?

Regulation

3. What are your views on current laws on controlled medicines, regulation and policies in Uganda? (probe on laws which respondents refer to)

4. In your opinion, how do these above laws affect availability, accessibility and affordability?

5. Can you think of any other factors that in your opinion influence accessibility and availability of ICEMS? (probe further on how the factors influence access)

6. In your opinion, what needs to be changed on a regulatory level to improve the access to ICEMs?

Enforcement

7. Can you tell me about the enforcement of the regulatory practices concerning ICEMs?

8. What are your views on the legal sanctions surrounding the use and misuse of ICEMs?

9. The WHO states that a balance should be found between protecting people from abusing controlled medicines and providing people with the needed controlled medicines. Would you say this is the case in Uganda?

Supply chain and distribution

10. Can you tell me about the process of the supply chain/ distribution system of ICEMs? (procurement, manufacturing, distribution)

11. What are the challenges that are being experienced? (provision, quantities)

12. Are there differences between the private and public sector?

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13. I know that health facilities must make an estimation of the needed ICEMs, do you believe this system functions well?

2.2

International level

14. In your opinion, do donors and international priority and attention influence accessibility and availability of ICEMs in any way?

Patient experience

15. What do you think are the main challenges experienced by patients in accessing controlled medicines?

16. Do you believe stigma is a factor that plays a role in the accessibility and availability of ICEMs? Why (not)?

Conclusion

17. In your opinion, what are the main strengths in the provision of controlled medicines in Uganda?

18. In your opinion, what are the main challenges Uganda faces?

19. Is there anything you would like to add?

2.3

THE IMPACT OF SCHEDULING KETAMINE AS AN INTERNATIONALLY CONTROLLED SUBSTANCE ON SURGICAL AND ANAESTHESIA CARE IN SUB-SAHARAN AFRICA: A CASE STUDY AND KEY INFORMANT INTERVIEWS

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Hendrika A van den Ham, Aukje K Mantel-Teeuwisse

ABSTRACT

Background

Access to anaesthesia and surgical care is a major problem for people living in Sub-Saharan Africa. In this region, ketamine is critical for the provision of anaesthesia care. However, efforts to control ketamine internationally as a controlled substance may significantly impact its accessibility. This research therefore aims to estimate the importance of ketamine for anaesthesia and surgical care in Sub-Saharan Africa and assess the potential impact on access to ketamine if it were to be scheduled.

Methods

This research is a mixed-methods study, comprising of a cross-sectional survey at the hospital level in Rwanda, and key informant interviews with experts on anaesthesia care in Sub-Saharan Africa. Data on availability of four anaesthetic agents were collected from hospitals (n=54) in Rwanda. Semi-structured interviews with 10 key informants were conducted, collecting information on the importance of ketamine, the potential impact of scheduling ketamine internationally, and opinions on misuse of ketamine. Interviews were transcribed verbatim and analysed using a thematic analysis approach.

Results

The survey conducted in Rwanda found that availability of ketamine and propofol was comparable at around 80%, while thiopental and inhalant agents were available at only about half of the hospitals. Significant barriers impeding access to anaesthesia care were identified, including a general lack of attention given to the speciality by governments, a shortage of anaesthesiologists and migration of trained anaesthesiologists, and a scarcity of medicines and equipment. Ketamine was described as critical for the provision of anaesthesia care as a consequence of these barriers. Misuse of ketamine was not believed to be an issue by the informants.

Conclusion

Ketamine is critical for the provision of anaesthesia care in Sub-Saharan Africa, and its scheduling would have a significantly negative impact on its availability for anaesthesia care.

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INTRODUCTION

Surgical care is defined by the Lancet Commission on Global Surgery as "the provision of operative, perioperative, and non-operative management; anaesthesia; and obstetric care for all surgical conditions" (1). Surgical care is a cross-cutting field of care, and surgical procedures are essential in the treatment of communicable and non-communicable diseases, maternal, neonatal and nutritional disorders, and injuries (1). It is estimated that conditions requiring surgery are responsible for around 30% of the global burden of disease, while access to safe, affordable and timely surgical and anaesthesia care is a major issue for more than 4.8 billion people worldwide (2,3). This treatment gap is felt the most by people living in low- and middle-income countries (LMICs): an additional 143 million surgical procedures are needed in LMICs annually to avert preventable disability and deaths, and more than 77 million disability-adjusted life-years (DALYs) could be averted with adequate provision of basic surgical care (1). Further, it is estimated that more than 100,000 maternal and 280,000 neonatal deaths could be prevented each year with increased access to caesarean delivery (4). Anaesthesia is a key component of surgical care.

Access to surgical and anaesthesia care is a major problem for people living in Sub-Saharan Africa (SSA), where it is beyond the reach of more than 95% of the population (3). In this region alone, an additional 41 million surgical procedures are needed each year (1). Lack of access to surgical and anaesthesia care in SSA is caused by a paucity of specialised healthcare workers, poor basic infrastructure, absence of surgical and anaesthesia equipment, and scarcity of essential medicines, including anaesthetics (5). It is estimated that in the World Health Organization (WHO) Africa Region, with the exclusion of South Africa due to its higher number of physician anaesthesia providers (PAPs), there are on average 0.41 PAPs per 100,000 population. This number is far below the 10 PAPs per 100,000 population as recommended by the World Federation of Societies for Anaesthesiologists (WFSA) (6). In comparison, in the WHO European Region there are 18.60 PAPs per 100,000 population (6). Research has shown that consistent access to electricity and running water remains problematic across SSA, and that availability of oxygen and functional anaesthetic machines is generally low (7–19). Essential medicines, such as local or general anaesthetics, remain in low supply (7,10,13,20–22).

Due to the lack of PAPs, infrastructure, equipment, and essential medicines in much of SSA, surgical procedures often take place without adequate anaesthesia or pain management (23). To alleviate the suffering of patients in these settings, hospitals have become reliant on ketamine. Ketamine was (almost) always available in 88% of health facilities in Liberia, always available in 95% of hospitals in Madagascar, and in 100% of hospitals in Malawi, Tanzania and Zambia (7,12,14). Ketamine, a dissociative anaesthetic, has been used for humans since 1970, and is used primarily as anaesthetic, sedative and for pain management (24). The WHO Model List of Essential Medicines lists ketamine for use as an anaesthetic (25,26). Its use

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in low-resource settings is popular as ketamine does not decrease respiratory function in patients while it increases blood pressure, and can therefore be used when access to airway equipment is lacking and monitoring of vital signs is challenging (23,25). Because of these properties, ketamine can also be used by non-physician providers, if they have been appropriately trained (23).

2.3

Ketamine is misused in high-income countries, especially in China, Hong Kong, Taiwan, and Japan, and more generally in East and Southeast Asia (5,25,27). It is used as a recreational drug due to its effects on sensory perceptions; it produces the same effects as psychedelic drugs, including feeling dream-like and detached, feelings of euphoria or fear, and has hallucinogenic properties (5,28,29). Long-term effects of recreational use of ketamine may impact brain function and structure, bladder function, increase the chance of sleeping disturbances, and can lead to depression and impaired memory (27).

Because of the misuse in these countries, China has repeatedly submitted a request to schedule ketamine as a Schedule I drug under the Single Convention on Narcotic Drugs in 2006, 2012 and 2014, and submitted a request to have it scheduled as a schedule IV drug under the Convention on Psychotropic Substances in 2015 (25,29–32). Drugs scheduled as a Schedule I drug in the Single Convention are subject to all measures of control under the Convention; only Schedule IV drugs are more tightly regulated within this Convention (31). Measures include, amongst others, obligatory annual estimates, full documentation of quantities produced, manufactured, used, imported and/or exported, and special licenses for distribution. Schedule IV substances in the Convention on Psychotropic Substances are subject to control measures such as special licenses for manufacture, trade and distribution, full documentation similar to the Single Convention provision, import and export is only allowed when tightly regulated, and countries are allowed to prohibit the import of any psychotropic substance (32).

All four instances that scheduling was requested, the WHO Expert Committee on Drug Dependence (ECDD) declined, stating that ketamine poses no great global public health risk, while scheduling it would have a significant impact on medical care in LMICs and in emergency situations (27,29,30). Subsequently, the United Nations Commission on Narcotic Drugs (CND) has not scheduled ketamine as a Schedule I drug in the Single Convention, or as a Schedule IV drug in the Convention on Psychotropic Substances (27,29,30). However, it is likely that similar requests will be made in the future.

While the importance of ketamine for anaesthesia care has been discussed in an article in the Guardian and in editorials, no research has been undertaken in which anaesthesiologists from the field provide their insights into the issue (28–30,33). This research therefore aims to estimate the importance of ketamine for anaesthesia and surgical care in SSA, and assess the potential impact on access to ketamine if it were to be scheduled, through a case study

of essential anaesthesia commodities availability in Rwanda, and key informant interviews with experts from SSA.

METHODS

Study design

This research is a mixed-methods study, comprising of a cross-sectional survey at the hospital level in Rwanda, and key informant interviews with experts on anaesthesia care in SSA. The survey on the availability of anaesthesia commodities was part of a larger project in Rwanda on access to essential medicines for the management and treatment of snakebites. In this study, 34 commodities were surveyed, including four commodities that are used in anaesthesia care (ketamine, thiopental, inhalant agents, and propofol). The survey functioned as a case-study to gain insight into the availability of a range of anaesthesia commodities in a specific SSA country. Semi-structured interviews were conducted with key informants from the whole of SSA to gather a more generalised insight into the importance of ketamine for anaesthesia and surgical care in the entire region, given the situation in Rwanda may not be representative of the region.

Study participants and recruitment

In Rwanda, all general, non-specialised hospitals from the public and private sectors were sampled for the survey, resulting in a sample of 55 hospitals. This included four private hospitals, and 51 public district-, provincial- and referral hospitals. The hospitals were contacted beforehand by email or telephone to schedule a study visit.

Key stakeholders identified for participation in the interview component of this study were anaesthesiologists with expertise in anaesthesia care in SSA. They were identified and recruited through document desk review, the network of the World Federation of Societies of Anaesthesiologists (WFSA) and its national chapters, and the professional network of the researchers. Inclusion criteria for participation were: participants are 18 years or older, knowledgeable on anaesthesia care and ketamine use in SSA, and able to communicate in English. Participants were invited over email and provided with background information on the study. Multiple follow-up emails were sent in case of non-response.

Data collection

The WHO-WFSA *International Standards for a Safe Practice of Anesthesia* guided the selection of the general anaesthesia commodities (34). Information on electricity, running water, and functional anaesthesia machines was also recorded. Data within the Rwandan hospitals was collected in February 2023. A mobile application, KoboCollect, was used for data collection. Data collectors received a two-day training from one of the authors (GO), which included a field-test. Data collectors collected data in pairs and were supervised by an in-country lead investigator. Data on availability of the commodities was recorded only when they could be

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physically seen. A commodity was considered available if it was present at the hospital at the time of data collection. A photo was taken of each available, surveyed commodity as an additional validity measure.

A semi-structured key-informant interview guide was developed based on literature to guide the interviews (see Supplementary File 1). Questions focused on the contextual situation of anaesthesia care, including barriers to access, in the countries in which participants have work experience, their beliefs about ketamine and its relevance for anaesthesia care in these respective countries, and their perceived potential impact of ketamine scheduling on anaesthesia and surgical care in these contexts. We also sought the participants' opinions on the level of misuse of ketamine in their countries, and about recommendations to safeguard access to anaesthesia care while at the same time preventing misuse of ketamine. Interviews were conducted from May to July 2023 with 10 participants. Nine interviews took place online through virtual meeting platform Zoom, and one interview was conducted via email, where the key informant responded to the questions in written form due to language barriers. Interviews were recorded, and Zoom's build-in automatic transcription setting was used.

Data management and analysis

Survey data were uploaded to the KoboToolbox server by the data collectors after completion, after which the data was downloaded into Microsoft Excel. The data was double-checked and cleaned by the researchers, and was analysed in Microsoft Excel using descriptive statistics. Availability was calculated as the proportion of hospitals where the commodity was present at the time of the survey.

The automatic, verbatim interview transcripts were checked by the researchers for errors and corrected when necessary after a consensus was reached. The interviews were analysed using a thematic analysis approach by one researcher (GIO), and consisted of coding text into predetermined themes, which were based on the interview topics.

Quality assurance

The qualitative component of this research was guided by the Consolidated Criteria for Reporting Qualitative Research (COREQ) framework (35). Triangulation occurred in two ways: informant triangulation through the inclusion of stakeholders from multiple countries, and data triangulation through the use of both quantitative and qualitative research methods. Transferability of the research is increased through a detailed description of the context of the research, the data collection, and data analysis.

Ethical considerations

Ethical approval for the hospital survey was granted by the University of Global Health Equity Institutional Review Board, approval number UGHE-IRB/2022/056, and by

the Rwanda National Health Research Committee, approval number NHRC/2022/PROT/050. Informed consent was given by all participants (see Supplementary File 2). Ethical approval for the interviews was granted by the Ethics Review Board of the faculties of Science and Geosciences, Utrecht University, approval number S-23008.

RESULTS

Availability of general anaesthetics in Rwandan hospitals

In total, 54 hospitals participated in this study. One hospital declined participation. The general anaesthetic with highest availability was propofol (81.5%), followed by ketamine (77.8%) (see **Table 1**). Inhalant agents, such as halothane, isoflurane or sevoflurane were available at 53.7% of the hospitals, and thiopental at 44.4%. When asked what anaesthetic was most commonly used at their hospital, 43.4% of medical professionals indicated it was ketamine, 37.7% indicated it was propofol, while the remaining medical professionals (18.9%) indicated it was halothane. All hospitals had running water and electricity, and 90.7% had a functional anaesthetic machine.

When ketamine was indicated as the general anaesthetic most commonly used at the hospital, it was also the anaesthetic with the highest availability; in these hospitals, ketamine was available at 82.6%, followed by an availability of 73.9% of propofol, a 65.2% availability of inhalant agents, and a 39.1% availability of thiopental. In hospitals where other general anaesthetics were indicated to be most commonly used, highest availability was

Table 1. Availability of anaesthesia commodities in Rwanda.

	Availability					
	General anaesthetic most commonly used at the hospital					
	Total (N=54)		Ketamine (N=23)*		Other general anaesthetic (N=30)*	
	N	%	N	%	N	%
General Anaesthesia						
Ketamine	42	77.8	19	82.6	23	76.7
Thiopental	24	44.4	9	39.1	15	50.0
Inhalant agents (halothane, isoflurane, sevoflurane)	29	53.7	15	65.2	14	46.7
Propofol	44	81.5	17	73.9	27	90.0
Infrastructure						
Running water	54	100.0	23	100.0	30	100.0
Electricity	54	100.0	23	100.0	30	100.0
Functional anaesthetic machine	49	90.7	21	91.3	27	90.0

*Missing data for one hospital.

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found for propofol (90.0%), followed by a 76.7% availability of ketamine, a 50.0% availability of thiopental, and a 46.7% of inhalant agents.

Key informant interviews

Sixty-nine individuals or national anaesthesia societies were contacted for participation in the study, of which ten agreed to participate. Key informant characteristics are provided in **Table 2**. Nine informants were knowledgeable about a country-specific context, while one informant had knowledge about the region in general.

Barriers to anaesthesia care

Multiple barriers to anaesthesia care were highlighted by the key informants. One of the main issues raised by all participants, was the lack of anaesthesiologists (**Table 3, Quote 1**). The number of anaesthesiologists was said to be critically low, with all anaesthesiologists primarily located in urban locations, in the more specialised hospitals. The key informant from the Democratic Republic of Congo (DRC) sketched this situation (**Table 3, Quote 2**). As a consequence, anaesthesia care is provided by non-physician providers, such as nurses and medical officers. However, eight of the key informants reported that these non-physician providers often had limited training in anaesthesia care, and do not have the skills or knowledge to provide more complex anaesthesia. This issue was highlighted by the key informant from Zambia (**Table 3, Quote 3**). One key informant also reported that protocols are not followed in some locations when providing anaesthesia care.

Another issue raised by the two informants from South Africa and Zimbabwe, was migration of trained anaesthesiologists, both within the country and abroad. For example, anaesthesiologists moved towards the private sectors, as they are offered better wages and working conditions there (**Table 3, Quote 4**). Crucially, the lack of medicines and equipment was also a significant barrier to anaesthesia care. Nine of the informants reported that

Table 2. Key informant characteristics.

Participant number	Country	Profession	Sex
P1	Regional	Anaesthesiologist	Female
P2	Democratic Republic of Congo	Anaesthesiologist	Male
P3	Ethiopia	Anaesthesiologist	Male
P4	The Gambia	Anaesthesiologist	Male
P5	Namibia	Anaesthesiologist; critical care	Male
P6	Nigeria	Anaesthesiologist	Male
P7	Somaliland	Nurse-anaesthetist	Male
P8	South Africa	Anaesthesiologist	Female
P9	Zambia	Anaesthesiologist; critical care	Male
P10	Zimbabwe	Anaesthesiologist	Female

the lack of medicines and equipment experienced in health facilities impedes the provision of anaesthesia care (**Table 3, Quote 5**). The respondent from Zimbabwe mentioned that the government, as part of the National Surgical, Obstetrician and Anaesthesia Strategy is purchasing equipment to tackle this problem. In South Africa, the respondent shared that availability of medicines has improved and is not a major issue there.

Lastly, four informants specifically mentioned the lack of training opportunities and attention, and subsequently the lack of budget, given to anaesthesia care. The informant from Ethiopia referred to the government's primary policy focus on prevention of infectious diseases, not on chronic diseases. The respondent from Namibia shared that only since 2018, doctors can train to become anaesthesiologists as part of the Namibian medical curriculum; before they needed to travel to other countries, such as South Africa, to study. In the Gambia there is no training available yet for anaesthesiologists. The informant from Zambia referred to the lack of attention among medical professionals and the public, as well as policy makers, as the main barrier to anaesthesia care (**Table 3, Quote 6**).

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Table 3. Barriers to accessing anaesthesia care, selected quotes.

Quote number	Quote (participant number)
1	*"In Somaliland still, they don't have any single local physician anaesthesia provider."* (P7)
2	*"The DRC is a large country with more than one hundred million inhabitants, but the number of anaesthetists is still low, less than 100 and all concentrated in the big cities: Kinshasa the majority, Lubumbashi (5 and doctors in training), East of the country (six), Central Kongo (two), and the rest of the provinces do not have anaesthetists and therefore the anaesthesia is done by anaesthesia technicians (anaesthesia nurses) or even nurses and general practitioners."* (P2)
3	*"Very, very few of the of the hospitals in Zambia have physician anaesthesiologists. Most of them have people that are below that level of training, and so they may not be able to provide very complex anaesthetics."* (P10)
4	*"More than 85% of our anaesthetists in South Africa that qualifies annually, leaves for the private sector. And the private sector sees less than 40% of the patient burden. So the number is really very skewed in our country. And now, with all the economic things that is happening, a lot of us are leaving the country as well."* (P8)
5	*"In general, anaesthesia care is growing. But it is highly challenged by availability of equipment and drugs. Like modern equipment, anaesthesia machines, monitoring equipment, like in the ICU too, […] and drugs like sevoflurane, the wide variety of modern drugs are lacking, it's not available. Access is highly limited."* (P3)
6	*"I would say the biggest barrier is maybe ignorance about the importance of anaesthesia. What anaesthesia's role is in the hospitals, and how big of an impact a good anaesthetic service would have on our health system. I think that ignorance translates into poor funding into the field. It translates into poor recruitment. It translates into poor sponsorships for healthcare workers who do want to study anaesthesia."* (P9)

DRC: Democratic Republic of Congo; ICU: Intensive Care Unit.

Ketamine for anaesthesia care

Ketamine was described as critical for the provision of anaesthesia care in their respective countries by all of the key informants. Five of the informants reported that in more specialised hospitals, where anaesthesiologists provide anaesthesia care, propofol, also a non-controlled substance, was the preferred anaesthetic. However, ketamine is also commonly used in these hospitals, specifically for haemodynamically unstable patients, hypotensive patients, patients who are in shock, and as a sedative in paediatric patients, patients with asthma or patients on the intensive care unit (ICU). Ketamine is also used for pain management. Four of the informants also referred to shortages of anaesthetics, such as propofol, that occurred in the specialised hospitals, which made them reliant on ketamine (**Table 4, Quote 1**).

Table 4. The importance of ketamine for anaesthesia care, selected quotes.

Quote number	Quote (participant number)
1	*"Propofol is the preferred one. The issue is, it's costly, and its availability is limited. […] So I would say, until recently, the majority of the cases are being induced by ketamine. But you know, request for propofol is highly increasing. We are getting, at least at my institution, We are getting more propofol these days."* (P3)
2	*"Ketamine is very important in DRC because it is available, cheaper, and easy to use even without an anaesthesia machine. Everyone – specialists, general practitioners, nurses – can use it."* (P2)
3	*"Some […] of the providers don't have the skill or knowledge of how to perform a spinal anaesthetic, and the majority of surgeries that are done in rural settings tend to be for obstetric emergencies in which a spinal anaesthetic may be, would be warranted. But because they don't have that skill, they would prefer to use a drug like ketamine that would […] keep the patient breathing on their own, and would allow for surgery to be done."* (P9)
4	*"Because out of the operation theatre, the [health] facility, in case if the patient lost breathing effort, the facility is not appropriate. So we will feel safe only when we are using ketamine, because, as compared to other sedative agents, its adverse effects, loss of breathing and so on, is very much minimal with ketamine compared to others. Because of all this, I think I would say ketamine is very important, you know."* (P3)
5	*"Ketamine is about the cheapest. The one we have here […] so that bottle is sold, in our local currency, that's about 500 Naira which is less than 1 USD. So, yeah, so it's always available. Propofol goes for 2,500 per ampoule. And that is about 4 times or 5 times the price of ketamine. Now, fentanyl goes for about 5,000 Naira. Which is about 10 times the price of ketamine. […] Then for regional anaesthesia, we're using bupivacaine, bupivacaine goes for 4,000. Which is about 8 times the price of ketamine per ampoule. So ketamine is somehow cheap and is available for us to use."* (P6)
6	*"Ketamine, eight months ago I would have said that number is very close to 100%. Because of how important it was. But with what's happening right now, the supply, I would say maybe under 10% of hospitals have it. We are one of the largest hospitals in the country, and we don't have ketamine. And usually we're the last to get hit. So I think that if we don't have ketamine I can't imagine many others will."* (P9)

DRC: Democratic Republic of Congo; ICU: Intensive Care Unit.

One of the primary reasons given for the importance of ketamine by all of the informants, is that it can easily be used by non-physician providers, who provide the bulk of anaesthesia services, especially in rural areas (**Table 4, Quote 2**). Informants shared that non-physician providers prefer to use ketamine as they are uncomfortable providing anaesthesia with alternatives because of potential side effects. Further, these providers often have only received a basic training in anaesthesia care and are not experienced with providing other anaesthetics (**Table 4, Quote 3**). Related, in lower-level hospitals and in rural areas, a lack of equipment, such as anaesthetic machines, exacerbated the difficulties of providing anaesthesia, and increased the reliance on ketamine, as they were fearful of the adverse consequences, and the possibility of death, when using other anaesthetic agents (**Table 4, Quote 4**). The informants from Somaliland and Nigeria raised the issue of affordability of medicines, and that next to ketamine being the most available anaesthetic agent, it was also the most affordable (**Table 4, Quote 5**).

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When the key informants were asked about the availability of anaesthetic agents in their respective countries as compared to the findings of the survey conducted in Rwanda, variations were reported. First, the informants emphasised it is difficult to report exact availabilities of the anaesthetics without conducting a similar survey. However, the informants shared that ketamine availability would be similar, or even higher, in their countries. Zambia was an exception, as the informant reported that for months preceding the interview, there had been critical shortages of ketamine (**Table 4, Quote 6**). The informant did not know the reason for the shortages. Informants from the DRC, Ethiopia, Nigeria, Somaliland and Zambia shared that the availability of propofol would be (slightly) lower than in Rwanda, especially in rural hospitals, while the informants from the Gambia, Namibia and South Africa shared that it would be more or less similar.

Misuse of ketamine

None of the key informants reported that misuse of ketamine was a significant issue in their respective countries, as far as they were aware. Three informants offered anecdotal evidence of specific instances of misuse that they knew or had heard about. The informant from the DRC had heard about a sickle cell patient misusing it for the treatment of vaso-occlusive crisis. Two informants shared that there was some misuse of ketamine among medical professionals in their countries. The Zambian informant shared that a medical professional had died as a consequence of the misuse. The South African informant reported that while she was aware of medical professionals that had misused ketamine and this issue should not be overlooked, the balance between control and access should be kept in mind (**Table 5, Quote 1**).

In all the other countries, the informants were unaware of misuse cases among medical professionals. Additionally, all of the informants shared that ketamine misuse among

the general public was not an issue. The informant from Nigeria shared their opinion that ketamine may be misused among the internally displaced. Some of the informants also shared that if misuse is occurring in high-income countries, it might eventually also happen in their countries (**Table 5, Quote 2**).

International scheduling of ketamine as a controlled substance

In three of the nine countries in which the informants work, ketamine is scheduled or regulated to some extent at the national level. In the Gambia, Namibia and South Africa, ketamine is stored in a locked cabinet, and medical professionals are required to request ketamine, and the release is signed off in a logbook by both the requesting medical professional as well as an in-charge nurse. However, in Namibia and South Africa informants shared that this procedure is not always followed as tightly as it might need to be (**Table 5,**

Table 5. Ketamine misuse and international scheduling, selected quotes.

Quote number	Quote (participant number)
1	"With the Schedule 5 [of ketamine] in South Africa, ketamine is also still locked. And ketamine is also still signed for. And I think education and the enforcement of patient-by-patient administration and access to ketamine is the best way for patient care and for protecting the provider, from […] exposing themselves to the risk of ketamine misuse." (P8)
2	"So when ketamine is being abused in other places, then it's likely that it will come here later. So I mean restricting those drugs not to be accessible for individuals, other than hospitals, has to be, I think, considered. But now it is not a major of a concept." (P3)
3	"In smaller hospitals, however, I have found that it's not as tightly controlled. So the ketamine ampoule will be given, and it will be placed on your product trolley for the day." (P8)
4	"I think in our local hospitals, there should be protocols on who to use ketamine. So if there are protocols and there are controls within the hospitals, such that whoever uses ketamine signs in and signs out. […] Whatever prescription has been, that he has written, should be stated clearly so that such can be traced. And also people handling ketamine. So we can now start using it as a [controlled] drug within the anaesthesia room. Such that it is not left in the open. So that it is only accessed when we need to use it." (P6)
5	"I think it's going to affect a lot of us who practice in rural communities. Because one, it's going to affect the availability. And how we access. And it's also going to make it very, very expensive. Because there will be a lot of controls, bottlenecks, trying to import ketamine, and make it available." (P6)
6	"It will just affect it as it is affecting the opioid supplies in our country. And having an opioid medication for analgesia is the hardest challenge that one can have. And we know the exact reason why. Because of the categorization of the medication." (P4)
7	"We can't be seen as part of the international group, if our resources and operational profile is completely different. I mean, I don't think it can be standardized that a drug that can potentially be life-saving, and a drug that is definitely part of our armoury for effective analgesia in a resource-limiting setting, that we are then under the same strict scheduling as a developed country that might have access to multiple other options." (P8)

Quote **3**). In the other countries, ketamine was not subject to additional, national control. Some of the informants from these countries could see the added value of having such controls at the national level for better stewardship (**Table 5, Quote 4**).

If ketamine were to be scheduled as a controlled substance at the international level, it was believed it would negatively impact access in the informants' respective countries, especially in the more rural locations. They all emphasised the critical importance of ketamine (**Table 5, Quote 5**). Informants from Namibia, the Gambia and Somaliland also made the comparison to already controlled substances, fearing the availability of ketamine would decrease to similar levels (**Table 5, Quote 6**). Next to the availability, some informants also raised concerns about increased costs of ketamine as a consequence of its scheduling, which would hamper access. In Zambia, where there is currently a shortage of ketamine, the informant shared their fears of this being the new reality. Lastly, one of the informants argued that LMICs and high-income countries should not be subjected to the same measures as they have very different resources available to them (**Table 5, Quote 7**).

Recommendations to improve access to anaesthesia care

Recommendations made by the key informants to improve access to anaesthesia care were related to increasing attention and budgets for anaesthesia care, training and retention of anaesthesiologists and non-physician providers, improving availability of medicines and equipment, and decentralisation of care. For example, the key informant with a regional perspective argued that countries need to take responsibility and put resources into anaesthesia care (**Table 6, Quote 1**). Similarly, the key informant from the Gambia argued for increasing the incentives to work in anaesthesia (**Table 6, Quote 2**). In line with this, the informant from Ethiopia argued for better collaboration between medical professionals and the Ministry of Health to ensure the medicines provided are the ones needed. The informant from Zimbabwe highlighted that, while much can still be improved, in the last few years, more and more attention has been paid to anaesthesia care. The informant from Nigeria pointed to COVID-19 for the increased availability of equipment, but also stressed the need for better policies without waiting for another pandemic to occur (**Table 6, Quote 3**). The importance of training of medical professionals was highlighted by the informant from Namibia (**Table 6, Quote 4**), while the informant from South Africa added the need to find a way to retain their trained specialists, as many are leaving to work in high-income countries. Last, the same informant also emphasised the importance of decentralisation of care, in which anaesthesiologists should go to rural areas to treat patients, instead of patients travelling far to come to the specialised hospitals in the big cities (**Table 6, Quote 5**).

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Table 6. Recommendations to improve access to anaesthesia care, selected quotes.

Quote number	Quote (participant number)
1	*"Unless the countries, governments, themselves do not take action, we will not succeed. So what has been done with those national anaesthesia, surgical and obstetric plans is important, that we must have the countries' governments to take responsibility. And that goes for training, […] and all kind of medications we are using, and so on."* (P1)
2	*"Incentivise the department of anaesthesia. Give more opportunity to those that are ready to go into it, because the competition is between specialities. So obviously everyone wants to go to an area where they have a better chance in their academic progress. So if you incentivise the department of anaesthesia, we will have so many clinicians or nurse anaesthetists who are giving safe anaesthetic care within the country."* (P4)
3	*"There should be a policy, a deliberate policy by government. […] COVID-19 came with a lot of problems. it opened our eyes to our emptiness. So after COVID-19, a lot of things have been done, provided. For example, anaesthetic machines, monitors, multi-parameter monitors, and even pulse oximeters, and the rest of them. [...] So what I will say is, we shouldn't wait for such things to happen."* (P6)
4	*"Training more people, having more staff in the department. So we have limited number of theatres, we're trying to expand the number of theatres that we have, but one of the stumbling blocks is limited number of [staff in the] anaesthesia department. So we're trying to push for more staff."* (P5)
5	*"Decentralisation of care is definitely, I feel, a buzzword, and is something that we need to do nationally and in sub-Saharan Africa really look at. That we don't spend all our money that is already limited, in bringing amounts and amounts of patients, 700, 900, 1000 kilometres, them staying in hospital for three, four, five nights, versus two specialists travelling down, sleeping over and delivering the same quality of care at the patient. So I do think decentralisation is definitely the way to go in sub-Saharan Africa for us to make… to actually make our healthcare service accessible to our patients"* (P8).

DISCUSSION

This is a first-of-its kind research on the importance of ketamine as detailed by anaesthesiologists working in SSA. It also studied the availability of ketamine compared to other anaesthetic agents specifically in Rwandan hospitals. The interviews with the key informants from across SSA found that there were significant barriers impeding access to anaesthesia care, including a general lack of attention given to the speciality by governments, a shortage of anaesthesiologists and migration of trained anaesthesiologists, and a scarcity of medicines and equipment. Ketamine was described as critical for the provision of anaesthesia care as a consequence of these barriers, and its scheduling would have a significantly negative impact on the quality of anaesthesia care that can be provided. The survey conducted in Rwanda found that availability of ketamine and propofol was comparable at around 80%, while thiopental and inhalant agents such as halothane, isoflurane or sevoflurane were available at only about half of the hospitals.

These barriers to anaesthesia care identified in this study have been identified previously in different contexts, and this research supports those findings (5,7,16–22,8–15). When the key informants were asked whether the availability in their respective countries was comparable to the availability found in Rwanda, the responses were variable. This is in line with previous research studying the availability of anaesthetic agents (7,10,22). For instance, a study from Liberia found that ketamine was available 76%-100% of the time in 88% of surveyed facilities, and this was the case for propofol in only 46% of facilities (7). Similarly, while anaesthesia using ketamine was available in 13 of 14 health facilities surveyed in Somalia, anaesthesia using inhalational agents was available at five of the facilities (10). Further, all surveyed hospitals in Rwanda had running water and electricity. Previous studies in Nigeria and Somalia found that access to running water and electricity was not guaranteed; the study in Nigeria found that hospitals suffered daily power outages ranging from 10-22 hours, and only 15% had running water (11). In Somalia, 28% of surveyed health facilities never or only sometimes had access to running water, and only 50% had consistent access to electricity (10). Last, in this study it was found that 90.7% of hospitals had a functional anaesthesia machine. In Tanzania, Nigeria and Somalia, 67%, 23% and 15% of hospitals, respectively, had a functional anaesthesia machine available (10,11,19).

The case study of Rwanda thus may not be representative of the availability in other countries in the region. However, this research has shown that even when other anaesthetic agents, such as propofol, are available, much of anaesthesia care is still provided using ketamine. This is due to the lack of trained anaesthesiologists, and the subsequent reliance on non-specialist anaesthesia providers, such as nurses and medical officers. These non-physician providers feel better prepared to provide anaesthesia using ketamine, as there are much fewer potential side-effects than the other agents. This has also been described elsewhere (30,36). Further, also in more specialised hospitals where anaesthesiologists are present to provide anaesthesia care, key informants shared ketamine is still one of the main anaesthetics used due to shortages of propofol that occur. A study conducted in district hospitals in Malawi, Zambia and Tanzania reported similar findings, showing that anaesthesia care at the district level is provided only by non-physician anaesthesia providers, and that ketamine was widely used to mitigate shortages of other anaesthetic agents (12).

In this study, the key informants reported that, as far as they were aware, misuse of ketamine is not a significant issue in their respective countries. A few did provide anecdotal evidence of specific instances of misuse among medical professionals. However, all informants believed scheduling ketamine internationally as a controlled substance would have a negative impact on access to anaesthesia care, as its availability would likely decrease. This fear is not unsubstantiated, as multiple informants referred to the difficulties with accessing opioids in their countries. In line with this, while in Liberia and Ethiopia ketamine was (almost) always available in 88% and 100% of facilities, respectively, morphine was (almost) always

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available at only 35% and 27% of facilities, respectively (7). Consequences of international scheduling are restrictions on production, manufacturing, importation, distribution and use of medicines, resulting in severely limited access to controlled medicines (37). It is thus paramount that ketamine does not become a scheduled substance. Instead, to safeguard against potential ketamine misuse in their respective countries, key informants believed in strengthening prescribing and dispensing practices in the healthcare setting. In many countries, ketamine is still freely available for all healthcare workers. Limiting ketamine so it is only obtainable for those allowed to use it may prevent future misuse. In Namibia, for example, ketamine is a Schedule 3 substance, and subsequently needs to be locked away and can only be sold or provided by designated personnel, on the basis of a prescription. The amount sold or provided has to be recorded in a logbook or prescription book (38).

LIMITATIONS

While this is the first study collecting experts' insights into the importance of ketamine for anaesthesia care in SSA, some limitations should be noted. In the survey conducted in Rwandan hospitals, no price or stock data was collected for the anaesthetic agents. This might have provided insights into the differences in costs between the different agents, and the availability over time. While the hospitals in Rwanda were contacted beforehand to schedule a visit for the survey, because the data collected for this study was part of a larger study on snakebites, it is believed that hospitals could not have taken measures that might have changed the availability numbers. Further, while more than 60 individuals and national anaesthesia societies were contacted, only ten individuals agreed to participate. Of these, only two were from West Africa. Due to this low number of respondents, it is difficult to assess whether topical fully saturation was reached. However, after initial analysis of eight interviews, the subsequent analysis of the last two interviews did not yield new insights, indicating potential data saturation. This study thus gives a first, detailed insight into the importance of ketamine for anaesthesia care in SSA. Further research may be undertaken to tease out more detailed, contextual factors that may not have been caught in this study.

CONCLUSION

This study has shown that ketamine is a critical medicine for the provision of anaesthesia care in SSA, as this field faces barriers related to its workforce and availability of medicines and equipment. If accessibility of ketamine changes as a result of its international scheduling, millions of people's access to safe surgical care will be in danger. Countries should strengthen prescribing and dispensing practices in the healthcare setting. Further, concerted efforts should focus on improving anaesthesia care in SSA in general, so in the future there can be less of a reliance on ketamine. Governments should focus more of their attention on the speciality, allocating more budget, facilitating training of more anaesthesiologists and non-physician providers, improving availability of medicines and equipment, as well as focusing efforts on retaining their anaesthesia workforce.

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CONTRIBUTION STATEMENT

GIO, HAvdH and AKM designed the study. GIO collected and analysed the data, and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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2.3

SUPPLEMENTARY DATA

Supplementary File 1. Interview gu ide

Introduction

1.   As an introduction, can you share a little about yourself and the work you do?

2.   Can you describe the anaesthesia care situation in [country] in general?

Ketamine in general

3.   I explained before that in this study we would like to get to know more about the use of ketamine as an anaesthetic in Sub-Saharan Africa. Can you describe in what way and to what extent ketamine is used in [country] for anaesthesia and surgical care?

4.   Can you describe ketamine availability and use for anaesthesia in relation to other anaesthetics and their availability and use in [country]?

5.   What would you say the importance is of ketamine for anaesthesia in [country]?
    a.   If it is important: why is ketamine an important anaesthetic in [country]?

Barriers to anaesthesia care

6.   You already described the anaesthesia care situation, but what do you think the main barriers to anaesthesia care are in [country]?

7.   Does ketamine play a role in alleviating some of these barriers?
    a.   If yes, how?

Rwanda Case Study

8.   In a study we recently conducted in Rwanda, we looked at the availability of anaesthesia commodities at hospital level and higher. Availability of general anaesthetics was:

	Availability	
	N	%
Ketamine	42	77.8
Thiopental	24	44.4
Inhalant agents (halothane, isoflurane, sevoflurane)	29	53.7
Propofol	44	81.5

How do these findings compare to the situation in your country? (Is Rwanda different compared to other Sub-Saharan African countries?)

International Scheduling

9. Are you familiar with the three international drug control conventions, which together establish internationally applicable control measures on narcotics and psychotropic substances (such as opioids, benzodiazepines, antipsychotics, etc.)? Their aim is to ensure the availability of these medicines for medical and scientific purposes, while at the same time preventing them from being diverted into illegal channels.
    (If yes, continue asking the question)
    (If no, explain about the conventions)

2.3

10. Ketamine is at the moment not internationally scheduled as a controlled substance. However, due to misuse in some high-income countries, especially in East and Southeast Asian countries like China, Hong Kong, Taiwan, and Japan, multiple attempts have been made to make ketamine an internationally controlled substance as well. What are your thoughts on the discussion at the international level about regulating ketamine more strictly?

11. In your opinion, do you think having ketamine scheduled internationally as a controlled substance, with subsequently the same types of measures put in place that regulate medicines such as morphine, oxycodone or fentanyl, would have an impact on its availability and use in [country]?
    ➔ *(Probe for more insights if necessary)*

12. Are there any special regulations in place for the manufacturing, distributing, use and handling of ketamine in [country]?

Misuse of ketamine

13. Are you aware of any incidences of misuse of ketamine in [country]?

14. Do you think ketamine misuse is a problem in your [country]?

15. How do you think misuse of ketamine can be prevented while at the same time ensuring it remains accessible for medical use?

16. Do you have any suggestions on how in the future access to anaesthesia care can be safeguarded or improved in [country], both with regards to ketamine but also looking broader than that?

17. Is there anything else you would like to share with me before we conclude?

Supplementary File 2. Informed Consent Form
The impact of scheduling ketamine as an internationally controlled substance on surgical and anaesthesia care in Sub-Saharan Africa

2.3

Principal Researcher	**Organisation**
Gaby Ooms	Health Action International
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	Amsterdam, The Netherlands

Study background

Access to surgical and anaesthesia care is a major issue for many people living in Sub-Saharan Africa, where more than 95% of the population does not have adequate access to it. In this region alone, an additional 41 million surgical procedures are needed each year. Lack of access to surgical and anaesthesia care in Sub-Saharan Africa is caused by lack of specialised healthcare workers, lack of basic infrastructure, lack of surgical and anaesthesia equipment, and lack of essential medicines. As a consequence, in much of Sub-Saharan Africa, surgical procedures often take place without anaesthesia or pain management. To alleviate the suffering of patients in these settings, hospitals have become reliant on ketamine for anaesthesia. Ketamine is listed as an anaesthetic on the WHO Model List of Essential Medicines.

Unfortunately, ketamine is misused in high-income countries, and especially in East and Southeast Asia, like China, Hong Kong, Taiwan, and Japan. Because of the misuse in these countries, China has submitted multiple requests to schedule ketamine internationally as a controlled substance, which would lead to more stringent regulation. The requests were denied, but it is likely that more will be made in the future. This research therefore aims to estimate the importance of ketamine for anaesthesia and surgical care in Sub-Saharan Africa, and what the impact might be of international scheduling of ketamine on access. This will be done through key informant interviews.

Research team

The principal investigator of this study is Gaby Ooms (HAI/Utrecht University, the Netherlands), who is supported by Dr. Mohammed Usman (Federal Medical Centre Birnin Kudu, Nigeria), Dr. Rianne van den Ham (Utrecht University, the Netherlands), Dr. Aukje Mantel-Teeuwisse (Utrecht University, the Netherlands), and Dr. Tim Reed (HAI, the Netherlands). Should you have any questions about the project, please feel free to contact the researchers.

Data Collection

This research project consists of key informant interviews. We would like to ask you to participate in an interview to get your insights on the relevance of ketamine for surgical and

anaesthesia care in the country/countries where you work. The interview is expected to take about 30 minutes of your time. The interview is semi-structured and will be guided by a set of questions. It will be completed online (Zoom, Teams) or over telephone, according to your preference. With your permission, the interview will be recorded and transcribed for analysis purposes afterwards.

Discomforts/risks

The research team does not believe there are any foreseeable risks associated with this project. If you have any concern on this matter, we do encourage you to get in touch with us via the contact information at the end of this letter.

Benefits

Research is fundamental in healthcare. This project attempts to estimate the importance of ketamine for anaesthesia and surgical care in Sub-Saharan Africa, and what the impact will be of international scheduling of ketamine on access, so fitting action may be taken if necessary.

Compensation

No compensations can be granted for your participation in the study.

Participant's rights

Participation in this study is completely voluntary. You are not under any obligation to participate. If you agree to participate, you can withdraw from the study at any time without consequences. Any data collected from you will be deleted and will not be used in the research. If you agree to take part, you are asked for your consent at the start of the interview. You will be provided with a copy of the information sheet and the consent form for your records.

Questions

Any time during or directly before or after the interview, the participant can ask the researchers questions related to the research. If the participant has questions after the research, the researchers can be reached by the email address as written on the first page of this participant information sheet.

Confidentiality

Information gathered about you will be held in strict confidence. Your name and any other identifying information will be removed from any data. A key (E.g., P1, P2, P3, etc.) will be used to refer to participants within the research. No individual respondents will be able to be identified in any publications or presentations. All data will be stored on a secure Drive and will only be made available to the researchers. The recordings of the interviews will be

deleted after transcription is completed. The transcripts will be stored securely for a period of ten years, after which they will also be deleted.

Study findings

The findings of the research project will be published in a scientific peer-reviewed journal and may be presented at meetings and conferences. You can choose to receive a copy of the publication when the study is published. Should you wish to, then please indicate so in the interview.

Complaints or concerns

If you wish to make a complaint regarding the manner in which this research project is conducted, it should be directed to Tim Reed (tim@haiweb.org, +31 (0) 20 412 4523). If you have any worries or complaints about your privacy, please contact privacy-beta@uu.nl. Any complaint or concern will be treated in confidence and will be fully investigated. You will be informed about the outcome.

The interviewer has discussed this information with me and offered to answer my questions. For any further questions, I may contact Gaby Ooms.

STATEMENT OF CONSENT

This is the statement you will be asked to consent to at the start of the interview.

... has described to me what is going to be done, the risks, the benefits involved and my rights regarding this study. I understand that my decision to participate in this study will not negatively affect me. In the use of the study information, my identity will be concealed. I am aware that I may withdraw at any time. I understand that by consenting to this statement, I do not waive any of my legal rights but merely indicate that I have been informed about the research study in which I am voluntarily agreeing to participate. A copy of this form will be provided to me.

Do you consent to participate in this research?
I hereby declare that I have read the information letter about the "impact of scheduling ketamine as an internationally controlled substance on surgical and anaesthesia care in Sub-Saharan Africa" study and agree to participate in the study.

Name **Signature**

Date

3

TREATMENT OF SNAKEBITE ENVENOMING

"Snakebite is essentially a disease of the poor. [It] is the biggest public health crisis you have likely never heard of."

– Kofi Annan

3.1

THE BURDEN OF SNAKEBITE IN RURAL COMMUNITIES IN KENYA: A HOUSEHOLD SURVEY

Gaby I Ooms, Janneke van Oirschot, Benjamin Waldmann,
Dorothy Okemo, Aukje K Mantel-Teeuwisse,
Hendrika A van den Ham, Tim Reed

ABSTRACT

Background

Annually, about 2.7 million snakebite envenomings occur worldwide, primarily affecting those living in rural regions. Effective treatment exists but is scarce, and traditional treatments are commonly used. To inform context-specific policies in Kenya, this study aimed to determine the health-seeking behaviour, and the health, social, and economic burden of snakebites in rural communities.

Methods

Non-probability sampling was used to survey 382 respondents from four snakebite-endemic counties, from February to August 2020 using a structured questionnaire. Descriptive statistics, fisher's exact tests, binary logistic regressions and Mantel-Haenszel tests were used for analysis.

Results

Life-time experience with snakebites included 13.1% of respondents who reported being personally bitten and 37.4% who reported knowing of a community member being bitten. Respondents reported death after a snakebite in 10.5% of bitten community members and 14.6% of bitten family members. Risk of snakebite was not significantly associated with sex, educational level, or occupation. Snakebite victims were most often walking (38%) or farming (24%) when bitten. Of those bitten, 58% went to a health facility, 30% sought traditional treatment, and 12% first went to a traditional healer before visiting a facility. Significant differences existed in perceptions on the financial consequences of snakebites among those who had been personally bitten and those who had observed a snakebite. Most commonly mentioned preventive measures were wearing shoes and carrying a light in the dark.

Conclusion

Community engagement, including engagement with traditional healers, is needed to reduce snakebites. This should be done through education and sensitisation to improve used preventive measures and effective health-seeking behaviour.

3.1

INTRODUCTION

Snakebite is a major public health problem, especially affecting those living in developing countries. The World Health Organization (WHO) estimates that each year about 5 million snakebites occur, of which 2.7 million are envenomings (1). In sub-Saharan Africa, up to 32,000 snakebite deaths are estimated to occur every year, but the actual number of deaths remains unknown (2). To draw attention to the devastating impact and to coordinate a response, snakebite was pronounced a Category A Neglected Tropical Disease by the WHO in 2017. A year later Member States passed a resolution at the World Health Assembly, and in 2019 the WHO launched a global snakebite strategy for prevention and control with the aim of reducing the morbidity and mortality due to snakebite envenoming by 50% by 2030 (3,4).

3.1

Despite these efforts, the health burden of snakebite, even though preventable, is enormous, and it mainly affects the poor. People living in rural regions, who often engage in some type of outdoor livelihood, are most prone to being bitten; estimates show that more than 95% of envenomings and snakebite deaths in sub-Saharan Africa occur in rural areas, especially in young, outdoor-working people and children (playing outside) (2,5,6).

Simple and effective treatment of snakebite envenoming has been around for decades. Good-quality antivenoms, if adequately and timely administered, can effectively reverse and cure envenoming, whereas consequences of snakebite, when not adequately and timely treated, can be death, disability, and psychological distress and stigmatisation (2). Unfortunately, in sub-Saharan Africa access to health services in general, and to antivenom specifically, is generally scarce in the remote areas highly affected by snakebite, contributing to the high death and disability rates among snakebite victims (7–11). If treatment is obtained, its costs can be catastrophic for households when this is not covered by health insurance or available for free in the public sector. In sub-Saharan Africa, the wholesale price of one vial of antivenom ranges from USD 18 to USD 200, and the average cost of a fully effective antivenom treatment regimen is USD 124 (9). Also, the sometimes permanent loss of income due to disability or death can result in additional financial hardship (2,6).

To improve the situation for people bitten by snakes, research is needed to fill the gaps in knowledge that exist in many sub-Saharan African countries. Evidence is needed on communities' beliefs on snakes and snakebites, on patient profiles and risk factors, and on health-seeking behaviour and health outcomes after a snakebite. To further explore the lived realities of people after a snakebite, more also needs to be known about its socio-economic consequences. Together, such evidence provides a clear picture of the snakebite burden, which is needed to create buy-in at the national level for the development of context-specific health policies and tailored community-informed educational campaigns to meet local needs. To contribute to this evidence base, a household survey was conducted in four counties in Kenya with a high snakebite prevalence to determine the health, social, and economic burden of snakebites in rural communities.

METHODS

This study was designed as a quantitative cross-sectional study, consisting of a household survey.

Study area and sampling

The study was conducted in four snakebite prevalent Kenyan counties: Kajiado County, Kilifi County, Kwale County, and Taita Taveta County (12). Kenya is divided into 47 counties, and each county is further divided into sub-counties. Kilifi, Kwale, and Taita Taveta counties are in the coastal region, and Kajiado County is located in the mainland, within the Nairobi Metropolis. The four counties share some of their borders. Venomous snakes commonly found in all four counties include the black mamba, eastern green mamba, red spitting cobra, James Ashe spitting cobra, puff adder, and boomslang. The Egyptian cobra (Kajiado County), Eastern forest cobra and yellow-bellied sea snake (Kwale and Kilifi counties), black-necked spitting cobra (Taita Taveta, Kwale, and Kajiado counties), and twig snake (Kilifi, Kwale, and Taita Taveta counties) are also venomous snakes found here (13).

In each county, the median subcounty in terms of population density was selected as the study area (14). These were Kajiado Central, Kaloleni, Samburu, and Mwatata, respectively. The four sub-counties have a total population of 634,366 inhabitants (14). To calculate the sample size, the following formula was used:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where n = sample size, Z = level of confidence, P = expected prevalence or proportion, and d = margin of error. With a 95% confidence interval, the Z value is 1.96, P is 0.5 when the expected proportion is unknown, and d is set at 0.05 (15). The subsequent sample size was 384.

A probability sampling technique was used to gather 100 respondents per subcounty. The specific communities to be surveyed were randomly selected by the data collectors. They were free to choose the communities based on convenience sampling as long as the communities met the following selection criteria: 1. the community consists of at least 40 households, and 2. communities surveyed within the subcounty cannot be neighbouring one another. Within a community, households were selected using systematic sampling, a fixed interval selection method that is easy to use, is low cost, and has relative validity (16). The first household selected was the dwelling closest to the data collectors when arriving in the community. If this household did not want to participate or if no one was home, the neighbouring dwelling was approached, until a first participant was found. Thereafter,

data collectors skipped two dwellings each time after finishing a survey. Community members included in the study had to meet the following criteria: 1. living in the selected community; 2. aged 18 years or older; and 3. ability to give consent.

Data collection

Data were collected using a structured questionnaire with a mix of open-ended and closed-ended questions. Specifically, questions gathered information on household composition; income and expenditure; occupation; personal or second-hand experience with snakebites; social, financial, and health outcomes; snakebite cases in the community; beliefs about snakes and snakebites; preventive measures; and actual and hypothetical health-seeking behaviour after a snakebite. The data collection tool was piloted among 10 community members in November 2019, after which slight alterations were made to improve understandability of the questions.

Due to the COVID-19 pandemic, data collection occurred in two time periods: February–March 2020 and August 2020. Data were collected using a mobile data collection application. Data collection was performed by local data collectors working in pairs and supervised by one of the authors (DO). Data collectors received a two-day training, which included a field test of the questionnaire. The survey was conducted in English or Kiswahili, with data collectors translating the questions from English to Kiswahili and back while conducting the survey. Questions pertaining to personal experiences with snakebite were only asked if the participant indicated to have been bitten by a snake. Questions about snakebite patient profiles, actual health-seeking behaviour, and health outcomes after a snakebite in the community were asked only if the participant had personal experience with a snakebite or knew a family member or community member who had been bitten by a snake. If the respondents knew a family member or community member who had been bitten, they were asked about the most commonly observed patient profiles, health-seeking behaviour, and health outcomes after a snakebite. All participants were asked about their beliefs on snakebites, preventive measures, and their presumed health-seeking behaviour if they were to be bitten by a snakebite.

Data management and analysis

Data were regularly uploaded to the server and downloaded into a Microsoft Excel spreadsheet by the researcher and imported into Stata. Data entries were checked for accuracy and cleaned when necessary. Missing data were excluded from the analysis. Analysis was carried out using Stata version 16. Descriptive analyses were performed to obtain frequencies and medians. Binary logistic regression and Mantel-Haenszel tests were performed to study the association between sociodemographic characteristics (sex, area, county of residence, level of education, occupation) and having experienced a snakebite. Two models were developed: 1. a model not correcting for potential confounders except

3.1

for the age of the respondent, and 2. a multivariate model in which all variables, including age of the respondent, were entered simultaneously. Associations are represented as odds ratios with 95% confidence intervals, and a significance level of 0.05 was used to determine statistical significance. Fisher's exact tests were performed to investigate the association between personal versus observed (among a family member or community member) snakebites and perceived social outcomes, and to test the association between personal, observed, or no experience with snakebites and beliefs on snakes, preventive measures, and health-seeking behaviour. The significance level was again determined at 0.05.

3.1 Ethical considerations

Ethical approval was granted by the Amref Health Africa Ethics and Scientific Review Committee (reference number P583-2019), and permission for the study was granted by the National Commission for Science, Technology an Innovation (license number NACOSTI/P/20/5492). Permission letters for the data collection were obtained from the counties' Directors of Health. Before starting the survey, participants were provided with information on the aim of the study and asked to sign an informed consent form.

COVID-19

Data collection in three counties took place from the end of February 2020 until the beginning of March 2020. As a consequence of the COVID-19 pandemic, data in Kwale County were collected in August 2020, only after the lockdown measures were lifted in Kenya and such research was allowed again. All necessary precautions to ensure the health of the respondents and data collectors were taken during this data collection period. These precautions included keeping to social distancing measures, providing all data collectors with face masks and hand sanitizer for themselves as well as for the respondents, and conducting the surveys only through one-on-one interviews to prevent crowding or unnecessary interaction. Further, Kwale County had a low incidence of COVID-19 cases at the time the data were collected, and data collectors adhered to the curfew measures in place during this time period.

RESULTS

In each county, respondents were surveyed from 9 to 11 different communities. Eight respondents refused to participate, and 12 were not at home at the time of the survey. Respondents were from Kajiado (N=100), Kilifi (N=93), Kwale (N=89), and Taita Taveta (N=100) counties (**Table 1**). About half (50.8%) of respondents were male, almost half of the sample had a lower (pre-primary or primary) level of education (45.8%), and 46.6% worked in the agricultural sector. The median age was 39.5 (range: 18.0–88.0) years, and respondents had a median monthly household income of USD 78.4 (range: 4.9–2,939.2) (Supplementary File 1).

Table 1. Characteristics of the sample, total and stratified by county.

	Total (N=382)		Kajiado (N=100)		Kilifi (N=93)		Kwale (N=89)		Taita Taveta (N=100)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
Sex										
Male	194	50.8	44	44.0	44	47.3	65	73.0	41	41.0
Female	188	49.2	56	56.0	49	52.7	24	27.0	59	59.0
Age										
18-25 years	46	12.0	24	24.0	7	7.5	5	5.6	10	10.0
26-35 years	105	27.5	39	39.0	25	26.9	21	23.6	20	20.0
36-45 years	91	23.8	16	16.0	27	29.0	28	31.5	20	20.0
46-55 years	69	18.1	12	12.0	17	18.3	16	18.0	24	24.0
56-65 years	46	12.0	4	4.0	15	16.1	14	15.7	13	13.0
66+ years	25	6.5	5	5.0	2	2.15	5	5.6	13	13.0
Head of Household										
No	159	41.6	51	51.0	41	44.1	19	21.4	48	48.0
Yes	223	58.4	49	49.0	52	55.9	70	78.7	52	52.0
Level of education										
No formal schooling	72	18.9	32	32.0	21	22.6	4	4.5	15	15.0
Lower	175	45.8	31	31.0	47	50.5	25	18.1	72	72.0
Higher	135	35.3	37	37.0	25	26.9	60	67.4	13	13.0
Occupation										
Agricultural	178	46.6	31	31.0	42	45.2	24	27.0	81	81.0
Indoor-based	108	28.3	38	38.0	31	33.3	30	33.7	9	9.0
Unemployed	83	21.7	30	30.0	17	18.3	28	31.5	8	8.0
Retired	13	3.4	1	1.0	3	3.2	7	7.9	2	2.0

[a]Low: pre-primary, primary; Middle: vocational secondary, secondary; High: post-secondary, university.

[b]Agricultural: herding, farming; Indoor-based: shop/service worker, teacher, civil servant, health worker, student, small business owner.

Snakebites, health outcomes, and patient profiles

Of the 382 respondents, 50 (13.1%) had ever been personally bitten by a snake, 55 (14.4%) had a family member who had ever been bitten, and 143 (37.4%) knew a community member who had been bitten (Supplementary File 2). Respondents indicated that in the previous 12 months, a median of 1 (range: 0–6) people had been bitten in their community. Reported permanent disability as a result of the snakebite ranged from 3.6% to 9.1%. A range of disabilities were mentioned, including amputations, swelling, tissue damage, nonhealing ulcers, and twisted limbs. Of the respondents who knew a family member or community member who had been bitten by a snake, 8 (14.6%) and 15 (10.5%) respondents, respectively, indicated the person bitten had died.

Snakebite was not significantly associated with sex, county, level of education, or occupation (**Table 2**). Although it was not statistically significant, no formal education seemed to

contribute to a higher snakebite incidence, as did having an outdoor occupation compared with an indoor-based occupation. The median age of people when bitten by a snake was 34.0 (range: 8.0–67.0) years. The most common activities at the time of the bite were walking (38%) and farming (24%), and the majority of respondents were bitten during daylight (60%) (**Table 3**). No clear difference was found in dry versus rainy season in occurrences of snakebites. The feet (48%) and legs (36%) were the most common bite sites. In one third of the cases, the respondent indicated that the snake was identified. Indicated snake types can be found in **Table 3**. In 20% of the cases, the snake was killed. The patient profiles and characteristics of the bite of those personally bitten by a snake were similar to those as most commonly described by the respondents who had observed a snakebite (Supplementary File 3).

3.1

Table 2. Associations between snakebite and sociodemographic characteristics.

				Total population (n=382)	
	N (total)	*N* (bitten)	%	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)
Sex					
Male	194	30	15.5	Ref	Ref
Female	188	20	10.6	0.72 (0.38-1.34)	0.61 (0.30-1.24)
County					
Kajiado	100	7	7.0	Ref	Ref
Kilifi	93	13	14.0	1.51 (0.55-4.16)	1.59 (0.56-4.46)
Kwale	89	16	16.9	1.82 (0.67-4.93)	2.10 (0.71-6.27)
Taita Taveta	100	15	15.0	1.63 (0.61-4.37)	1.73 (0.59-5.13)
Level of education[c]					
No formal schooling	72	11	15.3	Ref	Ref
Lower	175	27	15.4	1.14 (0.51-2.54)	0.84 (0.35-2.04)
Higher	135	12	8.9	0.67 (0.27-1.68)	0.43 (0.14-1.37)
Occupation[d]					
Agricultural	178	27	15.3	Ref	Ref
Indoor-based	108	9	7.4	0.57 (0.24-1.34)	0.75 (0.27-2.04)
Unemployed	83	10	12.1	1.08 (0.47-2.49)	1.32 (0.53-3.33)
Retired	13	5	38.5	2.13 (0.59-7.71)	2.31 (0.56-9.50)

CI = Confidence interval; OR = Odds ratio; Ref = reference.

[a]Variables were entered separately into the model. The model was corrected for age of the respondent.

[b]All variables were entered simultaneously into the model. The model was also corrected for age of the respondent.

[c]Low: pre-primary, primary; High: vocational secondary, secondary, post-secondary, university.

[d]Agricultural: herding, farming; Indoor-based: shop/service worker, teacher, civil servant, health worker, student, small business owner.

Table 3. Characteristics of the snakebite and health-seeking behaviour.

			Personally bitten (n=50)		
	N	*%*		*N*	*%*
Age when bitten			**Care sought**		
0-17 years	7	14	Traditional treatment	15	30
18-25 years	9	18	Healthcare at facility	29	58
26-35 years	13	27	Traditional treatment and healthcare	6	12
36-45 years	12	25	**Traditional treatment received**		
46+ years	8	16	Black stone	12	57
Activity at time of bite			Healing plants	12	57
Walking	19	38	Suck out venom	9	43
Farming	12	24	Cut bite	5	24
Collecting firewood	5	10	Tourniquet	2	10
Herding	4	8	Wash bite	2	10
Sleeping	3	6	Burn bite	1	5
Charcoal burning	2	4	**Outcome traditional treatment**		
Activity inside house	2	4	Fully healed	15	71
Playing	1	2	Not fully healed, went to facility	6	29
Don't know	2	4	**Reason for visiting traditional healer**		
Part of the day when bitten			Close by, facility too far away	18	90
During daylight	30	60	Cheap, facility too expensive	7	35
In the dark	20	40	Only one who can treat snakebite	3	15
Season when bitten[a]			No treatment available at facility	3	15
Dry season	18	36	Provides first aid	1	5
Rainy season	15	30	**Sector facility visited**		
Don't know	17	34	Public	28	85
Body part bitten			Private	2	6
Foot	24	48	Private not-for-profit	3	9
Leg	18	36	**Treatment received at facility**		
Arm	6	12	Antivenom	14	42
Hand	2	4	Antibiotics	12	36
Snake identified			Painkillers	9	27
No	17	34	Anti-tetanus injection	8	24
Yes	17	34	Referred to another facility	6	18
Don't know	16	32	Fluids	3	9
Type of snake[b]			Adrenaline	2	6
Black mamba	10	59	Antihistamine	1	3
Red spitting cobra	5	29	Surgery	1	3
Egyptian cobra	1	6	Don't know	4	12
Vine snake	1	6			
What happened to snake					
It slithered away	36	72			
It was killed	10	20			

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Table 3. (continued)

			Personally bitten (n=50)		
	N	%		*N*	%
It stayed in the same place	3	6			
It was not seen	1	2			

[a]Dry season: January, February, March, July, August, September; Rainy season: April, May, June, October, November, December.

[b]Type of snake as identified by the victim. Correct identification of the type of snake is therefore not certain.

Health-seeking behaviour after a snakebite

Almost 60% of those personally bitten by a snake went to a health facility after their bite, and 12% first went to a traditional healer before they went to a health facility (**Table 3**). Thirty percent only sought traditional treatment. The most common traditional treatments received were the use of a black stone or healing plants (57%), sucking the venom from the bite (43%), and cutting the bite (24%). Of those who had visited a traditional healer, 29% went to a health facility afterward because they were not healed. Respondents indicated that the most common reason for consulting a traditional healer after their snakebite was because the traditional healer was close by and the health facility far away (90%). Another reason was that it was cheaper than going to the health facility (35%). When the respondents visited a health facility after the bite, in more than 80% of the cases they went to a public facility. In 42% of the cases, the respondents indicated they had received antivenom at the health facility. A visit to a health facility after a snakebite was more quickly initiated than a visit to a traditional healer (31.0 [range: 5.0–270.0] minutes versus 60.0 [range: 0.0–3,600.0] minutes, respectively) (Supplementary File 4).

Financial and social consequences of the snakebite

Snakebites had an impact on people's work life: 44% indicated their ability to work was affected, 60% reported they were not able to do the same job after the snakebite as before, and 14% stated they had lost their job as a consequence of the snakebite (**Table 4**). Their financial situation was also affected, with 38% noting a loss of income and 20% declaring they went into debt due to the snakebite. There was a significant difference in perceptions of those who had been personally bitten by a snake and those who had observed a snakebite regarding whether the snakebite caused a loss of job (P=0.001), loss of income (P<0.001), or debt (P=0.002). Almost half of the respondents (46%) also indicated they were unable to afford the hospital bills for the snakebite treatment; the median out-of-pocket cost of snakebite treatment was USD 24.5 (range: 0.0–734.8) (Supplementary File 3). Again, perceptions on this differed among those personally bitten and those who had observed a snakebite (P<0.001). Social exclusion or stigmatisation was reported by 6% of those personally bitten and by 3.6% of those who had observed a snakebite.

Beliefs on snakes and snakebite prevention and potential health-seeking behaviour

All respondents were asked about their beliefs on snakes, preventive measures, and health-seeking behaviour if they were to be bitten by a snake (hypothetical scenario). The majority of respondents (68.4%) thought snakes bite when you step on them or disturb them (**Table 5**). When stratifying by personal experience with a snakebite, observing a snakebite among a family member or community member, and no experience with a snakebite, responses differed significantly between the groups for the answer option "snakes bite when

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Table 4. Financial and social consequences of a snakebite, personally experienced and observed.

	Personally bitten (n=50)		Observed snakebite (n=141)		
	N	%	*N*	%	p-value
Ability to work affected by snakebite					
No	27	54.0	NA	NA	-
Yes	22	44.0	NA	NA	
Don't know	1	2.0	NA	NA	
Able to do same job after snakebite as before					
No	30	60.0	NA	NA	-
Yes	17	34.0	NA	NA	
Don't know	3	6.0	NA	NA	
Loss of job due to snakebite					
No	42	84.0	99	70.2	0.001
Yes	7	14.0	10	7.1	
Don't know	1	2.0	32	22.7	
Loss of income due to snakebite					
No	29	58.0	100	70.9	<0.001
Yes	19	38.0	17	12.1	
Don't know	2	4.0	24	17.0	
Debt due to snakebite					
No	38	76.0	93	66.0	0.002
Yes	10	20.0	14	9.9	
Don't know	2	4.0	34	24.1	
Unable to afford hospital bills for snakebite treatment					
No	26	52.0	93	66.4	<0.001
Yes	23	46.0	16	11.4	
Don't know	1	2.0	31	22.1	
Socially excluded or stigmatized because of snakebite					
No	45	90.0	114	80.9	0.063
Yes	3	6.0	5	3.6	
Don't know	2	4.0	22	15.6	

NA: Not applicable.

Table 5. Beliefs on snakes and snakebite prevention, and hypothetical health-seeking behaviour if a snakebite occurred, stratified per snakebite experience.

	Total (n=382)		Personal snakebite (n=50)		Observed Snakebite (n=141)		No experience (n=191)		
	N	*%*	*N*	*%*	*N*	*%*	*N*	*%*	p-value
Reasons why snakes bite									
Hungry	11	2.9	1	2.0	4	2.8	6	3.2	1.000
Scared	61	16.1	15	30.6	25	17.7	21	11.1	**0.004**
Stepped on/disturbed	260	68.4	32	65.3	98	69.5	130	68.4	0.851
Animals in house	30	7.9	5	10.2	11	7.8	14	7.4	0.774
Accident	9	2.4	2	4.1	3	2.1	4	2.4	0.651
Sent by bad spirits	37	9.7	2	4.1	15	10.6	20	10.5	0.388
Sent by somebody to harm	39	10.3	8	16.3	15	10.6	16	8.4	0.238
No reason	23	6.1	2	4.1	12	8.5	9	4.7	0.336
Don't know	44	11.6	4	8.2	9	6.4	31	16.3	**0.015**
Preventive measures									
Wear shoes	187	49.5	25	51.0	66	47.1	96	50.8	0.797
Carry a light in the dark	169	44.7	23	46.9	54	38.6	92	48.7	0.179
Ensure no snake can enter house	97	25.7	11	22.5	38	27.1	48	25.4	0.821
Do not hurt or touch snakes	88	23.3	14	28.6	31	22.1	43	22.8	0.636
Kill snake	78	20.6	7	14.3	27	19.3	44	23.2	0.364
Preventive herbs around house	55	14.6	7	14.3	21	15.0	27	14.3	0.979
No animals in house	49	13.0	5	10.2	22	15.7	22	11.6	0.489
Preventive spray around house	49	13.0	5	10.2	16	11.4	28	14.8	0.607
Clear bushes around house	30	7.9	2	4.1	7	5.0	21	11.1	0.092
Don't know	8	2.1	2	4.1	4	2.9	2	1.1	0.221
Type of care after bite									
Traditional healer	23	6.1	6	12.2	7	5.0	10	5.3	0.185
First aid	200	52.6	23	46.9	81	57.5	96	50.5	0.315
Community health worker	71	18.7	9	18.4	23	16.3	39	20.5	0.620
Health facility	321	84.5	33	67.4	115	81.6	173	91.1	**0.001**
First aid after bite[a]									
Tourniquet	157	78.5	17	73.9	59	72.8	81	84.4	0.141
Black stone	93	46.5	12	52.2	29	35.8	52	54.2	**0.044**
Cut the bite	49	24.5	3	13.0	23	28.4	23	24.0	0.329
Wash the bite	16	8.0	0	0.0	7	8.6	9	9.4	0.397
Pain killers	13	6.5	1	4.4	5	6.2	7	7.3	1.000
Antibiotics	11	5.5	1	4.4	3	3.7	7	7.3	0.624

[a]Only asked if respondent indicated they would use first aid after a snakebite.

they are scared" (P=0.004), which was more often selected by those who had personally experienced a snakebite, and "don't know" (P=0.015), which was more often selected by those with no experience with snakebites.

There was a range of preventive measures mentioned by the respondents, including wearing shoes (49.5%), carrying a light in the dark (44.7%), and ensuring no snakes can enter the house by covering holes and openings (25.7%). Not hurting or touching a snake was mentioned by 23.3% of the respondents, whereas its opposite measure, killing a snake, was mentioned by 20.6% of the respondents. No significant differences in responses were found when stratified based on experience with snakebites.

When respondents were asked about their hypothetical health-seeking behaviour after a snakebite, the majority would use (traditional) first aid methods (52.6%) and would go to a health facility (84.5%). Only 6.1% indicated they would go to a traditional healer. When stratified by experience with snakebite, there was a significant difference in the choice of going to a health facility after a snakebite or not, with those having experienced a snakebite choosing the option of going to a health facility less often than the other two groups (P=0.001). When asked about the traditional first aid they would use, using a tight bandage or tourniquets (78.5%), using a black stone (46.5%), and cutting the bite (24.5%) were the most commonly mentioned practices. The potential use of a black stone if the respondent were to be bitten by a snake differed significantly between the stratified groups (P=0.044). The fact that the health facility is far away (52.8%) and care at the health facility being expensive (34.0%) were the reasons given why respondents would not visit a health facility if they were to be bitten by a snake. The medicines that were most commonly indicated by respondents that should be used after a snakebite were antivenom (58.9%), antibiotics (39.1%), and pain killers (32.3%).

DISCUSSION

This study aimed to provide a broad overview of the extent of the problem and impact of snakebite in four snakebite-prevalent counties in Kenya. Although it does not intend to provide a generalizable incidence or prevalence of snakebites in the counties, it does indicate the extent to which these communities are affected by snakebite and can be used as a baseline to guide the development of policies and programmes shaped to local needs. It is especially important in the current context where shifting priorities due to the COVID-19 pandemic are likely to affect snakebite prevention and care on all levels negatively. Therefore, within a rapidly changing environment, evidence on the effects of snakebite, both past and present, within rural communities can provide the authorities with valuable insights to shape policies informed by realities on the ground. This is even more necessary in the absence of any mechanisms to collect robust data on snakebites in communities in Kenya.

Our results show that snakebites were common in the surveyed communities; more than one-third of the surveyed community members had some experience with snakebites, and it frequently led to death or disability. This study also provides evidence of the demographic characteristics of those affected: the median age of those bitten was 34.0 years, with

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the majority aged 26–45 years. Further, traditional healing still played an important role in the treatment of snakebites in the surveyed communities. Some of the known preventive measures included wearing shoes and carrying a light in the dark, although these measures were not known by all. The most common first aid methods that would be used after a bite, which were all ineffective practices, included the use of tourniquets, black stones, and cutting the bite. Last, snakebites affect victims both socially and financially. **Box 1** provides a summary of recommendations following from this research, which are explained in more detail below.

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The age profile found in our study is similar to what has been found in other sub-Saharan African countries (17–21). Our sample showed no significant differences in snakebites between sex, occupation, or level of education. Previous studies undertaken in sub-Saharan Africa found the same (17, 22, 23), with the exception of one study that showed that farmers were more likely to be bitten than those with any other occupation (20). The relatively small sample size in our study might explain why we did not find any associations, although our results seemed to imply that no formal education and having an outdoor occupation contributed to a higher snakebite incidence. Other studies not testing for significance showed patterns of higher snakebite incidence among farmers and those with a lower educational status similar to our findings (12, 21, 24, 25). Further, although occupation was not shown to be associated with snakebite, this study does show snakebite victims were most often outside, performing activities such as walking, farming, or collecting firewood, when they were bitten by a snake. This is in line with studies in other countries (24, 26) and with one study done in Kenya (27).

1. Community sensitisation on effective preventive measures and first-aid practices to reduce snakebite incidences and the use of ineffective practices.
2. Include traditional healers as first-responders in health-seeking pathways, as first aid providers and for referrals to health facilities.
3. Ensure availability of free, effective antivenom and supportive treatment at health facilities.
4. Strengthen existing health surveillance systems to adequately collect, report and evaluate snakebite cases in communities and health facilities.
5. Undertake frequent qualitative research to capture the broader societal and economic impacts on snakebite-affected victims, families, and communities.
6. Identify and address the holistic needs of snakebite victims with disabilities through the development of community-led and community-based projects and services.
7. Ensure snakebite is prioritised by the Kenyan Ministry of Health within broader health policy frameworks and master plans, while ensuring translation of all four pillars specified within the WHO's snakebite strategy.

Box 1. Recommendations to reduce the burden of snakebite in rural Kenyan communities.

This study further showed that, although many of the snakebite victims visited a health facility after the bite, there was still a considerable proportion that also made use of traditional treatment, either solely or in combination with their visit to the health facility. This has also been shown to be the case in another study conducted in Western Kenya (27). Traditional treatments, such as the use of a black stone, healing plants, tourniquets, sucking the venom from the bite, or cutting the bite, have not been proven to be effective against envenomings; on the contrary, research has shown that these methods can have adverse consequences because they might cause infections or additional health problems and delay the administration of effective treatment such as antivenom (28). These traditional treatments are also adopted as first aid by many of the community members: almost 80% said they would use a tourniquet after a bite, and almost half would put a black stone on the wound, indicating that sensitisation efforts should focus on teaching communities what effective first aid entails. Further, efforts to include traditional healers in the health-seeking pathways in Kenya might reduce the delay in snakebite victims receiving proper medical care after envenomings: If traditional healers are able to provide effective and appropriate first aid, after which they refer victims directly to health facilities, serious disabilities and even deaths could be prevented.

When snakebite victims went to a health facility, 42% reported to have received antivenom. This finding should, however, be interpreted cautiously. It is possible that respondents' knowledge on the specific medications administered is uncertain, especially in emergency situations such as snakebites. It is further unknown whether antivenom was not provided to all the patients in our research because not all bites were envenomings or because it was unavailable. However, previous research conducted in Kenya showed that antivenom was available at only 27% of surveyed health facilities and that unavailability and stock-outs were common (12,25). Further, the cases in this study are only those that survived their snakebite; snakebite victims who might have died because there was no antivenom treatment available could not be surveyed. Ensuring that effective antivenom is available at health facilities is thus crucial. To facilitate this, snakebite should be prioritised by the Kenyan Ministry of Health within its broader health policy frameworks and master plans while at the same time ensuring translation of all four pillars specified within the WHO's snakebite strategy (29). Further, to properly capture the prevalence of snakebites, existing health surveillance systems need to be strengthened to adequately collect, report, and evaluate snakebite cases in both communities and health facilities.

This study is one of the first in sub-Saharan Africa that specifically included questions on the socio-economic impact of snakebite and showed that financial consequences are common: Many had experienced a loss of income and high hospital bills, and ability to work or do the same job afterward was also often affected. Further, we found that, in our sample, costs incurred for snakebite treatment were as high as USD 734.80, whereas

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the median monthly household income was USD 78.40. Such findings have also been reported in Bangladesh, India, and Sri Lanka (30–32). This research is also the first to ask community members who had only observed a snakebite but who had not experienced it personally about the socio-economic consequences of snakebite. Interestingly, they gave lower estimates of the financial impact of snakebites on those bitten. This finding might not be surprising because financial difficulties are seen as a personal problem and therefore might not be shared openly with others. It is also possible that others might underestimate the impact snakebite has had on victims because the impact of diseases is generally underestimated by outsiders, especially if the disease is stigmatized or not prioritized within a health system. These findings underscore the considerable financial impact snakebite has, which is not only felt by the victims but also by their families because income and jobs are regularly lost. Combined with the patient profile outlined in this study, our findings confirm that the impact of snakebite is felt strongly by those who might already be struggling to support themselves and their dependents. Efforts should focus on reducing snakebite incidences. For those that do occur, decreasing the financial and health burden for victims by ensuring adequate treatment, including antivenom, is available at the nearest public health facilities, where treatment is offered for free to the patient, is paramount. This will directly affect the financial burden because the victim will not need to pay for their treatment out-of-pocket and indirectly because ensuring proper treatment is available will diminish the chance of long-term disability or death. In the future, in-depth studies on the socio-economic consequences of snakebites, including the impact on victims' and their families' mental health, should be undertaken to enable full understanding of the long-term impact of snakebite.

More than 80% of the snakebite victims in our sample were bitten in the foot or leg, underscoring how wearing closed shoes or boots might help prevent a large proportion of the snakebites. A study conducted in coastal Kenya showed that less than 50% of the population wears shoes (33). Community sensitisation should focus on this specifically because, in line with those findings, only half of respondents indicated the wearing of shoes as a preventive measure. This study also showed that knowledge on recommended preventive measures in general has room for improvement and should be covered in sensitisation efforts because none of the effective measures was mentioned by a majority of the respondents, whereas incorrect measures (e.g., killing snakes when you see them) were indicated, and other effective measures (e.g., using mosquito nets to prevent snakes from entering your bed) were not mentioned at all (34).

Strengths and limitations

Although this is the first study in Kenya to quantitatively research the burden of snakebite in rural communities, some limitations to this study should be noted. First, recall bias of snakebite victims might have played a role in our study because we asked about lifetime

experience with snakebite, and not just about, for example, snakebites in the previous year. Nevertheless, snakebites are often experienced as being traumatic, which we believe allows for better knowledge retainment of the event than for events that happen in everyday life. Second, our study might be affected by its sample size, specifically the sample of those personally bitten, which limited the strength of the association analyses. Increasing the sample size and using cluster sampling is suggested for future research to establish the effects found in this research with more certainty. Third, no questions about the patient profiles or health-seeking behaviour of snakebite victims who had died were asked. As a consequence, we might have missed information about the most severe cases that occurred in the community. It is therefore also possible that the snakebite problem is even bigger than illustrated in our research. This might be researched in the future through interviews with the victims' relatives. Related, despite ongoing concerns on the availability of certain antivenom products that may lack efficacy in Kenya, we were unable to identify what antivenom products were administered to the patients in our sample and the performance of those products on the patient outcomes. This could be researched in the future, making use of patient medical records that comprehensively document snakebite cases, including treatment efficacy and patient outcomes. Fifth, respondents were asked about their occupation at the time of the survey but were not asked about their occupation at the time of the bite. This might have led to a distortion in the relationship between occupation and snakebite. Nevertheless, this study provides a useful, first indication of the extent to which Kenyan communities are affected by snakebite and highlights the gaps in knowledge on prevention strategies and proper first-aid methods. This study can be used as a baseline to guide the development of context-specific programmes, targeting these knowledge gaps.

CONCLUSION

This study conducted in four snakebite-endemic counties in Kenya showed that snakebites are a common occurrence in rural communities, leading to death and disability. The majority of snakebite victims were 26–45 years of age and were often walking or farming when the bite occurred. Traditional healing still plays an important role in the treatment of snakebites in Kenya, and snakebites have a considerable impact on victims, both socially and financially. To reduce this burden felt by rural communities, a multipronged approach is needed, consisting of on the one hand community engagement, including engagement with traditional healers, through education and sensitisation efforts to improve used preventive measures and effective health-seeking behaviour. On the other hand, health system strengthening is needed so snakebite victims who present to health facilities can be quickly and adequately treated with appropriate antivenom and supportive care that is affordable to them. For this, the government needs to adopt policies and programmes financed to ensure healthcare workers are adequately trained, antivenom and supportive treatments are supplied, cases are recorded, and communities are fully engaged.

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CONTRIBUTION STATEMENT

GIO, JvO and BW designed the study. GIO and DO collected the data. GIO analysed the data and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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3.1

SUPPLEMENTARY DATA

Supplementary File 1. Age, household composition, and financial situation of participant.

	Total population (N=382)	
	N	**Median (range)**
Age	382	39.5 (18.0-88.0)
Number of adults in household[a]	382	3 (0-11)
Number of children in household	382	4 (0-16)
Monthly household income (USD)	212	78.4 (4.9-2939.2)
Monthly household living expenses (USD)	223	49.0 (0.0-391.9)
Monthly household healthcare expenditure (USD)	211	9.8 (0.0-147.0)

USD = United States Dollar.
[a]Excluding the participant.
[b]Currency conversion on March 1, 2020: USD 1.000 = KSH 102.068.

3.1

Supplementary File 2. Snakebites and health outcomes after a snakebite as indicated by the respondent, stratified per snakebite experience.

	Total population (n=382)					
	Personal snakebite		**Family member bitten**		**Community member bitten**	
	N	**%**	**N**	**%**	**N**	**%**
Bitten by snake						
No	332	86.9	313	81.9	239	62.6
Yes	50	13.1	55	14.4	143	37.4
Don't know	NA	NA	14	3.7	0	0.0
Health outcome after snakebite						
Fully healed	48	96.0	45	81.8	113	79.0
Permanent disability	2	4.0	2	3.6	13	9.1
Death	NA	NA	8	14.6	15	10.5
Don't know	NA	NA	0	0.0	2	1.4

NA: Not applicable.

Supplementary File 3. Snakebite characteristics and health-seeking behaviour, as observed by respondents among family members or community members.

	Total (N=141)	
	N	%
Sex of people bitten		
Primarily males	29	22.1
Same number of males and females	63	48.1
Primarily females	20	15.3
Don't know	19	14.5
Age groups most often bitten[a]		
0-10 years	8	5.7
11-20 years	23	16.3
21-30 years	42	29.8
31-45 years	51	36.2
46-65 years	28	19.9
66+ years	1	2.6
Don't know	32	22.7
Common activities at time of bite[a]		
Walking	83	58.9
Farming	70	49.7
Collecting firewood	62	44.0
Herding	66	46.8
Sleeping	14	9.9
Charcoal burning	29	20.6
Activity inside the house	9	6.4
Playing	15	10.6
Don't know	3	2.1
Season		
Dry season	43	33.1
Rainy season	23	17.7
Any season	36	27.7
Don't know	28	21.5
Care sought by snakebite patient		
Traditional treatment	16	11.5
Healthcare at facility	101	72.7
Traditional treatment and healthcare	11	7.9
Don't know	11	7.9

[a]Respondents could indicate up to three categories so totals may sum to more than 100%.

3.1

Supplementary File 4. Time to care and financial costs of a snakebite.

	Total population (n=50)	
	N	**Median (range)**
Time between bite and visit to traditional healer (minutes)	20	60.0 (0.0-3600.0)
Time between bite and visit to health facility (minutes)	34	31.0 (5.0-270.0)
Cost of treatment by traditional healer (USD)[a,b]	8	1.0 (0.0-2.0)
Cost of treatment at health facility (USD)[a]	22	24.5 (0.0-734.8)

USD = United States Dollar.

[a]Currency conversion on March 1, 2020: USD 1.000 = KSH 102.068

[b]Non-monetary compensation included a goat and a chicken.

3.1

3.2

AVAILABILITY, AFFORDABILITY AND STOCKOUTS OF COMMODITIES FOR THE TREATMENT OF SNAKEBITE IN KENYA

Gaby I Ooms, Janneke van Oirschot, Dorothy Okemo, Benjamin Waldmann, Eugene Erulu, Aukje K Mantel-Teeuwisse, Hendrika A van den Ham, Tim Reed

ABSTRACT

Background

Annually, about 2.7 million snakebite envenomings occur globally. Alongside antivenom, patients usually require additional care to treat envenoming symptoms and antivenom side effects. Efforts are underway to improve snakebite care, but evidence from the ground to inform this is scarce. This study, therefore, investigated the availability, affordability, and stock-outs of antivenom and commodities for supportive snakebite care in health facilities across Kenya.

Method

This study used an adaptation of the standardised World Health Organization (WHO)/Health Action International methodology. Data on commodity availability, prices and stock-outs were collected in July-August 2020 from public (n=85), private (n=36), and private not-for-profit (n=12) facilities in Kenya. Stock-outs were measured retrospectively for a twelve-month period, enabling a comparison of a pre-COVID-19 period to stock-outs during COVID-19. Affordability was calculated using the wage of a lowest-paid government worker (LPGW) and the impoverishment approach. Accessibility was assessed combining the WHO availability target (≥80%) and LPGW affordability (<1 day's wage) measures.

Results

Overall availability of snakebite commodities was low (43.0%). Antivenom was available at 44.7% of public- and 19.4% of private facilities. Stock-outs of any snakebite commodity were common in the public- (18.6%) and private (11.7%) sectors, and had worsened during COVID-19 (10.6% versus 17.0% public sector, 8.4% versus 11.7% private sector). Affordability was not an issue in the public sector, while in the private sector the median cost of one vial of antivenom was 14.4 days' wage for an LPGW. Five commodities in the public sector and two in the private sector were deemed accessible.

Conclusion

Access to snakebite care is problematic in Kenya and seemed to have worsened during COVID-19. To improve access, efforts should focus on ensuring availability at both lower- and higher-level facilities, and improving the supply chain to reduce stock-outs. Including antivenom into Universal Health Coverage benefits packages would further facilitate accessibility.

3.2

INTRODUCTION

Snakebite has been recognised by the World Health Organization (WHO) as a neglected tropical disease (NTD) that seriously impacts people living in rural areas in Africa, Asia, Central and South America, and Oceania. It is estimated that each year, about 2.7 million snakebite envenomings occur (1). Envenomation takes place following the bite of a venomous snake, when a mixture of toxins (venom) is injected during the bite, and can only be effectively treated with high-quality antivenom (1). Antivenom is therefore listed on the WHO Model Essential Medicines List (EML) of priority medicines that at a minimum ought to be available in every basic healthcare system (2). In addition to antivenom, patients usually require further care to treat the symptoms of envenoming and side effects of antivenom administration, such as anaphylactoid reactions and serum sickness (3). Supportive care can include inter alia adrenaline, tetanus vaccine, antibiotics, airway support, intravenous fluids, pain management, blood transfusions, and assisted ventilation (3,4).

Unfortunately, in many countries antivenom is not regularly available, and sub-Saharan Africa in particular has been facing an antivenom supply crisis for at least the last 20 years (5,6). Multiple factors contribute to this, including the limited financial resources available to sub-Saharan African countries for procurement and quality-assurance, market disincentives for manufacturers, and high dependency on antivenom imports, which have been described previously as interacting in a vicious cycle (6–11). Also, governments generally do not prioritise snakebite, which is also reflected in insufficient funding allocated to snakebite. For example, in 2017 the Nigerian government allocated USD 192,000 (USD 980 per million population) to its snakebite programme, which is estimated to treat only 4% of all snakebite patients (6).

Efforts to tackle this crisis are underway at the international level, with the WHO's strategy "Snakebite envenoming: A strategy for prevention and control" specifically focusing on this problem through four overarching objectives: empower and engage communities; ensure safe, effective treatment; strengthen health systems, and; increase partnerships, coordination and resources (3). To realise these objectives, evidence from the ground is crucial (3). Most studies on antivenom availability have been estimating the availability compared to the needs; it is estimated that the number of effective treatments available in sub-Saharan Africa may be as low as 2.5% of what is needed (7). However, to date, in very few countries in sub-Saharan Africa has the availability of antivenoms in health facilities been methodically studied, while the availability of supportive treatment has rarely been studied in any country globally (12–14). Further, studies on antivenom costs in sub-Saharan Africa primarily focus on wholesale prices, not on patient (out-of-pocket) prices or patient affordability (7,13). The aim of this study was therefore to determine the availability, affordability, and stock-outs of antivenom and commodities used for supportive snakebite treatment in health facilities across Kenya to build the evidence needed to take targeted action to reduce the burden of snakebite.

3.2

Of note is that this research was undertaken in 2020, the year in which coronavirus disease 2019 (COVID-19) had an unprecedented impact on the world. Countries and their health systems were severely affected, exposing weaknesses in health systems across the globe (15). One of the consequences of the COVID-19 pandemic has been the disruption in the manufacturing and supply of commodities (16,17). This research provided a unique and timely opportunity to study stock-outs of snakebite commodities in Kenya during the first few months of the COVID-19 pandemic.

METHODS

Ethics statement

This study was approved by the Amref Health Africa Ethics and Scientific Review Committee (P816/2020) and the National Commission for Science, Technology and Innovation (NACOSTI/P/20/5492). Also, letters of endorsement were obtained from the County Directors of Health of the respective counties.

Study design and sampling

This study adopted a quantitative cross-sectional survey design with a retrospective component, using an adapted version of the standardised, gold-standard WHO/Health Action International (HAI) methodology measuring the availability, stock-outs and affordability of commodities (18). Per this methodology, in six survey regions, 24 health facilities were randomly selected from the public, private, and private not-for-profit (PNFP) sectors, in both urban and rural locations, to function as a representative sample. A rural location was defined as an area with a population of less than 2,000 people (19). This sampling strategy has been validated in many countries (18,20). The six survey regions in this study were purposively sampled: four were highly snakebite endemic and HAI programme counties (Kajiado County, Kilifi County, Kwale County and Taita Taveta County), and two were less endemic (Kirinyaga County and Nyandarua County). Using the Kenya Master Health Facility List, in each county, the main public hospital was selected for inclusion, after which the other 23 licensed facilities were randomly selected under the prerequisite that they were within about an hour's drive from the main public hospital (21). The master list used consisted of 52 facilities in Kajiado-, 26 in Kilifi-, 48 in Kirinyaga-, 40 in Kwale-, 33 in Nyandarua- and 26 in Taita Taveta County. The selected facilities were categorised according to sector and location. The levels of health facilities surveyed ranged from level 2: dispensaries and clinics to level 6: tertiary hospitals, thereby only excluding level 1: community health services, which are not expected to stock most of the commodities surveyed in this study.

Data collection tool

A mobile data collection application, KoBoCollect, was used to collect information about the availability, stock-outs and prices of 45 different snakebite treatment commodities. They included antivenoms, prophylactics, medicines for pain management and anaesthesia,

medicines to treat complications, and several instruments and tests. Commodities were selected based on the WHO's "Guidelines for the Prevention and Clinical Management of Snakebite in Africa" (4), the "Guidelines for Prevention, Diagnosis and Management of Snakebite Envenoming in Kenya" (22), the Kenya EML 2019 (23), and consultations with clinicians and recognised snakebite experts (24). For a full list of surveyed commodities, including their formulations and use, see Supplementary File 1.

Data collection

Data collectors received a one-day training, collected data in pairs, and were supervised by one of the authors (DO). They visited each of the health facilities, where a licenced healthcare worker employed at the facility assisted data collection. The presence of each commodity and formulation was recorded. Availability was defined as the presence of a survey medicine in pre-specified dose and formulation at the time of the data collection in the health facility. Patient prices were noted in Kenyan Shillings (KSH). If multiple brands of the same commodity were available, the one with the lowest patient price was taken as reference. Stock information was collected only when health facilities recorded this information in a stock-taking database, and this could be physically seen by the data collectors. Data were collected from July 28 to August 19, 2020.

Data analysis

Data were downloaded from the server and analysed in Microsoft Excel. Data were checked for errors and outliers by the researchers (GO and DO), and double-checked with the data collectors if inconsistencies were noted. Simple descriptive statistics were used to describe the availability and affordability of commodities, and results were categorised according to sector (public, private or PNFP), and location (urban or rural).

To determine the average availability of a commodity, only health facilities that were of the level at which a specific commodity was supposed to be available as per the Kenya EML 2019 (see Supplementary File 1), were included in the calculations (23). An availability of 80% or higher was used as the benchmark for accessibility as per WHO guidance (25). The combined availability of commodities that were surveyed for multiple formulations, such as amoxicillin, was calculated to provide the overall availability of that specific commodity at the facility.

Stock-outs were measured retrospectively over a twelve-month period, from 1 August 2019 to 31 July 2020. A commodity was considered stocked out if the facility usually stocked the commodity, but the stock-taking database indicated it had been out of stock at times in the past year. Stock-out information was asked for all commodities supposed to be available at that level of care, regardless of whether they were in or out of stock at the time of the survey. Taking into consideration the COVID-19 pandemic and its possible effect on the supply of

3.2

commodities, stock-out data were collected for two time periods: from 1 August 2019 to 31 January 2020, and from 1 February 2020 to 31 July 2020. Stock-outs were only calculated for commodities that had stock information available at a minimum of ten facilities per sector. Stock-outs were calculated as the percentage of facilities that reported at least one stock-out of the selected commodity over the measured time period, with stock-out days calculated as the average number of days stock-outs of a commodity lasted per facility.

Two-sample F-tests for variance and two-sample t-tests, paired t-tests, Fisher's Exact tests or binomial tests assessed whether significant differences in availability and stock-outs between and within the sectors, and between the two different time periods existed, using a significance cut-off value of 0.05.

3.2

Unit prices were calculated by dividing pack price by pack size. To calculate the affordability, two approaches were used. First, the median price of the starting dosage or full treatment course of a commodity was compared to the official salary of the lowest-paid-government worker (LPGW), which was 452.40 Kenyan Shillings (KSH) per day in 2020 (26). If a commodity's price exceeded one day of wages, it was considered unaffordable (18). Second, since the LPGW measure knows some limitations with representativeness as the wage of an LPGW is much higher than the income of a large proportion of the population, the impoverishment approach as developed by Van Doorslaer et al. (2006) was also used (27,28). In this approach the impoverishing effect of purchasing a medicine is calculated by comparing the proportion of a population that is pushed below a poverty line after purchasing a medicine with the population that was already living below the poverty line (27). The international poverty line (IPL) of USD 1.90 per person per day was used (29). As income indicator, we used the household final consumption expenditure (HHFCE), income share per population quintile data and population size of Kenya to calculate HHFCE per capita (30). The impoverishing effect of buying a commodity was compared to the monthly HHFCE.

Accessibility was calculated using the availability and LPGW affordability measures, resulting in a composite measure in which accessibility was achieved with an 80% or higher availability and a price of less than a day's wage for an LPGW.

COVID-19 precautions
Data collectors took all necessary precautions as advised by the Kenyan Ministry of Health to limit the risk of COVID-19 transmission, including keeping 1.5 metres distance, wearing face masks and distributing them to participating healthcare workers, and using hand sanitiser.

RESULTS

Sample

One hundred forty-four health facilities were approached to participate in the study, of which data was collected from a total of 133 health facilities from Kajiado (n=22), Kilifi (n=24), Kirinyaga (n=21), Kwale (n=24), Nyandarua (n=20) and Taita Taveta (n=22) counties (participation rate 92.4%). An overview of the sample characteristics is provided in **Table 1**. Due to the low number of facilities surveyed from the PNFP sector (n=12), PNFP facilities were only included in the totals and were not analysed as a distinct sector.

Availability

Availability of all surveyed commodities can be found in **Table 2**. Overall mean availability of the surveyed snakebite commodities in Kenya was 43.0%. No significant differences in overall mean availability between location or sector existed. Antivenom was available in 44.7% of public facilities, and in 19.4% of private facilities (p = 0.009). Availability differed significantly between urban and rural locations within the public sector (p = 0.003). None of the level 2 facilities stocked antivenom, while more than 70% of level 4 and 5 public facilities (primary and secondary hospitals) did stock antivenom (see **Table 3**). Availability of both antivenom and adrenaline, which should be available in case of anaphylaxis as a consequence of antivenom usage, was lower: 36.4% and 25.0% of level 4 and 5 facilities, respectively, had both available. Availability of antivenom in highly endemic counties was 41.8%, availability in less endemic counties was 19.0% (p=0.01). The most commonly stocked antivenom brands in the public sector were Snake Venom Antiserum (African IHS) by VINS Bioproducts Ltd (66.7% of facilities), and Inoserp PAN-AFRICAN by INOSAN Biopharma (33.3% of facilities) (see Supplementary File 2).

In general, antibiotics had a relatively high availability of 46.8% to 91.0%. Availability of commodities used for the management of complications was more variable, with hydrocortisone having the highest availability (79.7%). Significant differences in availability existed for adrenaline, chlorpheniramine, and prednisolone. Paracetamol had the highest availability of commodities used for pain management. Blood products had a very low availability across sectors, and variability in availability of medical instruments and materials was observed.

Stock-outs

Stock information was available for 121 of 133 facilities (91.0%, see **Table 1**). Overall, on average 18.6% of all public facilities reported at least one stock-out of any of the surveyed commodities over a twelve-month period, with stock-outs lasting on average 30.5 days per facility (see **Table 4**). In the private sector, stock-outs occurred on average in 11.7% of the facilities over the twelve-month period and lasted on average 24.0 days per facility. In

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Table 1. Number of surveyed facilities with availability, price and stock information available, by sector, location and level of care.

	Public	Private	PNFP	Total
Availability and price information				
Total	85	36	12	133
Location				
Urban	26	22	8	56
Rural	59	14	4	77
Level of care				
Dispensary/clinic	13	7	2	22
Health centre	53	18	5	76
Primary hospital	11	3	2	16
Secondary care hospital	4	4	1	9
Tertiary hospital	4	4	2	10
Stock information				
Total	78	33	10	121
Location				
Urban	23	20	6	49
Rural	55	13	4	72
Level of care				
Dispensary/clinic	12	6	2	20
Health centre	50	17	5	72
Primary hospital	8	3	1	11
Secondary care hospital	4	4	0	9
Tertiary hospital	4	3	2	9

PNFP: Private not-for-profit.

both sectors stock-outs of almost all commodities occurred significantly more often from February to July 2020 than from August 2019 to January 2020.

Over a twelve-month period, 20.0% of all public facilities experienced a stock-out of antivenom, averaging 13.6 days per facility. No data on antivenom stock-outs in the private sector was available due to the small sample of health facilities with stock information for antivenom. Duration of stock-outs was longest for oxygen cylinders, hydrocortisone and chlorpheniramine (10mg/1ml) in the public sector, and for metronidazole and tetanus vaccine in the private sector.

Affordability

Pricing information was not provided for 11.2% (110/979) and 32.4% (145/303) of available commodities in the public and private sectors, respectively. Using the wage of an LPGW, in the public sector all commodities were affordable to the patient; none of the commodities cost more than a day's wage if the median price was considered

Table 2. Availability of snakebite commodities in Kenya, per sector and location.

Commodities	Overall[a] Urban	Rural	p-value	Total	Public Urban	Rural	p-value	Total	Private Urban	Rural	p-value	Total	p-value[h]
Total	44.5	42.2	0.751	44.0	45.0	47.8	0.708	43.4	45.1	47.2	0.773	46.3	0.700
Antivenom and anti-tetanus													
Antivenom	44.6	28.6	0.056	35.3	69.2	33.9	**0.003**	44.7	27.3	7.1	0.078	19.4	**0.009**
Tetanus vaccine	66.1	79.2	0.089	73.7	53.8	74.6	0.059	68.2	77.3	92.9		83.3	0.088
Antibiotics													
Benzylpenicillin	58.9	64.9	0.480	62.4	61.5	64.4	0.800	63.5	72.7	64.3	0.592	69.4	0.053
Metronidazole[b]	87.5	93.5		91.0	88.5	96.6		94.1	86.4	85.7	0.956	86.1	0.144
Gentamicin[c]	69.6	68.8	0.920	69.2	73.1	71.2	0.858	71.8	72.7	57.1	0.245	66.7	0.575
Amoxicillin[d]	94.6	93.5		94.0	96.2	94.9		95.3	90.9	85.7		88.9	0.195
Amoxicillin + clavulanic acid[f]	53.1	41.9	0.243	46.8	62.5	45.8	0.355	51.4	44.4	27.3	0.182	37.9	0.220
Complications management													
Adrenaline	60.7	41.6	**0.029**	49.6	61.5	35.6	**0.026**	43.5	54.5	71.4	0.311	61.1	0.077
Hydrocortisone	82.1	77.9	0.550	79.7	80.8	79.7	0.906	80.0	81.8	71.4	0.645	77.8	0.783
Chlorpheniramine[e,f]	40.8	11.3	**<0.001**	24.3	29.2	4.2	**0.002**	12.5	61.1	27.3	0.077	48.3	**<0.001**
Prednisolone[g]	73.2	45.5	**0.002**	57.1	53.8	32.2	0.060	38.8	86.4	85.7		86.1	**<0.001**
Neostigmine[g]	18.2	0.0	0.508	17.1	21.1	NA	NA	21.1	22.2	0.0	0.461	18.2	0.850
Atropine[f]	55.1	54.8	0.978	55.0	50.0	54.2	0.738	52.8	66.7	45.5	0.260	58.6	0.594
Pain management													
Paracetamol	96.4	88.3	**0.010**	91.7	96.2	84.7	**0.012**	88.2	95.5	0.0		97.2	0.116
Dihydrocodeine phosphate[f]	10.2	0.0		4.5	12.5	0.0	NA	4.2	5.6	0.0	0.426	3.4	0.867
Morphine[g]	15.2	0.0	0.552	14.3	15.8	NA	NA	15.8	22.2	0.0	0.461	18.2	0.865
Local anaesthesia													
Lidocaine	71.4	76.6	0.498	74.4	73.1	76.3	0.753	75.3	77.3	71.4	0.693	75.0	0.973
Fluids													

Mean Availability (%)

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3.2

Table 2. (continued)

Commodities	Overall[a]				Public				Private				p-value[h]
	Urban	Rural	p-value	Total	Urban	Rural	p-value	Total	Urban	Rural	p-value	Total	
Saline	66.1	79.2	0.089	73.7	76.9	83.1	0.505	81.2	54.5	78.6	0.143	63.9	0.042
Fresh frozen plasma[g]	6.1	0.0	0.720	5.7	5.3	NA	NA	5.3	0.0	0.0	NA	0.0	0.439
Blood platelets[g]	3.0	0.0	0.803	2.9	5.3	NA	NA	5.3	0.0	0.0	NA	0.0	0.439
Red blood cells[g]	9.1	0.0	0.656	8.6	5.3	NA	NA	5.3	11.1	0.0	0.621	9.1	0.685
Whole blood[g]	15.2	0.0	0.552	14.3	15.8	NA	NA	15.8	11.1	0.0	0.621	9.1	0.603
Medical instruments, materials													
Bandage	66.1	85.7	0.007	77.4	61.5	88.1	0.005	80.0	72.7	85.7	0.004	77.8	0.783
Splint[f]	0.0	6.5	0.070	3.6	0.0	4.2	0.310	2.8	0.0	18.2	0.061	6.9	0.337
Sticking plaster[f]	26.5	27.4	0.917	27.0	29.2	25.0	0.705	26.4	27.8	45.5	0.331	34.5	0.416
Oxygen cylinder	44.6	41.6	0.723	42.9	53.8	37.3	0.155	42.4	36.4	64.3	0.102	47.2	0.622
Laryngoscope	7.1	5.2	0.641	6.0	3.8	1.7	0.547	2.4	13.6	14.3	0.956	13.9	0.013
Cuffed endotracheal tube[f]	12.2	16.1	0.563	14.4	16.7	12.5	0.630	13.9	5.6	36.4	0.033	17.2	0.668
Nasal prong	41.1	49.4	0.344	45.9	38.5	45.8	0.532	43.5	45.5	64.3	0.270	52.8	0.351
Ambu bag	55.4	63.6	0.336	60.2	69.2	69.5	0.981	69.4	45.5	42.9	0.878	44.4	0.010
Oral airway[f]	18.4	25.8	0.352	22.5	12.5	20.8	0.386	18.1	27.8	54.5	0.149	37.9	0.034
Ventilator[f]	14.3	3.2	0.034	8.1	8.3	4.2	0.467	5.6	16.7	0.0	0.153	10.3	0.391
Intravenous cannula	67.9	80.5	0.095	75.2	73.1	78.0	0.624	76.5	63.6	92.9	0.048	75.0	0.862
Catheter	64.3	66.2	0.816	65.4	73.1	66.1	0.524	68.2	50.0	64.3	0.400	55.6	0.183
Syringe + needle	92.9	98.7	0.080	96.2	92.3	98.3	0.167	96.5	95.5	100.0	0.418	97.2	0.833
IV administration set	71.4	85.7	0.043	79.7	76.9	84.7	0.383	82.4	68.2	92.9	0.083	77.8	0.558
Urine dipstick	57.4	58.4	0.210	57.9	57.7	57.6	0.212	57.6	59.1	57.1	0.650	58.3	0.944
Creatinine clearance blood test	14.3	5.2	0.071	9.0	11.5	0.0	0.008	3.5	13.6	28.6	0.270	19.4	0.004
Blood urea nitrogen testing	10.7	5.2	0.233	7.5	3.8	1.7	0.547	2.4	13.6	21.4	0.541	16.7	0.004

Mean Availability (%)

Table 2. (continued)

Commodities	Mean Availability (%)												
	Overall[a]				Public				Private				
	Urban	Rural	p-value	Total	Urban	Rural	p-value	Total	Urban	Rural	p-value	Total	p-value[h]
20WBCT	10.7	5.2	0.233	7.5	11.5	0.0	**0.008**	3.5	13.6	21.4	0.541	16.7	**0.012**
Point-of-Care INR device	5.4	1.3	0.176	3.0	0.0	0.0	NA	0.0	9.1	7.1	0.837	8.3	**0.007**

20WBCT: 20-minute whole blood clotting test; INR: International normalised ratio; IV: Intravenous; NA: Commodity not surveyed because no facility was included that ought to have the commodity available.

[a]Availability includes the private not-for-profit sector.

[b]Metronidazole combines the availability of metronidazole 200mg, 400mg and 200mg/5ml.

[c]Gentamicin combines the availability of gentamicin 10mg/2ml, 20mg/2ml, 40mg/2ml and 80mg/2ml.

[d]Amoxicillin combines the availability of amoxicillin 250mg and 500mg.

[e]Chlorpheniramine combines the availability of chlorpheniramine 10mg/1ml and 2mg/5ml.

[f]Available from the health centre level and up.

[g]Available from the primary hospital level and up.

[h]Level of significance between public and private sector.

Availability:

<20% 20-39.9% 40-59.9% 60-79.9% ≥80%

3.2

Table 3. Availability of antivenom, and antivenom and adrenaline, per level and sector.

| | Antivenom availability (%) | | | | | | | | |
| | Overall[a] | | | Public | | | Private | | |
	Urban	Rural	Total	Urban	Rural	Total	Urban	Rural	Total
Level 2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Level 3	37.5	36.7	36.8	60.0	41.7	43.4	33.3	11.1	22.2
Level 4	47.4	0.0	45.0	72.7	NA	72.7	25.0	0.0	20.0
Level 5	62.5	0.0	55.6	75.0	NA	75.0	33.3	0.0	25.0
Level 6	83.3	NA	83.3	100.0	NA	100.0	50.0	NA	50.0

| | Antivenom and adrenaline availability (%) | | | | | | | | |
| | Overall[a] | | | Public | | | Private | | |
	Urban	Rural	Total	Urban	Rural	Total	Urban	Rural	Total
Level 2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Level 3	25.0	18.3	19.7	40.0	20.8	22.6	22.2	0.0	11.1
Level 4	26.3	0.0	25.0	36.4	NA	36.4	25.0	0.0	20.0
Level 5	37.5	0.0	33.3	25.0	NA	25.0	33.3	0.0	25.0
Level 6	83.3	NA	83.3	100.0	NA	100.0	50.0	NA	50.0

3.2

NA: Not applicable.

Level 2: Dispensary/clinic; level 3: Health centre; level 4: Primary hospital; level 5: Secondary hospital; level 6: Tertiary hospital.
[a]Includes the private not-for-profit sector.

Availability:
☐ <20% ☐ 20-39.9% ☐ 40-59.9% ☐ 60-79.9% ☐ ≥80%

the benchmark (see **Table 5**). However, when looking at the maximum price paid for the commodities at public facilities, one vial of antivenom can cost up to 44.2 days of wages. In the private sector, four commodities were unaffordable for an LPGW, with the median cost of one vial of antivenom being 14.4 days of wages. Benzylpenicillin, gentamicin (10mg or 20mg/2ml), and morphine were also unaffordable in the private sector. Using the impoverishment approach, it was calculated that 24.2% of the population was already living below the IPL. In the public sector, purchasing any medicines at median price had a minimal impoverishing effect. In the private sector, however, purchasing one vial of antivenom at median price would push 39.0% of the population below the IPL. Other impoverishing purchases included benzylpenicillin, gentamicin, hydrocortisone and morphine. When purchasing a vial of antivenom at the maximum price at a public or private facility (KSH 20,000.00), for 63.3% of the population treatment would be unaffordable and they would be impoverished. **Box 1** provides a real-life example of the affordability of treatment received by a snakebite patient with a typical disease course.

Accessibility

In the public sector, five of 23 commodities were deemed accessible, as they cost less than a day's wage for an LPGW and were available at 80% or more of health facilities (see **Figure 1** and Supplementary File 3). These commodities were: metronidazole (200mg or 400mg), amoxicillin (250mg), paracetamol, hydrocortisone and saline. In the private sector, two of 23 commodities (paracetamol and prednisolone) were accessible. In both sectors the main problem was low availability, as 18 of 23 commodities in the public sector and 15 of 23 commodities in the private sector cost less than a day's wage for an LPGW but had an availability of below 80%.

Accessibility of antivenom was variable (see **Figure 2**). Antivenom was accessible (both available and affordable) in 35% of public- and in 3% of private facilities, and available but not affordable in 8% of public- and 13% of private facilities. In the remaining facilities no antivenom was available.

3.2

A five-year-old boy was bitten by an unidentified snake near the Tana River in Southern Kenya. As traditional treatment, a black stone was applied to the site of the bite, after which the patient was taken to the nearest dispensary (public sector). There he was given a hydrocortisone injection* and tetanus toxoid vaccine. After, the patient was referred to a general hospital (public sector) 100km away. There he was administered two vials of antivenom and referred to a private nursing home. The patient stayed 11 days at the nursing home, he was discharged due to the family's financial constraints. During the 11-day stay, the patient received two more vials of antivenom, one vial of adrenaline as premedication, amoxicillin + clavulanic acid twice daily for the entire treatment and gentamicin 40mg/2ml once daily for five days after developing bite site soft tissue sepsis, and paracetamol four times daily for six days. Final health outcome is unknown due to his return to his hometown.

The costs of treatment alone, using the median treatment costs found in this study, would amount to KSH 14,258.00. For an LPGW, this would be 31.5 days of wage, and an additional 59.0% of the population would be pushed below the IPL if they needed this treatment. If the entire treatment were provided in private health facilities, an LPGW would need to work for 60.7 days to pay for the treatment, and 66.9% of the population would be pushed below the IPL.

*Hydrocortisone was provided even though it was not appropriate at that moment.

Box 1. Affordability of snakebite treatment for a patient.

Table 4. Facilities reporting stock-outs of snakebite commodities and average number of stock-out days per facility ove

| | **% of facilities reporting a stock-out** | | | | | | | | |
| | **Public** | | | | **Private** | | | | |
	Aug-Jan[a]	Feb- July[a]	p-value	Aug- July[b]	Aug-Jan[a]	Feb- July[a]	p-value	Aug- July[b]	p-value[c]
Total	10.6	17.0	**<0.001**	18.6	8.4	11.7	**0.005**	11.7	0.141
Antivenom and anti-tetanus									
Antivenom	20.0	11.4	0.685	20.0	NA	NA	NA	NA	NA
Tetanus vaccine	15.0	30.0	**0.039**	35.0	22.7	22.7	0.382	27.3	0.509
Antibiotics									
Benzylpenicillin	16.3	16.3	0.405	20.4	12.5	12.5	0.323	12.5	0.479
Metronidazole (200mg or 400mg)	6.9	6.9	0.372	8.6	13.0	17.4	0.171	17.4	0.257
Metronidazole (200mg/5ml)	0.0	7.7	**<0.001**	7.7	18.2	18.2	0.323	18.2	0.439
Gentamicin (10mg or 20mg/2ml)	6.5	9.7	0.242	9.7	NA	NA	NA	NA	NA
Gentamicin (40mg or 80mg/2ml)	5.0	7.5	0.138	7.5	18.2	18.2	0.323	18.2	0.291
Amoxicillin (250mg)	3.2	6.5	**0.048**	6.5	9.1	9.1	0.323	9.1	0.680
Amoxicillin (500mg)	13.6	47.7	**<0.001**	47.7	9.5	14.3	0.133	14.3	**0.009**
Amoxicillin + clavulanic acid	17.1	25.7	0.064	31.4	NA	NA	NA	NA	NA
Complications management									
Adrenaline	17.9	30.8	**0.015**	33.3	5.0	15.0	**0.016**	15.0	0.133
Hydrocortisone	10.0	13.3	0.142	13.3	7.7	15.4	**0.046**	15.4	0.801
Chlorpheniramine (10mg/1ml)	52.4	71.4	**0.023**	71.4	7.7	23.1	**0.014**	23.1	**0.006**
Chlorpheniramine (2mg/5ml)	33.3	53.3	**0.031**	53.3	14.3	21.4	0.128	21.4	0.077
Prednisolone	26.8	43.9	**0.006**	43.9	4.2	8.3	0.078	8.3	**0.003**
Neostigmine	30.0	40.0	0.150	40.0	NA	NA	NA	NA	NA
Atropine	7.1	19.0	**0.006**	19.0	16.7	16.7	0.395	16.7	0.851
Pain management									
Paracetamol	1.5	6.0	**0.003**	6.0	3.8	3.8	**<0.001**	3.8	0.684
Local anaesthesia									
Lidocaine	7.0	14.0	**0.017**	14.0	10.0	5.0	0.323	10.0	0.644
Fluids									
Saline	1.6	4.9	**0.017**	4.9	0.0	5.3	**<0.001**	5.3	0.952
Instruments and materials									
Bandage	0.0	0.0	**<0.001**	0.0	4.3	13.0	**0.016**	13.0	**0.007**
Sticking plaster	15.0	30.0	**0.022**	30.0	NA	NA	NA	NA	NA
Oxygen cylinder	11.1	5.6	0.609	11.1	NA	NA	NA	NA	NA
Nasal prong	3.8	11.5	**0.016**	11.5	NA	NA	NA	NA	NA
Ambu bag	0.0	0.0	**<0.001**	0.0	NA	NA	NA	NA	NA
Intravenous cannula	2.3	2.3	**<0.001**	2.3	0.0	0.0	**<0.001**	0.0	0.569
Catheter	0.0	2.4	**<0.001**	2.4	0.0	0.0	**<0.001**	0.0	0.601
Syringe + needle	0.0	0.0	**<0.001**	0.0	0.0	0.0	**<0.001**	0.0	NA
IV administration set	0.0	0.0	**<0.001**	0.0	0.0	6.3	**<0.001**	6.3	0.067
Urine dipstick	5.4	5.4	0.323	5.4	NA	NA	NA	NA	NA

NA: Not included due to small sample; NS: No stock-out.

[a]Stock-outs measured over a six-month period.

[b]Stock-outs measured over a twelve-month period.

[c]Level of significance between public and private sector.

3.2

r a six- and twelve-month period, per sector.

	Average number of stock-out days per facility								
	Public				Private				
	Aug-Jan[a]	Feb-July[a]	p-value	Aug-July[b]	Aug-Jan[a]	Feb-July[a]	p-value	Aug-July[b]	p-value[c]
	22.9	16.9	0.457	30.5	14.3	13.2	0.861	24.0	0.589
	11.9	3.0	0.316	13.6	NA	NA	NA	NA	NA
	46.3	19.3	0.248	36.4	27.6	27.2	0.986	45.7	0.769
	26.4	30.3	0.797	45.3	8.5	12.5	0.726	21.0	0.571
	4.3	3.0	0.681	5.8	3.7	16.8	0.435	19.5	0.401
	NS	7.0	NA	7.0	97.5	45.0	0.617	142.5	NA
	11.0	3.0	0.347	10.3	NA	NA	NA	NA	NA
	25.0	6.3	**0.030**	23.0	5.5	5.5	1.00	11.0	0.491
	3.0	3.0	1.00	4.5	11.0	16.0	0.349	27.0	**0.002**
	2.3	17.7	**0.002**	18.4	10.5	7.0	0.080	14.0	0.711
	22.2	20.3	0.911	28.7	NA	NA	NA	NA	NA
	9.1	18.1	0.267	21.6	4.0	13.7	0.629	15.0	0.371
	37.0	48.1	0.782	75.9	4.0	3.5	0.900	5.5	0.172
	45.2	41.0	0.868	74.3	1.0	6.7	0.425	7.0	**0.039**
	9.0	8.3	0.909	13.9	3.0	3.3	0.913	5.3	0.248
	34.1	28.1	0.735	48.9	5.0	10.0	0.602	12.5	**0.045**
	8.3	14.3	0.500	20.5	NA	NA	NA	NA	NA
	5.7	19.5	0.105	21.6	18.7	20.3	0.895	39.0	0.273
	40.0	38.0	0.965	48.0	20.0	15.0	NA	35.0	0.788
	12.3	10.8	0.849	16.9	6.5	20.0	0.269	16.5	0.982
	1.0	5.7	NA	6.0	NS	10.0	NA	10.0	NA
	NS	NS	NS	NS	3.0	3.3	NA	4.3	NA
	12.0	27.5	0.438	33.5	NA	NA	NA	NA	NA
	180.0	60.0	NA	210.0	NA	NA	NA	NA	NA
	1.0	1.3	NA	1.7	NA	NA	NA	NA	NA
	NS	NS	NS	NS	NA	NA	NA	NA	NA
	2.0	1.0	NA	3.0	NS	NS	NS	NS	NA
	NS	1.0	NA	1.0	NS	NS	NS	NS	NS
	NS	NS	NS	NS	NS	NS	NS	NS	NS
	NS	NS	NS	NS	NS	2.0	NA	2.0	NA
	1.0	1.5	NA	2.0	NA	NA	NA	NA	NA

3.2

3.2

Table 5. Affordability of snakebite commodities, using the wage of an LPGW and the impoverishment approach, per sector.

	Treatment regimen	Affordability for LPGW (days of wage)[a]		Additional population below IPL, post-purchase (%)[b]	
		Public	Private	Public	Private
Antivenom and anti-tetanus					
Antivenom	1 vial[c]	0.0 (0.0-44.2)	14.4 (0.7-44.2)	0.0 (0.0-63.3)	39.0 (2.5-63.3)
Tetanus vaccine	1 vial	0.0 (0.0-0.2)	0.2 (0.0-0.6)	0.0 (0.0-0.8)	0.8 (0.0-2.1)
Antibiotics					
Benzylpenicillin	20 vials	0.0 (0.0-4.4)	4.4 (0.0-22.1)	0.0 (0.0-15.1)	15.1 (0.0-51.2)
Metronidazole (200mg or 400mg)	15 tablets	0.0 (0.0-1.0)	0.2 (0.0-2.3)	0.0 (0.0-3.9)	0.6 (0.0-8.4)
Metronidazole (200mg/5ml)	15 vials	0.0 (0.0-2.1)	0.1 (0.0-13.3)	0.0 (0.0-7.7)	0.0 (0.0-45.8)
Gentamicin (10mg or 20mg/2ml)	5 vials	0.0 (0.0-1.1)	2.2 (1.7-2.2)	0.0 (0.0-4.0)	8.0 (6.3-8.0)
Gentamicin (40mg or 80mg/2ml)	3 vials	0.0 (0.0-0.7)	0.6 (0.0-1.3)	0.0 (0.0-2.5)	2.3 (0.0-5.1)
Amoxicillin (250mg)	15 tablets	0.0 (0.0-0.2)	0.2 (0.0-1.0)	0.0 (0.0-0.6)	0.8 (0.0-3.8)
Amoxicillin (500mg)	15 tablets	0.0 (0.0-2.0)	0.3 (0.0-2.3)	0.0 (0.0-7.3)	1.3 (0.0-8.4)
Amoxicillin + clavulanic acid	15 tablets	0.0 (0.0-8.3)	1.0 (0.0-1.7)	0.0 (0.0-7.7)	3.8 (0.0-6.3)
Complications management					
Adrenaline	1 vial[c]	0.0 (0.0-0.1)	0.2 (0.0-0.4)	0.0 (0.0-0.4)	0.8 (0.0-1.7)
Hydrocortisone	6 vials	0.0 (0.0-1.3)	1.3 (0.0-2.7)	0.0 (0.0-5.1)	5.1 (0.0-9.0)
Chlorpheniramine (10mg/1ml)	6 vials	0.1 (0.0-1.3)	0.7 (0.0-2.7)	0.5 (0.0-5.1)	2.5 (0.0-9.0)
Chlorpheniramine (2mg/5ml)	6 vials	0.0 (0.0-4.1)	0.3 (0.0-1.3)	0.0 (0.0-14.3)	1.3 (0.0-5.1)
Prednisolone	20 tablets	0.0 (0.0-0.2)	0.1 (0.0-0.4)	0.0 (0.0-0.8)	0.5 (0.0-1.7)
Neostigmine	1 vial[c]	0.1 (0.0-0.2)	0.5 (0.2-0.8)	0.2 (0.0-0.8)	1.8 (0.6-3.0)
Atropine	1 vial[c]	0.0 (0.0-0.1)	0.2 (0.0-0.4)	0.0 (0.0-0.6)	0.1 (0.0-1.7)
Pain management					
Paracetamol	18 tablets	0.0 (0.0-0.1)	0.1 (0.0-0.4)	0.0 (0.0-0.3)	0.3 (0.0-1.5)
Dihydrocodeine phosphate	3 tablets[c]	0.0 (0.0-0.0)	NP	0.0 (0.0-0.3)	NP
Morphine	1 vial[c]	0.2 (0.0-0.3)	1.1 (0.0-2.2)	0.7 (0.0-1.1)	4.2 (0.0-8.0)

Table 5. (continued)

	Treatment regimen	Affordability for LPGW (days of wage)[a]		Additional population below IPL, post-purchase (%)[b]	
		Public	Private	Public	Private
Local anaesthesia					
Lidocaine	1 tube	0.0 (0.0-0.2)	0.0 (0.0-3.3)	0.0 (0.0-0.8)	0.1 (0.0-11.6)
Fluids					
Saline	2 litres	0.0 (0.0-0.9)	0.6 (0.0-6.2)	0.0 (0.0-3.4)	2.4 (0.0-20.8)

IPL: international poverty line; LPGW: Lowest-paid government worker. NP: no price information available.

[a]Calculated using the median price of a medicine.

[b]IPL of USD 1.90 was equal to KSH 202.58 on August 1 2020.

[c]Starting dose.

[d]Repeat after one, six and twelve months.

3.2

DISCUSSION

This study is the first to research the availability, stock-outs and affordability of 45 commodities used in the treatment of snakebites in Kenya. It showed that overall availability of the commodities was low (43.0%). Antivenom was available at 44.7% of public facilities and 19.4% of private facilities. Stock-outs of commodities were common in both the public (18.6%) and private (11.7%) sectors, lasting on average about a month in the public sector and 24 days in the private sector over a twelve-month period. Stock-outs seemed to have worsened during COVID-19, with facilities reporting stock-outs significantly more often in the period of February to July 2020 than in August 2019 to January 2020. Affordability was not an issue in the public sector, as most commodities were free to the patient. In the private sector, affordability was a slightly bigger problem, especially when buying antivenom: it cost an LPGW 14.4 days of wages, and would impoverish 39.0% of the population if they required treatment. This study further showed that only five commodities in the public sector and two in the private sector could be considered accessible. The biggest issue in both sectors was availability.

Mean availability in rural public facilities was higher than in urban public facilities. One of the explanations is that rural facilities in Kenya are often lower-level facilities where more specialised commodities such as morphine and blood products are not supposed to be available as per the Kenya EML. This shows that not only availability is affected by supply chain issues such as stock-outs, but patients accessing care at lower-level facilities are facing a barrier that is inherent to the system: these more specialised commodities are never available at these levels of care. Further, antivenom availability was generally low in Kenya, and was higher for urban facilities than rural facilities. While the Kenya EML stipulates antivenom to be available at the dispensary/clinic level and up, in reality this is not the case. Since most snakebites occur in rural areas where often only lower level facilities such as health centres are found, this study confirms the discrepancy in antivenom availability which is often referred to in literature: it is most often unavailable in the places where it is most needed (31). These findings also confirm that snakebite patients are often forced to travel greater distances to reach a health facility where antivenom is available. To improve availability, specific attention should be paid to availability at lower-level facilities, especially in the case of antivenom, where timely administration is crucial. Further, 20% of the facilities that did stock antivenom experienced stockouts, which lasted on average 13.6 days per facility. This seems to suggest that while one-fifth of facilities experienced stock-outs of antivenom, the supply is more or less consistent, with stock-outs, although still troubling, not occurring for extended periods of time. Nevertheless, this study did not ask about the number of vials available at the facility. Since several vials are required per treatment per patient, the supply could be consistent for a period but not necessarily meet treatment demand. Focus should therefore be on making antivenom adequately available in facilities, especially where it is not yet stocked.
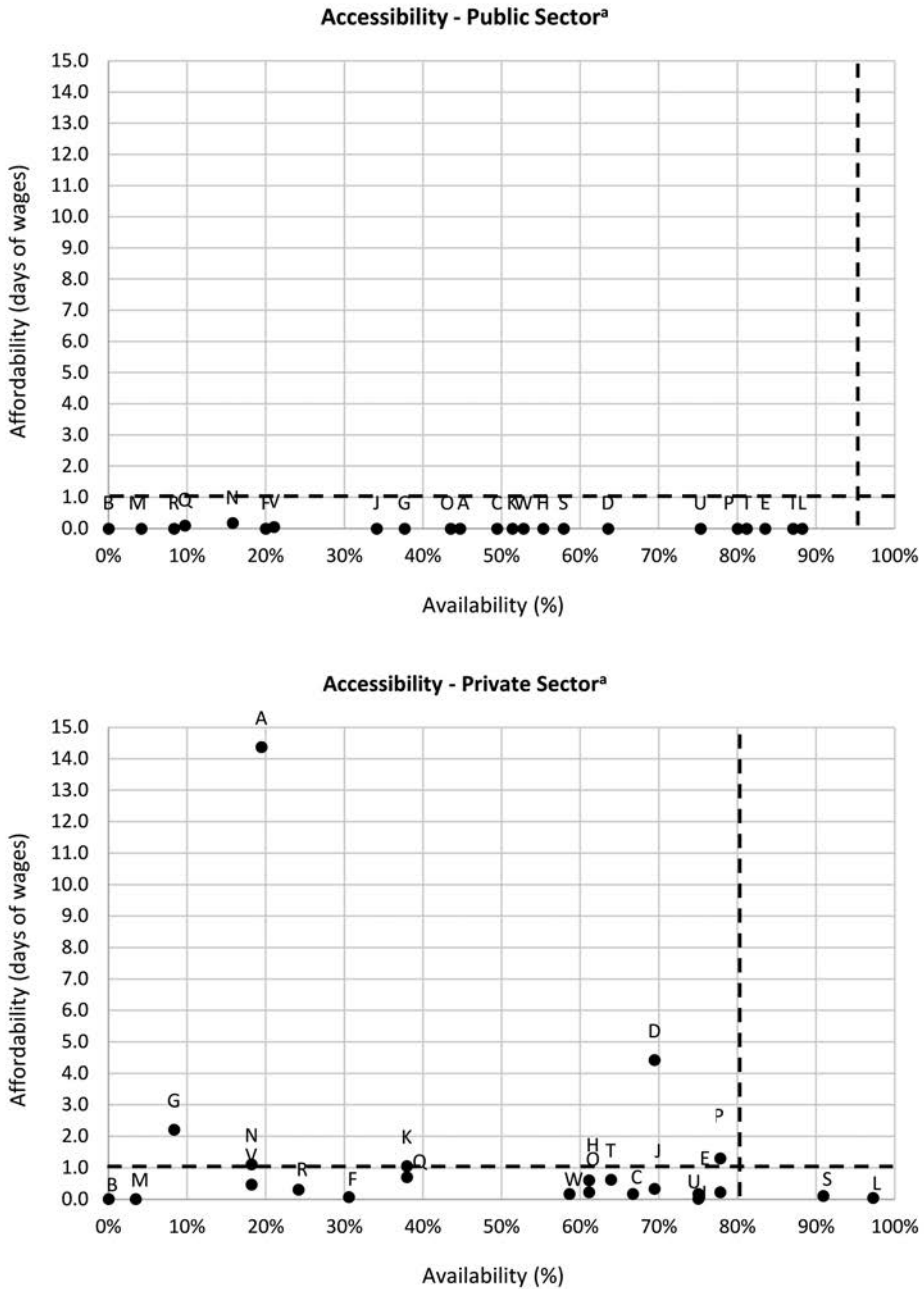
Figure 1. Accessibility of snakebite commodities, per sector.

[a]A: antivenom; B: anti-tetanus immunoglobulin; C: tetanus vaccine; D: benzylpenicillin; E: metronidazole (200mg or 400mg); F: metronidazole (200mg/5ml); G: gentamicin (10mg/2ml or 20mg/2ml); H: gentamicin (40mg/2ml or 80mg/2ml); I: amoxicillin (250mg); J: amoxicillin (500mg); K: amoxicillin + clavulanic acid; L: paracetamol; M: dihydrocodeine phosphate; N: morphine; O: adrenaline; P: hydrocortisone; Q: chlorpheniramine (10mg/1ml); R: chlorpheniramine (2mg/5ml); S: prednisolone; T: Saline; U: lidocaine; V: neostigmine; W: atropine.
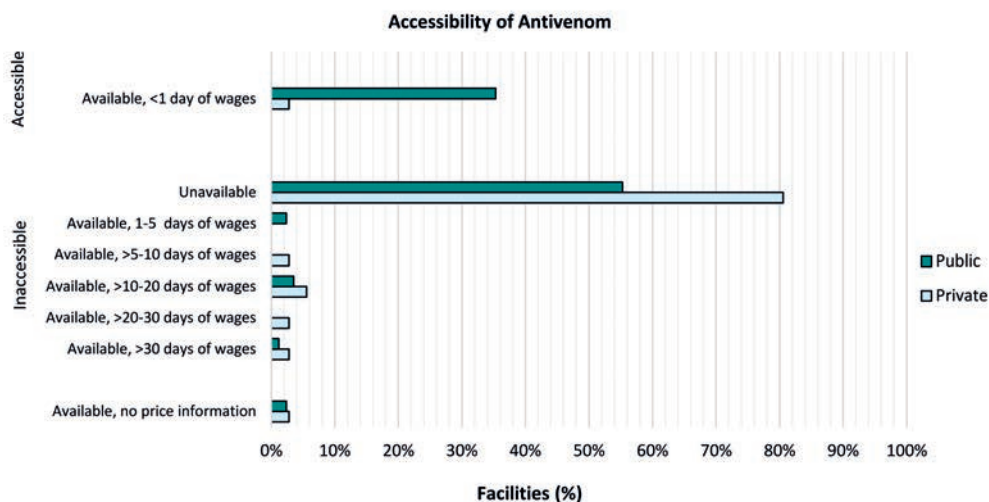
Figure 2. Accessibility of antivenom, per sector.

This study further showed that Snake Venom Antiserum (African IHS) produced by VINS Bioproducts Ltd, and Inoserp PAN-AFRICAN produced by INOSAN Biopharma were the most commonly stocked antivenom products, which have been shown to be ineffective in preclinical tests for some of the most commonly found snakes in Kenya. Especially for the VINS antivenom, its use is not supported by any pre-clinical data (10). Important to further note is that no antivenom in use in Kenya is supported by data from a randomised controlled trial. The use of ineffective antivenoms has been shown in some studies to lead to avoidable deaths. In Ghana, for instance, a switch from Sanofi's FAV-Afrique antivenom, one of the only safe and effective antivenoms previously used in Africa but discontinued due to commercial interests, to another antivenom led to an increase in mortality rate, from 1.8% to 12.1% (32).

Similarly, Médecins Sans Frontières reported an increase in mortality rate, from 0.47% to 10%, after they switched to another antivenom for six months due to unavailability of FAV-Afrique (33). Because of this, patients lose trust in the snakebite care offered, leading to delays in seeking care and increased use of traditional treatments by victims, and loss of trust in antivenom efficacy by healthcare workers (11,32). In Ghana, when the snakebite mortality rate in health facilities dropped again, a 50% increase in snakebite patients' attendance was observed (32).

Depending on the type of antivenom administered, several severe complications can arise, including anaphylactic reactions, occurring in up to 40% of patients, and serum sickness, occurring five to 14 days after antivenom administration (34–36). Adrenaline is the recommended prevention and treatment method for anaphylactic reactions, while

chlorpheniramine and prednisolone are used for mild and severe cases of serum sickness, respectively (34–36). In neurotoxic envenomings there is also a risk of respiratory failure, which is managed through ventilatory support, consisting of endotracheal intubation or assisted ventilation, and in the case of neurotoxic cobra bites also with neostigmine and atropine (4,35,37). We have shown, however, that availability of these commodities for managing complications is very low across facilities in Kenya, a situation exacerbated by stock-outs. Considering these adverse reactions are common in envenomings and can lead to death if not managed, ensuring the availability of both antivenom and associated commodities at facilities for quick access is critical. To facilitate this, snakebite should be made a part of routine national surveillance, with mandatory recording of the number of snakebites admitted to health facilities at all levels. Second, more data is needed on the effectiveness of the available antivenoms in Kenya. A case reporting system should therefore be established, in which snakebite cases presenting to health facilities and the subsequent care provided are recorded. This system should include the reporting of the type of antivenom administered, other commodities used, and the health outcomes of the patients, including any adverse reactions. This would allow policymakers to map facilities with a high case rate and respond by stocking suitable antivenom and other supportive treatments.

Even if antivenom and supportive commodities to manage adverse reactions are adequately available, the question remains whether healthcare workers have the skills to properly manage the patient. Research in Kenya has shown, for example, that only 12.4% of healthcare workers had received training on snakebite management (12). In line with this, we found that the 20-minute whole blood clotting test (20WBCT), which is a simple test using a glass tube to test for coagulability to identify hemotoxic envenomings, was indicated to be available at only 7.5% of Kenyan facilities (4). The question here, however, is whether the availability was actually so low, or if it was indicated to be unavailable because the healthcare workers were unfamiliar with this test, which requires only a glass tube. Efforts should therefore not only focus on improving availability of snakebite commodities, but also on increasing healthcare worker knowledge on snakebite management.

Antivenom affordability was not shown to be generally problematic in the public sector. However, in the private sector, where patients might have to buy antivenom if it is not available in the public sector, affordability can be problematic. The cost of one vial of antivenom would already impoverish 39.0% of the population if they required treatment. Considering that the average dose for seven antivenoms on the market in 2011 in sub-Saharan Africa, based on the manufacturers' recommendations, was 4.5 vials, which can go up to as many as 12 vials depending on the manufacturer and response of the patient to treatment, antivenom becomes unaffordable for almost the entire Kenyan population (7). This catastrophic health expenditure that might be incurred by snakebite victims is also illustrated by the case example, which highlights that incurred costs are not only

due to the purchasing of antivenom but are also an accumulation of the costs of treating the symptoms and complications. A study conducted in Kenya underscores the impact snakebite can have: 46% of the snakebite victims in the study noted they were unable to afford the hospital bills for their snakebite treatment, and 20% also noted they went into debt because of it (38). Of note is that both approaches used here to calculate affordability provide only an indication of what the affordability of a commodity is. In the case of a snakebite, costs incurred are acute and of short duration, but often present an immediate financial pressure to the victim and their family. Affordability calculations like this do not take into account that patients might need to sell their valuables, livestock or land to pay for the treatment, which has long-lasting financial consequences not assessed here (39,40). To fully understand the socio-economic burden of snakebite on victims and their families, future research should specifically study all components of treatment affordability.

To tackle the unaffordability of snakebite treatment, the cost of antivenom should be evaluated by what constitutes an effective dose rather than by the number of vials. Procurement agencies are sometimes misled by the cost per vial rather than the entire cost of effective treatment. To prevent higher total costs for an effective treatment, recommended dosages should be backed up by independent, evidence-based studies and real-world data measuring product efficacy with treatment outcomes (7). Further, the Ministry of Health should focus efforts on ensuring antivenom is available for free to the patient at public facilities to avoid catastrophic health expenditure otherwise incurred in the private sector. The roll-out of Universal Health Coverage (UHC) in Kenya provides the perfect opportunity for improving affordability of antivenom. Including antivenom and commodities for supportive treatment and complications management in the UHC benefits package could greatly reduce the impact purchasing commodities has on a family's financial situation. Efforts should therefore focus on advocating for inclusion of these commodities, especially antivenom, in this package.

This research showed that stock-outs seemed to have worsened during COVID-19, with facilities reporting stock-outs significantly more often in the period after COVID-19 measures were implemented. These results seem to confirm stories in the media that COVID-19 has disrupted supply chains, and are in line with findings from studies on the impact of COVID-19 on the availability of antiretrovirals, which reported low levels of stock or delays in deliveries (41,42). Health system strengthening is needed to ensure that in future emergencies or pandemics the supply of commodities is not hampered or de-prioritised, and those in need are still able to access the care they need. Further, the WHO will pilot an antivenom stockpiling programme in sub-Saharan Africa as a way to ensure access to effective antivenom treatments, which might solve some of the issues related to availability and stock-outs. At the same time, questions related to the sustainability of such an approach have been raised by Habib et al (2020) (6).

Strengths and limitations

This research is the first to study the availability, stock-outs and affordability of not only antivenom, but also commodities used for supportive treatment when managing snakebites. A standardised and validated methodology was used (20). Nevertheless, this research also knows some limitations. Due to the non-probability sampling and the distribution of public, private and PNFP facilities within the counties, we only surveyed a limited number of private not-for-profit facilities, which made it impossible to analyse this sector separately. Furthermore, the WHO/HAI methodology measures availability of commodities at one point in time. To mitigate this, we included commodity stock information for a period of twelve months to provide an indication of what the availability might be throughout the year. However, because availability of some of the commodities was very low, stock information could not be analysed for all the commodities as the commodity was never stocked at that facility. The WHO/HAI methodology further calculates affordability using the wage of a lowest-paid government worker. However, as seen in this study, the wage of a lowest-paid government worker was KSH 452.40 per day, while 24.2% of the population was living below the poverty line of USD 1.90, which was equal to KSH 202.58. The wage of a LPGW is thus not a sufficient benchmark for affordability in Kenya. Anticipating this, we also used the impoverishment approach, which provides a better indication of the actual affordability for the Kenyan population. However, as described by Niëns et al., this affordability measure also provides merely an indication due to the assumptions inherent to the HHFCE calculations and the linearity of the income distribution between groups (43). Further, the impoverishment approach is often used for calculating affordability of medicines for chronic conditions, making it easier to calculate daily costs of a medicine. Since snakebite treatment costs are not chronic and instead incurred over a very short time period, we used the HHFCE per month to calculate affordability.

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CONCLUSION

This study has shown that access to antivenom and supportive treatment to manage snakebites is problematic in Kenya. Availability was low, and while affordability was not a problem in the public sector, stock-outs of commodities force patients to buy them from the private sector, where antivenom in particular was unaffordable to many. Stock-outs seemed to have worsened during COVID-19, highlighting the needed for a strengthened health system that can secure continuity of care during emergencies or pandemics. To improve availability and reduce stock-outs, snakebite should be made a part of routine national surveillance, with mandatory recording of the number of snakebites admitted to health facilities to allow policymakers to map facilities with a high case rate and respond by stocking suitable antivenom and other supportive treatments. Further, in hotspot areas, a reporting system should be set up, in which snakebite cases, the provided care, and the treatment and patient outcomes are recorded and reported. Inclusion of antivenom into the UHC packages being rolled out in Kenya would further facilitate accessibility.

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CONTRIBUTION STATEMENT

GIO, JvO, BW and TR designed the study. DO collected the data. GIO analysed the data and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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SUPPLEMENTARY DATA

Supplementary File 1. Surveyed snakebite commodities.

Commodity	Formulation	Level of care available	Use
Antivenom	10ml	2	Specific antibody treatment for envenomings.
Tetanus toxoid vaccine	10ml	2	Prevention of tetanus.
Benzylpenicillin	600mg	2	Prevention of bacterial infections.
Metronidazole	200mg, 400mg	2	Prevention of bacterial infections.
Metronidazole	200mg/5ml	4	Prevention of bacterial infections.
Gentamicin	10mg/2ml, 20mg/2ml	2	Prevention of bacterial infections.
Gentamicin	40mg/2ml, 80mg/2ml	3	Prevention of bacterial infections.
Amoxicillin	250mg, 500mg	2	Prevention of bacterial infections.
Amoxicillin + clavulanic acid	250mg + 62.5mg, 875mg + 125mg	2	Prevention of bacterial infections.
Adrenaline	1mg/ml	2	Treatment of anaphylaxis.
Hydrocortisone	100mg	2	Treatment of serum sickness.
Chlorpheniramine	10mg/1ml, 2mg/5ml	2	Treatment of serum sickness.
Prednisolone	5mg	4	Treatment of serum sickness.
Neostigmine	2.5mg/ml	4	Reversion of neuromuscular blockage
Atropine	1mg/ml	4	Reversion of neuromuscular blockage
Paracetamol	500mg	1	Management of mild pain.
Dihydrocodeine phosphate	30mg	3	Management of moderate to severe pain.
Morphine	10mg/ml	2	Management of severe pain.
Lidocaine	30ml	2	Topical anaesthetic.
Saline (sodium chloride)	500ml	2	Treatment of anaphylaxis/circulatory failure.
Fresh frozen plasma	NA	4	Blood transfusion.
Blood platelets	NA	4	Blood transfusion.
Red blood cells	NA	4	Blood transfusion.
Whole blood	NA	4	Blood transfusion.
Bandage	NA	1	Bind up a wound or part of the body.
Splint	NA	3	Pressure immobilisation.
Sticking plaster	NA	3	Pressure immobilisation.
Oxygen cylinder	NA	2	Provision of oxygen to patients.
Laryngoscope	NA	2[a]	Examination of the throat, insertion of tube into throat.
Cuffed endotracheal tube	NA	3	Maintains an open airway to provide oxygen.
Nasal prong	NA	2	Deliver supplemental oxygen through the nose.
Ambu bag	NA	2	Manual ventilation.
Oral airway	NA	3	Maintains an open airway.

Supplementary File 1. (continued)

Commodity	Formulation	Level of care available	Use
Ventilator	NA	3[a]	Assist the function of the lungs of a patient.
Intravenous cannula	NA	2	Administration of fluids and medicines.
Catheter	NA	2	Drainage of bladder.
Syringe + needle	NA	2	Administration of fluids and medicines.
IV administration set	NA	2	Administration of fluids and medicines.
Urine dipstick	NA	2	Envenoming test.
Creatinine clearance blood test	NA	2[a]	Envenoming test.
Blood urea nitrogen testing	NA	2[a]	Envenoming test.
20-minute whole blood clotting test	NA	2[a]	Envenoming test.
Point-of-Care INR device	NA	2[a]	Envenoming test.

IV: Intravenous; INR: International normalised ratio; NA: Not applicable.

Level 1: Community health services; level 2: Dispensary/clinic; level 3: Health centre; level 4: Primary hospital; level 5: Secondary hospital; level 6: Tertiary hospital.

[a]Commodity not included on essential medicines or medical supplies list.

Supplementary File 2. Antivenom brands stocked at health facilities, per sector.

Brand	Number of Facilities		
	Public N (%)	Private N (%)	Total[a] N (%)
Snake Venom Antiserum (African IHS)	24 (66.7)	6 (100.0)	30 (70.2%)
VINS Bioproducts Ltd			
Inoserp PAN-AFRICAN	13 (33.3)	0 (0.0)	13 (29.8%)
INOSAN Biopharma			
SAIMR Polyvalent Snake Antivenom	1 (2.6)	0 (0.0)	1 (2.1%)
South African Vaccine Producers (SAVP) (PTY) Ltd			
Brand information missing	1 (2.6)	0 (0.0)	1 (2.1%)

[a]Availability includes the private not-for-profit sector.

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Supplementary File 3. Accessibility of snakebite commodities, per sector.

	Public		Private	
	Availability	**Affordability**	**Availability**	**Affordability**
Antivenom	44.7%	0.0	19.4%	14.4
Tetanus vaccine	68.2%	0.0	83.3%	0.2
Benzylpenicillin	63.5%	0.0	69.4%	4.4
Metronidazole (200 or 400mg)	83.5%	0.0	75.0%	0.2
Metronidazole (200mg/5ml)	20.0%	0.0	30.6%	0.1
Gentamicin (10mg/2ml or 20mg/2ml)	37.6%	0.0	8.3%	2.2
Gentamicin (40mg/2ml or 80mg/2ml)	55.3%	0.0	61.1%	0.6
Amoxicillin (250mg)	87.1%	0.0	77.8%	0.2
Amoxicillin (500mg)	34.1%	0.0	69.4%	0.3
Amoxicillin + clavulanic acid	51.4%	0.0	37.9%	1.0
Paracetamol	88.2%	0.0	97.2%	0.0
Dehydrocodeine phosphate	4.2%	0.0	3.4%	N/A
Morphine	15.8%	0.2	18.2%	1.1
Adrenaline	43.5%	0.0	61.1%	0.2
Hydrocortisone	80.0%	0.0	77.8%	1.3
Chlorpheniramine (10mg/1ml)	9.7%	0.1	37.9%	0.7
Chlorpheniramine (2mg/5ml)	8.3%	0.0	24.1%	0.3
Prednisolone (5mg)	38.8%	0.0	86.1%	0.1
Saline	81.2%	0.0	63.9%	0.6
Lidocaine	75.3%	0.0	75.0%	0.0
Neostigmine	21.1%	0.1	18.2%	0.5
Atropine	52.8%	0.0	58.6%	0.2

Accessibility:

☐ <80% availability, >1 day's wage ☐ <80% availability, <1 day's wage

▨ ≥80% availability, >1 day's wage ■ ≥80% availability, <1 day's wage

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3.3

THE CURRENT STATE OF SNAKEBITE CARE IN KENYA, UGANDA, AND ZAMBIA: HEALTHCARE WORKERS' PERSPECTIVES AND KNOWLEDGE, AND HEALTH FACILITIES' TREATMENT CAPACITY

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ABSTRACT

Introduction

Snakebites continue to be a public health concern in sub-Saharan Africa, where availability of appropriate medical treatment is rare, even though death and disability can be prevented with timely intervention. A challenge is the lack of socio-political studies to inform health policies. This study aimed to identify snakebite patient profiles, healthcare workers' (HCWs) knowledge of snakebite, and facilities' snakebite treatment capacity in Kenya, Uganda, and Zambia to inform interventions to improve access to appropriate treatment.

Methods

The research comprised a cross-sectional key informant survey among HCWs from health facilities in Kenya (n=145), Uganda (n=144), and Zambia (n=108). Data were collected between March 2018 and November 2019.

Results

The majority of HCWs suggested that the number of snakebite incidents was similar between the sexes, that most patients were aged 21 to 30 years, and most people were bitten when farming or walking. Overall, only 12% of HCWs had received formal training in snakebite management. Only about 20% of HCWs in each country said their health facility had the medicines needed to treat snakebites, with antivenom available in 0% to 34% of facilities across the sectors and countries, and snakebites were not systematically recorded.

Conclusion

This research shows that an integrative approach through policies to increase resource allocation for health system strengthening, including community education, HCW training and improved access to snakebite treatment, is needed. Part of this approach should include regulations that ensure antivenoms available in health facilities meet quality control standards, and that snakebites are accommodated into routine reporting systems to assess progress.

INTRODUCTION

Globally, it is estimated that snakebite envenoming is responsible for more than 138,000 deaths and more than 400,000 permanent disabilities each year (1). In sub-Saharan Africa, 314,000 snakebite envenomings cause between 5,900 to 14,600 amputations and 7,000 to 32,000 deaths annually (2,3). While displaying a large range, these estimated incidences are also believed to be a gross underestimation of the actual situation, given that studies have shown that up to 70% of snakebite cases remain unreported (4–6). A study on the burden of snakebite in West Africa estimated that the disability-adjusted life years caused by snakebites exceeded those of many other neglected tropical diseases which currently receive more attention (7). In addition to a range of morbidities, such as tissue necrosis, persistent nerve damage, and amputation, victims may suffer from psychological distress and stigmatisation in their communities (3,8).

Adequate and timely medical treatment can prevent serious health complications of snakebite envenomings. However, in sub-Saharan Africa, effective treatment is scarce, and issues of poor antivenom production, inadequate distribution, and poor efficacy of antivenom prevail (9,10). In the past 10 years, the production of antivenom has failed to expand, and the antivenom supply chain is currently inadequate and unstable (11,12). The lack of access to appropriate antivenom, in combination with traditional beliefs surrounding snakebite, leads victims to seek ineffective or adverse treatment from traditional healers. This also delays evidence-based treatment when time is of the essence (3,8).

Snakebite envenomings have a massive impact on households and communities, and disproportionally affect poor communities. In sub-Saharan Africa, 97% of snakebite deaths occur in rural areas which depend on outdoor activities for livelihood, such as farming, fishing, hunting, and herding (2,8,13,14). Snakebite incidents are highest among the most economically productive members of the community, and poor geographical access to and quality of healthcare in remote communities diminish the chance of receiving adequate treatment (8,11,14). Moreover, even if people do make it to health facilities and treatment is available, treatment costs could cause catastrophic expenditure and additional financial hardship (10,15). As such, snakebites aggravate socioeconomic inequalities.

Fortunately, with the right training, medicines, and equipment, combined with appropriate health-seeking behaviour, snakebite patients can be properly managed, and the burden of snakebite morbidity and mortality can be significantly relieved (16). To date, however, there are very little research efforts on snakebite in sub-Saharan Africa. In Kenya, Uganda, and Zambia, for instance, the few existing studies that involve primary data collection are generally of limited scale and scope or outdated (17–21). To contribute to evidence about the country-specific snakebite burden and to inform policy intervention, a survey was conducted among healthcare workers (HCWs) employed in health facilities in Kenya,

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Uganda, and Zambia to identify snakebite incidents, patient profiles, HCWs knowledge, and health facilities' capacity to adequately treat snakebites.

METHODS

Study area and sampling

The sampling strategy used to identify health facilities was adapted from the WHO/Health Action International gold-standard methodology "Measuring medicine prices, availability affordability, and price components," which recommends surveying 144 facilities from six regions to obtain a representative facility sample to create a picture of the country situation (22). The methodology has been validated in many countries (23,24). In Kenya and Zambia, data were collected across six counties and regions, respectively, of which three were thought to be snakebite-endemic areas and three were not. Uganda was divided into six survey regions from which data were collected. Furthermore, according to the sampling methodology, officially in each survey region, 24 health facilities should be randomly selected to participate in the research, equally divided across sectors (public, private, or private not-for-profit [PNFP]) and locations (urban or rural) (see Supplementary File 1). The national definition of urban varies in each of the countries; for the purpose of this study, an urban area was defined as a locality with a population of a minimum of 5,000 people where the main economic activity is non-agricultural and where basic modern facilities are present (25,26). In this research, 24 facilities were randomly selected per survey region from a list, with allocation to sector and area performed afterward. In Zambia, the levels of health facilities surveyed ranged from health posts to general hospitals, and in Kenya from health posts to national university teaching hospitals. Similarly, in Uganda, the levels ranged from health centres II to regional referral hospitals.

Within each facility, one informant was selected to participate in a qualitative survey through convenience sampling. This informant needed to be a licensed HCW who had been working at the facility for more than a year.

Data collection tool

A HCW questionnaire was used, which collected informant information about snakebite incidents, patient profiles, HCW's knowledge, and the facility's capacity to treat snakebites. The questionnaire was informed by scientific literature and developed in collaboration with recognized snakebite experts from the Global Snakebite Initiative and local civil society experts. The questionnaire contained 33 questions and inquired about the number of snakebite cases in the last 6 months (Uganda) or 12 months (Kenya, Zambia), proportion of male–female snakebite patients, age of patients, the availability of antivenom at the facility, the type of snakebite treatment offered at the facility, HCWs' training on snakebites, and their perceived knowledge on snakebite treatment. To provide exact numbers on the amount of snakebite incidents and stock availability of antivenom, the HCW was asked to refer to

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their medical records. The remaining questions were based on the informants' experience. The questionnaire was pilot-tested in 2017 in 108 facilities in Kilifi County, Kenya, after which the tool was refined. The pilot test data were not included in this research. Furthermore, in each country, local partners provided feedback on the questionnaire, resulting in the slightly different phrasing of four questions (age, number of registered cases, knowledge on snakebite treatments, and consultation of traditional healer) between the countries, even though the essence remained the same.

Data collection

Data collection was performed by local organisations with experience in conducting similar research. Data collection teams worked in pairs and were supervised by a local survey manager. Data collectors received a 1-day training course in person (Kenya and Uganda) or through video-calling (Zambia), led by one of the investigators (SvB or GIO). In Uganda, data were collected in March 2018, in Zambia in July 2018, and in Kenya from March to November 2019.

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Data analysis

All data collection forms were manually entered into Excel and cross-checked by two researchers for accuracy. Missing data and incorrectly answered questions were excluded from the analysis. Data analysis was performed in Microsoft Excel 365 (Microsoft, Redmond, WA), where an analysis tool was used to calculate medians, minimums, maximums, and frequencies using descriptive statistics.

Ethical considerations

In Zambia, approval was sought from the National Health Research Authority, and in Kenya, by the Amref Health Africa Ethics and Scientific Review Committee. In Uganda, no ethical approval was necessary, but permission for the research and letters of introduction to health facilities were secured from the Ministry of Health. These letters were also acquired in Kenya and Zambia. Informed consent was obtained from all participants, and all identifiers were replaced with codes to maintain anonymity and confidentiality.

RESULTS

Sample

A total of 118 HCWs in Zambia, 144 HCWs in Uganda, and 145 HCWs in Kenya were surveyed. In Kenya and Uganda, HCWs in facilities across the public, private, and PNFP sectors were included. In Zambia, data were collected from HCWs in the public and PNFP sectors only, as the private (for-profit) sector is of very limited scale. Healthcare workers working in PNFP facilities were subsequently excluded from analysis because of the small sample size. Hence, the included sample for Zambia totalled 108 HCWs working in public sector facilities. **Table 1** is an overview of the participants' characteristics.

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Table 1. Characteristics of study participants from Kenya, Uganda, and Zambia, per sector.

| | Kenya (n=145) | | | | | | | | Uganda (n=144) | | | | | | | | Zambia (n=108) | |
| | Public | | Private | | PNFP | | Total | | Public | | Private | | PNFP | | Total | | Public | |
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Facility location																		
Urban	11	(10.6)	11	(47.8)	3	(16.7)	25	(17.2)	26	(40.6)	28	(66.7)	16	(42.1)	70	(48.6)	33	(30.6)
Rural	93	(89.4)	12	(52.2)	15	(83.3)	120	(82.3)	38	(59.4)	14	(33.3)	22	(57.9)	74	(51.4)	75	(69.4)
Profession																		
Assistant	2	(1.9)	1	(4.3)	1	(5.6)	4	(2.8)	9	(14.1)	1	(2.4)	2	(5.3)	12	(8.3)	15	(13.9)
Nurse	60	(57.7)	7	(30.4)	9	(50.0)	76	(51.7)	30	(46.9)	17	(40.5)	17	(44.7)	64	(44.4)	61	(56.5)
Physician	37	(35.6)	15	(65.2)	8	(44.4)	60	(41.4)	24	(37.5)	24	(57.1)	19	(50.0)	67	(46.5)	31	(28.7)
Pharmacist	5	(4.8)	0	(0.0)	0	(0.0)	5	(3.4)	1	(1.6)	0	(0.0)	0	(0.0)	1	(0.7)	1	(0.9)
Facility level[a]																		
Level I	45	(43.3)	12	(52.2)	11	(61.1)	68	(46.9)	17	(26.6)	11	(26.2)	13	(34.2)	41	(28.5)	33	(30.6)
Level II	37	(35.6)	10	(43.5)	5	(27.8)	52	(35.9)	36	(56.3)	27	(64.3)	15	(39.5)	78	(54.2)	63	(58.3)
Level III	16	(15.4)	0	(0.0)	1	(5.6)	17	(11.7)	6	(9.4)	4	(9.5)	10	(26.3)	20	(13.9)	7	(6.5)
Level IV	6	(5.8)	1	(4.3)	1	(5.6)	8	(5.5)	5	(7.8)	0	(0.0)	0	(0.0)	5	(3.5)	5	(4.6)

PNFP: Private Not-For-Profit.

[a]Health facility levels in Kenya: I. Community Health Services and Dispensary/Clinic; II. Health Centre; III. Sub-County Hospital; IV. County Hospital and above. Health facility levels in Uganda: I. Health Centre; II. Health Centre III and IV; III. Hospital; IV. Regional Referral Hospital and above. Health facility levels in Zambia: I. Health Post; II. Health Centre; III. District Hospital; IV. General Hospital and above.

Snakebite demographics

Over a 6-month period in Uganda, 593 snakebite cases were registered in 140 facilities. In Kenya and Zambia, a respective 801 cases in 108 facilities and 662 cases in 86 facilities were registered over a 12-month period. In all three countries, most of the cases were registered in rural health facilities (see **Table 2**). In Kenya, the highest median number of registered cases was noted in level IV facilities; in Uganda and Zambia, it was noted in level III facilities.

In Kenya, HCWs' experiences regarding the months in which they saw most snakebites varied, and no clear patterns could be distinguished. Multiple months could be chosen. In Zambia, a clear majority of HCWs saw most snakebites in November to January. In Uganda,

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Table 2. Total or median number of registered snakebites per location, geographic region and facility level in Kenya, Uganda, and Zambia.

	Kenya[a]		Uganda[b]		Zambia[a]	
	Facilities tracking cases *N* (%)	# of cases (12-month period) *N* (range)	Facilities tracking cases *N* (%)	# of cases (6-month period) *N* (range)	Facilities tracking cases *N* (%)	# of cases (12-month period) *N* (range)
Per location, total						
Urban	16 (64.0)	211	67 (95.7)	231	22 (66.7)	149
Rural	92 (76.7)	590	74 (100.0)	362	64 (85.3)	513
Per geographic region, total[c]						
Region I	23 (100.0)	191	29 (93.5)	183	16 (69.6)	229
Region II	12 (50.0)	99	34 (94.4)	123	26 (92.9)	171
Region III	15 (60.0)	53	36 (100.0)	160	29 (100.0)	174
Region IV	20 (83.3)	392	41 (100.0)	127	15 (53.6)	88
Region V	24 (100.0)	12	NA	NA	NA	NA
Region VI	14 (58.3)	54	NA	NA	NA	NA
Per facility level, median[d]						
Level I	48 (70.6)	1.0 (0-22)	41 (100.0)	1.0 (0-10)	29 (87.9)	3.0 (0-20)
Level II	39 (75.0)	1.0 (0-76)	76 (97.4)	2.0 (0-39)	50 (79.4)	6.0 (0-65)
Level III	16 (94.1)	8.0 (0-48)	20 (100.0)	5.5 (0-23)	5 (71.4)	17.0 (3-30)
Level IV	5 (62.5)	12.0 (1-47)	4 (80.0)	3.0 (0-41)	2 (40.0)	5.5 (3-8)

NA: Not applicable.

[a]Snakebites registered over the previous 12 months.

[b]Snakebites registered over the previous 6 months.

[c]In Kenya Region I: Kajiado County; Region II: Kilifi County; Region III: Kirinyaga County; Region IV: Kwale County; Region V: Nyandarua County; Region VI: Taita Taveta County. In Uganda Region I: Central Region; Region II: Eastern Region; Region III: Northern Region; Region IV: Western Region; Region V-VI: NA. In Zambia Region I: Luapula Province; Region II: Muchinga Province; Region III: North Western Province; Region IV: Northern Province; Region V-VI: NA.

[d]Health facility levels in Kenya: I. Community Health Services and Dispensary/Clinic; II. Health Centre; III. Sub-County Hospital; IV. County Hospital and above. Health facility levels in Uganda: I. Health Centre II; II. Health Centre III and IV; III. Hospital; IV. Regional Referral Hospital and above. Health facility levels in Zambia: I. Health Post; II. Health Centre; III. District Hospital; IV. General Hospital and above.

the largest proportions of HCWs saw more snakebite cases from October to December, and from April to June (see **Figure 1**).

Snakebite patient profile

In Kenya, almost half of HCWs claimed that the male–female ratio among snakebite patients was equal, whereas 30.4% thought there were mostly male patients and 18.8% thought there were mostly female patients. In Uganda and Zambia, the responses were similar (see **Table 3**). When asked about the age of those bitten by snakes, HCWs from all three countries indicated that individuals aged 21–30 years were most often bitten by snakes. In Uganda and Zambia, this was followed by the 11–20 years age-group, whereas the second most commonly mentioned age-group in Kenya was 31–45 years (see **Table 3**). According to HCWs in all three countries, farming was the most common activity performed by people at the time of the bite (55.3–75.4%), followed by simply walking, collecting firewood, and herding (depending on country) (see **Table 3**).

In Kenya, the survey further asked about the most commonly bitten body part. Multiple body parts could be chosen. More than eight in 10 HCWs believed the legs to be one of the most commonly bitten body parts, whereas about 30% of HCWs mentioned the feet, hands, and fingers (see Supplementary File 2).
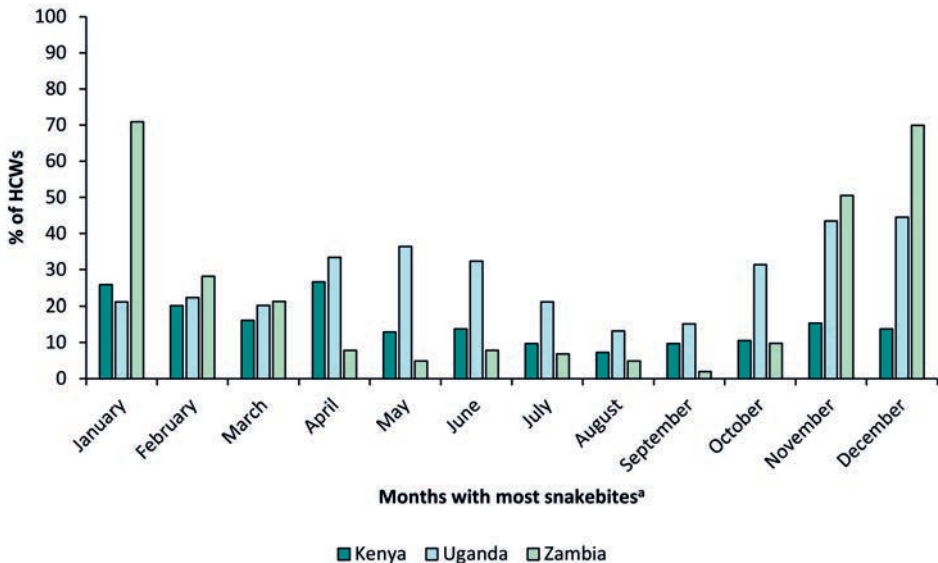
Figure 1. Months in which healthcare workers (HCWs) reported to see most snakebite cases, per country. [a]Healthcare workers could indicate multiple months, so totals may sum to more than 100%.

Table 3. HCWs' perspectives on snakebite patient characteristics.

	Kenya HCWs (overall)		Uganda HCWs (overall)		Zambia HCWs (public)	
	N	(%)	N	(%)	N	(%)
Proportion of male-female patients						
Only male	6	(5.4)	3	(2.2)	3	(2.9)
Mostly male	34	(30.4)	41	(30.6)	37	(36.2)
Same number of males and females	50	(44.6)	48	(35.8)	41	(39.0)
Mostly female	21	(18.8)	29	(21.6)	23	(21.9)
Only female	1	(0.9)	13	(9.7)	0	(0.0)
Age of snakebite patients[a]						
0-10 years	20	(18.1)	33	(24.6)	18	(17.1)
11-20 years	26	(23.6)	64	(47.8)	55	(53.3)
21-30 years	61	(55.5)	93	(69.4)	63	(61.0)
31-45 years	58	(52.7)	61	(45.5)	40	(38.1)
46-65 years	9	(8.2)	11	(8.2)	6	(5.7)
>65 years	1	(0.9)	0	(0.0)	1	(1.0)
Activity at time of snakebite[a]						
Playing	12	(10.5)	26	(19.4)	21	(19.8)
Herding	36	(31.6)	22	(16.4)	1	(0.9)
Sleeping	15	(13.2)	20	(16.4)	4	(3.8)
Farming	63	(55.3)	101	(75.4)	67	(64.2)
Walking	30	(26.3)	63	(47.0)	64	(60.4)
Charcoal burning	10	(8.8)	6	(4.5)	5	(4.7)
Fishing	0	(0.0)	7	(5.2)	7	(6.6)
Collecting firewood	32	(28.1)	6	(4.5)	33	(31.1)
Activities inside the house	24	(21.1)	3	(2.2)	0	(0.0)
Other	0	(0.0)	9	(6.7)	7	(6.6)

[a]HCWs could indicate up to three categories so totals may sum to more than 100%.

Health facilities' resources and response

Training and knowledge of snakebite management

Training of HCWs on snakebites was found to be uncommon, ranging from 2.6% in the PNFP sector in Uganda to 22.2% in the PNFP sector of Kenya (see **Table 4**). Low percentages were also obtained for questions related to knowledge to treat snakebite adequately. In Uganda, less HCWs in the public sector believed they had the knowledge to adequately treat snakebites than those in the private and PNFP sectors (28.6% versus 65.9% and 57.9%, respectively) (see **Table 4**). In Zambia, 58.5% of the HCWs believed there was someone in the health facility, not specifically the HCW surveyed, who had the knowledge to treat snakebites, whereas in Kenya, 34.8% of HCWs believed they could differentiate a venomous snakebite from a nonvenomous snakebite. The overwhelming majority of HCWs in Uganda

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Table 4. HCWs' perspectives on treatment and their health facilities' capacity to treat snakebite.

|	Kenya (n=145)								Uganda (n=144)								Zambia (n=108)	
	Public		Private		PNFP		Total		Public		Private		PNFP		Total		Public	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Training on snakebite treatment																		
Yes	11	(10.6)	3	(13.0)	4	(22.2)	18	(12.4)	6	(9.4)	5	(11.9)	1	(2.6)	12	(8.3)	17	(16.0)
No	93	(89.4)	20	(87.0)	14	(77.8)	127	(87.6)	58	(90.6)	37	(88.1)	37	(97.4)	132	(91.7)	89	(84.0)
Knowledge on snakebite treatment																		
Yes	34	(34.3)	11	(52.4)	3	(16.7)	48	(34.8)	18	(28.6)	27	(65.9)	22	(57.9)	67	(47.2)	62	(58.5)
No	65	(65.7)	10	(47.6)	15	(83.3)	90	(65.2)	45	(71.4)	14	(34.1)	16	(42.1)	75	(52.8)	44	(41.5)
Treats snakebite[a]																		
Assistant	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.7)	11	(18.0)	1	(2.4)	5	(14.3)	17	(12.4)	8	(7.6)
Nurse	56	(57.1)	7	(30.4)	9	(52.9)	72	(52.2)	43	(70.5)	21	(51.2)	22	(62.9)	86	(62.8)	69	(65.7)
Physician	61	(62.2)	18	(78.3)	9	(52.9)	88	(63.8)	44	(72.1)	36	(87.8)	27	(77.1)	107	(78.1)	60	(57.1)
Not treated at facility	8	(8.2)	1	(4.3)	2	(11.8)	11	(8.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Commodities available to treat snakebite																		
Yes	23	(23.2)	3	(13.6)	3	(18.8)	29	(21.2)	9	(14.1)	9	(21.4)	10	(26.3)	28	(19.4)	20	(19.0)
No	73	(73.7)	19	(86.4)	13	(81.3)	105	(76.6)	55	(85.9)	30	(71.4)	28	(73.7)	113	(78.5)	72	(68.6)
I don't know	3	(3.0)	0	(0.0)	0	(0.0)	3	(2.2)	0	(0.0)	3	(7.1)	0	(0.0)	3	(2.1)	13	(12.4)
Antivenom available at facility																		
Yes	33	(33.7)	0	(0.0)	4	(23.5)	37	(26.8)	4	(6.3)	1	(2.4)	1	(2.7)	6	(4.2)	9	(8.7)
Not at the moment	29	(29.6)	14	(60.9)	9	(52.9)	52	(37.7)	9	(14.1)	3	(7.1)	12	(32.4)	24	(16.9)	5	(4.9)
Generally not	36	(36.7)	9	(39.1)	4	(23.5)	49	(35.5)	50	(78.1)	36	(85.7)	24	(64.9)	110	(77.5)	53	(51.5)
I don't know	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.6)	2	(4.8)	0	(0.0)	2	(1.4)	36	(35.0)
Outcome of antivenom treatment																		
Desired effect	NA		NA		NA		NA		35	(61.4)	25	(64.1)	21	(61.8)	81	(62.3)	37	(38.1)
No effect	NA		NA		NA		NA		0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Negative effect	NA		NA		NA		NA		22	(38.6)	14	(35.9)	13	(38.2)	49	(37.7)	0	(0.0)

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and Zambia referred to a lack of training and the need for more specialised training on how to manage snakebite patients as the reason for their lack of knowledge.

Treatment

In all three countries, both nurses and physicians are the ones commonly providing care to snakebite patients, with assistants not commonly treating snakebites (see **Table 4**). Only about 20% of HCWs across the countries said they had the necessary equipment and medicines available at the health facility to treat snakebites. In all countries, supportive treatment, comprising painkillers, fluids, tetanus vaccines, antibiotics, and hydrocortisone, was the most commonly offered treatment for snakebite patients (see **Figure 2**). Health facilities also commonly referred patients to other facilities.

Traditional treatment, such as black stone and tourniquets, was offered at 0.8% of Kenyan, 7.0% of Ugandan, and 14.6% of Zambian facilities. In addition, considerable numbers of HCWs believed the majority of patients sought traditional treatments before visiting the health facility (50.0% in Kenya, 39.0% in Uganda, and 30.8% in Zambia, see **Table 4**).

Administering antivenom was not a common treatment practice, offered by 32.3% of Kenyan facilities, and a respective 7.7% and 12.6% of Ugandan and Zambian facilities (see **Figure 2**). When asked about the general effect of antivenom, 62.3% of HCWs in Uganda and 38.1% of HCWs in Zambia believed it had the desired effect (see **Table 4**). This question was not included in the Kenyan survey. In Kenya, 33.7% of public facilities, 0% of private facilities, and 23.5% of PNFP facilities surveyed had antivenom available and in stock at the time of the survey (see **Table 4**). In Uganda and Zambia, this was the case for less than 10% of

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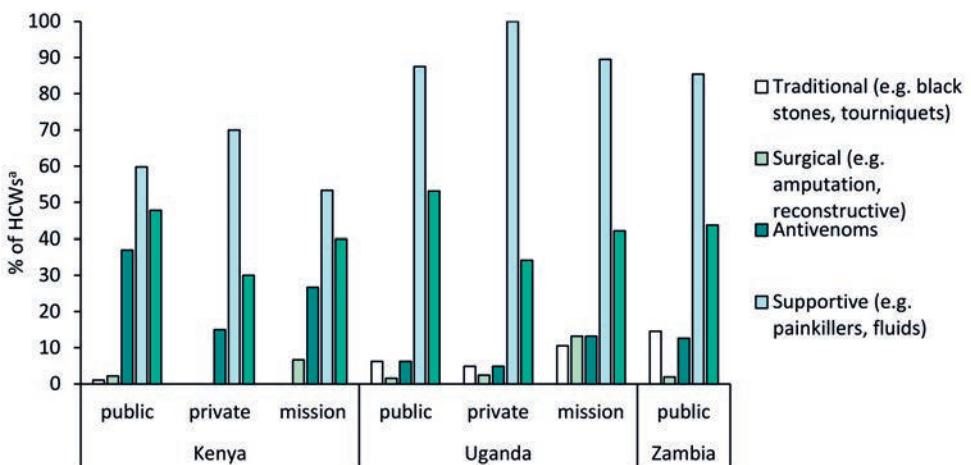
Figure 2. Type of treatment provided at health facility in response to snakebites, per country and sector. [a]HCWs could indicate multiple treatments, so totals may sum to more than 100%.

facilities across all sectors surveyed. The types of antivenom stocked in each country can be found in **Table 5**.

In all three countries, reasons given for the unavailability of antivenom included that it was not supplied to the facility, either because the level of care of the facility was too low, it was too expensive to stock, or the facility never stocked antivenom. In the non-endemic areas, a low snakebite incidence was also mentioned as reason for not having antivenom available.

Complications

In Kenya, HCWs were asked about the complications they most commonly observed after a snakebite. Multiple-answer options could be chosen. According to the HCWs, when complications occurred, the most common ones were swelling (55.9%), pain at the site of the bite (32.2%), cellulitis (23.7%), and respiratory distress (20.3%) (see Supplementary File 2).

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DISCUSSION

This research is one of the first to study HCWs' perspectives on snakebite demographics, their knowledge on treatment, and their health facilities' treatment capacity in Kenya, Uganda, and Zambia. According to most HCWs, there were no differences in snakebite incidents between genders, most patients were aged 21–30 years, and activities often performed when bitten were farming and walking. Supportive treatment was the most commonly offered type of treatment, and 85–90% of HCWs had not received any training in snakebite management. About 80% of HCWs across the countries thought their health facility did not have the necessary equipment and medicines available to treat snakebite. Accordingly, a mere 27.0% of HCWs in Kenya, 4.2% in Uganda, and 7.6% in Zambia stated they had antivenom in stock at the time of survey.

Snakebite envenoming is a significantly understudied neglected tropical disease. Existing studies cover just one hospital or are outdated (17–21). One Kenyan study had a similar research question and approach (albeit it only covered four high-level urban facilities) (27). The current study provided insight into the snakebite issue from the perspective of HCWs. Because none of the three countries have a national snakebite reporting and surveillance system, current evidence on snakebite incidents is mostly anecdotal (27–30). This research is an attempt to provide a comprehensive overview of snakebite incidents by randomly sampling health facilities throughout multiple regions in each country, which can be used as evidence for policy-makers to inform and strengthen snakebite policies, including reporting systems. Although these not insubstantial numbers registered at the facilities only give cautious indications toward the actual number of snakebites taking place, also because not all facilities registered the snakebites cases seen by the facility, they confirm that in general, health facilities regularly have to deal with a number of snakebites. Given that multiple studies have shown snakebite underreporting is as high as 70%, real snakebite incidents

Table 5. Type of antivenoms stocked in health facilities, per country and sector.

	Number of health facilities						
	Kenya			Uganda			Zambia
	Public	Private	PNFP	Public	Private	PNFP	Public
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Snake Venom Antiserum (African) VINS Bioproducts Ltd	28 (87.5)	0 (0.0)	3 (75.0)	4 (100.0)	0 (0.0)	0 (0.0)	6 (75.0)
SAIMR Polyvalent Snake Antivenom South African Vaccine Producers (SAVP) (PTY) Ltd	4 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	1 (12.3)
Inoserp PANAFRICAIN INOSAN Biopharma	2 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unclear origin	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.3)

PNFP: Private Not-For-Profit.

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will be much higher (4–6). Fortunately, in all three countries, ministries of health are willing to take encouraging steps to strengthen snakebite surveillance and reporting mechanisms. Reliable estimates of snakebite incidents and burden will improve opportunities for intervention and resource allocation (3).

Countries need to be prepared for seasonal variations in snakebite incidents. For example, in Zambia, HCWs reported an increase in snakebite cases from November to March. This might be explained by Zambia's climate, which has extreme droughts in May to August, and higher precipitation and temperatures from November to March (31). In Uganda, many HCWs also observed peaks in snakebite cases in months which corresponded to the rainy season (32). Other studies (in Costa Rica and Ghana) found similar patterns of increased snakebite incidents during the rainy season (33,34). In Kenya, the findings were not congruent with the rainy season (35). Information about snakebite incidents over the months can help authorities to anticipate on fluctuations in demand for treatments and adjust stock accordingly.

Although a few studies have investigated snakebite patient profiles in Kenya and other sub-Saharan African countries, to our knowledge, there are no such studies in Uganda and Zambia. Given most studies (including ours) are small scale, or based on experience, the level of generalisable and wholly reliable evidence is poor. Nevertheless, our findings largely correspond to those findings in the literature: a study of Kenyan case records showed roughly equal cases of males and females, whereas clinicians believed males were more likely to be bitten (27). Similar findings were also observed in Ghana and South Africa (34,36).

In our study, people aged 21–30 years were believed to be most prone to snakebites. This again resonates with previous research, which often finds highest incidence in relatively young age-groups (27,34,36). Also, HCWs suggest farming to be the most common activity performed at the time of the bite, which supports other studies' findings that it is people in rural areas, dependent on agriculture for livelihood, who are most at risk (13,34). At the same time, these people are most vulnerable to adverse health outcomes after snakebites because of poorer access to quality health care in rural areas (14).

This research underscores the paucity of HCW training on snakebite management: a mere 8–16% of HCWs had received any training. A similar percentage was found in a study in Cameroon (15%) (37). Healthcare workers' perspectives on their knowledge about snakebite treatment also exposed serious shortcomings. Although the questions in our research did not measure actual knowledge on snakebite treatment, the low numbers of trained HCWs and their own perceived lack of knowledge and confidence are alarming; an adequate treatment response can mean the difference between full recovery, and permanent disability or even death (38). Snakebite management training should be given to all HCWs during initial

training as part of the curricula, and in service as continuing professional development, especially in endemic areas.

Even if HCWs receive adequate training, there remains a considerable chance that resources are not available at health facilities. The health facilities in the sample mostly offered supportive treatment, with only a minority offering antivenom as part of the treatment pathway. This is supported by the finding of low antivenom availability, which remains a problem in many sub-Saharan African countries. The lack of trust in antivenoms we found among some HCWs might be explained by the overall lack of knowledge and the fact that ineffective antivenoms are regularly marketed and used in these countries (10,15,39–42). For instance, only a few health facilities across the countries had South African Institute for Medical Research polyvalent snake antivenom manufactured by South African Vaccine Producers (PTY) Ltd. available, which is seen as the "gold-standard" antivenom (43). Most facilities stocked snake venom antiserum (African) manufactured by VINS Bioproducts Ltd., which only showed signs of preclinical effectiveness for *Naja nigricollis* (black-necked spitting cobra), and ineffectiveness for other East and Southern African snake species such as *Bitis arietans* (puff adders) and *Dendroaspis polylepis* (black mambas), which are also found in Kenya, Uganda, and Zambia (43,44).

3.3

Ineffective traditional treatment, for example, using a black stone and tourniquets, is still sometimes offered by HCWs, particularly at Zambian health facilities. Interestingly, previous research in Cameroon showed that "pierre noire," similar to black stone, was believed effective for snakebite treatment by 64% of surveyed HCWs, whereas 37% believed use of tourniquets was recommended (37). Again, this is a training gap which needs to be addressed, as offering these types of treatments at health facilities can lead to negative health outcomes. It can cause infections from the method itself, as well as lead to a delay in providing appropriate medical care (45). Notably high was the number of HCWs who thought most snakebite patients sought traditional treatments before a health facility visit. This type of health-seeking behaviour leads to delays in seeking appropriate medical care, which in case of envenomings can lead to serious morbidity and death (46). Efforts should focus on engaging and empowering communities through strategies which improve their knowledge, attitudes, and practices on effective prevention measures, first aid, and health-seeking behaviour.

To gain a more in-depth understanding of snakebite incidence and its health and socioeconomic impact on fragile communities, it is vital to collect data from the community perspective. Household surveys and qualitative studies, which have been conducted in other countries, should also be completed in Kenya, Uganda, and Zambia (47,48). In addition, studies assessing availability and affordability of snakebite treatment and barriers to access are needed to inform resource allocation and intervention development.

Limitations

Although this study provides further insights into the snakebite situation in Kenya, Uganda, and Zambia, limitations should be noted. This research is based on data collected at health facilities, whereas a substantial portion of snakebite patients have limited access to health care and might instead visit a traditional healer (8,14). It therefore only provides part of the picture on the snakebite issue. In addition, although informants included were predominantly nurses and physicians, the fact that perspectives were obtained from just one informant per facility poses a risk for respondent bias. Their function in the facility, as well as the extent of their personal experience with treating snakebites, and knowledge about health facility resources and capacity may vary. Information on snakebites was collected retrospectively, which could have incurred recall bias. Except for obtaining the exact number of snakebite cases registered at the facilities, we did not make use of registries to identify the profile of snakebite patients, which might also have led to recall bias. Furthermore, with surveys, there is always a risk of interviewer bias, with informants answering in such a way that they think is desirable. We aimed to mitigate this by ensuring questions were phrased objectively, and they were asked by the data collectors as they are and not interpreted or paraphrased.

Data were collected consecutively in the three countries. After feedback from local partners, some adjustments were made, resulting in four differently phrased questions in the three countries. Furthermore, knowledge on how to treat snakebites was not tested, but the participants were asked to reflect on it themselves. This should be taken into consideration when looking at the numbers, as it is possible that the participants under or overrated their knowledge.

Finally, the sampling strategy also has limitations. Sampled regions included snakebite-endemic and non-endemic areas. This strategy was chosen to obtain insight into the country's situation in general, and to ensure random sampling did not include only endemic or non-endemic areas. In each survey region, facilities were randomly sampled, and afterward stratified per sector and location. As a consequence, the facilities were not equally distributed across these strata: fewer private and PNFP facilities were surveyed, as well as fewer urban locations than rural locations. However, this might provide a better representation of the division of facilities across the sectors and the snakebite-endemic locations. Snakebites occur more often in rural areas, and the public sector is the main provider of health care in the three countries (2,49–51). In Zambia, the 10 surveyed PNFP facilities were excluded as this sample was too small to be representative.

CONCLUSION

In conclusion, this study shows that snakebites most often affect agricultural workers of any gender in the age category 21–30 years, and that enormous gaps in snakebite care exist

as HCWs lacked training and equipment to properly manage snakebites. To tackle this, an integrative approach including community education, HCW training, and improved access to snakebite treatment is vital. Regulations should also ensure that antivenoms available in health facilities meet quality control standards, and that snakebites are accommodated into routine reporting systems to assess progress on snakebite treatment and management at the subnational and national levels. Snakebite envenoming, as a neglected tropical disease, has long suffered from lack of attention. The burden of disease still does not correspond with resources allocated to research and health system strengthening for snakebites. To make up the necessary ground, a significant increase in resources is essential.

ACKNOWLEDGEMENTS

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CONTRIBUTION STATEMENT

GIO, JvO, BW and SvB designed the study. GIO collected and analysed the data, and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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3.3

SUPPLEMENTARY DATA

Supplementary File 1. Division of health facilities per survey region.

	Public	Private	PNFP
Urban	4	4	4
Rural	4	4	4

PNFP: Private not-for-profit.

Supplementary File 2. Commonly bitten body parts and observed complications in Kenya, according to HCWs.

	Overall *N* (%)
Commonly bitten body part[a]	
Feet	38 (33.9)
Legs	92 (82.1)
Arms	20 (17.9)
Hands and fingers	31 (27.7)
Head	1 (0.9)
Stomach	0 (0.0)
Back	0 (0.0)
Complications commonly observed after a snakebite[a]	
Swelling	33 (55.9)
Pain at site of bite	19 (32.2)
Cellulitis	14 (23.7)
Respiratory distress	12 (20.3)
Gangrene	11 (18.6)
Neurological complications	9 (15.3)
Numbness	8 (13.6)
Vomiting	5 (8.5)

[a]HCWs could indicate up to three categories so totals may sum to more than 100%.

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4

SEXUAL AND REPRODUCTIVE HEALTH COMMODITIES

"Communities and countries, and ultimately the world, are only as strong as the health of their women."

– Michelle Obama

4.1

ACCESS TO SEXUAL AND REPRODUCTIVE HEALTH COMMODITIES IN EAST AND SOUTHERN AFRICA: A CROSS-COUNTRY COMPARISON OF AVAILABILITY, AFFORDABILITY AND STOCK-OUTS IN KENYA, TANZANIA, UGANDA AND ZAMBIA

Gaby I Ooms, Denis Kibira, Tim Reed, Hendrika A van den Ham,
Aukje K Mantel-Teeuwisse, Gemma Buckland-Merrett

ABSTRACT

Background

Access to sexual and reproductive health services continues to be a public health concern in Kenya, Tanzania, Uganda and Zambia: use of modern contraceptives is low, and unmet family planning needs and maternal mortality remain high. This study is an assessment of the availability, affordability and stock-outs of essential sexual and reproductive health commodities (SRHC) in these countries to inform interventions to improve access.

Methods

The study consisted of an adaptation of the World Health Organization/Health Action International methodology, *Measuring Medicine Prices, Availability, Affordability and Price Components*. Price, availability and stock-out data was collected in July 2019 for over fifty lowest-priced SRHC from public, private and private not-for-profit health facilities in Kenya (n=221), Tanzania (n=373), Uganda (n=146) and Zambia (n=245). Affordability was calculated using the wage of a lowest-paid government worker. Accessibility was illustrated by combining the availability (≥ 80%) and affordability (less than 1 day's wage) measures.

Results

Overall availability of SRHC was low at less than 50% in all sectors, areas and countries, with highest mean availability found in Kenyan public facilities (46.6%). Stock-outs were common; the average number of stock-out days per month ranged from 3 days in Kenya's private and private not-for-profit sectors, to 12 days in Zambia's public sector. In the public sectors of Kenya, Uganda and Zambia, as well as in Zambia's private not-for-profit sector, all SRHC were free for the patient. In the other sectors unaffordability ranged from 2 to 9 SRHC being unaffordable, with magnesium sulphate being especially unaffordable in the countries. Accessibility was low across the countries, with Kenya's and Zambia's public sectors having six SRHC that met the accessibility threshold, while the private sector of Uganda had only one SRHC meeting the threshold.

Conclusion

Accessibility of SRHC remains a challenge. Low availability of SRHC in the public sector is compounded by regular stock-outs, forcing patients to seek care in other sectors where there are availability and affordability challenges. Health system strengthening is needed to ensure access, and these findings should be used by national governments to identify the gaps and shortcomings in their supply chains.

INTRODUCTION

Worldwide, more than 800 women a day die due to complications related to pregnancy and childbirth, and annually an estimated 5.3 million children do not reach the age of five, with half of these deaths occurring in sub-Saharan Africa (1,2). In addition to the threat of death, 210 million women a year experience serious pregnancy-related injuries and disabilities, which often lead to long-term morbidity (3). Research has estimated that the lives of four million women, newborns and children in sub-Saharan Africa could be saved if coverage of interventions such as emergency obstetric care, breastfeeding counselling, and treatment for infections such as diarrhoea and pneumonia increased to 90% of families (4). Contraceptive prevalence rates remain low in many developing countries among both men and women, with over 214 million women experiencing unmet family planning needs, and the limited demand and uptake of reproductive health services and education around reproductive health issues pose significant challenges (5–8). In addition, it is estimated that in 2020 there will be an annual shortfall of $233 million needed to pay for contraceptive supplies (6). In 2016 alone, there were also an estimated 376 million new cases of one of the four most common curable sexually transmitted infections (STIs) (chlamydia, gonorrhoea, syphilis and trichomoniasis), with syphilis responsible for more than 200,000 stillborn and newborn deaths (9). Access to essential commodities and services for sexual and reproductive health (SRH) can prevent a significant proportion of these deaths and disabilities. However, access remains a problem for almost 2 billion people (10).

4.1

Reflecting global trends, access to SRH services continues to be a public health concern in Kenya, Tanzania, Uganda and Zambia. Ranging from 224 to 510 maternal deaths per 100,000 live births, the maternal mortality in these countries remains high, especially when comparing it to the maternal mortality rate in developed countries (12 per 100,000 live births) (11,12). The use of modern contraceptives is low, especially in Uganda and Tanzania, where only 27.5 and 33.5% of married women, respectively, used modern contraceptive methods. In Kenya, Tanzania and Zambia, about 20% of married women aged 15–49 had unmet family planning needs, while 30% of married women in Uganda were experiencing this problem (7). In Zambia, 81.9% of unmarried, sexually active adolescent girls aged 15–19 were not using contraception (13). The other three countries also have high percentages of unmarried, sexually active adolescent girls not using contraception (59.3 to 68.8%) (14–16). Not surprisingly, overall unmet needs for contraceptives among this population was high; across the four countries it ranged from 38.6 to 66.9% (14, 17). Consequences of unmet family planning needs can be serious, especially amongst adolescents: it can lead to unwanted pregnancies, unsafe abortions, and increased risks for morbidity and mortality (18). Further, teenage pregnancies can lead to school dropout, which diminishes the chances of girls finding employment opportunities later in life, continuing the poverty cycle (18). Significant changes are thus needed to reach the Sustainable Development Goals' targets of a global maternal mortality ratio of less than 70 per 100,000 live births and universal access to sexual and reproductive healthcare services (19).

Despite the clear need for access to sexual and reproductive health commodities (SRHC) in Kenya, Tanzania, Uganda and Zambia, access has not been fully achieved and unavailability, unaffordability, regulatory provisions and supply chain issues persist (20). Previous research in these countries has focused on identifying the barriers to access on both the supply and demand side (21–26), but detailed research on availability and affordability of these medicines at the health system level is lacking. In Uganda research on availability of medicines for SRH has been conducted previously, showing that access remains suboptimal (27, 28). However, this research did not cover an extensive list of SRHC, nor included medical devices essential in offering quality SRH services. The research presented here is an assessment of the availability, affordability and stock-outs of over fifty essential SRHC, including medicines and medical devices, in Kenya, Tanzania, Uganda and Zambia to identify current accessibility of SRHC and to inform interventions to improve access.

METHODS

Study design

4.1

The study was designed as a cross-sectional survey. Data collection comprised a health facility survey in which the availability, price, and stock-outs of SRHC were measured.

Ethical approval was granted by the Amref Ethics and Scientific Review Committee in Kenya, the National Institute for Medical Research in Tanzania, Makerere University School of Health Sciences in Uganda, and the National Health Research Authority in Zambia. Letters of introduction to health facilities were provided by County Directors of Health in Kenya, and Ministries of Health in Tanzania, Uganda and Zambia.

Study settings and participants

This survey was conducted in ten counties in Kenya, twelve counties in Tanzania, six regions in Uganda, and ten provinces in Zambia. The provinces selected included each country's main urban region and five or more other regions, using a random sampling strategy. Each survey area within a province covered a population of 100,000 to 250,000. Health facilities were identified for inclusion, using a stratification method, as public-, private-, and private not-for-profit (PNFP) facilities. Within each stratum, four health facilities were randomly sampled from rural and urban areas. In this study urban areas were defined per country according to the definition held by the corresponding National Bureaus of Statistics: an urban area was defined in Kenya and Uganda as an area with a population of 2,000 or higher, in Zambia with a population of 5,000 or higher, and in Tanzania with a population of 10,000 or higher (29). In each case, one of the selected urban areas included the main public provincial health facility. The inclusion criteria for the other health facilities were that facilities had to be within 3 h travel from the main public provincial health facility, and all selected health facilities had to provide SRH services.

Data collection tool

A data collection tool, adapted from the standardised World health Organization (WHO)/Health Action International (HAI) Medicine Prices Monitoring Tool and validated in many countries, was used for collecting data (30–34). The 'basket' of commodities assessed was developed by combining the WHO's Essential Medicines for Reproductive Health, the Interagency List of Essential Medicines for Reproductive Health, the Interagency List of Medical Devices for Essential Interventions for Reproductive, Maternal, Newborn and Child Health, and the United Nations Commission on Life Saving Commodities for Women and Children: Commissioner's Report (35–38). In combination with in-country expertise via a specialist advisory group and after piloting the methodology, after which slight alterations were made to the commodity basket, the commodities list presented was believed to be a selection of the most essential SRHC within the study region. Commodity strengths and dosage forms were based on the national essential medicine lists (NEMLs) (39–43). Commodities cover family planning, maternal and child health, and STI management, and when listed with multiple dosage forms or strengths, all the formulations were included in the survey (see Supplementary File 1 for a complete overview of surveyed commodities). Previous cycles of the research took place in 2017 and 2018 in Kenya, Tanzania, Uganda and Zambia.

4.1

Data collection

Data collection took place in July 2019 using a mobile data collection application. In each country, local data collectors were trained by the authors (GIO and DK) on how to use the data collection tool during a two-day workshop organised by Health Action International, which included a field test. During the workshop the data collectors were provided with one tablet each and taught how to use the mobile application through a step-by-step walkthrough. During the field test they practiced the use of the mobile application.

Data collectors worked in pairs, supervised in each country by a survey manager. Data on availability, patient prices, brand information and stock-out days was only collected when commodities were visibly present. Product name, name of manufacturer, actual pack size and pack price were recorded for the lowest price for each commodity available. Stock-outs were only recorded if a stock card was available and seen. Stock-outs were noted for the 6 months prior to the day of data collection.

Data analysis

After completion of data collection, data was uploaded to the server and downloaded into an excel spreadsheet. Data entries were double-checked for accuracy by the survey managers and researchers. If data was incompletely or incorrectly entered, such as if a wrong product or pack size was noted, or a wrong unit price was calculated, the data was rectified after verification with the data collectors or an 'X' was noted to denote only the availability of the commodity when pricing information could not be verified. Thereafter, analysis was completed in a previously developed Excel analysis tool using descriptive statistics.

The availability of a commodity was calculated as the mean of the sampled facilities where the medicine was found at the time of the survey, expressed as a percentage. Mean availability of SRHC per sector and country was calculated in a two-step manner: firstly, the mean availability per commodity across the sampled facilities was calculated, after which the mean of these mean availabilities was calculated. For each commodity, availability was only measured when the level of care at which a commodity should be available corresponded with the surveyed facility. For example, calcium gluconate should be available at hospital levels and up in Kenya, Tanzania and Zambia, and from health centre III level in Uganda. In the PNFP sector, availability of family planning commodities was only calculated if family planning services were provided by the facility. Availability was calculated per commodity, as well as in groups for similar use (the birth control pill, injectable contraceptive and implant) or for different formulations of the same medicine (i.e. for magnesium sulphate, amoxicillin, clotrimazole, ferrous salt, folic acid, zinc and ORS sachets). When availability was calculated for a grouping of commodities, it was an aggregate of the availability and calculated as the mean percentage of sampled facilities where either of the formulations or commodities with similar medicinal use were available. Availability of 80% or higher was considered acceptable as per WHO guidelines (44). Two-sample F-tests for variance were computed to test for normal distribution and independence, after which two-sample t-tests were calculated to test whether significant differences existed between means, using a significance cut-off value of 0.05.

Stock-outs were calculated longitudinally as the mean percentage of facilities that reported a stock-out of a commodity any time in the 6 months prior to the day of data collection. Stock-out days were also calculated longitudinally over a six-month period and were calculated as the average number of days a commodity was stocked out per month. Stock information was surveyed only for medicines, not for medical devices.

Affordability was calculated using the median price of a commodity, and the number of days a lowest-paid government worker (LPGW) needs to work in order to pay for a standard treatment regimen for a commodity. The daily wage of an LPGW was 449.40 Kenyan Shillings (Kenya), 3077.15 Tanzanian Shillings (Tanzania), 6169.65 Ugandan Shillings (Uganda), and 33.12 Kwacha (Zambia) (45–48). According to the WHO/HAI methodology, treatment was considered unaffordable if it cost more than a day's wage for an LPGW (30). Affordability was calculated only for medicines, not for medical devices.

Accessibility was illustrated combining the availability and affordability measures. This resulted in a categorical variable, in which accessibility was achieved when a commodity had an 80% or higher availability, and when a treatment regimen cost less than a day's wage of an LPGW.

RESULTS

Across the public, private and PNFP sectors, 221, 373, 146 and 245 facilities were surveyed in Kenya, Tanzania, Uganda and Zambia, respectively. Stock information was collected from 221 facilities in Kenya, 212 facilities in Tanzania, 105 facilities in Uganda, and 182 facilities in Zambia. An overview of the distribution of the facilities is provided in **Table 1**.
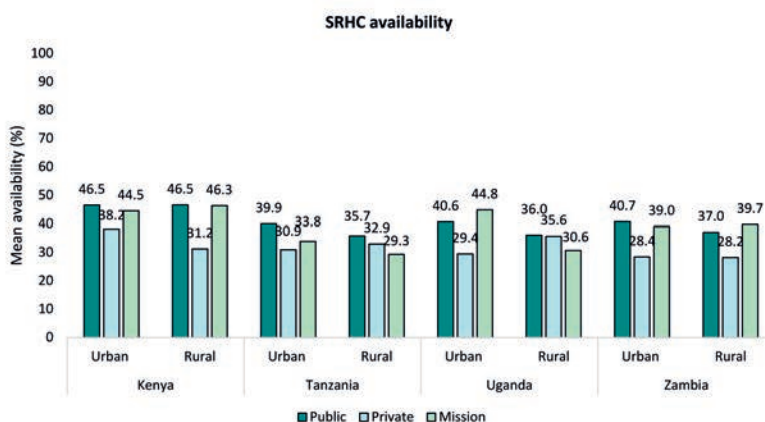
Availability of SRHC

Across countries

The research surveyed 55 commodities in Kenya, 56 in Tanzania and Zambia, and 59 in Uganda. Aggregation led to 43 surveyed SRHC in all countries. Mean availability of SHRC in general on the day of data collection was lower than 50% in all sectors. Highest mean availability was found in Kenya for all sectors, with the highest overall mean availability found in Kenya's public sector (46.6%). Mean availability in Tanzania's (37.9%), Uganda's (37.9%) and Zambia's (38.6%) public sectors was comparable to each other. Zambia's private sector had the lowest mean availability across the countries and sectors (28.3%). Comparing the countries to each other showed that mean availability of SHRC in the PNFP sector was significantly higher in Kenya (45.7%, n=55) than in Tanzania (33.5%, n=56) (p=0.01). No significant differences in mean availability were found across the countries for any other sectors.

4.1

Country level

In none of the countries did the mean availability of SHRC differ significantly between sectors. In Uganda mean availability within the PNFP sector differed significantly when comparing urban and rural facilities: mean availability of SRHC in urban PNFP facilities (44.8%, n=59) was significantly higher than in rural PNFP facilities (30.6%, n=59) (p=0.009) (**Figure 1**). There were no significant differences in mean availability when comparing urban and rural areas within a sector in the other countries.

Figure 1. Mean availability of SRHC across sectors and areas, by country.

Table 1. Distribution of surveyed facilities with availability, price and stock data, by country, sector and area.

	Public	Private	PNFP	Total
Kenya				
Availability and price data				
Urban	33	63	24	120
Rural	46	25	30	101
Total	79	88	54	221
Stock data				
Urban	33	63	24	120
Rural	45	25	30	100
Total	78	88	54	220
Tanzania				
Availability and price data				
Urban	131	55	35	221
Rural	132	5	15	152
Total	263	60	50	373
Stock data				
Urban	100	25	21	146
Rural	56	1	9	66
Total	156	26	30	212
Uganda				
Availability and price data				
Urban	22	33	23	78
Rural	33	15	20	68
Total	55	48	43	146
Stock data				
Urban	21	16	21	58
Rural	29	0	18	47
Total	50	16	39	105
Zambia				
Availability and price data				
Urban	59	58	4	121
Rural	77	9	38	124
Total	136	67	42	245
Stock data				
Urban	48	30	4	82
Rural	57	5	38	100
Total	105	35	42	182

PNFP: Private not-for-profit.

In all countries, the public sector had the most commodities with an 80% availability or more. Kenya's public sector had 10 SRHC with an 80% or higher availability, followed by Zambia (8 SRHC), and Uganda and Tanzania (both 6 SRHC) (see **Table 2**). In all countries, the private

sector had the most commodities available at 50% or less of facilities: 25 of 43 SRHC in Kenya, 27 of 43 SRHC in Uganda, 30 of 43 SRHC in Tanzania, and 33 of 43 SRHC in Zambia.

Family planning

In the countries, male condoms were most likely to be available in more than 80% of the facilities across the different sectors (see **Table 2**). Only in Kenya's and Tanzania's PNFP sector, and Tanzania's and Uganda's private sector was the availability below 80%. Female condoms were available at 60% or less of the facilities across the countries. Kenya's public sector had the most family planning commodities available at more than 80% of facilities, this included the combination measures of oral contraceptive, injectable contraceptive and the implant. Levonorgestrel 750 mcg, an emergency contraceptive, had a low availability across the countries, with Tanzania only providing it in 8% of public facilities, and in none of the private or PNFP facilities.

Maternal health

Maternal health commodities were on average less available than family planning commodities. Oxytocin only had an 80% or higher availability in the public sectors of Kenya, Uganda and Zambia. Misoprostol had a low availability across the countries; only in Uganda's public sector was availability above 80%. Zambia had lowest availability across the sectors, ranging from 11 to 27%. Methyldopa had a relative high availability in all sectors in Kenya and Tanzania, while in Uganda and Zambia it was much lower. Magnesium sulphate had a low availability across the countries, especially in Zambia and the countries' private sector.

Antibiotics and antifungals

In all countries, metronidazole had the highest availability in facilities. In Zambia, all sectors had an 80% or higher availability, while an 80% or higher availability was also found for the private and PNFP sectors in the other countries. Availability of clotrimazole, either the pessary or cream formulation, was considerably low in Tanzania and Zambia (less than 50% across the sectors), and only the PNFP sector in Kenya had either formulation available at more than 80% of facilities. Similarly, amoxicillin (125 mg or 250 mg), had a low availability in the countries; only in Zambia's private and PNFP sector did the availability go above 80%. The benzylpenicillins had a suboptimal availability in most of the countries' sectors.

Newborn and child health

Kenya had the best availability of newborn and child health commodities. Zinc had an 80% or higher availability across the sectors, while dexamethasone and ORS sachets also had a high availability. Overall, ORS sachets had the highest availability across the countries, with the exception of Zambia where availability was below 50% in the public and PNFP sectors. Chlorhexidine 4% had a low availability across all countries, with highest availability in Kenya's public sector (38%).

4.1

Table 2. Mean availability of individual SRHC across sectors, by country.

4.1

Commodities	Mean Availability (%)											
	Kenya			Tanzania			Uganda			Zambia		
	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP
Family Planning												
Oral contraceptive[a]	91	80	72	69	47	40	75	36	43	91	67	83
Levonorgestrel 750 mcg	47	71	32	8	0	0	35	30	24	41	61	41
Injectable contraceptive[b]	92	32	66	82	59	53	62	51	67	72	30	79
Male condoms	84	85	79	82	52	47	93	72	81	89	89	86
Female condoms	56	13	39	33	22	27	18	17	33	60	5	48
Intrauterine contraceptive device[n]	82	29	48	62	65	53	72	39	56	51	2	41
Implant[c,n]	87	30	79	84	78	73	89	64	67	71	0	62
Diaphragm	0	0	4	0	0	0	0	0	0	0	0	0
Maternal Health												
Oxytocin injection[n,p]	87	41	67	75	42	56	80	50	64	94	50	78
Misoprostol	33	34	35	49	35	22	82	48	56	11	27	26
Methyldopa[k,m,n]	77	77	83	76	73	73	24	14	36	12	51	17
Magnesium sulphate[d,n,p]	59	10	44	70	18	48	69	10	42	13	0	12
Calcium gluconate[k,m,n,q]	71	29	71	44	0	44	43	8	27	67	0	0
Ferrous salt	57	50	43	5	3	4	4	27	37	75	55	71
Folic acid	55	77	79	63	50	48	64	71	63	80	82	79
Ferrous Salt: Folic Acid Tablet[g]	62	8	48	20	5	14	27	10	33	1	7	2
Antibiotics and Antifungals												
Metronidazole	68	80	87	61	92	86	75	94	84	88	87	93
Clotrimazole[e]	70	74	83	39	47	38	67	63	67	24	45	17
Gentamicin[n]	58	39	61	43	45	40	30	67	67	48	33	50
Procaine benzylpenicillin	NS	NS	NS	26	33	36	33	48	44	2	34	7

Table 2. (continued)

Commodities	Kenya			Tanzania			Uganda			Zambia		
	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP
Benzathine benzylpenicillin[n]	39	16	30	80	60	70	70	72	67	60	69	74
Benzylpenicillin	46	34	50	NS	NS	NS	NS	NS	NS	82	34	86
Amoxicillin[f]	62	38	43	74	30	42	40	40	49	77	88	81
Newborn- and Child Health												
Dexamethasone[k,o,q]	81	82	63	10	27	32	76	50	46	67	50	0
Zinc ORS co-pack	68	28	41	29	3	4	44	6	26	13	5	17
Zinc[h]	86	82	93	36	75	74	44	70	67	53	46	60
ORS sachets[i]	77	73	83	75	72	82	53	70	63	32	57	48
Chlorhexidine 4%	38	9	30	7	3	6	26	6	19	6	3	10
SRH medical devices												
Vasectomy kit[k,l,n]	19	6	8	3	5	0	17	8	15	7	4	14
Tubal ligation kit[k,l,n]	23	35	13	13	9	5	17	11	24	10	1	10
Manual vacuum aspiration kit[j,n]	66	59	56	38	38	26	48	36	48	54	38	64
Speculum[j,o]	86	78	84	84	67	66	88	75	92	84	38	94
Cervical dilator[j,n]	34	41	49	12	17	14	46	31	58	28	25	25
Incubator	68	47	79	11	13	16	16	4	14	27	13	53
Monitor[k,n]	39	53	63	11	15	16	22	11	33	14	13	17
Ultrasound scan[k,o]	45	53	63	13	45	36	52	63	92	19	50	22
Ventilator[k,n]	32	41	42	5	5	6	9	8	3	9	25	17
Foetal scope[j,n]	82	78	88	97	80	92	94	92	91	86	63	78
Resuscitator (adult size)[j,n]	45	33	49	31	22	18	33	44	45	28	25	39
Resuscitator (infant size)[j,n]	63	44	53	63	38	46	65	56	70	50	38	72
Bag and mask (size 0)[j,o]	58	52	77	59	37	46	68	25	62	52	38	75

Mean Availability (%)

4.1

Table 2. (continued)

Commodities	Mean Availability (%)											
	Kenya			Tanzania			Uganda			Zambia		
	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP
Suction device[j]	68	67	79	71	52	62	65	54	81	75	50	81
Training mannequin (infant)[j,n]	20	15	23	36	22	32	26	6	27	26	0	33

NS: not surveyed.

[a] 'Oral contraceptive' combines availability of ethinylestradiol + levonorgestrel (multiple formulations) and/or ethinylestradiol + levonorgestrel (multiple formulations) and/or ethinylestradiol + desorgestrel (multiple formulations) and/or levonorgestrel 30mcg at the facility.

[b] 'Injectable contraceptive' combines availability of medroxyprogesterone acetate (150mg in 1ml vial or 104mg in 1 ml vial) and/or norethisterone enanthate 200mg/ml in 1ml vial and/or estradiol cypionate + medroxyprogesterone acetate (5mg + 25mg) at the facility.

[c] 'Implant' combines availability of levonorgestrel implant and/or etonogestrel implant at the facility

[d] 'Magnesium sulphate' combines availability of magnesium sulphate 500mg in 1ml and/or magnesium sulphate 500mg in 2ml and/or magnesium sulphate 500mg in 10ml at the facility.

[e] 'Clotrimazole' combines availability of clotrimazole cream (1%, 15g tube) and/or clotrimazole pessary (100mg, 200mg or 500mg) at the facility.

[f] 'Amoxicillin' combines availability of amoxicillin 125mg and/or amoxicillin 250mg at the facility.

[g] 'Ferrous salt: folic acid tablets' combines availability of the ferrous salt: folic acid (60mg + 400mcg) and/or ferrous salt: folic acid (150mg + 500mcg) and/or ferrous salt: folic acid (200mg + 500mcg) at the facility.

[h] 'Zinc' combines availability of zinc 10mg in 5ml syrup and/or zinc 20mg and/or zinc ORS co-pack at the facility.

[i] 'ORS sachets' combines availability of ORS sachets of 200ml and/or 500ml and/or 1L and/or zinc ORS co-pack at the facility.

[j] Available from health centre and up in Kenya.

[k] Available from primary/county hospital and up in Kenya.

[l] Available from health centre and up in Tanzania.

[m] Available from council hospital and up in Tanzania.

[n] Available from health centre III and up in Uganda.

[o] Available from health centre IV and up in Uganda.

[p] Available from general hospital and up in Zambia.

[q] Available from central hospital and up in Zambia.

4.1

SRH medical devices

Availability of SRH medical devices was generally low, with Kenya doing slightly better than the other countries. In all countries, availability of the vasectomy kit, tubal ligation kit, ventilator, resuscitator and infant-size training mannequin was below 50%. In Zambia's private sector, all commodities, with the exception of the foetal scope, were available at less than 50% of facilities. Availability of the foetal scope was also high in the other countries.

Stock-outs

Stock-out data was collected for 41 SRHC in Zambia, 42 SRHC in Kenya and Tanzania, and 45 SRHC in Uganda. Zambia had the highest percentage of SRHC stock-outs across the sectors. In the public sector, an average of 46.9% of facilities reported stock-outs, compared with 35.6% in Uganda, 25.1% in Tanzania and 23.2% in Kenya (see **Table 3**). In the private sector stock-outs occurred less often than in the public sector in Kenya and Uganda, while in Tanzania stock-outs occurred more often. Zambia's stock-outs in the private sector were similar to the public sector. Stock-outs in the PNFP sector were much higher in Zambia than in the other three countries.

4.1

The average duration of stock-outs was also highest in Zambia, where stock-outs lasted 9 to 12 days per month across sectors. Stock-out duration in the public and private sectors of Kenya, Tanzania and Uganda were similar, ranging from 6 to 8 days per month in the public sector, and 3 to 5 days in the private sector. Tanzania's PNFP sector stock-outs were comparable to Zambia's, while in Uganda and Kenya they were lower.

Affordability

Pricing information was missing for 0.6% (17/2946) of SRHC in Uganda, 1.1% (48/4469) of SRHC in Zambia, 2.5% (110/4316) of SRHC in Kenya and 6.5% (473/7289) of SRHC in Tanzania. In Kenya, Uganda and Zambia's public sector all commodities were affordable to the patient because commodities were provided for free (see **Table 4**). Zambia's PNFP sector also provided all SRHC for free to the patient. In Tanzania's public sector, two SRHC cost more than a day's wage for an LPGW: 2.27 days for a treatment of procaine benzylpenicillin, and 1.30 days for a treatment of gentamicin.

Uganda's private sector had the most commodities that cost more than a day's wage (n=9), with a magnesium sulphate 500 mg/10 ml treatment costing more than 16 days' wage. Two long-acting reversible contraceptives, levonorgestrel 750mcg and the intrauterine contraceptive device, also cost more than a day's wage. Kenya and Tanzania had 4 and 6 commodities, respectively, that cost more than a day's wage in the private sector, with a magnesium sulphate treatment also costing the most days. Zambia's private sector had seven commodities that cost more than a day's wage; all were maternal health commodities or antibiotics. Affordability patterns in the PNFP sector, although slightly better, were

Table 3. Percentage of facilities reporting stock-outs in the last six months, and number of stock-out days per month.

	Stock-outs	
	Facilities reporting stock-outs (%)	Average number of stock-out days/month
Kenya		
Public	23.2	6
Private	17.4	3
PNFP	12.0	3
Tanzania		
Public	25.1	8
Private	31.4	5
PNFP	14.5	9
Uganda		
Public	35.6	7
Private	16.6	4
PNFP	15.9	6
Zambia		
Public	46.9	12
Private	45.7	9
PNFP	41.7	10

PNFP: Private not-for-profit

4.1

comparative to their private sector counterparts in Kenya, Tanzania and Uganda, with many of the commodities that cost more than a day's wage in the PNFP sector also costing more than a day's wage in the private sector.

Accessibility

Accessibility was low across the countries. In the public sector, where medicines are often provided free of charge, Kenya and Zambia had the highest accessibility, with six commodities considered accessible, followed by Tanzania (four commodities) and Uganda (two commodities). Accessibility was lower in the private sector. For instance, in Tanzania only two SRHC were accessible: ORS sachets 1 L and metronidazole (**Figure 2**). Six commodities were both unaffordable and available in less than 80% of facilities: ferrous salt (1.22, 3%), gentamicin (4.06, 45%), magnesium sulphate 500 mg/10 ml (5.85, 11.7%), procaine benzylpenicillin (7.31, 33%), methyldopa (7.31, 73%) and magnesium sulphate 500 mg/2 ml (11.70, 6.7%). However, the problem for most SRHC seems to be availability, and not affordability, as many commodities are not available in 80% or more of facilities but do cost less than a day's wage.

In Zambia's private sector three SRHC met the accessibility threshold (amoxicillin 125 mg, male condoms and metronidazole), in Kenya two did (dexamethasone and male condoms),

**Table 4.** Affordability of SRHC for an LPGW, per country and sector.

Commodities	Treatment regimens	Affordability (Days of Wages)											
		Kenya			Tanzania			Uganda			Zambia		
		Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP
Ethinylestradiol + levonorgestrel	1 strip	0	0.13	0	0	0	0	0	0.16	0	0	0.30	0
Ethinylestradiol + norethisterone	1 strip	0	0.09	NA	0	0.19	NA	0	NA	NA	0	NA	NA
Ethinylestradiol + desorgestrel	1 strip	NA	NA	NA	0	0	NA	NA	NA	NA	NA	NA	NA
Levonorgestrel 30mcg	1 tablet	0	0.09	0.04	0	0	0	0	NA	NA	0	0.30	0
Levonorgestrel 750mcg	1 tablet	0	0.22	0.07	0	NA	NA	0	1.13	0.32	0	0.80	0
Medroxyprogesterone acetate 150ml	1 vial	0	0.22	0.09	0	0	0	0	0.81	0	0	0.60	0
Medroxyprogesterone acetate 104ml	1 vial	0	0.22	0.06	NA	NA	NA	0	0.32	0.08	NA	NA	NA
Norethisterone enanthate	1 vial	NA	NA	NA	NA	NA	NA	0	NA	NA	0	0.63	0
Male condoms	1 pack	0	0.11	0	0	0	0	0	0.11	0	0	0.15	0
Female condoms	1 pack	0	0	0	0	0	0	0	0	0	0	0.27	0
Intrauterine contraceptive device	1 device	0	1.00	0	0	0	0	0	2.43	0	0	0.00	0
Implants: levonorgestrel	1 device	0	0.67	0	0	0	0	0	0.81	0	0	NA	0
Implants: etonogestrel	1 device	0	0.89	0.33	0	0	0	0	1.62	0	0	NA	0
Diaphragm	1 device	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA
Oxytocin injection	1 vial	0	0.20	0.22	0	0.32	0	0	0.49	0.24	0	0.42	0
Misoprostol	1 vial	0	0.18	0.16	0	0.65	0	0	0.49	0.16	0	1.19	0
Methyldopa	90 tablets	0	1.00	1.00	0	7.31	5.85	0	1.46	3.65	0	3.80	0
Magnesium sulphate 500mg/ 2ml	18 vials	0	8.81	0.70	NA	11.70	0	NA	NA	NA	0	NA	0
Magnesium sulphate 500mg/ 10ml	18 vials	0	17.76	5.41	0	5.85	0	0	16.12	14.59	0	NA	0
Calcium gluconate	1 ampoule	NA	0.29	0.22	0	NA	0	0	2.92	14.59	0	NA	0
Ferrous salt	30 tablets	0	0.07	0.07	NA	1.22	NA	NA	0.02	0.01	0	0.45	0
Folic acid	30 tablets	0	0.13	0.07	0	0.97	0.02	0	0.49	0.24	0	1.59	0
Ferrous Salt: Folic Acid 60/400	30 tablets	0	0.67	0.07	0	0.97	0	0	0.49	0.16	0	0	0
Ferrous Salt: Folic Acid 150/500	30 tablets	0	NA	0.07	0	0.49	0	0	0.49	0.26	NA	2.26	NA

4.1

Table 4. (continued)

4.1

Commodities	Treatment regimens	Affordability (Days of Wages)											
		Kenya			Tanzania			Uganda			Zambia		
		Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP	Public	Private	PNFP
Metronidazole	30 tablets	0	0.07	0.13	0	0.97	0.88	0	0.49	0.49	0	0.45	0
Clotrimazole pessary	6 tablets	0	0.28	0.11	0.06	0.89	0.65	0	2.92	2.92	0	0.79	0
Clotrimazole cream	1 tube	0	0.13	0.1`	0.49	0.97	0.81	0	0.49	0.41	0	0.45	0
Gentamicin	10 amp	0	0.45	0.67	1.30	4.06	4.87	0	3.24	2.43	0	1.51	0
Procaine benzylpenicillin	10 vials	NA	NA	NA	2.27	7.31	6.50	0	6.48	3.24	0	3.62	NA
Benzyl penicillin	10 vials	0	1.11	1.11	NA	NA	NA	NA	NA	NA	0	3.62	0
Benzathine benzylpenicillin	1 vial	0	0.11	0.17	0.15	0.97	0.65	0	0.49	0.49	0	0.42	0
Amoxicillin 125mg	15 tablets	0	1.67	0.17	0.10	0.44	0.24	0	0.24	0.24	0	0.45	0
Amoxicillin 250mg	15 tablets	0	0.10	0.03	0	0.49	0.26	0	0.24	0.49	0	0.23	0
Dexamethasone	1 vial	0	0.11	0.11	0	0.97	0.49	0	0.41	0.32	0	0.60	0
Zinc syrup	1 bottle	0	0.33	0.22	NA	0.97	0.89	NA	0.41	NA	NA	0.68	NA
Zinc tablet	10 tablets	0	0.22	0.11	0	0.41	0.32	0	0.32	0.16	0	0.60	0
Zinc ORS co-pack	1 kit	0	0.22	0.13	0	0.32	0.02	0	0.32	0.24	0	0.06	0
ORS sachets 200ml	1 sachet	0	0.03	0.	NA	0.16	NA	NA	NA	NA	0	0.27	NA
ORS sachets 500ml	1 sachet	0	0.02	0.02	0	NA	NA	NA	NA	0.08	NA	NA	NA
ORS sachets 1L	1 sachet	0	NA	NA	0	0.16	0.16	0	0.08	0.08	0	0.09	0

PNFP: Private not-for-profit.
ORS: Oral rehydration salts.
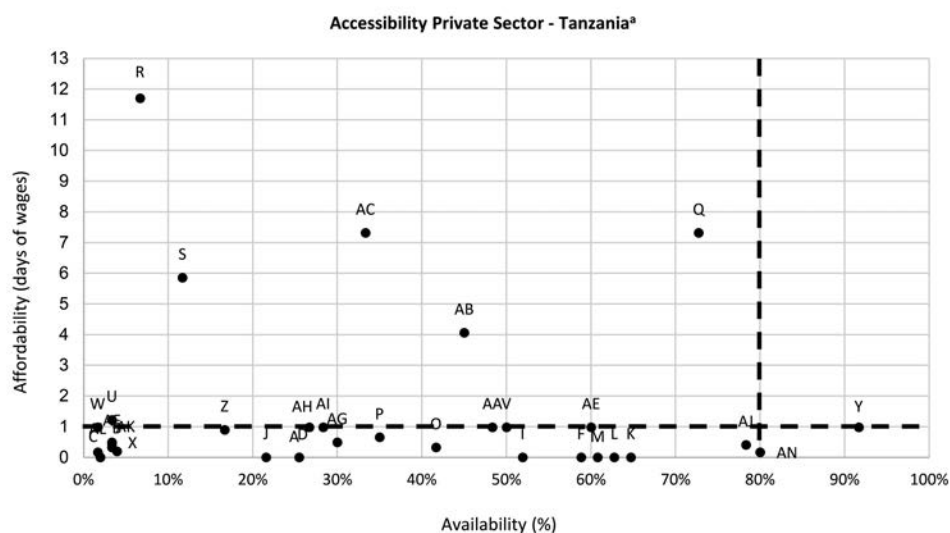
Figure 2. Accessibility of SRHC in Tanzania's private sector. [a]A: Ethinylestradiol + levonorgestrel; B: Ethinylestradiol + norethisterone; C: Ethinylestradiol + desorgestrel; D: Levonorgestrel 30mcg; E: Levonorgestrel 750mcg; F: Medroxyprogesterone acetate 150ml; G: Medroxyprogesterone acetate 104ml; H: Norethisterone enanthate; I: Male condoms; J: Female condoms; K: Intrauterine contraceptive device; L: Implants: levonorgestrel; M: Implants: etonogestrel; N: Diaphragm; O: Oxytocin injection; P: Misoprostol; Q: Methyldopa; R: Magnesium sulphate 500mg/ 2ml; S: Magnesium sulphate 500mg/ 10ml; T: Calcium gluconate; U: Ferrous salt; V: Folic acid; W: Ferrous Salt: Folic Acid 60/400; X: Ferrous Salt: Folic Acid 150/500; Y: Metronidazole; Z: Clotrimazole pessary; AA: Clotrimazole cream; AB: Gentamicin; AC: Procaine benzylpenicillin; AD: Benzyl penicillin; AE: Benzathine benzylpenicillin; AF: Amoxicillin 125mg; AG: Amoxicillin 250mg; AH: Dexamethasone; AI: Zinc syrup; AJ: Zinc tablet; AK: Zinc ORS co-pack; AL: ORS sachets 200ml; AM: ORS sachets 500ml; AN: ORS sachets 1L.

while in Uganda only one commodity (metronidazole) met the threshold. In Uganda and Zambia, six SRHC were also both unaffordable (more than a day's wage) and had a low availability (less than 80%). In Kenya this was the case for four commodities. The PNFP sector had similar accessibility patterns as the private sector in the countries, with two or three commodities considered accessible across the countries' PNFP sectors. Please refer to Supplementary File 2 for detailed information per country and sector.

DISCUSSION

Findings and implications

This study researched the availability, affordability, stock-outs and accessibility of more than fifty sexual and reproductive health commodities considered essential by the WHO, in four Eastern and Southern African countries. The research showed that overall availability of these commodities remains low at less than 50% in all sectors, areas and countries, with highest mean availability found in Kenyan public facilities (46.6%). Stock-outs were a common occurrence across the countries; average number of stock-out days per month ranged from

3 days in Kenya's private and PNFP sectors, to 12 days in Zambia's public sector. In the public sectors of Kenya, Uganda and Zambia, as well as in Zambia's PNFP sector, all SRHC were free for the patient. In the remaining sectors magnesium sulphate was the least affordable SRHC. Accessibility was low across the countries, with Kenya's and Zambia's public sectors having six SRHC that met the accessibility threshold, while the private sector of Uganda had only one SRHC meeting the threshold.

Similar trends highlighting in which aspects access to SRHC is lacking and where there is room for improvement were observed in the four countries. Availability of levonorgestrel 750mcg, the emergency contraceptive, was for example low across the countries, and this finding is reflected in the trends of use (49–52). Comparable to other studies, magnesium sulphate, critical in managing pre-eclampsia and eclampsia, also had a low availability in all countries, with an especially low availability in Zambia (28,53,54). Medical devices also had a suboptimal availability: tubal ligation and vasectomy kits had a very low availability across the countries, while availability of ultrasound scans was shown to be variable, with a higher availability in Kenya's and Uganda's public sector than in Tanzania and Zambia. An important note to make on the ultrasound scan is that according to the NEMLs, in Kenya it is available starting at county hospitals and in Uganda starting at Health Centres IV, while in Tanzania and Zambia it ought to be available at lower level facilities as well (40–43).

Low availability of many of the SRHC is exacerbated in these four countries by regular stock-outs, which often last for a significant part of the month. Further, even though affordability does not seem to aggravate access issues in the public sectors, it does constitute a problem in the private and PNFP sectors, where people turn to if SRHC are unavailable in the public sector (55,56). In these sectors, affordability might pose an even bigger issue than illustrated in this research due to the fact that a large proportion of the population does not earn the wage of an LPGW. For instance, in Kenya an LPGW earns the equivalent of about 4.50 USD, while in 2016 36.1% of the population was living below the poverty line of 1.90 USD (47,57).

Other health system challenges beyond the price and availability of the commodities at the health facility, which were not measured in this research, also influence accessibility. These challenges include policy and regulatory issues, infrastructural issues, lack of knowledge amongst the population and healthcare workers, cultural beliefs, and lack of skilled healthcare workers (25,58–67). The physical availability of an ultrasound scan, for example, does not mean it is routinely used or functional; lack of healthcare workers trained in its use, lack of electricity or high user costs are also barriers (61). Use and acceptability of male and female sterilization is also dependent on lack of knowledge and negative attitudes of clients and healthcare workers, religious beliefs, fear of surgery and side effects, lack of equipment, long travel distances, and long waiting times (62–66,68).

Barriers to access are also created by policies and regulations. When a commodity is expected to be provided only at higher levels, as is the case for ultrasound scans, it increases the distance patients have to travel and reduces access (60,66,68). Related, a slightly higher use of the emergency contraceptive in Kenya (1.7%) than in the other countries (0.2–0.5%), might be explained by the fact that only in Kenya is this contraceptive available without a prescription (49–52). Another example is that major barriers to the availability of magnesium sulphate previously identified in Zambia included lack of policy implementation, lack of procurement by the Ministry of Health and stock-outs at the central distributor (59). Efforts from governments thus ought to focus on improving availability, affordability, geographical accessibility and quality of offered SRH services on the one hand, and SRH client and community education on the other hand.

Key to improving access to SRHC is strengthening the health system, with a specific focus on the supply chain. Stock-outs are a serious issue across the countries, and governments ought to ensure that stock management systems are in place in health facilities; this research showed that especially in Tanzania and Zambia, there are still a number of facilities who do not have stock cards or an electronic stock management system in place. Further, better quantification of medicines is needed, as stock-outs are partly caused by the use of estimations for the needed medicines, and not on previous consumption data, and anticipated burden and need (55,69). Improved stock management at the central level is also critical, as poor stock management at this level results in commodities not delivered for extended periods, or commodities delivered that have not been ordered (26,69). In line with this, the government needs to ensure timely payment of commodity suppliers, as irregular or delayed payments can lead to a delayed or diminished supply until payment is received (55,70).

A tool that can be used by governments to improve availability is Universal Health Care (UHC) packages. At the moment, UHC is a priority on the countries' development agenda, and governments are adopting and implementing UHC and UHC packages (71–74). A simple way to increase availability of essential SRHC could be to include the SRHC in these packages.

To tackle the negative attitudes and lack of knowledge on use of family planning services among the community, and to improve healthcare workers' knowledge on SRHC and their professionalism, community sensitisation programmes and healthcare workers refresher trainings should be promoted and implemented. A review has shown that programmes using a combination of healthcare worker training, opening youth friendly health corners in health facilities, and sensitisation in communities and schools and through the media are most effective in improving knowledge of and demand for SRHC (75).

4.1

Strengths and limitations

The major strength of this study is the use of a standardised and validated methodology which allows for the measurement of medicine prices, availability and affordability (30,31). This research also used a combined measure of availability and affordability to illustrate accessibility, as first introduced by Ewen et al. (76). The added value of this combined measure is that it easily illustrates in what respects the WHO's target for availability and affordability of essential medicines is falling short (44). However, the used methodology also has some limitations, which have been previously identified (77). One of the limitations of the methodology is collection of availability data at only one point in time. This research included the collection of commodity stock-out information with the aim to provide a more accurate picture of the availability situation across time. However, stock data was collected only for the previous six months, so some seasonal or financial year differences might not have been captured.

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The methodology further calculates affordability using the wage of an LPGW to allow for easy comparisons of data across countries (30). However, in many developing countries, the wage of an LPGW is higher than what a large proportion of the population earns. It is therefore likely that the affordability projections here are an overestimation of the actual affordability. Further, in this study 'accessibility' should be construed in the basic sense of the word as it is explained here, and it should be noted that socioeconomic factors as potential determinants for low access were not taken into account as data on this went beyond the scope of the research. When considering the recommendations, this should be kept in mind.

Another limitation of the existing methodology is that it only collects data for the outcome measures for one dosage form or strength, while a commodity might be available in other dosage forms. This research tried to mitigate this by aligning the surveyed commodities' strengths and dosage forms to those on the countries' corresponding NEMLs. When a commodity was listed with multiple dosage forms or strengths, they were all included. Further, in the PNFP sector, availability of family planning commodities is likely to be an overestimation of the actual situation in the countries. In this sector, only facilities offering family planning services were included in the analysis for contraceptives availability. Lastly, in this research, the oral contraceptive is a combined measure of multiple formulations and strengths. Availability seems high, but this is the availability of any oral contraceptive, while for women it might make a difference which oral contraceptive is available. Switching on a regular basis between different oral contraceptives due to unavailability of the preferred method can easily lead to side effects or discontinuation of use.

CONCLUSION

This research has shown that accessibility of essential commodities for sexual and reproductive health remains a challenge in Eastern and Southern Africa. Low availability of SRHC in the public sector is compounded by regular stock-outs, which may force patients to seek care in private and PNFP sector facilities, where availability is also often low, where some services might not be offered or where the commodities might be unaffordable to a large proportion of the population. This research indicates that health system strengthening and community sensitisation is needed to ensure adequate access to essential SRHC. The findings of this research should be used by national governments and policy makers as a starting point to identify where the gaps and shortcomings in their health systems lie, and what commodities need priority attention.

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CONTRIBUTION STATEMENT

GIO, DK and GM designed the study and collected the data. GIO analysed the data and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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4.1

SUPPLEMENTARY DATA

Supplementary File 1. Surveyed sexual and reproductive health commodities.

Family Planning
    Ethinylestradiol + levonorgestrel 30mcg/150mcg
    Ethinylestradiol + norethisterone 50mcg/1.0mg[a,b,d]
    Ethinylestradiol + norethisterone 35mcg/1.0mg[b,c]
    Ethinylestradiol + norethisterone 30mcg/30mcg[a,c,d]
    Ethinylestradiol + desorgestrel 50mcg/250mcg[a,b,d]
    Ethinylestradiol + desorgestrel 30mcg/15mcg[a,c,d]
    Levonorgestrel 30mcg
    Levonorgestrel 750mcg
    Medroxyprogesterone acetate 150ml in 1ml
    Medroxyprogesterone acetate 104ml in 1ml[b,d]
    Estradiol cypionate + medroxyprogesterone acetate 5mg/25mg[b,c,d]
    Norethisterone enanthate 200mg/ml in 1ml[a]
    Male condoms: 3 per pack
    Female condoms: 1 per pack
    Intrauterine contraceptive device
    Implants: levonorgestrel
    Implants: etonogestrel
    Diaphragm
Maternal Health
    Oxytocin injection 10IU, 1ml
    Misoprostol 200mcg
    Methyldopa 250mg
    Magnesium sulphate 500mg/ 1ml[a,b,d]
    Magnesium sulphate 500mg/ 2ml
    Magnesium sulphate 500mg/ 10ml
    Calcium gluconate 100mg/ml in 10ml ampoule
    Ferrous salt 200mg
    Folic acid 5mg
    Ferrous Salt: Folic Acid 60mg/400mcg
    Ferrous Salt: Folic Acid 200mg/500mcg[a,b,d]
    Ferrous Salt: Folic Acid 150mg/500mcg[c]
Antibiotics and Antifungals
    Metronidazole 200mg
    Clotrimazole pessary 100mg[a,b,d]
    Clotrimazole pessary 500mg[c]
    Clotrimazole cream 1%, 15g tube
    Gentamicin 80mg/2ml[a,b,d]
    Gentamicin 40mg/1ml[c]
    Procaine benzylpenicillin powder for injection 3MU[a,b,c]
    Procaine benzylpenicillin powder for injection 4MU[a,d]
    Benzyl penicillin powder for injection 600mg[b,d]

4.1

Supplementary File 1. (continued)

    Benzyl penicillin injection 5MU[a,b,c]
    Benzathine benzylpenicillin 2.4MU in 10ml[a]
    Benzathine benzylpenicillin 900mg[b,c,d]
    Amoxicillin 125mg/5ml syrup[a,b,c]
    Amoxicillin 125mg[d]
    Amoxicillin 250mg

Newborn and Child Health
    Dexamethasone 4mg/ml
    Zinc syrup 10mg in 5ml syrup
    Zinc tablet 20mg
    Zinc ORS co-pack 10mg tablet/1L
    ORS sachets 200ml
   ORS sachets 500ml
    ORS sachets 1L
    Safe Delivery Kit
    Chlorhexidine 4%

4.1

SRH medical devices
    Vasectomy kit
    Tubal ligation kit
    Manual Vacuum Aspiration (MVA) kit
    Speculum
    Cervical dilator
    Incubator
    Monitor
    Ultrasound scan
    Ventilator
    Foetal scope
    Resuscitator (adult size)
    Resuscitator (infant size)
    Bag and mask (size 0)
    Suction device
    Training mannequin for infant resuscitation

[a]not surveyed in Kenya.
[b]Not surveyed in Tanzania.
[c]Not surveyed in Uganda.
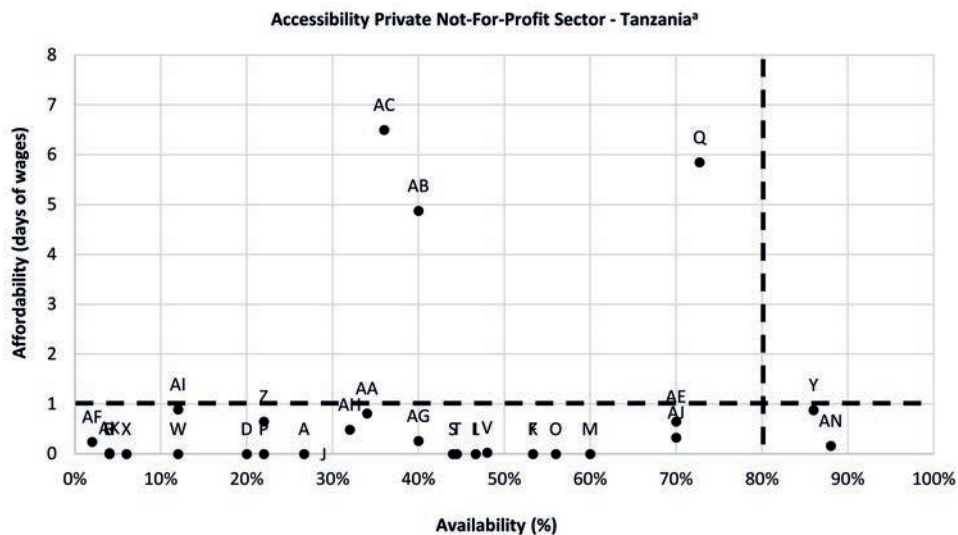[d]Not surveyed in Zambia.

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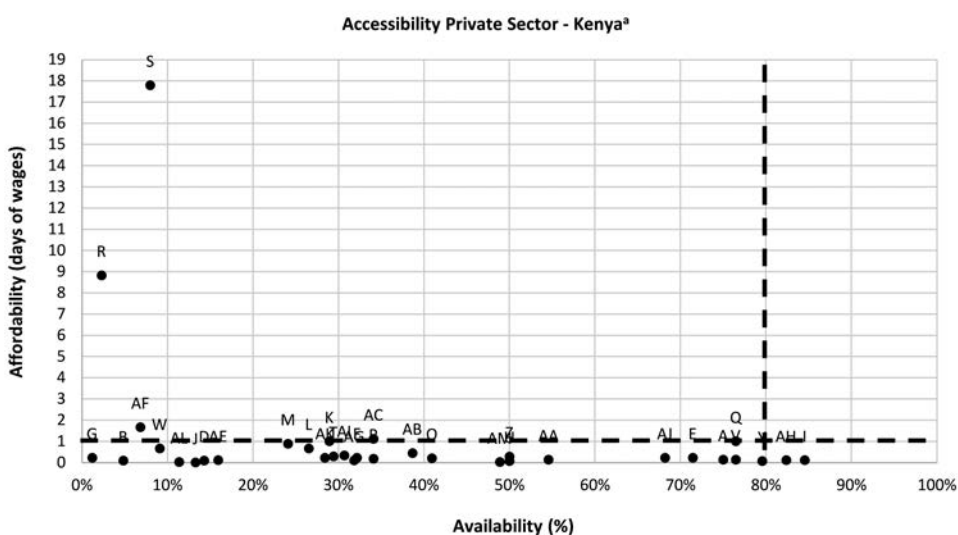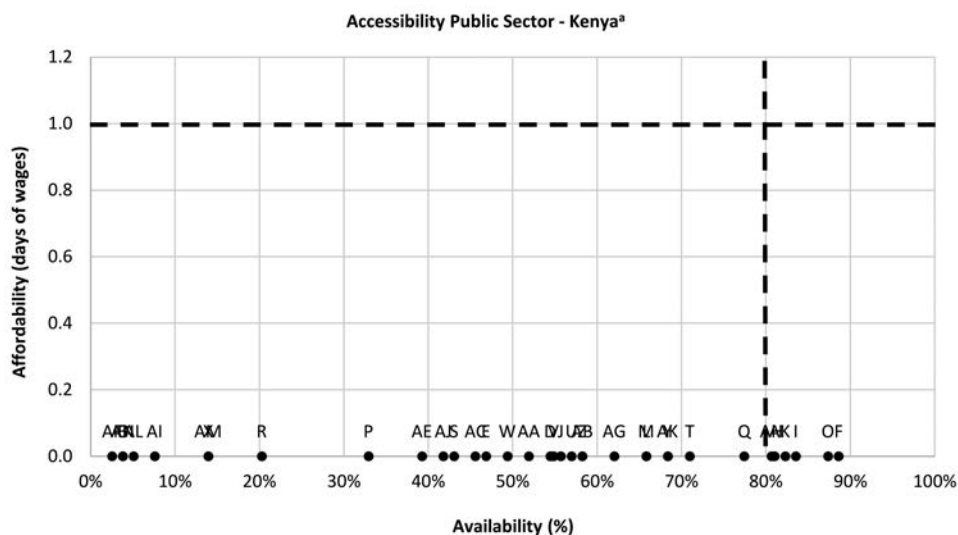
Supplementary File 2. Accessibility of SRHC in Kenya, Tanzania, Uganda and Zambia, per sector. [a]A: Ethinylestradiol + levonorgestrel; B: Ethinylestradiol + norethisterone; C: Ethinylestradiol + desorgestrel; D: Levonorgestrel 30mcg; E: Levonorgestrel 750mcg; F: Medroxyprogesterone acetate 150ml; G: Medroxyprogesterone acetate 104ml; H: Norethisterone enanthate; I: Male condoms; J: Female condoms; K: Intrauterine contraceptive device; L: Implants: levonorgestrel; M: Implants: etonogestrel; N: Diaphragm; O: Oxytocin injection; P: Misoprostol; Q: Methyldopa; R: Magnesium sulphate 500mg/ 2ml; S: Magnesium sulphate 500mg/ 10ml; T: Calcium gluconate; U: Ferrous salt; V: Folic acid; W: Ferrous Salt: Folic Acid 60/400; X: Ferrous Salt: Folic Acid 150/500; Y: Metronidazole; Z: Clotrimazole pessary; AA: Clotrimazole cream; AB: Gentamicin; AC: Procaine benzylpenicillin; AD: Benzyl penicillin; AE: Benzathine benzylpenicillin; AF: Amoxicillin 125mg; AG: Amoxicillin 250mg; AH: Dexamethasone; AI: Zinc syrup; AJ: Zinc tablet; AK: Zinc ORS co-pack; AL: ORS sachets 200ml; AM: ORS sachets 500ml; AN: ORS sachets 1L.
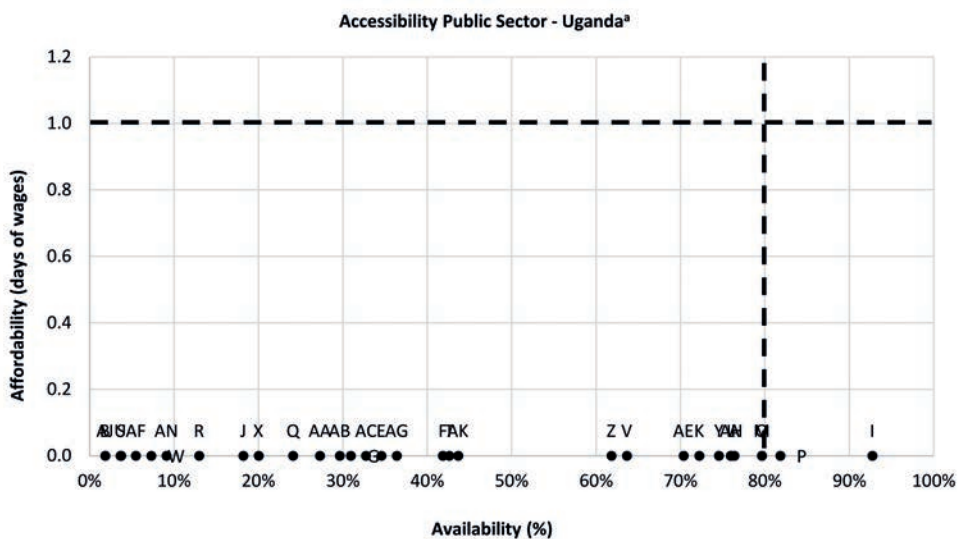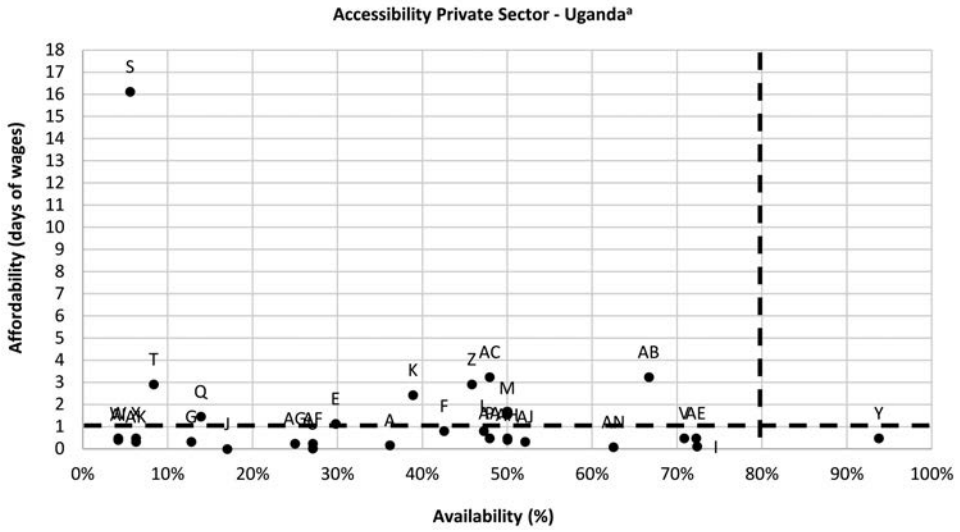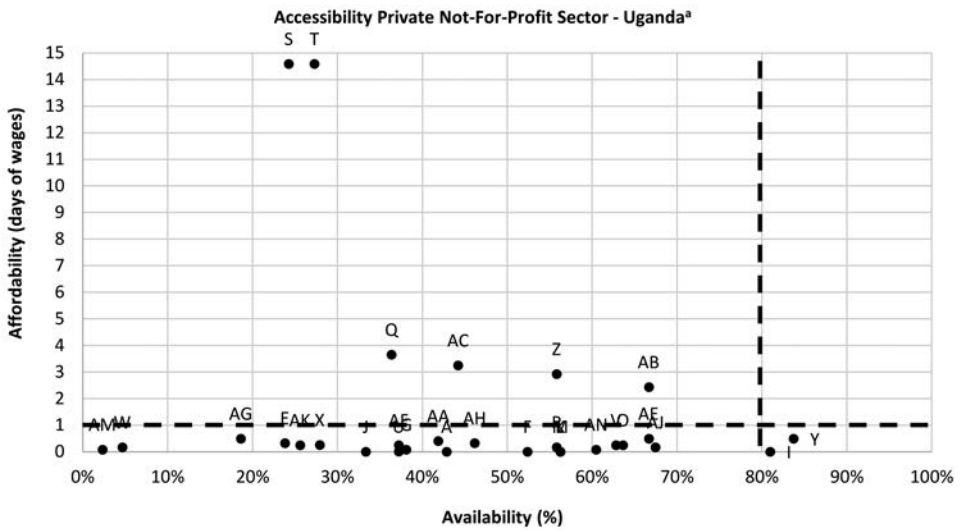
Accessibility Private Not-For-Profit Sector - Kenya[a]

4.1

Accessibility Public Sector - Tanzania[a]

Supplementary File 2. (continued)

Accessibility Private Not-For-Profit Sector - Tanzania[a]

4.1

Accessibility Public Sector - Uganda[a]

Supplementary File 2. (continued)

Accessibility Private Sector - Uganda[a]

4.1

Accessibility Private Not-For-Profit Sector - Uganda[a]

Supplementary File 2. (continued)

Accessibility Public Sector - Zambia[a]

Accessibility Private Sector - Zambia[a]

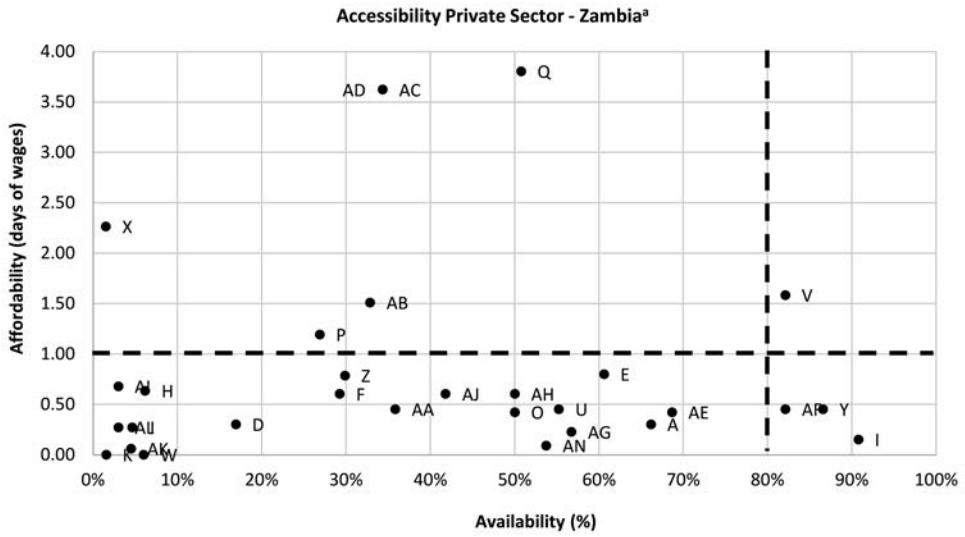**Supplementary File 2.** (continued)
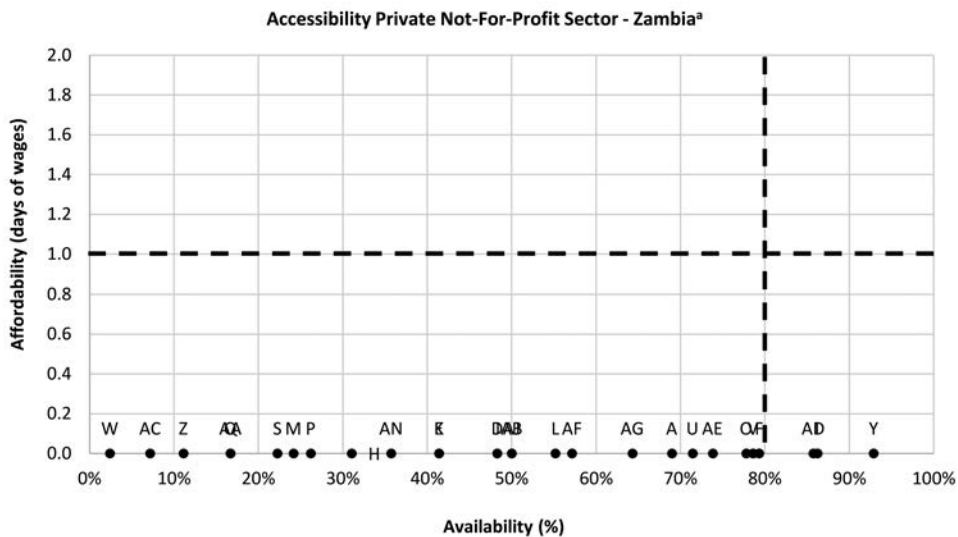
Supplementary File 2. (continued)

4.1

4.2

ACCESS TO OXYTOCIN AND MISOPROSTOL FOR MANAGEMENT OF POSTPARTUM HAEMORRHAGE IN KENYA, UGANDA AND ZAMBIA: A CROSS-SECTIONAL ASSESSMENT OF AVAILABILITY, PRICES AND AFFORDABILITY

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Juliet S Namugambe, Tim Reed,
Hubert GM Leufkens, Aukje K Mantel-Teeuwisse

ABSTRACT

Objective

To assess access (availability and affordability) to oxytocin and misoprostol at health facilities in Kenya, Uganda and Zambia to improve prevention and management of postpartum haemorrhage (PPH).

Design

The assessment was undertaken using data from Health Action International (HAI) research on sexual and reproductive health commodities based on a cross-sectional design adapted from the standardised WHO/HAI methodology.

Setting

Data were collected from 376 health facilities in in Kenya, Uganda and Zambia in July and August 2017.

Outcome measures

Availability was calculated as mean percentage of sampled medicine outlets where medicine was found on the day of data collection. Medicine prices were compared with international reference prices (IRP) and expressed as median price ratios. Affordability was calculated using number of days required to pay for a standard treatment based on the daily income of the lowest paid government worker.

Results

Availability of either oxytocin or misoprostol at health facilities was high; 81% in Kenya, 82% in Uganda and 76% in Zambia. Oxytocin was more available than misoprostol, and it was most available in the public sector in the three countries. Availability of misoprostol was highest in the public sector in Uganda (88%). Oxytocin and misoprostol were purchased by patients at prices above IRP, but both medicines cost less than a day's wages and were therefore affordable. Availability of misoprostol was poor in rural settings where it would be more preferred due to lack of trained personnel and cold storage facilities required for oxytocin.

Conclusion

Availability and affordability of either oxytocin or misoprostol at health facilities met the WHO benchmark of 80%. However, countries with limited resources should explore mechanisms to optimise management of PPH by improving access to misoprostol especially in rural areas.

4.2

INTRODUCTION

The risk of women dying due to pregnancy and childbirth remains a major global health challenge. In 2017, there were approximately 295 000 maternal deaths globally, of which 94% occurred in low-income and middle-income countries (LMICs). Sub-Saharan Africa contributed about 66% to these deaths (1). The global leading cause of maternal mortality is haemorrhage, accounting for 27% of all maternal deaths (2).

Postpartum haemorrhage (PPH) which occurs after childbirth accounts for most (72%) of the three forms of haemorrhage. Antepartum haemorrhage which occurs during pregnancy accounts for 24%, while intrapartum haemorrhage (during childbirth) accounts for 3% (2). PPH is responsible for 34% of maternal deaths in Kenya, 25% in Uganda and 34% in Zambia (3–5).

The WHO recommends oxytocin as the medicine of choice for management of PPH, and misoprostol as the second line alternative when injection capability is lacking and/or storage conditions for oxytocin are not met. Other uterotonics such as ergometrine and carbetocin are also recommended when the use of oxytocin is not feasible (1).

The relevance of oxytocin and misoprostol to health systems was further emphasised by the United Nations Commission on Life-saving Commodities for women and children when they were listed among the 13 lifesaving, low-cost medicines with greatest proven potential to avert preventable deaths (6). Both oxytocin and misoprostol are included in national essential medicine lists in Kenya, Uganda and Zambia (7–9).

4.2

The quality, efficacy and safety of oxytocin and misoprostol have been widely studied (10–23). Oxytocin is temperature sensitive and should therefore be stored under refrigeration at temperatures between 2°C and 8°C to prevent degradation expected at higher temperatures (10). Degradation reduces potency and consequently the effectiveness of the medicine. Oxytocin stability through the supply chain has proven a worry to policymakers and has been a subject of numerous investigations to ascertain quality and efficacy (11–13). Some studies on the quality of oxytocin found analysed samples to contain less active pharmaceutical ingredients than was claimed in the label, while some samples also failed sterility tests (14–16). LMICs with low resources may also lack facilities required for adequate storage conditions for oxytocin to ensure integrity of the product, while they may also lack trained health workers for its administration (17). Women living among displaced populations, in conflict areas, hard to reach areas, who deliver at home or with a traditional birth attendant seldom have access to a trained health worker. Hence, they do not have access to oxytocin or if they do, it is not safely used (24). As a result of these challenges, prevention and treatment of PPH in low-resource settings using oxytocin has not provided the desired impact (18,19).

Misoprostol, a prostaglandin, is an alternative to oxytocin in the management of PPH. It is cheap, stable at room temperature and more convenient to administer. It can be administered

sublingually, orally and vaginally (19,20,25,26). It has been demonstrated through various studies that the use of misoprostol is feasible, improves uterotonic coverage, reduces incidence of PPH and that it is effective for use at community and household level in low-resource settings (20–22).

In 2015, the WHO expert committee on the selection and use of medicines recommended the addition of misoprostol for the prevention and treatment of PPH when oxytocin is not available or cannot be used safely (23). At different occasions, the inclusion of misoprostol in the list of WHO recommended medicines was debated for both efficacy and safety reasons, but the 2015 decision to recommend misoprostol in addition to oxytocin for prevention of PPH was reaffirmed in 2019 by a WHO expert committee (27). Before 2015, misoprostol was indicated by WHO for use in induction of labour and management of spontaneous and induced abortion (28). The historical use of misoprostol for termination of pregnancies may have affected its acceptability for routine use in prevention of PPH, despite available convincing evidence of its therapeutic effect and relative safety in management of PPH. Another challenge is that the high doses of misoprostol required for postpartum haemorrhage often result in troublesome side effects such as vomiting and shivering (29). Furthermore, the longer half-life of the medicine means that it stays longer in the body and has potential to cause complications (30).

These two medicines could be used complementarily to overcome challenges and barriers in policy, health sector infrastructure and health service delivery that at the moment inhibit the optimal management of PPH (24,31). However, there is a knowledge gap on the accessibility of both medicines in low-resource settings. This is a missed opportunity in closing the gap in the reduction of maternal mortality in developing countries. This paper therefore assesses access to oxytocin and misoprostol in urban and rural health facilities in Kenya, Uganda and Zambia through a cross-sectional assessment of availability, prices and affordability at the patient level of the two medicines to facilitate the optimal management of PPH.

METHODS

A secondary assessment of availability and prices of oxytocin and misoprostol was undertaken using data from Health Action International (HAI) research on sexual and reproductive health commodities (SRHC): Measuring Prices, Availability and Affordability (32). The data were collected in Kenya, Uganda and Zambia in July and August 2017 using a cross-sectional design with quantitative methods adapted from the standardised WHO/HAI methodology (33), which has been validated (34) and used extensively in several countries (35–37).

4.2

Patient and public involvement

The research agenda for this study was set by the multistakeholder platform Medicines Transparency Alliance (MeTA) Councils in Kenya, Uganda and Zambia. The study protocols were reviewed and approved by MeTA Councils. Data collectors were selected from the membership of MeTA within the countries. Results were validated by stakeholders including civil society. Dissemination plans were made by MeTA councils and results were disseminated to wide country and intercountry platforms including Ministries of Health, Parliamentarians, private sector as well as civil society members to inform policy.

Data collection

For this study, the data on availability, price and affordability of the highest and lowest priced products of oxytocin 10 IU, 1 mL injections and misoprostol 200 μg tablets were extracted.

In each of the three countries, six geographical areas (districts, municipalities, or counties) were selected; the country's main urban centre and five other areas which were randomly selected. All survey areas were reachable within one hour's travel from the country's main urban centre using a car or bus. Each survey area covered a population of between 100,000 and 250,000 people.

4.2

The WHO/HAI methodology prescribes a minimum of 30 health facilities from each of the sectors, that is, public, private and mission sectors, giving a minimum total of 90 facilities per country (33). In each survey area, the main public hospital was selected first. Then, eight public health facilities, four each from urban and rural areas, representing levels of care at which SRHCs should be made available, were randomly selected (38). Additionally, eight private (for-profit) and eight mission sector (not-for-profit) health facilities (four each from urban and rural areas) that were within a three-hour drive radius of the main hospitals were selected. Thus, a total of 24 health facilities were sampled from each of the six survey areas in Kenya, Uganda and Zambia, respectively, giving a total of 144 facilities per country.

Eight data collectors with experience of conducting medicine surveys worked in pairs of a pharmacist and a social scientist under close supervision of a qualified survey manager. Prior to data collection, the team was trained on the methodology. Data collectors used a semi-structured questionnaire administered to facility managers while physically ascertaining the availability of surveyed medicines. Availability was measured by the physical presence of a product in the outlet at the time of the survey. For each medicine surveyed, data collectors recorded the product name for both the highest and lowest priced medicines available, the manufacturer and unit price of the product. In the public sector in Uganda and Zambia where medicines are

Once data collection was complete, survey data were entered into a preprogrammed Microsoft Excel Workbook provided as part of the modified methodology. Data input was

independently checked for errors. Additional quality control measures were executed at various stages throughout the study by a survey manager. The survey tools were pretested in Uganda in 2016 and a field test was conducted by all data collectors prior to data collection. Each data collection team had a supervisor who cross-checked the data on a daily basis for completeness, legibility and consistency and reported to the survey manager. Prior to data entry, all relayed data were checked for completeness and consistency.

Data analysis

The availability of oxytocin and misoprostol was calculated as the percentage of sampled medicine outlets where the medicine was found. Availability was also calculated for the presence of either oxytocin or misoprostol at a facility. Data were reported in aggregate as public, private or mission sector medicine outlets. Overall availability per sector was calculated as mean of the two medicines surveyed.

Patient prices were collected in local currency including Shillings in Uganda and Kenya, and Kwacha in Zambia. The mean, minimum and maximum unit prices were calculated. To facilitate cross-country comparisons, medicine prices obtained during the survey were expressed as ratios relative to a standard set of international reference prices (IRPs) by dividing the mean unit price (in dollars) by the Management Sciences for Health international buyers' reference unit price derived on 25 September 2018 (39). Mean price ratios (MPRs) were only calculated for oxytocin and misoprostol products that had price data from at least four medicine outlets per sector (33). The exchange rate used to calculate MPRs was 1 USD=102.67 Kenya Shillings (KES), 1 USD=3667.9 Uganda Shillings (UGX), 1 USD=8.85 Zambia Kwacha (ZMW) taken on 1 July 2017 prior to the first day of data collection (40,41).

Affordability was calculated using the number of days' wages it requires to pay for standard treatment or dose of treatment based on the daily income of the lowest paid government worker (LPGW) (33). The daily wage of a LPGW is approximately KES 411 (USD 4) in Kenya, 6255 UGX (USD 1.78) in Uganda and ZMW 96.7 (USD 10.92) in Zambia, as per public service salary structures (42). Treatments that required more than 1 hour's wages to purchase were considered unaffordable (33).

RESULTS

A total of 376 health facilities, including 120, 124 and 132 health facilities in Kenya, Uganda and Zambia, respectively, were surveyed as shown in **Figures 1** and **2**.

Availability across sectors

Figure 1 shows the availability of either oxytocin or misoprostol at the surveyed health facilities in the three countries. Overall availability of either oxytocin or misoprostol met the WHO benchmark of 80% in Kenya (81%) and Uganda (82%) but was marginally lower
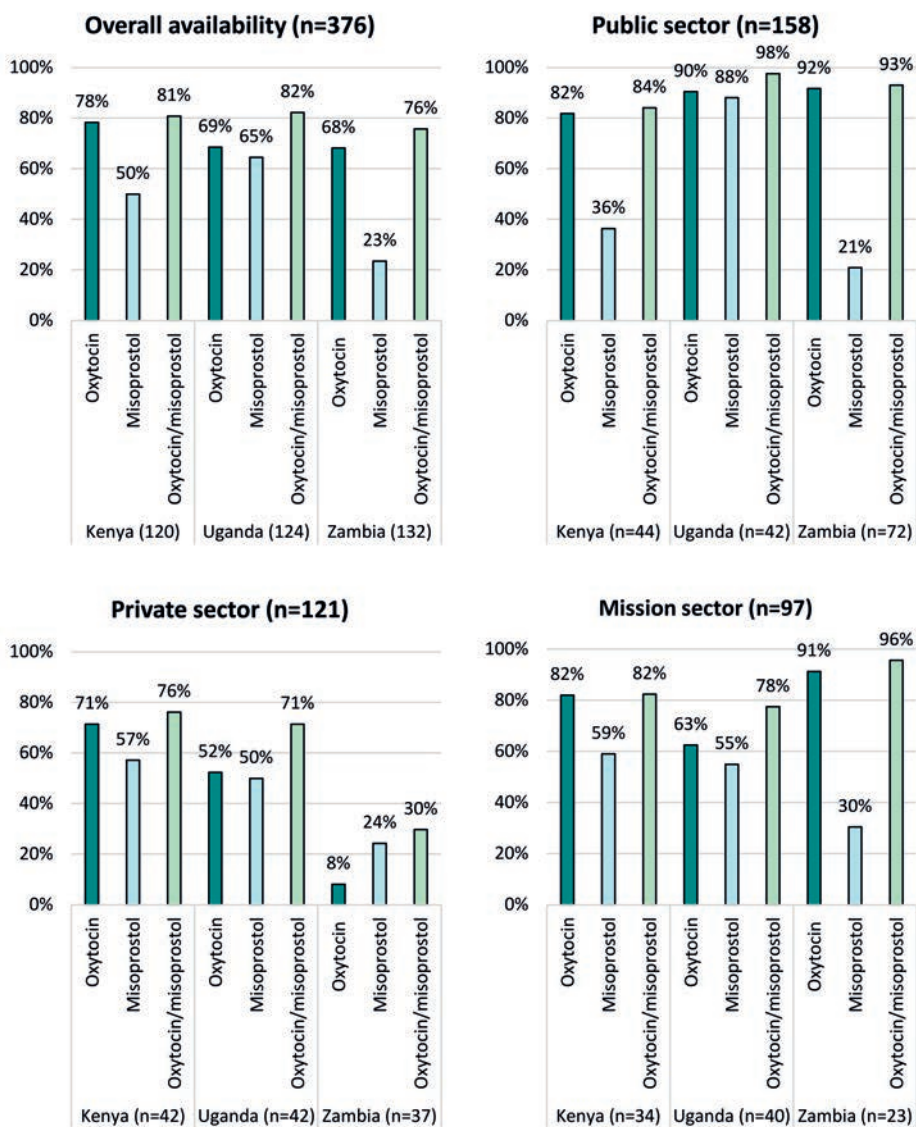
Figure 1. Availability of oxytocin and misoprostol across sectors in Kenya, Uganda and Zambia.

in Zambia (76%). Availability of oxytocin was higher than misoprostol except in Uganda. Availability of either oxytocin or misoprostol was comparable between the public and mission sectors. In the public sector, the three countries met the WHO benchmark for availability of oxytocin. Misoprostol was only optimally available in the public sector in Uganda (88%), with availability in Kenya and Zambia lower (36% and 21%, respectively). In the private sector, none of the countries met the WHO recommended availability for misoprostol. Availability in Zambia was especially low (24%).
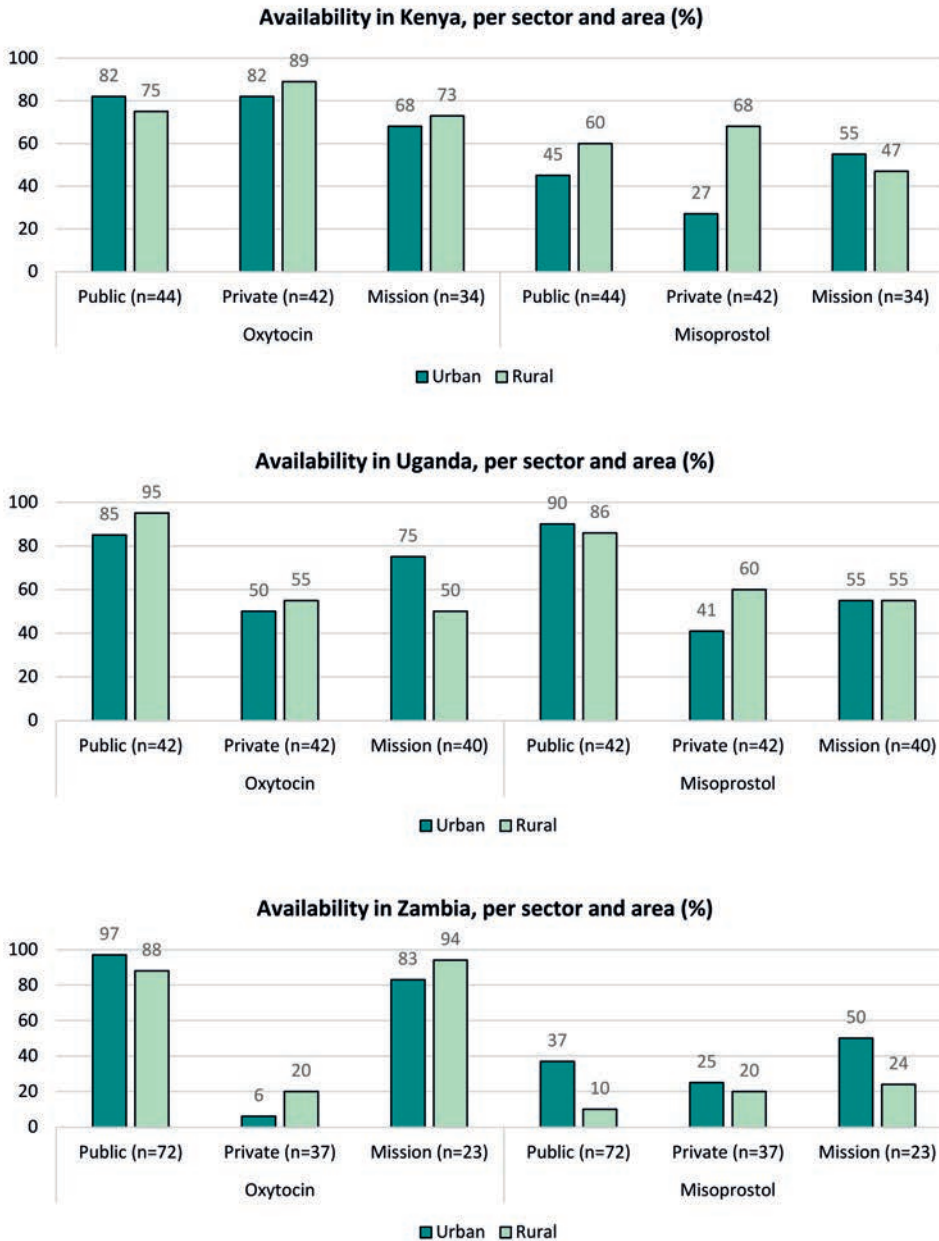
4.2

4.2

Figure 2. Availability of oxytocin and misoprostol in urban and rural facilities across countries.

Availability in urban versus rural areas

Figure 2 shows availability in urban versus rural areas. Oxytocin was available in over 80% of all public urban and rural facilities across the three countries. Optimum availability of 80% was further achieved for oxytocin in Kenya mission urban facilities (89%) and in Zambia's

mission sector for both urban and rural facilities (83% and 94%, respectively). Optimum availability of misoprostol was only achieved in Ugandan public urban and rural facilities (90% and 86%, respectively).

In Kenya, oxytocin had a higher availability than misoprostol across all urban and rural facilities in the three sectors. Availability of misoprostol was lowest in the public sector: availability in urban facilities was 45%, and 27% in rural facilities. In the private sector, there was a higher availability in rural facilities than in urban facilities for both oxytocin and misoprostol.

In Uganda, the public sector was optimally stocked with both oxytocin and misoprostol across urban and rural facilities. Rural public facilities had a higher availability of oxytocin than urban public facilities. In the private sector, rural facilities also had a higher availability of oxytocin and misoprostol compared with urban facilities.

Oxytocin had a high availability in Zambia's public and mission sectors across both urban and rural facilities. Availability in the private sector was very low. Availability of misoprostol was low across the sectors and areas, with highest availability found in urban mission facilities (50%). Although both oxytocin and misoprostol were poorly available in the private sector, oxytocin was more available in rural than urban facilities, while misoprostol had a higher availability in urban facilities than in rural facilities.

4.2

Prices and affordability

Oxytocin and misoprostol were free for patients in the public and mission sectors in Zambia, and in the public sector in Uganda. In Kenya's public sector, the lowest price was noted for oxytocin, with a MPR of USD 0.174 (**Table 1**). Both misoprostol and oxytocin cost less than a day's wages for an LPGW across all countries and sectors, and can therefore be considered affordable.

Notwithstanding the sectors in which the medicines were for free, the MPRs for oxytocin and misoprostol were above one in the countries, ranging from 1.37 for misoprostol in Kenya's public sector to 29.95 for misoprostol in the private sector in Zambia. This meant that both misoprostol and oxytocin were accessed by patients at prices that were more expensive compared with IRPs.

DISCUSSION

This paper assesses access to oxytocin and misoprostol in urban and rural health facilities in Kenya, Uganda and Zambia through a cross-sectional assessment of availability, prices and affordability at the patient level of the two medicines to facilitate the optimal management of PPH.

4.2

Table 1. Prices and affordability of misoprostol and oxytocin across countries.

		Public			Private			Mission		
		Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio*	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)
Kenya	Oxytocin	0.029	0.17	0.01	1.354	8.14	0.34	0.672	4.04	0.30
	Misoprostol	0.273	1.37	0.07	1.967	9.84	0.49	1.217	6.09	0.17
Uganda	Oxytocin	0	NA	NA	0.998	5.99	0.57	0.408	2.45	0.23
	Misoprostol	0	NA	NA	0.589	2.95	0.34	0.39	1.95	0.22
Zambia	Oxytocin	0	NA	NA	0.678	4.08	0.06	NA	NA	NA
	Misoprostol	0	NA	NA	5.989	29.95	0.55	NA	NA	NA

NA: Not applicable; USD: US Dollar.

Overall, availability of uterotonics, expressed as the presence of either oxytocin or misoprostol, was high in Kenya and Uganda, and just below the WHO benchmark of 80% in Zambia. Misoprostol was markedly less available than oxytocin. Oxytocin and misoprostol were accessed by patients in the private sector at prices that were more expensive than the IRPs. However, both medicines cost less than a day's wages, which is considered affordable. The availability of misoprostol across urban and rural areas did not show the expected pattern of having a higher availability of the medicine in rural areas, which are more prone to health system barriers for use of oxytocin.

Oxytocin availability was high in the public and mission sectors but lower in the private sector, particularly in Zambia. In the private sector, none of the countries met the WHO availability benchmark of 80% for the two medicines. Besides the public sector in Uganda, misoprostol was not optimally available in the other countries or sectors. Misoprostol had a low availability, particularly in rural areas where the medicine ought to play a major role given that facilities in these areas tend to lack adequately trained health workers and the health infrastructure required to maintain cold chain to safeguard the quality of oxytocin (17). Its poor availability in Kenya and Zambia may be a result of slow diffusion of the intervention into the health system (43,44). Moreover, misoprostol has been recommended by WHO for use in PPH since 2015 after several rounds of weighing the benefits and risks, but the debate about its role in PPH prevention has continued over the years (23,27). The fear and stigma among health workers about the use of misoprostol to induce abortions may also have contributed to the situation (29). In contrast, Uganda's efforts as an early adaptor (43,44) to ensure availability of misoprostol through government procurement and community level distribution strategies may explain why it has a higher availability of misoprostol, as well as lower PPH levels compared with Kenya and Zambia (25% in Uganda vs 34% in both Kenya and Zambia) (3–5).

Urban facilities have better health infrastructure such as cold chain facilities, and also tend to have more health workers compared with rural facilities (45–47). It would therefore be expected that these urban areas would have a higher availability of oxytocin and lower availability of misoprostol than rural facilities. However, there were instances when rural facilities had a higher availability of oxytocin and a lower availability of misoprostol. This may indicate that stocking of oxytocin and misoprostol by health facilities does not take into consideration challenges faced by the facilities to administer the medicines. It will require more research in this area to better understand the data and for policymakers to look into how to address context-specific barriers related to these medicines by ensuring that they are deployed where they can have maximum impact (48,49). For example, efforts should be made to deploy more misoprostol in rural areas where there is a lack of adequately trained personnel and a lack of health infrastructure to properly use oxytocin, and to ensure that both medicines are available to complement one another depending on circumstances.

4.2

PPH levels across the countries are high despite health facilities having reached the WHO benchmark for availability of either oxytocin or misoprostol across the three countries. This may confirm the finding from a study by Ononge et al (5) that despite the use of uterotonics, incidence of PPH remains high. It may be that some oxytocin found at health facilities may not have the quality and efficacy for optimum management of PPH (14–16). Countries should strive for universal access as the 80% availability benchmark by WHO still leaves one in five facilities without required medicine. However, availability of a medicine alone does not guarantee that it is used, health worker beliefs and knowledge as well as necessary infrastructure such as electricity and equipment are needed to reduce PPH levels.

Studies have shown that combinations of uterotonics have proven to be more effective. For example, a misoprostol plus oxytocin combination was found to be more effective in preventing PPH than the currently used standard of oxytocin only (50). This argument further emphasises that having both oxytocin and misoprostol available at the health facility could help to improve PPH management.

4.2

Although oxytocin and misoprostol were affordable to patients, the private sector prices were varied and more expensive compared with IRPs. For example, the MPR of misoprostol ranged from 1.37 in Kenya to 29.95 in Zambia. Therefore, even though availability met the WHO benchmark, individual patients may still be confronted with unavailability in the public sector, pushing them to seek care in the private sector where they may not be able to afford the prices of medicines. This suggests that countries need to explore pricing policies to improve affordability of the medicines.

Strengths and limitations

The WHO/HAI methodology that was used for this study is tested, reliable, standardised and validated for the measurement of medicine prices and availability (34). The study provides details on availability, price and affordability of individual medicines across three sectors (public, private and mission). The methodology uses a cross-sectional design and therefore historical data trends were not traced. The study only used two frontline medicines for PPH, while countries may have had other alternative therapies including carbetocin which were not captured. The number of mission facilities surveyed in Zambia (n=23) was below the minimum (n=30) recommended for the methodology per sector (33). The findings presented here may not be used to predict country pharmaceutical supply chain but are intended to stimulate policy discussions on deliberate targeting and the use of available technologies to improve access.

CONCLUSION

Availability of oxytocin and misoprostol met the WHO benchmark in Kenya and Uganda but was just below the WHO benchmark in Zambia. In general, oxytocin was more available

than misoprostol. Oxytocin and misoprostol were purchased by patients at prices above IRPs but both medicines cost less than a day's wages for a LPGW and were therefore considered affordable. However, there was no strategy in place that looked at which medicine could be best utilised in which area. Countries with limited resources should explore mechanisms to balance access to both oxytocin and misoprostol between rural and urban areas to optimise management of PPH.

ACKNOWLEDGEMENTS

CONTRIBUTION STATEMENT

GIO and DK designed the study and analysed the data. DK wrote the draft manuscript, and GIO revised and critically reviewed the manuscript. All other co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript.

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HEALTHCARE WORKERS' PERSPECTIVES ON ACCESS TO SEXUAL AND REPRODUCTIVE HEALTH SERVICES IN THE PUBLIC, PRIVATE AND PRIVATE NOT-FOR-PROFIT SECTORS: INSIGHTS FROM KENYA, TANZANIA, UGANDA AND ZAMBIA

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ABSTRACT

Background

Access to sexual and reproductive health services remains a challenge for many in Kenya, Tanzania, Uganda and Zambia. Health service delivery in the four countries is decentralised and provided by the public, private and private not-for-profit sectors. When accessing sexual and reproductive health services, clients encounter numerous challenges, which might differ per sector. Healthcare workers have first-hand insight into what impediments to access exist at their health facility. The aim of this study was to identify differences and commonalities in barriers to access to sexual and reproductive health services across the public, private and private not-for-profit sectors.

Methods

A cross-sectional survey was conducted among healthcare workers working in health facilities offering sexual and reproductive health services in Kenya (n=212), Tanzania (n=371), Uganda (n=145) and Zambia (n=243). Data were collected in July 2019. Descriptive statistics were used to describe the data, while binary logistic regression analyses were used to test for significant differences in access barriers and recommendations between sectors.

Results

According to healthcare workers, the most common barrier to accessing sexual and reproductive health services was poor patient knowledge (37.1%). Following, issues with supply of commodities (42.5%) and frequent stockouts (36.0%) were most often raised in the public sector; in the other sectors these were also raised as an issue. Patient costs were a more significant barrier in the private (33.3%) and private not-for-profit sectors (21.1%) compared to the public sector (4.6%), and religious beliefs were a significant barrier in the private not-for-profit sector compared to the public sector (odds ratio=2.46, 95% confidence interval=1.69-3.56). In all sectors delays in the delivery of supplies (37.4%-63.9%) was given as main stockout cause. Healthcare workers further believed that it was common that clients were reluctant to access sexual and reproductive health services, due to fear of stigmatisation, their lack of knowledge, myths/superstitions, religious beliefs, and fear of side effects. Healthcare workers recommended client education to tackle this.

Conclusion

Demand and supply side barriers were manifold across the public, private and private not-for-profit sectors, with some sector-specific, but mostly cross-cutting barriers. To improve access to sexual and reproductive health services, a multi-pronged approach is needed, targeting client knowledge, the weak supply chain system, high costs in the private and private not-for-profit sectors, and religious beliefs.

INTRODUCTION

Sexual and reproductive health and rights (SRHR) encompass "efforts to eliminate preventable maternal and neonatal mortality and morbidity, to ensure quality sexual and reproductive health services, including contraceptive services, and to address sexually transmitted infections (STI) and cervical cancer, violence against women and girls, and sexual and reproductive health needs of adolescents" (1). Unfortunately, many in Kenya, Tanzania, Uganda and Zambia have poor access to the sexual and reproductive health (SRH) services that address these issues. As a result, their rights are not fulfilled which results in poor SRHR outcomes. Unintended pregnancy rates are high, which range from 105 per 1,000 women aged 15–49 in Tanzania, to 145 per 1,000 women in Uganda, especially when compared to the rate in Europe and Northern America (35 per 1,000 women) (2). In addition, each year, 340,000 women and 370,000 new-borns in Tanzania do not receive the care they need for major (obstetric) complications, with similar numbers found in Kenya, Uganda and Zambia (2). Related, the maternal mortality rate remains high in these countries, ranging from 213 per 100,000 live births in Zambia to 524 per 100,000 live births in Tanzania (3). Further, studies on the prevalence of STIs have shown infection rates to be high, especially among adolescents. In Kenya, two studies investigating the prevalence of chlamydia trachomatis among women found it to be around 11–13%, while a study in Uganda among more than 8,000 adolescents found a 19% self-reported history of STIs (4–6). Much thus still needs to be done to ensure the SRHRs of people in these countries are fulfilled.

In each country, service delivery is undertaken by three entities: the public sector, the private sector, and the private not-for-profit (PNFP) sector, which for a large part comprise faith-based organisations (7). In Zambia, the public sector owns 88% of registered facilities, the private sector 13% and the PNFP sector 6% (8). Ownership in Tanzania is comparable, with the public sector owning 74% of facilities, and the private and PNFP sectors 14% and 13%, respectively (9). In Kenya and Uganda, ownership between the public and private sector is more evenly distributed, with about 45% public and about 40% private sector ownership (10,11).

It is known that women and girls encounter numerous challenges in accessing SRH services. On the demand side, barriers include, amongst others, lack of knowledge on SRH, socio-cultural and religious beliefs and practices, poverty, stigmatisation, and healthcare workers' (HCWs) negative attitudes (12–15). On the supply side, barriers include unavailability and unaffordability of commodities and services, stockouts, distance to health facilities, staff shortages, and poorly trained HCWs (12–16). It is, however, unknown how these barriers compare between the three sectors that deliver SRH services. Previous research studied only one sector (17–19), studied multiple sectors but did not stratify results per sector (12), or did not specify which sector(s) were studied (14,15), which does not allow for comparison across sectors. One study that did measure the availability, affordability and stockouts of sexual and reproductive health commodities (SRHC) across the three sectors found that

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availability was comparable across sectors, while affordability for specific commodities was only problematic in the private and PNFP sectors (20).

It is essential to know more about how barriers to delivering SRH services vary across sectors. Among others, they have their own supply systems, methods of operation, and offering and pricing of services. Knowing what barriers play out in each of the sectors and how they compare can help to identify the need for and development of sector-specific action plans to address these barriers. The current study addresses this gap. It used a survey design to gather the perspectives of HCWs on the impediments to access to SRH services at their health facility. HCWs have first-hand insight on issues in service provision from their day-to-day work and can provide insights into barriers on both the supply and demand side. The aim of this study was to compare the barriers to access to SRH services across the public, private and private not-for-profit sectors of Kenya, Uganda, Tanzania and Zambia.

METHODS

Study design and settings

A cross-sectional survey among HCWs in health facilities providing SRH services was conducted in Kenya, Tanzania, Uganda, and Zambia. These countries were selected due to their similar health system structures and comparable performance on SRH indicators (2–6,8–11).

Study participants and sampling procedures

HCWs, at the forefront of care delivery, were used as key informants in this study. The HCW needed to be a licensed HCW providing SRH services and had to have worked at the facility for at least one year. The definition of 'HCW' included pharmacists, physicians, nurses, and clinical officers.

The sampling strategy used was based on the standardised World Health Organization's (WHO)/Health Action International's (HAI) methodology, *Measuring medicine prices, availability, affordability and price components*, in which each country's main urban region was selected, and in addition five or more other regions were randomly selected for inclusion (21). This sampling strategy has been shown to be a representative presentation of surveyed countries' price, availability and affordability situation through a validation study (22). Regions chosen included ten counties in Kenya, twelve districts in Tanzania, six regions in Uganda, and ten provinces in Zambia. In each survey region, at least 24 facilities, located in both urban and rural areas, were randomly selected from the public, private and PNFP sectors. Facilities where HCWs were working had to be within three hours travel from the main public provincial health facility. In total, the target sample size consisted of 912 HCWs in Kenya (n=240), Tanzania (n=288), Uganda (n=144), and Zambia (n=240). Urban was defined based on the definition used by the countries' national bureaus of statistics (23). The healthcare levels included in the study ranged from the health post/dispensary level to

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regional and national (referral) hospitals. In each facility, one HCW was asked to participate in the survey.

Data collection tool

The survey collected information about the HCWs' perceptions on the SRH services offered at their facility, key challenges to accessing SRH services, perspectives on SRHC stockouts, perspectives on clients' potential reluctance to access SRH services, and recommendations to improve access. The survey was developed in collaboration with in-country civil society experts, and consisted of seven open-ended and three close-ended questions (see Supplementary File 1). The survey was pilot-tested in 2018 in all four countries, after which it was refined and one question was added based on feedback from in-country experts. Refinement of the survey occurred in phrasing of the questions, and specification within the questions between supply- and demand-side barriers. Data were collected using a mobile data collection application in July 2019. In each country, local consultants specialised in this type of research undertook the data collection. They were trained during a two-day workshop by the authors (GO, DO), after which they piloted the survey during a field test. The local consultants worked in pairs and were supervised by an in-country lead. The survey took on average twenty minutes to complete.

Data management and analysis

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Data were regularly uploaded to the server and downloaded into Microsoft Excel after completion of the data collection. Data were double-checked by the researchers, responses were verified with the data collectors when questions about their meaning arose, and open-ended questions were categorised. Thereafter, data were imported into Stata version 17 for analysis. Simple descriptive statistics were used to daescribe the data, while binary logistic regression analyses were used to test for significant differences in access barriers and recommendations between sectors. In the analyses we controlled for country, location (urban vs. rural), and level of care of the health facility. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were reported to assess if some answers were more (or less) likely to be mentioned by HCWs in the private sector and PNFP sector compared to the public sector. A significance cut-off value of 0.05 was used.

Ethical considerations

Ethical approval for the study was obtained from the Amref Ethics and Scientific Review Committee (P394-2017) and National Commission for Science & Technology (NACOSTI/P/19/36,482/31,905) in Kenya, the National Institute for Medical Research in Tanzania (NIMR/HQ/R.8a/Vol. IX/2797), the Makerere University School of Health Sciences in Uganda (2018-017), and ERES Converge in Zambia (2018-Apr-010). Further, permission was granted by letter by the respective county/district Directors of Health and Ministries of Health. Participants were provided with an information sheet, and their informed consent

was obtained orally before the survey was undertaken. No identifying information was collected about the participants, and all data was stored on password-protected computers.

RESULTS

In total, 971 HCWs participated from Kenya (n = 212), Tanzania (n = 371), Uganda (n = 145) and Zambia (n = 243) (see **Table 1**). More than half of HCWs worked in the public sector, 25.9% worked in the private sector, and 19.5% in the PNFP sector. HCWs believed that family planning services experienced the most access challenges (41.2%), followed by maternal health (27.7%) and STI management (22.4%) services. Only 8.7% of HCWs indicated child health services to experience most access challenges of the SRH services.

HCWs' perspectives on access to SRH per sector

When HCWs were asked about the key challenges to accessing SRHC, the most commonly mentioned barrier in the public sector was issues with the supply to the health facility (42.5%). In the private sector patients' lack of knowledge (37.0%) was most often mentioned, which was also commonly mentioned in the other sectors (see **Table 2**). In the PNFP sector

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Table 1. Characteristics of study participants.

	N	%
Country		
Kenya	212	21.8
Tanzania	371	28.2
Uganda	145	14.9
Zambia	243	25.0
Sector		
Public	531	54.7
Private	251	25.9
PNFP	189	19.5
Area		
Urban	530	54.6
Rural	441	45.4
Level[a]		
I	416	42.8
II	190	19.6
III	235	24.2
IV	79	8.1
V	51	5.3

[a]Health facility levels in Kenya: I. Dispensary/clinic, pharmacy; II. Health centre; III. Primary hospital; IV. Secondary care hospital; V. Teaching/national hospital. In Tanzania: : I. Dispensary/clinic, pharmacy; II. Health centre; III. Council hospital; IV. Regional referral hospital; V. Zonal/national hospital. In Uganda: I. Dispensary/clinic, pharmacy; II. Health centre II; III. Health centre III; IV. Health centre IV; V. (Regional referral) hospital. In Zambia: I. Dispensary/clinic, pharmacy; II. Health post; III. Health centre; IV. District hospital; V. General hospital and above.

Table 2. HCW perspectives on access to SRH barriers and recommendations for improvement, per sector.

	Overall N (%)	Public N (%)	Private N (%)	OR (95% CI)[a]	PNFP N (%)	OR (95% CI)[a]
Key challenges to accessing SRHC						
Patient lack of knowledge on SRH	354 (37.1)	203 (38.8)	91 (37.0)	0.99 (0.69-1.42)	60 (32.4)	0.75 (0.52-1.09)
Issues with supply to HF	320 (33.5)	222 (42.5)	56 (22.8)	0.40*** (0.27-0.59)	42 (22.7)	0.44*** (0.29-0.65)
Frequent stockouts at HF	282 (29.6)	188 (36.0)	49 (19.9)	0.47*** (0.31-0.72)	45 (24.3)	0.57** (0.38-0.85)
Religious/cultural beliefs	272 (28.5)	142 (27.2)	47 (19.1)	0.75 (0.50-1.15)	83 (44.9)	2.46*** (1.69-3.56)
Stigma	207 (21.7)	113 (21.6)	56 (22.8)	0.97 (0.63-1.48)	38 (20.5)	0.75 (0.49-1.16)
Staff shortages	182 (19.1)	144 (27.5)	18 (7.3)	0.26*** (0.15-0.46)	20 (10.8)	0.34*** (0.21-0.57)
Staff training on SRH services	148 (15.5)	101 (19.3)	24 (9.8)	0.49** (0.28-0.83)	23 (12.4)	0.61 (0.37-1.01)
Patient costs	145 (15.2)	24 (4.6)	82 (33.3)	6.83*** (3.98-11.70)	39 (21.1)	4.58*** (2.61-8.03)
No demand	102 (10.7)	40 (7.7)	45 (18.3)	1.30 (0.74-2.28)	17 (9.2)	1.02 (0.55-1.91)
Frequent stockouts at central level	102 (10.7)	71 (13.6)	23 (9.4)	0.70 (0.39-1.25)	8 (4.3)	0.35** (0.16-0.75)
SRHC stockout causes						
Delay in supply delivery	471 (54.1)	320 (63.9)	83 (37.4)	0.36 (0.24-0.54)***	68 (46.0)	0.52** (0.34-0.77)
What is ordered is not what HF received	295 (33.9)	226 (45.1)	37 (16.7)	0.31 (0.20-0.49)***	32 (21.6)	0.35*** (0.22-0.54)
Problems with stock at medical stores	264 (30.3)	170 (33.9)	61 (27.5)	0.94 (0.62-1.41)	33 (22.3)	0.61* (0.39-0.95)
Demand higher than availability	185 (21.2)	120 (24.0)	37 (16.7)	0.49** (0.31-0.81)	28 (18.9)	0.76 (0.47-1.23)
Affordability for HF	138 (15.8)	33 (6.6)	67 (30.2)	5.59*** (3.27-9.53)	38 (25.7)	4.82*** (2.79-8.34)
Poor stock management at HF	128 (14.7)	63 (12.6)	34 (15.3)	1.37 (0.81-2.32)	31 (21.0)	1.84* (1.11-3.04)
Lack of storage space at HF	80 (9.2)	58 (11.6)	14 (6.3)	0.54 (0.28-1.08)	8 (5.4)	0.48 (0.21-1.07)
Problems with medicine transport to HF	71 (8.2)	51 (10.2)	10 (4.5)	0.49 (0.22-1.08)	10 (6.8)	0.67 (0.32-1.39)
Recommendations for improvement – supply side						
Improve supply chain	523 (55.6)	346 (66.4)	104 (43.2)	0.40*** (0.27-0.57)	73 (41.0)	0.38*** (0.27-0.56)
Timely supply of SRHC	430 (45.7)	274 (52.6)	84 (34.9)	0.48*** (0.33-0.70)	72 (40.5)	0.61** (0.42-0.87)
Prevent stockouts of SRHC at HF	326 (34.7)	192 (36.9)	80 (33.2)	1.04 (0.71-1.50)	54 (30.3)	0.75 (0.51-1.10)
Ensure sufficient stock available at HF	275 (28.7)	180 (34.2)	56 (22.6)	0.65* (0.44-0.97)	39 (21.2)	0.57** (0.38-0.85)
Supply SRHC that were ordered	247 (26.3)	179 (34.4)	46 (19.1)	0.56** (0.37-0.86)	22 (12.4)	0.28*** (0.17-0.46)

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Table 2. (continued)

	Overall N (%)	Public N (%)	Private N (%)	OR (95% CI)[a]	PNFP N (%)	OR (95% CI)[a]
(Continued) staff training	216 (23.0)	140 (26.9)	42 (17.4)	0.63* (0.41–0.97)	34 (19.1)	0.66 (0.43–1.03)
Increase staff	203 (21.6)	143 (27.5)	30 (12.5)	0.51** (0.32–0.82)	30 (16.9)	0.57** (0.36–0.90)
Increase budget for SRHC	176 (18.7)	112 (21.5)	33 (13.7)	0.50*** (0.30–0.81)	31 (17.4)	0.76 (0.48–1.20)
Provide greater choice of SRHC	147 (15.6)	71 (13.6)	49 (20.3)	1.60* (1.00–2.55)	27 (15.2)	1.05 (0.63–1.73)
Recommendations for improvement – demand side						
Client and community education	778 (81.1)	437 (82.9)	194 (78.2)	0.77 (0.50–1.20)	147 (79.9)	0.89 (0.57–1.39)
Increase male partner involvement	357 (37.2)	222 (42.1)	82 (33.1)	0.82 (0.57–1.18)	53 (28.8)	0.57** (0.39–0.83)
Offer/improve SRH outreach services	280 (29.2)	164 (31.1)	62 (25.0)	0.77 (0.52–1.14)	54 (29.4)	0.86 (0.58–1.26)
Increase choice of contraceptives	222 (23.2)	129 (24.5)	59 (23.8)	0.76 (0.50–1.16)	34 (18.5)	0.76 (0.49–1.18)
Professionalise HCW-patient relationship	173 (18.0)	102 (19.4)	49 (19.8)	0.88 (0.56–1.36)	22 (12.0)	0.43** (0.26–0.73)
Reduce costs for clients	202 (21.0)	38 (7.2)	113 (45.2)	7.60*** (4.79–12.04)	51 (27.7)	4.10*** (2.53–6.63)
HF at times unable to provide client with SRHC and services						
Yes	359 (37.0)	155 (29.2)	123 (49.0)	1.57* (1.09–2.26)	81 (42.9)	1.47* (1.02–2.12)
Reasons why unable to provide client with SRHC and services						
SRHC was stocked out	131 (37.3)	84 (56.4)	35 (28.2)	0.30*** (0.16–0.56)	12 (15.4)	0.11*** (0.07–0.28)
HF does not offer FP services	65 (18.6)	13 (8.8)	24 (19.5)	1.88 (0.82–4.30)	28 (35.9)	6.38*** (2.97–13.72)
Client unable to pay for service	60 (17.2)	4 (2.7)	44 (35.8)	15.13*** (4.85–47.18)	12 (15.4)	6.88** (2.08–22.70)
Client was too young	58 (16.6)	19 (12.8)	26 (21.1)	1.72 (0.78–3.83)	13 (16.7)	1.15 (0.51–2.60)
Service not culturally or religiously acceptable	56 (16.1)	13 (8.7)	5 (4.1)	0.42 (0.13–1.37)	38 (49.4)	12.65*** (5.75–27.81)
Service would not benefit client	25 (7.2)	11 (7.4)	9 (7.3)	1.26 (0.42–3.81)	5 (6.4)	0.60 (0.19–1.90)
Lack of HCW knowledge	23 (6.6)	16 (10.7)	5 (4.0)	0.53 (0.16–1.74)	2 (2.6)	0.22* (0.05–0.99)
Client was unmarried	17 (4.9)	6 (4.1)	4 (3.3)	0.59 (0.13–2.64)	7 (9.0)	1.63 (0.49–5.45)

CI = confidence interval; FP = family planning; HCW = healthcare worker; HF = health facility; OR = odds ratio; SRH = sexual and reproductive health; SRHC = sexual and reproductive health commodities.

[a]The model was corrected for country, location, and level of care of the health facility.

* p<0.05, ** p<0.01, *** p<0.001

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the barrier most cited was religious or cultural beliefs on both the supply- and demand side (44.9%); HCWs in this sector had higher odds (OR=2.46, 95% CI=1.69–3.56) of mentioning this barrier than their counterparts in the public sector. In the private and PNFP sectors, HCWs were less likely to mention issues with the supply to the health facility, frequent stockouts at the health facility, and staff shortages than HCWs in the public sector. In the private sector, HCWs were also less likely to indicate staff training on SRH as a key challenge to accessing SRHC than those in the public sector (9.8% vs. 19.3%, OR=0.49, 95% CI=0.28–0.83), while in the PNFP sector HCWs were less likely to mention stockouts at the central level as a barrier than HCWs in the public sector (4.3% vs. 13.6%, OR=0.35, 95% CI=0.16–0.75). Both the HCWs in the private (33.3%, OR=6.83, 95% CI=3.98–11.70) and PNFP sectors (21.1%, OR=4.58, 95% CI=2.61–8.03) were more likely to mention patient costs as barrier than HCWs from the public sector (4.6%).

When HCWs were asked about the causes of SRHC stockouts at their facilities, in all sectors they most commonly said that it was due to delays in the delivery of the SRHC (37.4-63.9%). In the public sector, another commonly mentioned cause of SRHC stockouts was a difference between supplies ordered by the facility, and those received (45.1%). Both of these reasons were less likely to be mentioned as a cause of stockouts in the private and PNFP sector. HCWs in these two sectors did have a 5.59 (95% CI=3.27–9.53) and 4.82 (95% CI=2.79–8.34) higher odds, respectively, of giving poor affordability of SRHC as a reason for stockouts than in the public sector.

HCWs also shared what they believed could be done, on both the supply- and demand side, to improve access to SRHC. On the supply side, the most often shared recommendation was the general recommendation to improve the supply chain (41.0-66.4%). Nevertheless, HCWs in the private (OR=0.40, 95% CI=0.27–0.57) and PNFP (OR=0.38, 95% CI=0.27–0.56) sectors were less likely to mention this recommendation than HCWs in the public sector. Ensuring the timely supply of SRHC and preventing stockouts of SRHC at the facility were also commonly provided recommendations across the three sectors. Public sector HCWs also often recommended increasing number of staff offering SRH services (27.5%) and increasing staff training on SRH service provision (26.9%).

To improve the demand for commodities, more than 80% of HCWs across the sectors saw a need for community education on SRH. Offering or improving outreach services and increasing male partner involvement were also commonly recommended across the sectors. Nevertheless, PNFP sector HCWs were less likely to recommend increasing male partner involvement than public sector HCWs (42.1% vs. 28.8%, OR=0.57, 95% CI=0.39–0.83). In the private and PNFP sectors, HCWs were more likely to recommend reducing costs for clients than their counterparts in the public sector (OR=7.60, 95% CI=4.79–12.04 and OR=4.10, 95% CI=2.53–6.63, respectively).

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HCWs were also asked if they were at times unable to provide clients with SRHC and SRH services; 29.2% of HCWs in the public sector indicated this was the case, with HCWs in the private sector (49.0%) and PNFP sector (42.9%) being significantly more likely to state they experienced this issue. The most commonly provided reason for this in the public sector was that the SRHC was out of stock (56.4%), which was a less likely reason given in the private (28.2%, OR=0.30, 95% CI=0.16–0.56) and PNFP (15.4%, OR=0.14, 95% CI=0.07–0.28) sectors. In the private sector, the most indicated reason was that clients were unable to pay for the service (35.8%).The most common reasons given in the PNFP sector were because the service was not culturally or religiously acceptable (49.4%) and because the health facility did not offer family planning services (35.9%).

Further, 39.3% of HCWs thought that clients were reluctant to access SRHC (see **Table 3**). The most commonly provided reasons for clients' reluctance were fear of stigmatisation (63.0%), patients' lack of knowledge (50.0%), myths or superstitions (44.7%), religious beliefs (39.2%) and fear of side effects (38.6%). HCWs from the PNFP sector were less likely (OR=0.43, 95% CI=0.19–0.97) than public sector HCWs to believe low support from male partners was a reason for client reluctance. Conversely, they were more likely (OR=2.46, 95% CI=1.05–5.73) to believe poverty and costs played a role in their reluctance.

To tackle clients' reluctance, almost all HCWs (97.4%) recommended expanding client education. Other commonly mentioned recommendations included creating youth-friendly health corners (35.8%) and involving partners in the SRH care (28.9%). The youth-friendly health corners were less likely to be recommended by HCWs from the private and PNFP sectors than by those from the public sector, while involving partners was also less likely to be recommended by PNFP sector HCWs compared to public sector HCWs. Staff training was also less likely to be recommended by HCWs from the private (OR=0.46, 95% CI=0.21–0.99) and PNFP (OR=0.43, 95% CI=0.20–0.95) sectors than by those in the public sector. These HCWs were more likely than public sector HCWs to recommend reducing costs for patients to tackle their reluctance. In the PNFP sector, HCWs were also more likely (OR=3.19, 95% CI=1.18–8.60) to recommend providing free family planning services than their counterparts in the public sector.

The presented adjustments in the models for country, location, and level of care of the facility did not substantially change the results compared to the crude results (see Supplementary File 2). The barriers and recommendations shared by the HCWs were comparable across the four countries (see Supplementary File 3).

DISCUSSION

This study looked at what barriers to accessing SRH services exist at both the supply- and demand side in the public, private and PNFP sectors and what ought to be done to improve

Table 3. HCW perspectives on client reluctance to access SRH services, per sector.

	Overall N (%)	Public N (%)	Private N (%)	OR (95% CI)[a]	PNFP N (%)	OR (95% CI)[a]
Clients reluctant to access SRH services						
Yes	381 (39.3)	195 (36.7)	108 (43.0)	1.03 (0.72-1.49)	78 (41.5)	0.92 (0.64-1.31)
Reasons for reluctance to access SRH services						
Fear of stigmatisation	238 (63.0)	115 (59.6)	70 (65.4)	0.69 (0.36-1.32)	53 (68.0)	0.83 (0.44-1.58)
Patient lack of knowledge	189 (50.0)	100 (51.8)	57 (53.3)	0.96 (0.53-1.73)	32 (41.0)	0.64 (0.36-1.15)
Myths or superstitions	169 (44.7)	95 (49.2)	43 (40.2)	0.86 (0.48-1.56)	31 (39.7)	0.83 (0.47-1.48)
Religious beliefs	148 (39.2)	84 (43.5)	33 (30.8)	0.89 (0.47-1.67)	31 (39.7)	1.40 (0.76-2.59)
Fear of side effects	146 (38.6)	71 (36.8)	46 (43.0)	1.45 (0.78-2.68)	29 (37.2)	0.88 (0.48-1.62)
Low support - male partner	78 (20.6)	49 (25.4)	20 (18.7)	0.64 (0.31-1.33)	9 (11.5)	**0.43* (0.19-0.97)**
Poverty/costs	48 (12.7)	13 (6.7)	20 (18.7)	2.14 (0.85-5.38)	15 (19.2)	**2.46 (1.05-5.73)***
Frequent stockouts at HF	32 (8.5)	23 (11.9)	4 (3.7)	0.31 (0.08-1.19)	5 (6.4)	0.58 (0.20-1.73)
Distance to HF	28 (7.4)	18 (9.3)	5 (4.7)	1.24 (0.34-4.50)	5 (6.4)	0.68 (0.21-2.15)
Low support - female partner	21 (5.6)	10 (5.2)	7 (6.5)	0.99 (0.28-3.52)	4 (5.1)	1.00 (0.27-3.72)
Recommendations to tackle client reluctance						
Expand client education	367 (97.4)	189 (97.4)	101 (97.1)	0.78 (0.11-5.68)	77 (97.5)	1.39 (0.19-10.42)
Create youth-friendly health corners	135 (35.8)	76 (39.2)	35 (33.7)	**0.43* (0.21-0.84)**	24 (30.4)	**0.42* (0.22-0.82)**
Involve partners	109 (28.9)	67 (34.5)	26 (25.0)	0.56 (0.29-1.08)	16 (20.3)	**0.46* (0.24-0.91)**
Staff training	75 (19.9)	45 (23.2)	19 (18.3)	**0.46* (0.21-0.99)**	11 (13.9)	**0.43* (0.20-0.95)**
Improve HCW-patient relationship	63 (16.7)	33 (17.0)	17 (16.4)	0.84 (0.39-1.84)	13 (16.5)	0.77 (0.36-1.65)
Improve stock availability	57 (15.1)	34 (17.5)	15 (14.4)	0.56 (0.23-1.33)	8 (10.1)	0.48 (0.20-1.15)
Empower people economically	51 (13.5)	18 (9.3)	22 (21.2)	1.70 (0.69-4.18)	11 (13.9)	1.24 (0.52-2.96)
Reduce costs for patients	36 (9.6)	5 (2.6)	23 (22.1)	**6.97** (2.20-22.07)**	8 (10.1)	**3.47* (1.04-11.56)**
Provide free FP services	32 (8.5)	9 (4.6)	11 (10.6)	1.95 (0.66-5.77)	12 (15.2)	**3.19* (1.18-8.60)**

CI = confidence interval; FP = family planning; HCW = healthcare worker; HF = health facility; OR = odds ratio; SRH = sexual and reproductive health.

[a]The model was corrected for country, location, and level of care of the health facility.

* p<0.05, ** p<0.01, *** p<0.001

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the situation, from the perspective of HCWs. It found that some significant differences existed in perspectives of HCWs across the different sectors, even though in general many barriers were cross-cutting. One of the most commonly raised barriers to accessing SRH services was patient lack of knowledge. Issues with supply of commodities and frequent stockouts were often raised in the public sector. Patient costs were a significant barrier in the private and PNFP sectors, and religious and cultural beliefs were commonly mentioned in the PNFP sector. HCWs in all sectors mentioned delay in delivery of supplies as main reason for stockouts, with affordability of commodities being a significant problem in the private and PNFP sectors. Further, HCWs believed that clients were often reluctant to access SRH services, caused by fear of stigmatisation, their lack of knowledge, myths and superstitions, religious beliefs, and fear of side effects. Main recommendations to improve access were similar across the sectors and in line with the raised barriers.

Patient lack of knowledge about SRH and SRH services, raised as a main challenge by HCWs across the sectors, is an often-raised barrier to accessing SRH services (24–27). Related to this, HCWs believed that clients' reluctance to access SRH services was caused for a large part by their lack of knowledge, as well as myths or superstitions, and fear of side effects. Again, this has been well-documented elsewhere, and has been perceived by both HCWs and clients themselves as barriers (14,25,27–29). Thus, more should be done to improve clients' knowledge about SRH services and commodities, including on offered services, on how to properly use certain commodities (e.g. condoms), and on true side effects of commodities (e.g. the birth control pill). This because many misunderstandings persist, including that contraceptives cause infertility (14,28,29). However, research has shown that only tackling client knowledge may only have a limited effect on health-seeking behaviour (24,25). A multi-pronged approach is thus needed, tackling the other factors which also influence access to SRH services.

For instance, religious and cultural beliefs were also seen as one of the key challenges to accessing SRH services. Especially in the PNFP sector, which in these countries constitutes for the most part faith-based facilities, it seemed to negatively impact access. HCWs in this sector who indicated they were at times unable to provide clients with SRH services gave as most common reasons that the service was not culturally or religiously acceptable and that the health facility did not offer family planning services. These arguments were both much less relevant across the other sectors.

Research has shown that adolescents saw unsupportive attitudes from HCWs as a major barrier to access to SRH services. In contrast, the HCWs themselves did not think their attitudes interfered with the use of services among adolescents (26). In other studies, however, HCWs did recognise that HCWs' negative attitudes impacted access (19,30). Previous research has shown that some HCWs might be reluctant to provide family planning services because

they believe the use of any type of contraceptive is inappropriate, especially to adolescents or unmarried women and girls (14,18,19). Our study found that HCWs who work at PNFP sector facilities acknowledge that religious beliefs form a barrier to access to SRH services. Many Catholic health facilities in the four countries also do not provide contraceptives, with the exception of condoms, which forms a significant issue for those dependent on these facilities for their healthcare services (31,32). HCWs, especially those in PNFP sector facilities, are an important group to target for continuous education. Improvements in their knowledge and attitudes will improve access to services (33). Secondly, engaging them in campaigns with civil society and communities to fulfil a more activist role can be a powerful tool to improve access (34).

Next to knowledge and attitudinal barriers, this study also highlighted the high costs of care to patients in the private and PNFP sectors. This finding is not surprising, as out-of-pocket health expenditure in the countries ranges from 10% of all health expenditure in Zambia, to 38% of all health expenditure in Uganda (35). In sub-Saharan Africa, many countries are focusing on attaining universal health coverage (UHC). They often establish public-private partnerships (PPPs), through which the government collaborates with the private sector to provide health services (36). As part of these PPPs, countries are implementing prepayment health financing schemes such as social insurance or national health insurance (NHI). Members of such schemes pay a fee which allows them to access care at private facilities for 'free', with private facilities reimbursed for the care provided (37). However, rollout of NHI schemes differs across the four countries. About 15% and 30% of Kenya's and Tanzania's population is covered by such a scheme, while in Zambia, as of October 2021, only 191 of 1956 registered health facilities had been accredited. Uganda has no NHI in existence yet (8,38–41).

PPPs and NHI can be useful tools to reduce costs for clients and improve access to medicines when it is functioning well and has a high population coverage (42–44). However, at the moment many bottlenecks exist in the two study countries where NHI has been implemented for a longer time that limit its potential. Premiums paid by the insured are unaffordable to parts of the population, stockouts or lack of commodities at facilities force clients to buy out-of-pocket at non-accredited facilities, shortages of HCWs affect quality of services, a pro-urban distribution of health facilities results in clients needing to travel long distances to accredited facilities in rural areas, and delays in provider reimbursement by the NHI scheme result in co-payments by clients, denial or limiting of services, and long waiting times (39,40,45,46). To fulfil its potential, governments ought to focus on tackling these bottlenecks.

Logistical problems were also raised by the HCWs as causing significant challenges. These included issues with supply to the facility as well as stockouts, which were said to be caused by delays in deliveries, incorrect orders and deliveries, and problems with the stock at

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the medical stores. Problems with stockouts have also been identified previously in the four countries (14,18,20,47). Strengthening the supply chain systems should be one of the main priorities of the countries' governments. Stockouts can be prevented, or at least minimised, with a well-functioning logistic management information system, staff trained in supply chain management, and sufficient budget allocations to commodity procurement (48).

It is important to note that not only barriers at the provider or supply chain level influence commodity availability and stockouts; they are also influenced by global forces. For instance, sufficient budget allocations to commodity procurement are dependent on the health budget available. These budgets are still dependent on donor funding, making them vulnerable to the whims of donors, and challenging sustainable programme implementation (49–52). This is especially the case as over the past years, the countries have seen a decrease in this type of funding (49–52). In Kenya, for example, donor funding made up 33% of the health budget in financial year 2017/18, which decreased to 16% in financial year 2019/20 (53). Even though the government has increased their own spending on the health budget, it has been inadequate to offset the decrease in donor aid (53). Further, the global gag rule re-instated and expanded during President Trump's presidency had far-reaching consequences on access to SRH services far beyond abortion care. In Uganda, for instance, organisations that had lost funding due to the global gag rule were forced to scale down or close down community sensitisation programmes on family planning, outreach services focusing on long-term contraceptives, and health facility collaborations on family planning with community health workers (54). Another organisation had to shut one of their health facilities due to the lost funding (54). Last, preferences of international development organisations and donors also impact the availability of commodities. The female condom, for example, invented in 1984, has for decades been met with scepticism and neglect by international development organisations and donors. They referenced a lack of user demand and high prices, resulting in lack of rollout at the national level and subsequent low availability (55). To offset the impact of global forces and decrease the dependency on donor aid, and ensure sustainable and improved access to SRH services, the governments ought to increasingly and continuously invest in their health systems.

Strengths and limitations

This study provides quantitative insights into commonalities and differences of the barriers to accessing SRH services across public, private and PNFP sector health facilities in four sub-Saharan African countries. This type of study was selected as it is a proven manner to investigate beliefs and opinions of specific target groups within a limited amount of time, with high representativeness. Although these types of surveys may be prone to socially acceptable answers, we have no indication that this was the case in our study when looking at the results. Further, data collectors were experienced in conducting this type of research and were trained on how to make participants feel safe and comfortable, how to ask questions

in an open-ended manner, and how to guarantee the participants' privacy. A limitation is that we used the experiences of HCWs providing SRH services to identify barriers on both the supply- and demand side. However, they do not have full insights into the barriers as experienced by those seeking SRH services. Therefore, demand side barriers provided here should be considered in that light and not as a complete picture of all barriers clients might experience when accessing SRH services. It is also possible that HCWs might not have been as reflective about their health facilities or colleagues' shortcomings as clients might have been. Further, logistic regressions were performed to correct for influences of variables such as country, location of health facility and level of health facility, with relatively wide 95% CIs. Less value should therefore be given to the exact ORs and focus should instead be put on the directions of the found associations.

CONCLUSION

This study showed that HCWs experienced both demand and supply side barriers across the public, private and PNFP sectors, with some sector-specific, but mostly cross-cutting barriers. To improve access to SRH services across the sectors in the four countries, a multipronged approach is needed, targeting these barriers on both the supply- and demand side. Efforts should focus on improving knowledge through client education, HCW sensitisation and education regarding unhelpful religious and cultural beliefs, improving supply chain systems through strengthening logistic management information systems, training staff in supply chain management, and allocating sufficient budget to commodity procurement. Last, unaffordability in the private and PNFP sectors can be tackled through a well-functioning NHI scheme.

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CONTRIBUTION STATEMENT

GIO and TR designed the study. GIO, DO and JvO collected the data. GIO analysed the data and wrote the manuscript. All co-authors provided input for the analysis and data interpretation, and critically reviewed the manuscript. GIO revised the manuscript based on the co-authors' feedback.

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SUPPLEMENTARY DATA

Supplementary File 1. Healthcare worker survey.

1. **In your opinion, which of the following categories of Sexual and Reproductive Health (SRH), and Mother and Child Health services (MCH) faces the most challenges related to access to commodities?**
   (Choose only one option)
   o   Family Planning
   o   Maternal Health
   o   STI Management
   o   Child Health

2. **Based on the first question, what do you think are the key challenges related to accessing these essential SRH and MCH commodities?**
   Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.
   o   There is no demand for the commodities
   o   Issues or delays with supply of the commodities to the facility
   o   Frequent stock-outs at facility level
   o   Frequent stock-outs at central level
   o   Shortage of staff
   o   Training of staff
   o   Costs of medicines to patients
   o   Lack of knowledge of patients about SRH services/commodities available
   o   Religious or cultural beliefs
   o   Perceived stigma associated with accessing the commodities
   o   Health professionals' reluctance to provide certain client groups with commodities or services (because of age, marital status, religion etc.)
   o   Drugs are not supplied as per the supply cycle
   o   Other (specify on next page)

2a. **Other:**_____

3. **In your opinion, what are the causes of stock-outs of SRH and MCH commodities at your facility?**
   Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.
   o   What is ordered is not what the facility received
   o   Delay in supplies being delivered
   o   Poor stock management at the facility
   o   Lack of storage space at the facility

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- o   Problems with the transport of the medicines to the facility
- o   Problems with the stock at the central/ distribution level
- o   Affordability of the medicines for the facility
- o   Demand is higher than the supplied medicines
- o   Other (specify on next page)

3a. Other:_____

4.   What can be done to improve access to SRH and MCH commodities and services on the supply side (e.g. healthcare workers, health facilities, suppliers, the health system and the government)?
Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.

- o   Improve supply chain
- o   Timely supply of the commodities
- o   Supply commodities that have been ordered
- o   Ensure availability of commodities at the facility
- o   Improve stock management (ordering and reporting) at the facility
- o   Increase staff
- o   (Continued) staff training
- o   Reduce costs
- o   Provide greater choice of SRHC
- o   Improve infrastructure
- o   Increase budget for SRH
- o   More supervision from central level
- o   Other (specify on next page)

4a. Other:_____

5.   What can be done to improve access to SRH and MCH commodities and services on the demand side (e.g. the client and community)?
Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.
- o   Client and community education
- o   Reduce costs
- o   Increase male partner involvement
- o   Professional healthcare worker – patient relationship
- o   Offer/improve outreach SRH services
- o   Increase choice of contraceptives

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    o   Ensure enough stocks are available at the facility

    o   Other (specify on next page)

5a. Other:_____

6.   Do you think clients are reluctant to access sexual and reproductive health commodities?

    o   Yes

    o   No

7.   If you answered 'Yes', please explain why you think clients are reluctant to access/ request SRHC.

Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.

    o   Fear for stigmatization from family members or the community

    o   Myths or superstition

    o   Religious beliefs

    o   Fear of side effects

    o   Low support from male partners

    o   Low support from female partners

    o   Patient lack of knowledge

    o   Poverty/ costs

    o   Distance to clinic

    o   Frequent stock-outs at the facility

    o   Unprofessional healthcare workers

    o   Other (specify on next page)

7a. Other:_____

8.   How could this reluctance be tackled?

Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.

    o   Expand client education for ALL (male and female)

    o   Empower people economically

    o   Create youth/adolescent friendly health corners

    o   Involve partners in SRH services

    o   Improve stock availability

    o   Improve/create professional healthcare worker – patient relationships

    o   Training of staff to improve quality of services

    o   Provide free family planning services

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    o   Reduce costs for patients

    o   Other (specify on next page)

8b. Other:_____

9. Are there ever clients that come to your health facility whom you cannot provide with the services or commodities they request?

    o   Yes

    o   No

10. If yes, please specify why you cannot provide these clients with sexual and reproductive health services or commodities.

Do not read. Listen to their answer and choose all that apply. If other answer options are given than those below, choose 'other' and note it on the next page.

    o   The client was too young

    o   The client was unmarried

    o   The client was unable to pay for the services

    o   The client did not have health insurance

    o   We do not offer family planning services

    o   I do not believe that the service/commodity would benefit the client

    o   The service requested by the client is not culturally or religiously acceptable

    o   The SRH commodity was stocked out

    o   Lack of knowledge about the service by the HCW

    o   Other (specify on next page)

10b. Other:_____

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Supplementary File 2. HCWs perspectives on access to SRH barriers and recommendations for improvement, per sector. Crude and adjusted models.

	Overall N (%)	Public N (%)	Private N (%)
Key challenges to accessing SRHC			
Patient lack of knowledge on SRH	354 (37.1)	203 (38.8)	91 (37.0)
Issues with supply to HF	320 (33.5)	222 (42.5)	56 (22.8)
Frequent stockouts at HF	282 (29.6)	188 (36.0)	49 (19.9)
Religious/cultural beliefs	272 (28.5)	142 (27.2)	47 (19.1)
Stigma	207 (21.7)	113 (21.6)	56 (22.8)
Staff shortages	182 (19.1)	144 (27.5)	18 (7.3)
Staff training on SRH services	148 (15.5)	101 (19.3)	24 (9.8)
Patient costs	145 (15.2)	24 (4.6)	82 (33.3)
No demand	102 (10.7)	40 (7.7)	45 (18.3)
Frequent stockouts at central level	102 (10.7)	71 (13.6)	23 (9.4)
SRHC stockout causes			
Delay in supply delivery	471 (54.1)	320 (63.9)	83 (37.4)
What is ordered is not what HF received	295 (33.9)	226 (45.1)	37 (16.7)
Problems with stock at distribution level	264 (30.3)	170 (33.9)	61 (27.5)
Demand higher than availability	185 (21.2)	120 (24.0)	37 (16.7)
Affordability for HF	138 (15.8)	33 (6.6)	67 (30.2)
Poor stock management at HF	128 (14.7)	63 (12.6)	34 (15.3)
Lack of storage space at HF	80 (9.2)	58 (11.6)	14 (6.3)
Problems with medicine transport to HF	71 (8.2)	51 (10.2)	10 (4.5)
Recommendations for improvement – supply side			
Improve supply chain	523 (55.6)	346 (66.4)	104 (43.2)
Timely supply of SRHC	430 (45.7)	274 (52.6)	84 (34.9)
Prevent stock-outs of SRHC at HF	326 (34.7)	192 (36.9)	80 (33.2)
Ensure sufficient stock available at HF	275 (28.7)	180 (34.2)	56 (22.6)
Supply SRHC that were ordered	247 (26.3)	179 (34.4)	46 (19.1)
(Continued) staff training	216 (23.0)	140 (26.9)	42 (17.4)
Increase staff	203 (21.6)	143 (27.5)	30 (12.5)
Increase budget for SRHC	176 (18.7)	112 (21.5)	33 (13.7)
Provide greater choice of SRHC	147 (15.6)	71 (13.6)	49 (20.3)
Recommendations for improvement – demand side			
Client and community education	778 (81.1)	437 (82.9)	194 (78.2)
Increase male partner involvement	357 (37.2)	222 (42.1)	82 (33.1)
Offer/improve SRH outreach services	280 (29.2)	164 (31.1)	62 (25.0)
Increase choice of contraceptives	222 (23.2)	129 (24.5)	59 (23.8)
Professionalise HCW-patient relationship	173 (18.0)	102 (19.4)	49 (19.8)
Reduce costs for clients	202 (21.0)	38 (7.2)	113 (45.2)
HF at times unable to provide client with SRHC and services			
Yes	359 (37.0)	155 (29.2)	123 (49.0)
Reasons why unable to provide client with SRHC and services			
SRHC was stocked out	131 (37.3)	84 (56.4)	35 (28.2)

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OR (95% CI)		PNFP	OR (95% CI)	
Model 1	Model 2ᵃ	N (%)	Model 1	Model 2 ᵃ
0.93 (0.68-1.27)	0.99 (0.69-1.42)	60 (32.4)	0.76 (0.53-1.08)	0.75 (0.52-1.09)
0.40*** (0.28-0.56)	**0.40*** (0.27-0.59)**	42 (22.7)	**0.45*** (0.30-0.66)**	**0.44*** (0.29-0.65)**
0.44*** (0.31-0.64)	**0.47*** (0.31-0.72)**	45 (24.3)	**0.57** (0.39-0.84)**	**0.57** (0.38-0.85)**
0.63* (0.44-0.92)	0.75 (0.50-1.15)	83 (44.9)	**2.18*** (1.54-3.09)**	**2.46*** (1.69-3.56)**
1.07 (0.74-1.54)	0.97 (0.63-1.48)	38 (20.5)	0.94 (0.62-1.42)	0.75 (0.49-1.16)
0.21*** (0.12-0.35)	**0.26*** (0.15-0.46)**	20 (10.8)	**0.32*** (0.19-0.53)**	**0.34*** (0.21-0.57)**
0.45** (0.28-0.73)	**0.49** (0.28-0.83)**	23 (12.4)	**0.59* (0.36-0.97)**	0.61 (0.37-1.01)
10.4*** (6.38-16.93)	**6.83*** (3.98-11.70)**	39 (21.1)	**5.55*** (3.23-9.54)**	**4.58*** (2.61-8.03)**
2.70*** (1.71-4.27)	1.30 (0.74-2.28)	17 (9.2)	1.22 (0.67-2.21)	1.02 (0.55-1.91)
0.66 (0.40-1.08)	0.70 (0.39-1.25)	8 (4.3)	**0.29*** (0.14-0.61)**	**0.35** (0.16-0.75)**
0.34*** (0.24-0.47)	**0.36 (0.24-0.54)*****	68 (46.0)	**0.48*** (0.33-0.70)**	**0.52** (0.34-0.77)**
0.24*** (0.16-0.36)	**0.31 (0.20-0.49)*****	32 (21.6)	**0.34*** (0.22-0.52)**	**0.35*** (0.22-0.54)**
0.74 (0.52-1.04)	0.94 (0.62-1.41)	33 (22.3)	**0.56** (0.36-0.86)**	**0.61* (0.39-0.95)**
0.64* (0.42-0.96)	**0.49** (0.31-0.81)**	28 (18.9)	0.74 (0.47-1.17)	0.76 (0.47-1.23)
6.13*** (3.89-9.66)	**5.59*** (3.27-9.53)**	38 (25.7)	**4.90*** (2.94-8.16)**	**4.82*** (2.79-8.34)**
1.26 (0.80-1.97)	1.37 (0.81-2.32)	31 (21.0)	**1.84* (1.14-2.96)**	**1.84* (1.11-3.04)**
0.51* (0.28-0.94)	0.54 (0.28-1.08)	8 (5.4)	**0.44* (0.20-0.94)**	0.48 (0.21-1.07)
0.42* (0.21-0.84)	0.49 (0.22-1.08)	10 (6.8)	0.64 (0.32-1.29)	0.67 (0.32-1.39)
0.38*** (0.28-0.53)	**0.40*** (0.27-0.57)**	73 (41.0)	**0.35*** (0.25-0.50)**	**0.38*** (0.27-0.56)**
0.48*** (0.35-0.66)	**0.48*** (0.33-0.70)**	72 (40.5)	**0.61** (0.43-0.86)**	**0.61** (0.42-0.87)**
0.85 (0.62-1.17)	1.04 (0.71-1.50)	54 (30.3)	0.75 (0.52-1.08)	0.75 (0.51-1.10)
0.56** (0.40-0.80)	**0.65* (0.44-0.97)**	39 (21.2)	**0.52** (0.35-0.77)**	**0.57** (0.38-0.85)**
0.45*** (0.31-0.65)	**0.56** (0.37-0.86)**	22 (12.4)	**0.27*** (0.17-0.44)**	**0.28*** (0.17-0.46)**
0.57** (0.39-0.84)	**0.63* (0.41-0.97)**	34 (19.1)	**0.64* (0.42-0.98)**	0.66 (0.43-1.03)
0.38*** (0.24-0.58)	**0.51** (0.32-0.82)**	30 (16.9)	**0.54** (0.35-0.83)**	**0.57* (0.36-0.90)**
0.58* (0.38-0.88)	**0.50** (0.30-0.81)**	31 (17.4)	0.77 (0.50-1.20)	0.76 (0.48-1.20)
1.62* (1.08-2.42)	**1.60* (1.00-2.55)**	27 (15.2)	1.13 (0.70-1.83)	1.05 (0.63-1.73)
0.74 (0.51-1.08)	0.77 (0.50-1.20)	147 (79.9)	0.82 (0.53-1.25)	0.89 (0.57-1.39)
0.68* (0.50-0.93)	0.82 (0.57-1.18)	53 (28.8)	**0.56** (0.39-0.80)**	**0.57** (0.39-0.83)**
0.74 (0.52-1.04)	0.77 (0.52-1.14)	54 (29.4)	0.92 (0.64-1.33)	0.86 (0.58-1.26)
0.96 (0.68-1.37)	0.76 (0.50-1.16)	34 (18.5)	0.70 (0.46-1.07)	0.76 (0.49-1.18)
1.03 (0.70-1.50)	0.88 (0.56-1.36)	22 (12.0)	**0.57* (0.34-0.93)**	**0.43** (0.26-0.73)**
10.68*** (7.06-16.15)	**7.60*** (4.79-12.04)**	51 (27.7)	**5.00*** (3.13-7.88)**	**4.10*** (2.53-6.63)**
2.33*** (1.71-3.18)	**1.57* (1.09-2.26)**	81 (42.9)	**1.82** (1.29-2.57)**	**1.47* (1.02-2.12)**
0.31*** (0.18-0.51)	**0.30*** (0.16-0.56)**	12 (15.4)	**0.14*** (0.07-0.28)**	**0.11*** (0.07-0.28)**

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Supplementary File 2. (continued)

	Overall N (%)	Public N (%)	Private N (%)
HF does not offer FP services	65 (18.6)	13 (8.8)	24 (19.5)
Client unable to pay for service	60 (17.2)	4 (2.7)	44 (35.8)
Client was too young	58 (16.6)	19 (12.8)	26 (21.1)
Service not culturally or religiously acceptable	56 (16.1)	13 (8.7)	5 (4.1)
Service would not benefit client	25 (7.2)	11 (7.4)	9 (7.3)
Lack of HCW knowledge	23 (6.6)	16 (10.7)	5 (4.0)
Client was unmarried	17 (4.9)	6 (4.1)	4 (3.3)
Clients reluctant to access SRH services			
Yes	381 (39.3)	195 (36.7)	108 (43.0)
Reasons for reluctance to access SRH services			
Fear of stigmatisation	238 (63.0)	115 (59.6)	70 (65.4)
Patient lack of knowledge	189 (50.0)	100 (51.8)	57 (53.3)
Myths or superstitions	169 (44.7)	95 (49.2)	43 (40.2)
Religious beliefs	148 (39.2)	84 (43.5)	33 (30.8)
Fear of side effects	146 (38.6)	71 (36.8)	46 (43.0)
Low support - male partner	78 (20.6)	49 (25.4)	20 (18.7)
Poverty/costs	48 (12.7)	13 (6.7)	20 (18.7)
Frequent stock-outs at HF	32 (8.5)	23 (11.9)	4 (3.7)
Distance to HF	28 (7.4)	18 (9.3)	5 (4.7)
Low support - female partner	21 (5.6)	10 (5.2)	7 (6.5)
Recommendations to tackle client reluctance			
Expand client education	367 (97.4)	189 (97.4)	101 (97.1)
Create youth-friendly health corners	135 (35.8)	76 (39.2)	35 (33.7)
Involve partners	109 (28.9)	67 (34.5)	26 (25.0)
Staff training	75 (19.9)	45 (23.2)	19 (18.3)
Improve HCW-patient relationship	63 (16.7)	33 (17.0)	17 (16.4)
Improve stock availability	57 (15.1)	34 (17.5)	15 (14.4)
Empower people economically	51 (13.5)	18 (9.3)	22 (21.2)
Reduce costs for patients	36 (9.6)	5 (2.6)	23 (22.1)
Provide free FP services	32 (8.5)	9 (4.6)	11 (10.6)

CI = confidence interval; FP = family planning; HCW = healthcare worker; HF = health facility; OR = odds ratio;

SRH = sexual and reproductive health; SRHC = sexual and reproductive health commodities.

[a]The model was corrected for country, location, and level of care of the health facility.

* p<0.05, ** p<0.01, *** p<0.001

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OR (95% CI)		PNFP	OR (95% CI)	
Model 1	Model 2[a]	N (%)	Model 1	Model 2 [a]
2.52* (1.22-5.19)	1.88 (0.82-4.30)	28 (35.9)	**5.82*** (2.79-12.11)**	**6.38*** (2.97-13.72)**
20.05* (6.95-57.86)**	**15.13*** (4.85-47.18)**	12 (15.4)	**6.55** (2.03-21.06)**	**6.88** (2.08-22.70)**
1.82 (0.95-3.48)	1.72 (0.78-3.83)	13 (16.7)	1.36 (0.63-2.92)	1.15 (0.51-2.60)
0.44 (0.15-1.28)	0.42 (0.13-1.37)	38 (49.4)	**10.19*** (4.94-21.01)**	**12.65*** (5.75-27.81)**
0.98 (0.39-2.46)	1.26 (0.42-3.81)	5 (6.4)	0.85 (0.29-2.55)	0.60 (0.19-1.90)
0.35* (0.12-0.98)	0.53 (0.16-1.74)	2 (2.6)	**0.22* (0.05-0.98)**	**0.22* (0.05-0.99)**
0.80 (0.22-2.89)	0.59 (0.13-2.64)	7 (9.0)	2.33 (0.76-7.20)	1.63 (0.49-5.45)
1.30 (0.96-1.77)	1.03 (0.72-1.49)	78 (41.5)	1.22 (0.87-1.72)	0.92 (0.64-1.31)
1.28 (0.79-2.10)	0.69 (0.36-1.32)	53 (68.0)	1.44 (0.82-2.51)	0.83 (0.44-1.58)
1.06 (0.66-1.70)	0.96 (0.53-1.73)	32 (41.0)	0.65 (0.38-1.10)	0.64 (0.36-1.15)
0.69 (0.43-1.12)	0.86 (0.48-1.56)	31 (39.7)	0.68 (0.40-1.16)	0.83 (0.47-1.48)
0.58* (0.35-0.95)	0.89 (0.47-1.67)	31 (39.7)	0.86 (0.50-1.46)	1.40 (0.76-2.59)
1.30 (0.80-2.10)	1.45 (0.78-2.68)	29 (37.2)	1.02 (0.59-1.75)	0.88 (0.48-1.62)
0.68 (0.38-1.21)	0.64 (0.31-1.33)	9 (11.5)	**0.38* (0.18-0.83)**	**0.43* (0.19-0.97)**
3.18 (1.51-6.97)**	2.14 (0.85-5.38)	15 (19.2)	**3.30 (1.49-7.31)****	**2.46 (1.05-5.73)***
0.29* (0.10-0.85)	0.31 (0.08-1.19)	5 (6.4)	0.51 (0.19-1.38)	0.58 (0.20-1.73)
0.48 (0.17-1.32)	1.24 (0.34-4.50)	5 (6.4)	0.67 (0.24-1.86)	0.68 (0.21-2.15)
1.28 (0.47-3.47)	0.99 (0.28-3.52)	4 (5.1)	0.99 (0.30-3.25)	1.00 (0.27-3.72)
0.89 (0.21-3.80)	0.78 (0.11-5.68)	77 (97.5)	1.02 (0.19-5.36)	1.39 (0.19-10.42)
0.79 (0.48-1.30)	**0.43* (0.21-0.84)**	24 (30.4)	0.68 (0.39-1.19)	**0.42* (0.22-0.82)**
0.63 (0.37-1.08)	0.56 (0.29-1.08)	16 (20.3)	**0.48* (0.26-0.90)**	**0.46* (0.24-0.91)**
0.74 (0.41-1.35)	**0.46* (0.21-0.99)**	11 (13.9)	0.54 (0.26-1.10)	**0.43* (0.20-0.95)**
0.95 (0.50-1.81)	0.84 (0.39-1.84)	13 (16.5)	0.96 (0.48-1.94)	0.77 (0.36-1.65)
0.79 (0.41-1.54)	0.56 (0.23-1.33)	8 (10.1)	0.53 (0.23-1.20)	0.48 (0.20-1.15)
2.62 (1.33-5.16)**	1.70 (0.69-4.18)	11 (13.9)	1.58 (0.71-3.52)	1.24 (0.52-2.96)
10.73* (3.94-29.22)**	**6.97** (2.20-22.07)**	8 (10.1)	**4.26* (1.35-13.45)**	**3.47* (1.04-11.56)**
2.43 (0.97-6.07)	1.95 (0.66-5.77)	12 (15.2)	**3.68** (1.48-9.13)**	**3.19* (1.18-8.60)**

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Supplementary File 3. HCWs perspectives on access to SRH barriers and recommendations for improvement, per country. Numbers represent percentage of HCWs that mentioned this barrier or recommendation.

	Kenya (%)	Tanzania (%)	Uganda (%)	Zambia (%)
Key challenges to accessing SRHC				
Patient lack of knowledge on SRH	42.7	42.1	32.4	27.2
Issues with supply to HF	26.5	41.5	25.4	32.3
Frequent stockouts at HF	23.2	32.0	32.4	29.8
Religious/cultural beliefs	33.2	33.1	15.5	25.1
Stigma	33.2	16.1	22.5	19.6
Staff shortages	12.3	26.0	15.5	16.6
Staff training on SRH services	12.3	17.5	14.1	16.2
Patient costs	21.3	8.5	29.6	11.5
No demand	14.2	5.7	14.1	13.2
Frequent stockouts at central level	7.1	14.2	4.2	12.3
SRHC stockout causes				
Delay in supply delivery	62.1	65.5	16.7	50.4
What is ordered is not what HF received	29.0	41.1	22.5	33.3
Problems with stock at distribution level	29.5	34.5	15.0	32.9
Demand higher than availability	12.1	21.9	25.0	25.9
Affordability for HF	21.1	12.9	33.3	6.6
Poor stock management at HF	13.7	15.0	27.5	8.3
Lack of storage space at HF	3.7	15.3	11.7	3.5
Problems with medicine transport to HF	7.4	8.4	5.8	9.7
Recommendations for improvement – supply side				
Improve supply chain	51.2	61.1	28.2	66.8
Timely supply of SRHC	56.6	50.4	28.2	39.2
Prevent stock-outs of SRHC at HF	30.2	40.3	43.0	25.1
Ensure sufficient stock available at HF	28.1	35.0	14.8	27.8
Supply SRHC that were ordered	25.9	32.9	11.1	25.1
(Continued) staff training	25.4	30.1	14.8	14.5
Increase staff	15.6	30.1	14.8	17.5
Increase budget for SRHC	19.5	18.9	12.6	21.3
Provide greater choice of SRHC	23.9	14.8	9.6	13.2
Recommendations for improvement – demand side				
Client and community education	82.4	85.3	76.1	76.8
Increase male partner involvement	34.8	43.2	30.3	34.4
Offer/improve SRH outreach services	37.1	33.6	25.4	17.8
Increase choice of contraceptives	21.0	22.1	14.1	32.0
Professionalise HCW-patient relationship	25.2	15.6	24.7	11.6
Reduce costs for clients	31.9	12.5	37.8	14.5
HF at times unable to provide client with SRHC and services				
Yes	52.8	24.5	51.7	33.3
Reasons why unable to provide client with SRHC and services				
SRHC was stocked out	22.7	57.1	41.9	47.4

4.3

Supplementary File 3. (continued)

	Kenya (%)	Tanzania (%)	Uganda (%)	Zambia (%)
HF does not offer FP services	22.7	19.1	17.6	13.2
Client unable to pay for service	19.1	6.7	21.6	22.4
Client was too young	30.9	11.2	8.1	10.5
Service not culturally or religiously acceptable	12.7	19.1	14.9	5.3
Service would not benefit client	14.6	5.6	2.7	2.6
Lack of HCW knowledge	2.7	8.8	9.5	6.6
Client was unmarried	10.0	0.0	5.4	2.6
Clients reluctant to access SRH services				
Yes	54.3	28.6	55.2	33.1
Reasons for reluctance to access SRH services				
Fear of stigmatisation	83.5	45.7	65.8	53.2
Patient lack of knowledge	52.2	55.2	46.8	43.0
Myths or superstitions	46.1	55.3	34.2	39.2
Religious beliefs	46.1	57.1	16.5	27.9
Fear of side effects	53.0	32.4	36.7	27.9
Low support - male partner	24.4	27.6	13.9	12.7
Poverty/costs	17.4	3.8	15.2	15.2
Frequent stock-outs at HF	9.6	11.4	2.5	8.9
Distance to HF	2.6	7.6	5.1	16.5
Low support - female partner	9.6	4.8	1.3	5.1
Recommendations to tackle client reluctance				
Expand client education	99.1	97.1	92.5	100.0
Create youth-friendly health corners	60.9	23.8	22.5	28.6
Involve partners	36.5	32.4	17.5	24.7
Staff training	33.0	18.1	8.8	14.3
Improve HCW-patient relationship	26.1	14.3	15.0	7.8
Improve stock availability	20.9	13.3	10.0	14.3
Empower people economically	20.9	5.7	12.5	14.3
Reduce costs for patients	15.7	2.9	8.8	10.4
Provide free FP services	18.3	3.8	3.8	5.2

4.3

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GENERAL DISCUSSION

"The way we work in public health is, we make the best recommendations and decisions based on the best available data."

– Tom Frieden

BACKGROUND

The right to the highest attainable standard of health is a human right recognised internationally in many treaties and conventions, such as the Universal Declaration of Human Rights, the International Covenant on Economic, Social and Cultural Rights, and the African Charter on Human Rights and Peoples' Rights, amongst other (1–3). In striving for the attainment of the right to health, access to medicines has been identified as a cornerstone (4–6). Nevertheless, both access to medicines and the subsequent realisation of the highest attainable standard of health have not been met for a significant proportion of the global population. Coverage by essential health services in low-income countries is as low as 12% to 27%, while 2 billion people worldwide are facing catastrophic or impoverishing health expenditure (7). This applies particularly to those living in regions such as Sub-Saharan Africa where many barriers to accessing medicines and health services exist, and people suffer due to a lack of proper care (8–14). Universal health services coverage (UHC) in this region is 44%, the maternal mortality rate stands at 534 per 100,000 live births, and there are only 0.6 pharmacists per 10,000 population and 0.2 physicians per 100,000 population (15,16).

The price, availability and affordability of medicines have been extensively studied in the past two decades using the World Health Organization/Health Action International (WHO/HAI) methodology 'Measuring medicine prices, availability, affordability and price components' (17). However, access to medicines and health services is not only a result of the availability and affordability of the medicines itself; there are a multitude of factors that impact their accessibility. With this in mind, Bigdeli et al. (2013) developed a framework, classifying barriers to access to medicines at five levels along the health system continuum: individuals, households and the community; service delivery; the health sector; and the national and international level (18).

To gain a deeper understanding of how barriers at the different levels of the health system influence access in Sub-Saharan Africa, and what lessons might be learned, this thesis focussed on three distinct cases: internationally controlled essential medicines (ICEMs), the treatment of snakebite envenoming, and sexual and reproductive health (SRH). These cases were chosen due to their controversial nature or neglect by the international community. They are used to illustrate the complexity of access to essential medicines in the region. This concluding chapter brings together the main findings of the research and places them in a single, broad framework. The question 'What are the commonalities and differences in access to essential medicines and services between these cases?' is answered. We reflect on what lessons might be learned from this research to improve access to essential medicines and discuss key policy recommendations to improve access in Sub-Saharan Africa. Last, used methodologies are discussed and opportunities for future research are suggested.

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ACCESS TO ESSENTIAL MEDICINES THROUGH THE LENS OF ICEMS, TREATMENT OF SNAKEBITE ENVENOMING, AND SRH: WHAT CAN WE LEARN?

Barriers and recommendations for the individuals, households and the community level

The level of individuals, households, and the community pertains to barriers on the demand side. Factors influencing access to medicines at this level include perceived quality of medicines and health services, ability to pay for health care, ability to reach health services, and social and cultural beliefs, including stigma (18). Previous research on access to medicines and health services has identified demand-side barriers related to income, social, cultural, religious and gender characteristics, knowledge about health care, education, and perceived or low quality of available services (19,20). Similar barriers were found in this thesis.

In **Chapters 2.1** and **2.2** barriers to accessing ICEMs are described, including those experienced on the demand side. Barriers identified in these studies relate to socio-cultural beliefs and the subsequent stigma, and lack of knowledge. ICEMs are for example associated with diseases or care that are stigmatised, such as epilepsy and end-of-life care, resulting in social exclusion or fear of using these medicines. In **Chapter 3.1** demand-side barriers to accessing treatment of snakebite envenoming that were identified include traditional beliefs surrounding snakes and snakebites, and, as a consequence, the use of ineffective traditional treatments. In Kenya, for example, 42.0% of snakebite victims sought only traditional treatment or first sought traditional treatment before going to a health facility. The study in this chapter also showed that in Kenya, 10.0% of the surveyed communities believed that snakes bite because they were sent by bad spirits or by somebody to harm the victim.

Demand-side barriers for accessing SRH services identified in **Chapter 4.3** were extensive, and included lack of knowledge, stigma, and socio-cultural and religious beliefs. Across Kenya, Tanzania, Uganda and Zambia, 37.1% of surveyed healthcare workers indicated that the lack of knowledge of patients on SRH is a key challenge to access, 28.5% referred to cultural and religious beliefs as a barrier, while 21.7% also made mention of stigma associated with accessing SRH services as a barrier to access. Religious beliefs were identified particularly as a barrier in the private not-for-profit sector, which is primarily composed of faith-based health facilities in the surveyed countries. When talking about clients' reluctance to access SRH services, fear of stigmatisation (63.0%), lack of knowledge (50.0%), myths or superstitions about SRH and services (44.7%), religious beliefs (39.2%), fear of side effects (38.6%), and low support from male partners (20.6%) were all commonly raised barriers across the four countries. These barriers to accessing SRH services and commodities have also been shown in other studies (21–24).

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While barriers identified at this level are specific to each of the studied cases, such as the fear of opioids or the belief that snakes are sent by spirits to harm the victim, the underlying causes can be linked to two main over-arching constraints: lack of knowledge, and socio-cultural beliefs. Mitigation strategies should thus focus on increasing knowledge of the public on these types of care fields, and aligning sensitisation messages with socio-cultural beliefs of the target populations. Because of the case-specific context in which these constraints materialise, public sensitisation programmes need to be adapted and tailored to the unique facets of each of the cases, as well as country contexts.

When sensitisation programmes are well-tailored, they can have a positive impact. However, research into such programmes have revealed mixed results (25,26). Comprehensive sexuality education (CSE) in schools is one tool that has been proven to improve knowledge, attitudes, practices and behaviours (KAPB) of adolescents (26). However, CSE programmes are often poorly implemented, with most curricula lacking basic information about condoms and contraceptives, with the focus instead put on abstinence, while the curricula also often lack inclusion of key aspects of SRH such as reproduction, sexually transmitted infections (STIs), abortion, and how to access SRH services. Many CSE programmes also lack modules on adolescents' empowerment (26,27). Moreover, teachers can be uncomfortable talking about sexuality and SRH and are not properly trained, and as a result are reluctant to teach CSE in the classroom (26,27). A second sensitisation tool is the engagement of peer educators and counsellors to transfer knowledge on SRH, and provide information and counselling on SRH through group discussions, one-on-one meeting, presentations, and distribution of information, education and communication (IEC) materials. Peer educators have been shown to significantly improve knowledge on SRH, but not on contraceptive use (28). However, other research has shown peer education to be less effective (25). Thirdly, mass media can be used to increase knowledge on SRH. Mass media includes print, television, radio, and social media. Studies have shown that the utilisation of mass media can decrease the likelihood of teenage pregnancy, and increase adolescents' knowledge on and testing for HIV, as well as increase maternal health awareness among women (29–32). Sensitisation of the community, including of parents, faith leaders and community leaders, is also critical to increase demand and uptake of SRH services. Studies have shown that community participation programmes, such as community mobilisation or education, can be successful in increasing use of SRH services and decreasing negative attitudes (25). While these tools can be successful when properly implemented, research has also shown that interventions combining the different sensitisation approaches are most effective in increasing knowledge and demand of SRH services, and decreasing negative attitudes (25,26,33).

Fewer evaluations of community interventions for snakebite prevention and care have been undertaken, with most of the studies that have been conducted taking place in Asia (34–37). One evaluation of a community sensitisation programme in Tamil Nadu, India, showed very

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promising results. The programme comprised a combination of engagement methods; distribution of leaflets, posters and documentaries, media and social media campaigns, community education, and school assemblies, reaching over three million people in the state (35). The evaluation showed that after 12 months, more than 90% of students who had attended the school assemblies had good recall of key messages, and there was an 85% recall amongst community members who had attended community education activities (35). On top of that, a pre- and post-campaign analysis of hospital admissions for snakebite envenoming (2018 and 2019), showed that significantly more patients were admitted in 2019 (223 patients versus 291 patients), and that patients were significantly more likely to arrive to the hospitals in under four hours after the bite in 2019 (95.0%) compared to 2018 (60.5%) (35). Further, in 2019, 97.3% of patients had arrived at the hospital without seeking traditional treatment, compared to 63.7% of patients in 2018, providing strong evidence that community engagement programmes can be successful in increasing knowledge and improving health-seeking behaviour (35).

Evaluations of programmes tailored to improving public perceptions on ICEMs are primarily related to palliative care and opioids, and epilepsy. Few have been developed for opioid agonist treatment (harm reduction), anaesthesia or for mental health, such as anxiety disorders. Further, most of the studies on palliative care and opioids were conducted in high-income countries (38,39). A study in Japan evaluating a three-year awareness-raising programme on palliative care, consisting of distribution of IEC materials and public lectures, found perceptions of palliative care and opioids had improved significantly among the public (39). Stigma-reducing epilepsy campaigns consisted of similar tools as used for snakebite envenoming and SRH, and included IEC materials, documentaries, mass media campaigns, school assemblies and education, and community engagement (40). A study in Ethiopia, for instance, found that knowledge, attitudes and awareness on epilepsy significantly increased among adolescents after reading an educational comic book on epilepsy (41).

Improving the knowledge and understanding of individuals and communities on ICEMs, snakebite envenoming and SRH should therefore comprise a combination of different sensitisation approaches. Further, inclusion of community- and faith-leaders in efforts to improve uptake of SRH services is important, as they play an important role in managing socio-cultural and religious beliefs (25,42). They can also play an important role in making palliative care and the use of opioids more acceptable at the end-stages of life: research in Kenya has shown that 28% of faith leaders believed use of opioids hastens death, and 8% believed it was morally the same as killing a patient (43). Sensitising and involving them in palliative care may allow people to die more comfortably. For snakebites, involvement of traditional healers should also be considered due to the significant role they still play in the health-seeking pathway of many victims. Including traditional healers in the health-seeking pathways might reduce the delay in snakebite victims receiving proper medical care after envenomings: if they are able to provide effective and appropriate first aid, after

which they refer victims directly to health facilities, serious disability and even death could be prevented.

While sensitisation programmes have been successful to some extent in changing behaviour, research has also shown that achieving real behaviour change is dependent on three conditions: capability, opportunity and motivation (44). In this model, known as the COM-B model, capability can be physical or psychological, opportunity can be physical or social, and motivation is either reflective or automatic (44).

Changes to peoples' capability, opportunity and motivation can be achieved through nine main interventions: education, persuasion, incentivisation, coercion, training, restriction, environmental restructuring, modelling, and enablement. The key to behaviour change is the interaction between capability, opportunity, and motivation. While sensitisation programmes may cover the intervention functions of education, persuasion, training, (social) environmental restructuring and modelling to some extent, not all intervention functions are covered. Individual's opportunity and capability are dependent on an enabling environment, including the accessibility of health services.

Health service delivery: barriers and mitigation strategies

At this level of the health system, barriers to access to medicines were found on the supply side, and specifically relate to the delivery of health services. Access to medicines is impacted by their availability, affordability, accessibility, acceptability and quality, as well by health information, health financing, human resources, and health infrastructure. Further, quality and equity of services are central to good service delivery (18). While price, availability and affordability of groups of essential medicines have been extensively studied in low-, middle- and high-income countries, the price, availability and affordability of SRH commodities and those for the treatment of snakebite envenoming have not (45).

Availability, stockouts, and affordability of medicines

In **Chapters 2.3, 3.2, 4.1** and **4.2**, the availability, stockouts, and affordability of commodities for the treatment of snakebites and of SRH commodities were studied, showing access to these commodities was inadequate in the study countries. **Chapter 2.3** studied the availability of four anaesthetic agents in Rwandan hospitals. It found that only propofol had an availability of more than 80%. Ketamine almost reached the WHO threshold with 77.8% availability. The other commodities (inhalant agents and thiopental) had and availability of around 50%. **Chapter 3.2** focussed on access to commodities for the treatment of snakebite envenoming in Kenya and found overall availability of the 45 surveyed commodities was only 43.0%. Antivenom itself was available at 44.7% of public facilities, and 19.4% of private facilities. Stockouts of snakebite commodities were common, with stockouts of antivenom occurring at 20.0% of health facilities, lasting on average 13.6 days. Affordability was not

an issue in the public sector; all commodities were considered affordable when measured against the daily wage of a lowest-paid government worker (LPGW). In the private sector the median cost of one vial of antivenom cost 14.4 days of wages for an LPGW. In this chapter, the 'accessibility' of commodities was also assessed by looking at both the availability and affordability of a commodity: If a commodity was available at 80% or more of health facilities and the price was less than a day's wage for an LPGW, it was deemed accessible. Only five commodities (metronidazole, amoxicillin, paracetamol, hydrocortisone and saline) in the public sector and two commodities (paracetamol and prednisolone) in the private sector were accessible. The biggest issue found in this study was with the availability of the commodities. **Chapter 3.3**, while having a broader focus on health facilities' treatment capacity and not following the WHO/HAI methodology, found that 27.0% of healthcare workers in Kenya indicated they stocked antivenom, with the percentages in Uganda and Zambia being as low as 4.2% and 7.6%, respectively.

Chapter 4.1 analysed the price, availability, affordability and stockouts of more than 50 essential SRH commodities in Kenya, Tanzania, Uganda and Zambia. It also found that overall availability was low at less than 50% across all countries, with stockouts being common occurrences. In the public sectors of Kenya, Uganda and Zambia, as well as in the private not-for-profit (PNFP) sector of Zambia, all SRH commodities were free to the patient. In the other sectors unaffordability was experienced most often for maternal health and STI treatments. 'Accessibility' was low across all the study countries: in the public sectors of Kenya and Zambia six commodities met the accessibility threshold, while in Tanzania and Uganda four and two commodities, respectively, were accessible. In the private and PNFP sectors 'accessibility' was lower. In **Chapter 4.2**, an in-depth assessment of the price, availability and affordability of oxytocin and misoprostol in Kenya, Uganda and Zambia was conducted. Oxytocin and misoprostol are recommended uterotonics for prevention and treatment of post-partum haemorrhage (46). It showed that overall availability of oxytocin and misoprostol did not meet the 80% availability threshold set by the WHO. However, when combining the availability of both commodities, oxytocin or misoprostol was available at 81% of facilities in Kenya and 82% of facilities in Uganda. In Zambia, the availability was 76%. Oxytocin was found to have a greater availability than misoprostol in all three countries. While oxytocin and misoprostol were purchased by patients at prices above international reference prices, both medicines cost less than a day's wage for an LPGW and were therefore deemed affordable.

Availability

This thesis shows that overall availability of commodities for the three study cases was comparable, and much lower than the 80% availability target set by the WHO (47). Within the basket of studied commodities, fluctuations in availability were seen, with some commodities more regularly available than others. For example, paracetamol, antibiotics, tetanus toxoid, hydrocortisone, lidocaine and saline, as well as some medical instruments

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such as IV administration sets and syringes, had a relatively high availability in Kenya's study on snakebite commodities, while commodities such as antivenom, chlorpheniramine, codeine or morphine, and blood products had a much lower availability. Similarly, while male condoms, oral contraceptives, contraceptive implants, oxytocin, some antibiotics, and zinc- and ORS sachets had on average a relatively high availability in the four countries studying the availability of SRH commodities, other commodities had a much lower availability, including female condoms, the emergency contraceptive (levonorgestrel 750 mcg), and tubal ligation- and vasectomy kits.

The review conducted in **Chapter 2.1** on access barriers to ICEMs in Sub-Saharan Africa also found fluctuations in the availability of ICEMs, with generally a better availability of diazepam compared to the availabilities of fentanyl, morphine, and phenobarbital across a range of Sub-Saharan African countries. In **Chapter 2.2**, key informants interviewed in Uganda also raised the issue of discrepancies in the availability of specific ICEMs, that there was a lack of availability of different formulations (e.g., morphine), and that there was a substantial gap between needs of the population, and actual availability. Recent studies using the WHO/HAI methodology also found similar low availabilities, and fluctuations in availabilities between different medicines (48–51). For example, one study from Cameroon found that availability of cardiovascular medicines was observably higher in urban locations compared to rural locations, with insulin available in 91.4% of urban facilities and 61.9% of rural facilities (52). A study conducted in Northern Ethiopia found that while amoxicillin, oral rehydration salts and paracetamol were available at more than 90% of facilities, morphine, vitamin A, artesunate and ampicillin were unavailable or available at less than 20% of facilities (53).

Differences in availability of commodities may be explained by several factors. While in **Chapter 3.2** overall availability of snakebite commodities was found to be higher in public health facilities located in rural areas than public health facilities located in urban areas, when looking at the availability of individual commodities, it becomes clear that this is often not the case. One of the explanations is that rural facilities in Kenya are often lower-level health facilities, where more specialised commodities such as antivenom, morphine, and blood products were not commonly available, or are not supposed to be available as per the Kenya Essential Medicines List (EML) (54). For instance, antivenom was available in 69.2% of urban health facilities, and 33.9% of rural health facilities, while morphine was available in 15.8% of urban health facilities, but not surveyed in rural areas because there are no primary hospitals located in rural areas, which is the level from which morphine is allowed to be available. Similarly, in **Chapter 2.1**, the review on barriers to accessing ICEMs in Sub-Saharan Africa found that availability of ICEMs was impacted by the location and level of the health facilities: in Mozambique diazepam was available at 55% of rural health facilities and 83% of more specialised health facilities. Morphine was available in only 2% of lower-level health facilities in Malawi, compared to an 31% availability in hospitals. This issue was also raised by key informants interviewed in **Chapter 2.3**: ketamine was the primary anaesthetic

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used, especially in lower-level facilities, due to shortages of other anaesthetics and lack of equipment. The findings in this thesis also show that availability is not only affected by supply chain issues. Patients accessing care at lower-level facilities also face a barrier that is inherent to the system: more specialised commodities are never available at these levels of care, and patients are often forced to travel greater distances to reach a health facility where these medicines are available. To improve availability and accessibility of these medicines, efforts should focus on improving availability at lower-level facilities. This can include regulatory changes such as making medicines available at lower-level facilities or allowing prescribing by less specialised healthcare workers.

Stockouts

In **Chapters 3.2** and **4.1** stock information about commodities was collected to gain a deeper understanding of availability of the commodities over time, which is the first time such a variable was added to the WHO/HAI methodology. Stockouts of both snakebite and SRH commodities were common: snakebite commodities were on average stocked out at 18.6% of public health facilities and 11.7% of private facilities over a 12-month period, while SRH commodities were on average stocked out at 12.0% to 46.9% of surveyed facilities across the countries and sectors over a six-month period. Specific snakebite commodities were stocked out at as much as 71.4% of health facilities in the public sector. Stockouts of snakebite commodities lasted on average 30.5 days and 24.0 days per facility over a twelve-month period in the public and private sectors, respectively. SRH commodity stockouts lasted on average 3 to 12 days per month across the countries and sectors, translating to 18 to 72 days per facility on average if a stockout occurred over the surveyed six months. These stockouts further exacerbated the already poor availability of commodities in the study countries.

Stockouts of essential medicines have been identified across Sub-Saharan Africa (55–58). Causes of stockouts have also been extensively studied, and can be linked to inadequate budget allocation, shortage of (trained) staff, poor supply chain management systems, commodity forecasting and stock records, inefficiencies in procurement processes, and weak monitoring and oversight (56–60). In the review conducted in **Chapter 2.1** it was found that the inadequate commodity quantification systems, which is mandatory as per the Single Convention on Narcotic Drugs of 1961, hampered countries' ability to estimate their annual needs of narcotics. This led to insufficient quantities being requested and acquired by countries. In **Chapter 2.2**, key informants interviewed about access to ICEMs in Uganda also raised the issues they experienced with the supply chain. They shared that health facilities only received a fraction of the ordered medicines at times due to problems experienced at the central level, or due to practical delivery issues. Similarly, in **Chapter 3.3**, commonly shared causes of stockouts of SRH commodities were delays in the deliveries (54.1%), stock

delivered to the facility does not match the order (33.9%), and that there were problems with stock at the central level (30.3%).

Key to improving access to essential medicines in the study countries is strengthening the supply chain. Stockouts can be prevented, or at least minimised, with a well-functioning logistic management information system, a sufficient number of staff trained in supply chain management and forecasting, and sufficient budget allocations to commodity procurement. Specifically for the quantification and estimation of ICEMs, the International Narcotics Control Board (INCB) has a responsibility to support countries in their capacity strengthening. In 2012, the INCB and WHO developed the 'Guide on Estimating Requirements for Substances under International Control' to support governments in calculating their requirements adequately (61). While in 2022 almost all 96 Member States surveyed by the INCB reported being aware of these guidelines, 40% still indicated that their estimates were not (fully) realistic and appropriate. Further, many countries' estimates did not reflect the real needs of their population (62). A discrepancy thus exists between awareness of these guidelines and its proper use, which should be an area of focus for the INCB.

Chapter 3.2 also studied the impact of COVID-19 on stockouts of commodities at the health facilities. The research showed that stockouts of almost all commodities occurred significantly more often from February to July 2020 (beginning of COVID-19) than from August 2019 to January 2020 (pre-COVID-19), suggesting they worsened as a consequence of the pandemic. Research conducted since then on the impact of COVID-19 on health supply chains has corroborated these findings, showing significant disruptions across the globe (63–65). COVID-19 showed that no country's health supply chain was resilient in the face of an emergency of such magnitude, and future supply chain strengthening is critical. Strengthening of local pharmaceutical manufacturing is one strategy that is now high on the agenda, which may offer the opportunity to strengthen supply chains (64,66).

Affordability

In **Chapter 4.1** and **4.2**, the affordability of SRH commodities was calculated using the WHO/ HAI methodology of comparing the price of a (month's) treatment, to the wage of a lowest-paid government worker (LPGW). In **Chapter 3.2**, the affordability of commodities for the treatment of snakebite envenoming was calculated using the wage of an LPGW, as well as through using the impoverishment approach as developed by van Doorslaer et al. (2006). In this approach, the proportion of a population that is pushed below a poverty line after purchasing a medicine is compared with the population that was already living below the poverty line. This approach was used in addition, as the LPGW approach knows some limitations with representativeness; in many LMICs, the wage of an LPGW is often higher than the income of a large proportion of the population. In Kenya, Uganda, Tanzania and Zambia, for example, 29.4% to 61.4% of the population lives below the international poverty

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line (IPL) of 2.15 USD a day, while an LPGW in Kenya earned an equivalent of around 4.50 USD at the time of the study (67,68). It is therefore assumed that affordability projections using the LPGW approach can be an overestimation of the actual affordability in many Sub-Saharan African countries, where there is a significant proportion of informal workers (69).

The affordability issues found in the private sector in this thesis, have also been identified previously in LMICs (48,50,70). Low availability in the public sector forces people to turn to the private and PNFP sectors, where affordability becomes problematic. In **Chapter 4.3**, 33.3% and 21.1% healthcare workers in the private and PNFP sector, respectively, highlighted the high costs of care to patients as a key challenge to accessing SRH commodities. The review conducted in **Chapter 2.1** found that 76.0% of healthcare workers in Zimbabwe indicated patients had to buy opioids themselves, and 74.0% of PLWE discontinued treatment for financial reasons. In **Chapter 3.1**, individuals were asked about the socio-economic impact of snakebites, which showed that many had experienced high hospital costs, with costs incurred for snakebite treatment being as high as 734.80 USD, while the median monthly household income was 78.40 USD.

The roll-out of UHC in Sub-Saharan Africa takes different forms in every country. It is, however, in many African countries characterised by public-private partnerships (PPPs), namely through the partnering of the government with the private and PNFP sectors to provide health services and/or insurance (71). PPPs have been shown to increase access to medicines and health services for a range of care fields, including SRH, infectious diseases such as HIV/ AIDS, tuberculosis and malaria, immunisation and vaccination, and environmental health (71,72). As part of these PPPs, countries are implementing prepayment health-financing schemes such as social insurance or national health insurance (NHI). Members of such schemes pay a premium which allows them to access care at private facilities for 'free' or for a low, flat rate, with private facilities receiving reimbursement from the insurance schemes (73). PPPs and NHI can be useful tools to reduce costs for clients in the private sector and improve access to medicines in general when they are well-functioning and have a high coverage (71,72,74–76). However, challenges with both programmes exist. With PPPs, challenges within the partnerships relate to hesitancy to work together and lack of trust, lack of adequate management of the PPP, inadequate financial resources to sustain the PPPs, lack of communication between partners, inadequate regulatory frameworks, and inadequate capacity of the government to manage PPP contracts (71,77). With regards to NHI schemes, challenges relate to unaffordability of premiums, stockouts at accredited health facilities, long waiting times, inadequate quality of services, shortages of healthcare workers, and delays in provider reimbursements by NHI schemes resulting in co-payments by clients, denial or limiting of services (78–82). Further, the rollout of NHI schemes is still poor in this thesis' four main study countries. Uganda has no NHI in existence yet, while in Zambia NHI has only recently been introduced, with only 344 of almost 2,000 health facilities NHI-accredited by April 2023. NHI coverage in Tanzania and Kenya is around 30% (79,83–86). Further, NHI

schemes are often dependent on tax revenues and/or compulsory payroll deductions from the formal sector. The issue is the large proportion of informal sector workers in Sub-Saharan Africa (339.4 million people), who would consequently not contribute to or be covered by, any insurance scheme (69).

Thus, while PPPs and NHI can be tools to increase access to medicines and services, for it to be successful in the study countries, coverage needs to be increased, and the programmes themselves need to be strong and properly implemented, managed, and financed. Lastly, while SRH commodities are more likely to be included in UHC packages, it is less likely that commodities for the treatment of snakebite envenoming and ICEMs are included without pro-active advocacy by civil society.

Human resources for health

One of the key determinants of access to medicines at the health service delivery level is human resources. However, healthcare workers, particularly those with specialised skills, are in short supply. The review on barriers to access to ICEMs conducted in **Chapter 2.1** found that the specialist workforce was very low. In Liberia, for example, the anaesthesiologist workforce density was 0.02 per 100,000 population. The shortage of specialised healthcare workers was found to be worse in rural areas. The review also found that a shortage of staff at import authorities, and their lack of training on how to properly issue import authorisations, impeded access to ICEMs. Stakeholders interviewed in **Chapters 2.2** and **2.3** raised this same issue. In **Chapter 4.3** 19.1% of healthcare workers surveyed in Kenya, Tanzania, Uganda and Zambia suggested that staff shortages were also one of the key challenges to access to SRH services. The shortage of (specialised) healthcare workers has been well documented, and a recent study has estimated a shortage of 1.9 million physicians, 5.6 million nurses and midwives, and 856,000 pharmacists and pharmacist assistants in Sub-Saharan Africa alone (87). This shortage is caused by a multitude of factors, including insufficient training capacity, migration of healthcare workers, inadequate governance, working conditions, war and political unrest, and limited funding (87,88).

To tackle the shortage of specialised healthcare workers, the WHO has recommended task-shifting and task-sharing. This entails transferring tasks to other cadres of HCWs with less experience, or delegating certain tasks to HCWs who receive training to obtain specific skills (89). Task-shifting/sharing is already taking place in Sub-Saharan Africa for a range of health services (90). In Uganda, Kenya and Sierra Leone, for example, nurses and clinical officers are permitted to prescribe opioids to patients independently, after completion of a training course, which has increased access, especially in rural areas (91–94). This programme was also referred to in **Chapter 2.2**. Roll-out of this type of programme in more countries in the region, and development of these programmes for other services, such as epilepsy and mental health, is recommended to improve access. Successful roll-out of an epilepsy nurse

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specialist programme in the UK is an example of task-shifting for this type of service that has already been implemented in a high-income country (95).

Task-shifting of anaesthesia care, which was mentioned by the interviewed anaesthesiologists in **Chapter 2.3**, is more common in the region, as the number of physician anaesthesia providers is critically low (0.41 per 100,000 population) (96). A 2018 review found that 36 of 37 studied Sub-Saharan African countries reported task-shifting for anaesthesia care, with tasks shifted mainly to clinical officers and nurse anaesthetists, similarly to the morphine prescribing task-shifting programmes (97). However, as also observed by the interviewed anaesthesiologists, these non-physician providers may not feel comfortable, may not have the skills, or may not have the equipment and medicines to offer all types of anaesthetics. Subsequently, they rely primarily on ketamine to provide anaesthesia care (98,99). The number of non-physician providers is often also inadequate, resulting in overworked providers, referrals to higher-level facilities, or non-trained healthcare workers providing the services (99).

Task-shifting/sharing also occurs among SRH services. A review of task-sharing programmes for family planning in Burkina Faso, Cote d'Ivoire, Ethiopia, Ghana and Nigeria found that tasks are primarily shared with community health workers, midwives, and nurses. They were trained to perform family planning tasks, including administering injectable contraceptives, implants and intra-uterine contraceptive devices (100). The programmes led to increased contraceptive prevalence rates and reduced fertility rates (100). Another review of task-shifting for maternal and reproductive health, including emergency obstetric care, abortion care and family planning, showed that task-shifting for these services can increase access while safeguarding patient outcomes (101). However, problems with availability of equipment and medicines, poor supervision, and insufficient funding were also reported in both reviews (100,101).

Task-shifting can thus be an important tool to improve access to services. However, to fully realize its potential, governments need to ensure that the healthcare workers have the necessary equipment and medicines, sufficient programme funding, and that the healthcare workers are appropriately prepared to provide these services through (continued) training and supervision.

A lack of training and knowledge among the health workforce in general was also identified in this thesis. In **Chapters 2.1** to **2.3** it was found that there was a lack of knowledge on ICEMs and anaesthetics among healthcare workers, and there was a lack of inclusion of ICEMs and related care fields, including anaesthesia, in medical curricula. Further, healthcare workers held misconceptions about ICEMs and were reluctant to prescribe opioids. It was also found that staff at import authorities lacked the skills to properly issue import authorisations, and that procurement was hampered by the countries' inability to appropriately quantify ICEMs

needs. Issues with commodity quantification and forecasting have been found across Sub-Saharan Africa, and affect all types of essential commodities (59,60,102). **Chapter 3.3** showed that healthcare worker training on snakebite management was critically low, as only 8% to 16% had received any training on snakebite management. This lack of knowledge can lead to the use of ineffective traditional treatments, such as using black stones and tourniquets, even in regular care settings. These treatments were at times still offered by healthcare workers, particularly in Zambia. Recent studies have shown that this lack of knowledge on snakebite management is common in many Sub-Saharan African countries (103–105). A study conducted in Rwanda, for example, showed that 35% of surveyed physicians and interns believed traditional healers could successfully treat snakebites, and 66% believed black stones were an appropriate first aid measure (106). Healthcare workers in **Chapter 4.3** raised the issue of lack of training as well: 15.5% pointed to staff training on SRH services as a key challenge to accessing SRH commodities and services, and 10.7% of public sector healthcare workers said lack of knowledge was a reason why healthcare workers are at times unable to provide a client with SRH commodities and services. In line with this, 23.0% of healthcare workers recommended (continued) staff training as a way to improve access.

Lack of training and knowledge thus seem to be a recurring issue across the three case studies, and evaluation of medical curricula is recommended to improve delivery of care. For ICEMs specifically, a better balance needs to be found between teaching healthcare workers about the possibility of misuse of the medicines, and the critical importance of them for medical purposes. For snakebite envenoming, better inclusion is needed in the curricula, so all healthcare workers have a basic understanding of snakebites that will allow them to diagnose envenomings quickly and provide appropriate treatment. Further, special programmes for in-service continuing professional development should be developed in snakebite-endemic areas, where expert knowledge is critical.

Faith-based SRH services

This thesis found that one of the barriers to accessing SRH services and commodities at the service delivery level, was related to the PNFP sector specifically. In **Chapter 4.3**, surveyed healthcare workers in Kenya, Tanzania, Uganda and Zambia indicated that in 35.9% of the PNFP health facilities, they were unable to provide clients with SRH commodities and services because family planning services were not offered. In the study countries, many Catholic health facilities do not provide contraceptives, which is a significant issue for those dependent on these facilities for their health services (107,108). Engaging with faith leaders and communities on issues of SRH through the use of SRH and rights-related scriptures is a recommended tool to improve access. In Nigeria, for example, the Christian Association of Nigeria endorsed an SRH handbook titled 'Christian perspectives on reproductive health and family planning in Nigeria'. It was developed by the Nigerian Urban Reproductive Health Initiative Project, in collaboration with representatives of different Christian denominations. In the handbook scriptures are used to substantiate support for family planning (109).

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Advice on modern contraceptive methods is also included in this handbook, along with advocacy for increased access to family planning information and services (109). Another way to improve access to family planning, which might be more feasible in the short-term, is establishing referral pathways between PNFP health facilities, and public and private health facilities. In Rwanda, for example, the government established a 'work-around' referral programme between Catholic health facilities and nearby public health facilities, in which Catholic facilities refer clients interested in modern contraceptive methods to the nearby facilities that provide such services (110).

Governance at the health sector, national, and international level: constraints and recommendations for improvement

Governance at the health sector, national and international level relates to legislative and organisational practices, such as procurement processes, health sector financing, and health and pharmaceutical policies. Constraints also relate to regional and international practices and regulations.

Health sector financing

Health sector financing constraints were found in **Chapters 2.1** to **2.3**, and **Chapter 4.3**. Constraints related to budgets for ICEMs and to care fields were identified in the scoping review conducted in **Chapter 2.1**, where it was found that limited health budgets led to a lack of prioritisation of ICEM-related care fields. This in turn led to insufficient budget allocation. In **Chapter 2.2.** key informants in Uganda suggested that the Ministry of Health's budget was inadequate to meet the needs of its population, which resulted in prioritisation and ranking of health issues, of which the ICEMs-related care fields were not part. Similarly, anaesthesiologists from across Sub-Saharan Africa interviewed in **Chapter 2.3** shared that the lack of attention to their care field led to the lack of budget allocation for anaesthesia. Healthcare workers surveyed in **Chapter 4.3** about access to SRH services and commodities also believed budget constraints to be an issue, as 21.5% of healthcare workers in the public sector recommended increasing budget for SRH as a tool to improve access. These findings are not surprising, as health financing in Sub-Saharan Africa is the lowest in the world (111). Domestic government health expenditure as a percentage of gross domestic product (GDP) for Sub-Saharan Africa was 2.1% in 2020, compared to a 9.2% expenditure by Organisation for Economic Co-operation and Development (OECD) countries (67). Indeed, in spite of African governments signing the Abuja Declaration in 2001, which committed them to spend at least 15% of their annual budgets on health, very few have reached that target; in 2020 the study countries' spending ranged from 3.1% in Uganda to 9.4% in Tanzania (112,113).

Over the past decades, health in LMICs has been financed for a significant part by donor aid (114). In 2018, spending on development aid for health was 38.9 billion USD, with HIV/AIDS, new-born and child health, sector-wide approaches and health sector support receiving

most development aid (114). However, annual growth of development aid has recently levelled, with an estimated 1.3% annual growth from 2010 to 2018, compared with an annual growth of 10.0% from 2000 to 2010 (114). This donor dependency makes countries vulnerable to global economic pressures and the political whim of donors, combining to challenge sustainable programme implementation (115–118). In Kenya, for example, 33% of the health budget in financial year 2017/18 was funded by development aid, which decreased to 16% in financial year 2019/20 (119). Even though the government increased their own spending on the health budget, it has been insufficient to offset the downturn in development aid (119). This issue was also raised by key informants in **Chapter 2.2**, who questioned the sustainability of donor-supported programmes. Another example is the New Mexico City Policy, also known as the 'global gag rule', which was re-instated and expanded during the United States' (US) Trump presidency. This policy prevents foreign organisations receiving US development aid from advocating or providing information, referrals, or services for legal abortion. The reinstatement of the policy in 2017 had far-reaching consequences on access to SRH services. Studies conducted in Ethiopia, Kenya, Madagascar, Nepal and Uganda showed that next to abortion, access to family planning services and use of contraceptives also decreased as a consequence of the US' development policy (120–122). To decrease the dependency on development aid and the subsequent influence it can have on health services and provision, and move towards a more sustainable solution, governments need to increase their own spending on health. They should also invest enough into their health systems to ensure they can offer quality services to their population.

Legislation and regulatory practices

Regulatory practice demonstrably influenced access to medicines and services studies in this thesis, some of which have already been detailed above, such as the level at which commodities are allowed to be provided, or the healthcare workers who are allowed to prescribe specific medicines. Regulatory practices had particular impact on access to ICEMs. This is not surprising, as ICEMs are subject to tight regulation of manufacturing, licensing, distribution and dispensing as stipulated by the United Nations (UN) international drug control conventions (123–125). In the review conducted in **Chapter 2.1**, barriers that were identified included cumbersome procurement processes due to stringent regulations set by the conventions, which translated into strict regulations at the country level. Strict laws controlling ICEMs, which led to overly restrictive prescription practices, were also identified as hampering access. In **Chapter 2.2** key informants raised similar regulatory issues that were experienced in Uganda. They highlighted the issues caused by overly restrictive prescription practices, such as the extra workload due to the necessity of additional documentation books and special licenses for prescribing opioids. Fear of legal sanctions, such as license revocation, among some prescribers, were also pointed out, which not unsurprisingly influenced prescribing. In **Chapter 2.3** the key informants shared their fears of ketamine becoming as difficult to access as ICEMs if it were to be scheduled internationally, critically impacting access to safe anaesthesia care in Sub-Saharan Africa. In 2012, recognising the additional

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workload of national authorities due to the regulations set by the international drug control conventions, the INCB developed an electronic management tool, the International Import and Export Authorization System (I2ES), which countries can use to monitor and manage the import and export of controlled medicines more easily (126). I2ES, which was launched in 2015, has only 75 Member States actively using the system as of November 2022 (127). Thus, while the INCB suggests they are continuously assisting governments in its implementation and use, there is still room for improvement. More support for countries to implement the system is recommended, as well as continued support to governments already using the system, including support for training of staff to use the system. Further, while the INCB found a downwards trend in the past years in Member States' perceived importance of fear of prosecution and sanctions among healthcare workers, and onerous regulations as barriers to access, they remain an issue, which is also emphasised by the INCB itself (62). Recommendations to tackle these barriers are for governments to review their legislations and regulations on ICEMs prescribing and handling, to ensure that regulations find the balance between ensuring access to medicines for medical use, while preventing their misuse.

Summary of policy recommendations

To summarise, the policy recommendations across the different levels of the health system made in this thesis can be found in **Box 1**.

5 METHODOLOGICAL CHALLENGES AND LESSONS FOR FUTURE RESEARCH

This thesis aimed to provide a detailed picture of barriers that influence access to medicines across the health system, as access to medicine is not only a result of its availability and affordability. It is determined by many facets, from the individual level all the way up to the international level. By using a mixed methods approach, we tried to capture this complexity. The advantage of a mixed methods approach is that it allows for triangulation of the data: findings can be compared to each other, with one study providing nuances to the findings of the other. For instance, the WHO/HAI methodology used in **Chapters 3.2**, **4.1** and **4.2** found that while some commodities were unaffordable in the private and PNFP sectors, affordability did not seem to be the biggest issue with access to medicines. However, when we triangulated these findings with perspectives from healthcare workers in **Chapter 4.3** and community members in **Chapter 3.1**, it became clear that the affordability measure used in the WHO/HAI methodology may not be as representative, especially in rural locations. Another example of such a data triangulation approach was in **Chapters 3.1** and **3.3.** In **3.1** healthcare workers were surveyed about snakebite patients' characteristics, including on sex, age and activity undertaken at the time of the bite. In **3.3** community members, including snakebite patients and patients' family members, were also surveyed about these measures. This allowed for comparisons between data provided by healthcare

Individuals, households and the community
»   Development and implementation of sensitisation programmes, adapted to the unique facets of each case, taking into consideration the socio-cultural beliefs of the target population. The programmes should consist of a combination of sensitisation approaches. Inclusion of community- and faith leaders, both as participants and change leaders, is critical.

Health service delivery
»   Improving availability of medicines by lowering the healthcare level at which they are allowed to be available.
»   Strenghtening of the supply chain by:
    ›   Ensuring a well-functioning logistic management information system is in place;
    ›   Ensuring there are sufficient staff trained in supply chain management and forecasting;
    ›   Allocating sufficient budget to commodity procurement.
»   Roll-out of PPPs and NHI to increase access to medicines and services.
»   Task-shifting and sharing of tasks to cadres of healthcare workers with less experience. This can include allowing the prescribing of certain medicines by less specialised healthcare workers. Governments need to equip these cadres of healthcare workers with the necessary commodities, training, supervision and programme funding.
»   Evaluation of medical curricula to improve knowledge and training of the health workforce, especially on controversial and neglected topics, such as ICEMs and snakebite envenoming.
»   Increasing healthcare workers' opportunities for in-service continuing professional development.
»   Establishment of referral pathways between PNFP health facilities, and public and private health facilities to enable clients to access family planning services.

Governance at the health sector, national, and international level
»   Increasing government spending on health to ensure sustainable financing and sufficient investments are made to ensure provision of quality services, without donor dependence.
»   Review of legislations and regulations on ICEMs prescribing and handling by the governments to ensure a balance exists between access to medicines for medical use, and prevention of misuse.
»   Additional support of INCB to facilitate quantification, estimates and importation of ICEMs at country level.

Box 1. Summary of policy recommendations.

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workers, and data provided by patients and their families, confirming findings from the different studies.

The limitation of using the LPGW measure to calculate affordability has been mentioned previously in this chapter, as the wage of an LPGW in LMICs is often higher than the income of a large proportion of the population (67). In **Chapter 3.2**, anticipating this limitation and

to provide a comparison to the LPGW approach, we included the impoverishment approach, in which the proportion of a population that is pushed below a poverty line after purchasing a medicine is compared with the population that was already living below the poverty line. While this approach provides a better, contextual indication of affordability of snakebite commodities in Kenya, the approach still merely provides an indication of affordability due to the assumptions inherent to the approach, and the linearity of the income distribution used to calculate it (128). Since Niëns et al.'s proposed methods of measuring affordability of medicines using the abovementioned impoverishment approach, as well as a catastrophic expenditure method, in 2012, no significant fundamental research has been undertaken on this topic (129). Given affordability remains a critical component of access to medicines, a fundamental rethinking of affordability methods may be needed and future research should focus on this. Further, the affordability of a medicine at the health facility fails to capture indirect costs incurred by the patient, such as travel or loss-of-income due to sickness or ongoing morbidity/unemployment. Supplementing data collected using the WHO/HAI methodology with interviews, focus group discussions or household surveys that provide insights into the affordability of medicines and services of target populations would thus provide a more comprehensive picture of the context in which medicines and health services are accessed, and is recommended.

Another previously identified limitation of the WHO/HAI methodology is its cross-sectional design (128,130). Availability of commodities is measured at only one point in time. To mitigate this limitation, we added an additional outcome measure, stockouts, to the two surveys conducted in **Chapters 4.1** and **3.2**. In **Chapter 4.1**, information on stockouts of SRH commodities was collected for a six-month period to gain a better understanding of availability over a longer period of time. However, a limitation to a six-month period that we noted is that seasonal or financial year fluctuations are not fully captured. Consequently, in **Chapter 3.2**, stock information for snakebite commodities was collected over a 12-month period. This additional measure provides a much more comprehensive insight into availability of commodities and highlights potential issues with the supply chain. Stockouts of SRH commodities occurred for instance in 45.9% of public facilities in Zambia, with a stockout lasting on average 12 days per month. Stockouts of commodities for the treatment of snakebite envenoming lasted as long as 210 days during the 12-month period surveyed. It is thus recommended that future researchers using the WHO/HAI methodology add this measure to the survey.

While the additional stockout measure provides a more comprehensive picture of availability over time, to measure changes in access over a longer time period as a consequence of implemented policy interventions, time series data is needed. In 2016, the WHO developed the essential medicines price and availability monitoring (MedMon) mobile application, which enables rapid and inexpensive data collection of commodity prices and availability in health facilities (131). Its aim was to make data collection with the WHO/HAI methodology more

cost-effective by decreasing duplication of efforts and potential entry errors. The application is adaptable to a country's needs and allows for inclusion of national product registries, but not much has yet been published in the literature on its use and applicability (131). However, a problem that remains with this type of data collection is that in many LMICs, especially in Sub-Saharan Africa, health facilities in rural locations are not easily reached. This makes data collection costly and lengthy, in countries where governments do not usually have budgets for these types of activities. The development of a tool that is truly low-cost might be needed and might consist of an annual health facility inventory check completed by the healthcare workers themselves, using an easy-to-use application based on the WHO/HAI methodology and MedMon application.

A fourth limitation of the WHO/HAI methodology is related to the collection of data for only one formulation or strength (128,130). To mitigate this, we aligned the surveyed medicines' formulations and strengths to those on the countries' corresponding national EML. Second, when a medicine was listed with multiple formulations or strengths, they were all included in the survey. Future researchers making use of mobile data collection applications, can make use of conditional branching to easily include multiple formulations and strengths in one survey. Conditional branching automatically directs users to the next logical question based on their previous response, skipping non-relevant questions.

A last limitation that might be observed with the WHO/HAI methodology, is that it studies availability and affordability as two separate measures of accessibility. However, access to medicines is dependent on both its availability and its affordability, as emphasised by the Sustainable Development Goals indicator 3.b.3: the proportion of health facilities that have a core set of relevant essential medicines available and affordable on a sustainable basis (132). Subsequently, in **Chapters 3.2 and 4.1**, we included a combined measure, as first introduced by Ewen et al. (2017), where 'accessibility' of a commodity was defined as it having an 80% or higher availability, and costing less than a day of wages for a LPGW (70). The added value of this combined measure is that it illustrates in what respects the WHO's targets for availability and affordability of essential medicines are falling short.

In **Chapter 4.3**, a cross-sectional survey was conducted among healthcare workers to identify barriers to SRH services on both the supply and demand side. While healthcare workers have insights into a range of barriers on both, they do not appear to have a comprehensive overview into the barriers as experienced by those seeking SRH services. Further, healthcare workers might not be as reflective or aware of their health facilities', colleagues', or own shortcomings, or how it might affect access. In these types of situations, data triangulation involving patients and/or citizens through the use of interviews, focus group discussions or household surveys would have provided more comprehensive insights on demand side barriers. The results should be interpreted with this in mind.

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The qualitative methodologies used in this thesis also know some limitations. In **Chapter 2.2**, while aiming for the inclusion of a broad range of stakeholders, not all perspectives were captured. For example, no patients were interviewed due to ethical considerations, which may have provided valuable insights into the lived experiences of people accessing ICEMs. Similarly, while in **Chapter 2.3** more than 60 national anaesthesia societies or individuals were contacted for participation in the study, only ten took part, and only two came from the West African region. Even though most of the themes emerged from all of the interviews, it is difficult to conclude whether data saturation was reached with this limited sample. Unfortunately, research of this type is always dependent on the goodwill of participants, and it can be challenging to find stakeholders willing to share insights. Notwithstanding this potential shortcoming, in **Chapter 2.3**, the findings provide a first, qualitative insight into the importance of ketamine for anaesthesia care in Sub-Saharan Africa, and future research can build onto it to tease out more of the specifics within the region.

CONCLUSION

The right to the highest attainable standard of health is a human right recognised internationally, and access to medicines has been identified as a cornerstone in its fulfilment. Nevertheless, access to medicines remains a critical issue for the majority of people living in Sub-Saharan Africa, demonstrated in this thesis for internationally controlled essential medicines, treatment of snakebite envenoming and sexual and reproductive health commodities. In this thesis, by studying these three distinct cases, it has been shown that while access to essential medicines for specific care fields or diseases may be subject to topic-specific barriers, many of the barriers are transcendent and are the result of an interplay of conditions across the health system that affect all areas of access. By looking at the similarities between care fields and diseases, and not the dissimilarities, this thesis shows that a multi-pronged, system-wide approach is needed to strengthen health systems in the Sub-Saharan region. It should be targeted at individuals, households and the community, the delivery of health services, and governance at the health sector, national and international level. Such a complex issue needs active involvement from all actors, including patients and communities, community- and faith leaders, healthcare workers, civil society, governments, researchers, and international actors such as international aid organisations, donors, UN agencies, and in the case of internationally controlled essential medicines, the INCB.

CONTRIBUTION STATEMENT

GIO wrote the general discussion of this thesis. Her supervisors reviewed previous versions of the manuscript, and GIO implemented their feedback.

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APPENDICES

6.1 SUMMARY

INTRODUCTION

The right to the highest attainable standard of health is a human right recognised internationally. In striving for the attainment of this right to health, access to medicines has been identified as a cornerstone. Nevertheless, both access to medicines and the subsequent realisation of the highest attainable standard of health have not been met for a significant proportion of the global population, which is especially the case for those living in Sub-Saharan Africa (SSA).

The price, availability and affordability of medicines have been extensively studied in the past two decades using the World Health Organization/Health Action International (WHO/HAI) methodology 'Measuring medicine prices, availability, affordability and price components'. As outlined in the general introduction in **Chapter 1**, access to medicines and health services is not only a result of the availability and affordability of the medicines itself; it is impacted by barriers across the five levels of the health system continuum: individuals, households and the community; service delivery; the health sector; and the national and international level. To gain a deeper understanding of how barriers at the different levels of the health system influence access in SSA, and what lessons might be learned, this thesis focussed on three distinct cases: internationally controlled essential medicines (ICEMs, medicines listed on WHO's Essential Medicines List and one of three international drug control conventions), the treatment of snakebite envenoming, and commodities for sexual and reproductive health (SRH). These cases were chosen because of their controversial nature or neglect by the international community, and are used to illustrate the complexity of access to essential medicines in the region. The questions that are answered in this thesis are: *What are the commonalities and differences in access to essential medicines and services between these cases?* And *what lessons might be learned in order to improve access to essential medicines, both case-specific and in general?*

6.1

INTERNATIONALLY CONTROLLED ESSENTIAL MEDICINES

Chapter 2 studied access to ICEMs, and consists of three sub-chapters. In **Chapter 2.1** existing literature on barriers to accessing ICEMs in SSA between 2012-2022 was reviewed.

The search identified 97 articles that met the inclusion criteria. Numerous barriers hindering access to ICEMs were reported, and these barriers were prevalent across the ICEMs drug classes. The main barriers can be grouped according to the health system levels:

1. *Individuals, household and the community level:* Limited or lack of public understanding of ICEMs and the fear of opioid addiction.

2. *Health service delivery level:* Stockouts, unaffordability, long distances to health facilities, medicine quality, lack of specialised healthcare workers, lack of ICEMs knowledge and training among healthcare workers, misconceptions about ICEMs, and a lack of

infrastructure to store and distribute medicines. General low availability of medicines was exacerbated by the controlled status of ICEMs.

3.   *Health sector level*: Lack of prioritisation of ICEM-related healthcare fields by governmental authorities, leading to inadequate budget allocation.

Cross-cutting governance-related barriers pertained to the lack of proper quantification systems, cumbersome procurement processes, and strict national laws regulating ICEMs, which result in overly restrictive prescription practices.

This study showed that a multitude of barriers, spanning all levels of the health system, impede access to ICEMs and the related healthcare fields, and that a multifaceted approach is necessary to improve access.

Chapter 2.2 consisted of a qualitative study, its aim to identify the social, cultural, and regulatory barriers that influence access to ICEMs in Uganda. Semi-structured interviews with 15 stakeholders revealed that barriers arose from several factors, with some ICEMs-specific and some for medicines in general. Factors that influenced access to medicines in general in Uganda included the use of an estimate system to quantify medicine needs, practical and logistical supply issues, lack of healthcare workers, unaffordability, and physical and geographical availability. ICEM-specific factors were their lack of prioritisation, difficulties in finding a balance between control and access in laws and regulations, a lack of knowledge on ICEMs among the public and healthcare workers, and stigma related to ICEMs and related healthcare fields. The outcomes of this study underscore the necessity of comprehensive health system strengthening in Uganda. To improve access to ICEMs, a collaborative approach and active involvement from all stakeholders are imperative. Such efforts should not only promote access but also mitigate the risk of misuse.

Access to anaesthesia and surgical care is a major problem for people living in SSA. In this region, ketamine is critical for the provision of anaesthesia care. However, efforts to regulate ketamine internationally as a controlled substance may significantly impact its accessibility. In **Chapter 2.3** the impact of scheduling ketamine as an internationally controlled substance was therefore estimated. Two methods were used, a cross-sectional survey at the hospital level in Rwanda and key informant interviews with experts on anaesthesia care in SSA. In 54 hospitals, data on four anaesthetic agents (ketamine, propofol, thiopental and inhalant agents) were collected. Semi-structured interviews with 10 key informants were conducted.

The survey found that availability of ketamine and propofol was comparable at around 80%, while thiopental and inhalant agents such as halothane, isoflurane or sevoflurane were available at about 50% of the hospitals. The interviews found significant barriers impeding access to anaesthesia care including a general lack of attention given to the speciality by

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governments, a shortage of anaesthesiologists and migration of trained anaesthesiologists, and a scarcity of medicines and equipment. As a consequence, all key informants described ketamine as critical for the provision of anaesthesia care in SSA, and that its scheduling would have a significantly negative impact on the quality of anaesthesia that can be provided in the region. As far as they were aware, misuse of ketamine was not to an issue.

This study has shown that ketamine is a critical medicine for the provision of anaesthesia care in SSA, and that millions of people's access to safe surgical care may be in jeopardy. Concerted efforts are needed to improve anaesthesia care in SSA in general, so in the future there can be less of a reliance on ketamine.

TREATMENT OF SNAKEBITE ENVENOMING

Chapter 3 focussed on snakebite envenoming. **Chapter 3.1** aimed to provide a broad overview of the extent of the problem and impact of snakebite in four snakebite-prevalent counties in rural Kenya to inform context-specific policies. It studied the health-seeking behaviour, and the health, social and economic burden of snakebites through a household survey. Non-probability sampling was used to survey 382 respondents from the four counties using a structured questionnaire.

The findings showed that snakebites were common in the surveyed communities, as 13% of participants had been personally bitten by a snake, and more than one-third knew of a community member who had been bitten. Victims were most often walking (38%) or farming (24%) when bitten. Death of a community member or family member was reported by 9% and 15% of participants, respectively. The majority of those bitten were aged 26–45 years. Risk of snakebite was not significantly associated with sex, educational level, or occupation. Further, traditional healing played an important role in the treatment of snakebites: while 58% of those bitten went to a health facility after the bite, 42% either only went to a traditional healer, or first went to a traditional healer before visiting a health facility. The most common first aid methods that people would use after a bite, which were all ineffective practices, included the use of tourniquets, black stones, and cutting the bite. Last, snakebites affected victims both socially and financially.

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To reduce the burden of snakebite felt by rural communities, community engagement, including with traditional healers, is needed to improve used preventive measures and effective health-seeking behaviour. Second, health system strengthening is needed so snakebite victims can be quickly and adequately treated with appropriate and affordable antivenom and supportive care.

In **Chapter 3.2** the availability, affordability and stockouts of commodities used to treat snakebites in health facilities in Kenya was assessed. This study was undertaken because while efforts are underway to improve snakebite care, evidence from the ground on access

to treatment is scarce. The study used an adaptation of the WHO/HAI methodology. Data on availability, prices and stockouts were collected for 45 commodities from public (n=85), private (n=36), and private not-for-profit (PNFP) (n=12) facilities in Kenya in July-August 2020. Availability was defined as the presence of a survey medicine in pre-specified dose and formulation at the time of the data collection in the health facility. Stockouts were measured retrospectively for a twelve-month period. A commodity was considered stocked out if the facility usually stocked the commodity, but the stock-taking database indicated it had been out of stock at times in the past year. Affordability was calculated using the wage of a lowest-paid government worker (LPGW). Accessibility was assessed combining the WHO availability target (≥80%) and LPGW affordability (<1 day's wage) measures.

Overall availability of snakebite commodities was low (43%). Antivenom was available at 45% of public- and 19% of private facilities. Stockouts of any snakebite commodity were common in both the public (19%) and private (12%) sectors, lasting on average about a month in the public sector and 24 days in the private sector over a twelve-month period. Since most of the commodities were free to the patient in the public sector, affordability was not an issue there. In the private sector affordability was more of an issue, with the median cost of one vial of antivenom costing 14 days' wage for an LPGW. Only five commodities in the public sector and two in the private sector were considered accessible.

To improve access, efforts should focus on ensuring availability at both lower- and higher-level facilities, and improving the supply chain to reduce stock-outs. Inclusion of antivenom into the universal health coverage packages being rolled out in Kenya would further facilitate access.

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Chapter 3.3 investigated the capacity of health facilities and healthcare workers to treat snakebites in Kenya, Uganda and Zambia, as a challenge to the development of evidence-based health policies is the lack of socio-political studies. The research comprised a cross-sectional key informant survey between March 2018 and November 2019 among healthcare workers from health facilities in Kenya (n=145), Uganda (n=144), and Zambia (n=108).

The majority of healthcare workers suggested that the number of snakebite incidents was similar between the sexes, that most patients were aged 21-30 years, and victims were often farming or walking when bitten. Supportive treatment was the most commonly offered type of treatment at the health facilities. In the three countries, 85–90% of the healthcare workers had not received any training in snakebite management. Further, about 80% of healthcare workers across the countries thought their health facility did not have the necessary equipment and medicines available to treat snakebite. Accordingly, a mere 27% of healthcare workers in Kenya, 4% in Uganda, and 8% in Zambia stated they had antivenom in stock at the time of survey. Snakebites were not systematically recorded.

This research showed that a significant gap exists in snakebite care in the three countries. An integrative approach is needed to increase resource allocation for health system strengthening, including community education, healthcare worker training and improved access to snakebite treatment. Part of this approach should include regulations that ensure antivenoms available in health facilities meet quality control standards, and that snakebites are accommodated into routine reporting systems to assess progress.

SEXUAL AND REPRODUCTIVE HEALTH COMMODITIES

Chapter 4 studied access to SRH services and commodities. **Chapter 4.1** is a cross-country comparison of the availability, stockouts and affordability of SRH commodities in Kenya, Tanzania, Uganda and Zambia. Price, availability and stockout data was collected in July 2019 for over fifty lowest-priced SRH commodities from public, private and PNFP facilities in Kenya (n=221), Tanzania (n=373), Uganda (n=146) and Zambia (n=245). The availability and affordability were calculated according to the WHO/HAI methodology.

Overall availability of SRH commodities was low (<50%) in all sectors, areas and countries, with highest mean availability found in Kenyan public facilities (47%). Stockouts were common; average number of stockout days per month in the six months prior to data collection ranged from three days in Kenya's private and PNFP sectors, to 12 days in Zambia's public sector. In the public sectors of Kenya, Uganda and Zambia, and Zambia's PNFP sector, all SRH commodities were free for the patient. In the remaining sectors magnesium sulphate was the least affordable commodities. Accessibility was low across the countries, with Kenya's and Zambia's public sectors having six SRH commodities that met the accessibility threshold. The private sector of Uganda had only one SRH commodity that met the threshold.

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This study has shown that access to SRH commodities remains a challenge. Low availability in the public sector is compounded by regular stockouts, forcing patients to seek care in other sectors where there are availability and affordability challenges. Health system strengthening is needed to ensure access.

In **Chapter 4.2** the focus was on two key commodities for the treatment of post-partum haemorrhage: oxytocin and misoprostol. Their availability, prices and affordability was measured in Kenya, Uganda and Zambia. Data were collected from 376 health facilities in Kenya, Uganda and Zambia in July-August 2017. Availability and affordability were again calculated according to the WHO/HAI methodology. Medicine prices were compared with international reference prices (IRP) and expressed as median price ratios.

Availability of either oxytocin or misoprostol at health facilities was high; 81% in Kenya, 82% in Uganda and 76% in Zambia. Oxytocin was markedly more available than misoprostol, and it was most available in the public sector in all three countries. Availability of misoprostol

was highest in the public sector in Uganda (88%). Oxytocin and misoprostol were purchased by patients at prices above IRP. However, both medicines cost less than a day's wages and were therefore considered affordable. Availability of misoprostol was low in rural settings where it would be more preferred due to the lack of trained personnel and cold-storage facilities required for oxytocin. While the study showed that availability and affordability of either oxytocin or misoprostol at health facilities met the WHO benchmark of 80%, countries with limited resources should explore mechanisms to optimise management of post-partum haemorrhaging by improving access to misoprostol especially in rural areas.

Chapter 4.3 studied healthcare workers' perspectives on access to SRH services in the public, private and PNFP sectors in Kenya, Tanzania, Uganda and Zambia to gain insights into existing barriers per sector. A cross-sectional survey was conducted among healthcare workers working in health facilities offering SRH services in Kenya (n=212), Tanzania (n=371), Uganda (n=145) and Zambia (n=243). Data were collected in July 2019.

Some significant differences existed in perspectives of healthcare workers across the different sectors, even though in general many barriers were cross-cutting. The most common barrier in all sectors was poor patient knowledge (37%). Following, issues with supply of commodities (43%) and frequent stockouts (36%) were most often raised in the public sector; they were also raised in the other sectors. Patient costs were a more significant barrier in the private (33%) and PNFP sectors (21%) compared to the public sector (5%), while religious beliefs were a significant barrier in the PNFP sector (45%) compared to the public sector (27%). In all sectors delays in the delivery of supplies (37%-64%) was given as main stockout cause. Healthcare workers further believed that clients were often reluctant to access SRH services due to fear of stigmatisation, lack of knowledge, myths/superstitions, religious beliefs, and fear of side effects.

This study showed that to improve access to SRH services, efforts should focus on client education, the weak supply chain system, high costs in the private and PNFP sectors, and religious beliefs.

LESSONS LEARNED

Chapter 5 described the lessons learned from each of the studies, demonstrating through the three cases that access to medicines remains a critical issue for the majority of people living in SSA. It argues that while access to essential medicines for specific care fields or diseases may be subject to topic-specific barriers, many of the barriers are transcendent and are the result of an interplay of conditions across the health system that affect all areas of access. By looking at the similarities between care fields and diseases, and not the dissimilarities, this thesis has shown that a system-wide approach is needed to strengthen health systems in the Sub-Saharan region. Such an approach

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should be targeted at individuals, households and the community, the delivery of health services, and governance at the health sector, national and international level. A complex issue such as this needs active involvement from all actors, including patients and communities, community- and faith leaders, healthcare workers, civil society, governments, researchers, and international actors. Specific policy recommendations drawn from this thesis, and categorised according to the health system levels, are:

Individuals, households and the community

› Development and implementation of sensitisation programmes, adapted to the unique facets of each case, taking into consideration the socio-cultural beliefs of the target population. Programmes should consist of a combination of sensitisation approaches. Inclusion of community- and faith leaders, both as participants and change leaders, is critical.

Health service delivery

› Improving availability of medicines by lowering the healthcare level at which they are allowed to be available.

› Strengthening of the supply chain by:
  » Ensuring a well-functioning logistic management information system is in place;
  » Ensuring there are sufficient staff trained in supply chain management and forecasting;
  » Allocating sufficient budget to commodity procurement.

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› Roll-out of public-private partnerships and national health insurance to increase access to medicines and services.

› Task-shifting and sharing of tasks to cadres of healthcare workers with less experience. This can include allowing the prescribing of certain medicines by less specialised healthcare workers. Governments need to equip these cadres of healthcare workers with the necessary commodities, training, supervision and programme funding.

› Evaluation of medical curricula to improve knowledge and training of the health workforce, especially on controversial and neglected topics, such as ICEMs and snakebite envenoming.

› Increasing healthcare workers' opportunities for in-service continuing professional development.

› Establishing referral pathways between PNFP health facilities, and public and private health facilities to enable clients to access family planning services.

Governance at the health sector, national, and international level

› Increasing government spending on health to ensure sustainable financing and sufficient investments are made to ensure provision of quality services, without donor dependence.

› Reviewing of legislations and regulations on ICEMs prescribing and handling by the governments to ensure a balance exists between access to medicines for medical use, and prevention of misuse.

› Additional support of the International Narcotics Control Board to facilitate quantification, estimates and importation of ICEMs at country level.

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SAMENVATTING

INLEIDING

Het recht op de hoogst haalbare standaard van lichamelijke en geestelijk gezondheid is een internationaal erkend mensenrecht. Toegang tot geneesmiddelen is een van de bouwstenen om dit recht te realiseren. Helaas wordt voor een groot deel van de bevolking, vooral voor de inwoners van Sub-Sahara Afrika (SSA), zowel de toegang tot geneesmiddelen als de daaropvolgende verwezenlijking van de hoogst haalbare gezondheidsstandaard niet behaald.

De prijs, beschikbaarheid en betaalbaarheid van geneesmiddelen zijn de afgelopen twintig jaar uitgebreid bestudeerd met behulp van de methodologie *'Measuring medicine prices, availability, affordability and price components'* van de Wereldgezondheidsorganisatie en Health Action International (WHO/HAI). Zoals wordt beschreven in de algemene inleiding in **hoofdstuk 1**, is de toegang tot geneesmiddelen en de gezondheidszorg niet alleen het resultaat van de beschikbaarheid en betaalbaarheid van de geneesmiddelen zelf, maar wordt deze beïnvloed door barrières op de vijf niveaus van het zorgsysteem: individuen, huishoudens en de gemeenschap; de uitvoering van de gezondheidszorg; de zorgsector; en het nationale en internationale niveau.

Om een beter inzicht te krijgen in hoe barrières op deze verschillende niveaus van invloed zijn op de toegang tot gezondheidszorg in SSA, en welke lessen daaruit kunnen worden getrokken, richtte dit proefschrift zich op drie verschillende casussen: i. internationaal gereguleerde essentiële geneesmiddelen (ICEMs, geneesmiddelen die zijn opgenomen in de lijst van essentiële geneesmiddelen van de WHO en in een van de drie internationale verdragen inzake verdovende middelen en psychotrope stoffen), ii. de behandeling van slangenbeten, en iii. geneesmiddelen voor seksuele en reproductieve gezondheid (SRG). Deze casussen zijn gekozen vanwege hun controversiële karakter of verwaarlozing door de internationale gemeenschap en worden gebruikt om de complexiteit van de toegang tot essentiële geneesmiddelen in de regio te illustreren. De vragen die in dit proefschrift worden beantwoord zijn: *Wat zijn de overeenkomsten en verschillen in toegang tot essentiële geneesmiddelen tussen deze casussen?* En *welke lessen kunnen worden geleerd om de toegang tot essentiële geneesmiddelen te verbeteren*?

INTERNATIONAAL GEREGULEERDE ESSENTIËLE GENEESMIDDELEN

Hoofdstuk 2 beschrijft de toegang tot ICEMs en bestaat uit drie subhoofdstukken. In **hoofdstuk 2.1** werd bestaande literatuur over barrières voor de toegang tot ICEMs in SSA tussen 2012-2022 bestudeerd.

De zoekstrategie leverde 97 artikelen op die aan de inclusiecriteria voldeden. Er werden talloze barrières gerapporteerd die de toegang tot ICEMs belemmerden en deze barrières

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kwamen voor bij alle ICEM-medicijnklassen. De belangrijkste barrières kunnen worden gegroepeerd aan de hand van de niveaus van het zorgsysteem:

1. *Individuen, huishoudens en de gemeenschap:* Beperkte of gebrekkige kennis onder het publiek over ICEMs, angst voor opioïdenverslaving.

2. *Gezondheidszorg:* Geneesmiddelentekorten, onbetaalbaarheid, lange afstanden naar gezondheidscentra, kwaliteit van de geneesmiddelen, gebrek aan gespecialiseerd zorgpersoneel, gebrek aan kennis en opleiding over ICEMs onder het zorgpersoneel, misvattingen over ICEMs, gebrekkige logistieke infrastructuur. De algemene lage beschikbaarheid van geneesmiddelen in SSA werd verergerd door de gereguleerde status van ICEMs.

3. *Zorgsector*: Gebrek aan prioritering van ICEM-gerelateerde gezondheidszorggebieden door overheidsinstanties, wat leidt tot ontoereikende begrotingstoewijzingen.

Overkoepelende barrières op het gebied van bestuur hadden betrekking op het gebrek aan goede schattingen om de behoefte aan geneesmiddelen te kwantificeren, omslachtige inkoopprocessen en strenge nationale wetten die ICEMs reguleren, wat leidt tot te restrictieve voorschrijfpraktijken voor deze geneesmiddelen.

Dit onderzoek toonde aan dat meerdere barrières, verspreid over alle niveaus van het zorgsysteem, de toegang tot ICEMs belemmeren en dat een veelzijdige aanpak nodig is om de toegang te verbeteren.

Hoofdstuk 2.2 bestond uit een kwalitatief onderzoek, met als doel het identificeren van de sociale, culturele en wettelijke barrières die de toegang tot ICEMs in Uganda beïnvloeden. Uit semigestructureerde interviews met 15 experts bleek dat de barrières voortkwamen uit verschillende factoren, waarvan sommige specifiek waren voor ICEMs en andere golden voor geneesmiddelen in het algemeen. Factoren die de toegang tot geneesmiddelen in het algemeen in Uganda beïnvloedden waren onder andere het gebruik van schattingen om de behoefte aan geneesmiddelen te kwantificeren, praktische en logistieke leveringsproblemen van geneesmiddelen, gebrek aan gezondheidspersoneel, onbetaalbaarheid van geneesmiddelen en de fysieke en geografische barrières in de toegang tot geneesmiddelen. Specifieke barrières voor ICEMs waren het gebrek aan prioritering, een disbalans in de wetten die regulering prefereert boven de toegang tot de geneesmiddelen, een gebrek aan kennis over ICEMs onder zowel de bevolking als het zorgpersoneel en het heersende stigma met betrekking tot ICEMs en de gerelateerde gezondheidszorggebieden. De resultaten van dit onderzoek onderstrepen de noodzaak tot het versterken van het zorgsysteem in Uganda. Om de toegang tot ICEMs te verbeteren zijn een gecoördineerde aanpak en actieve betrokkenheid van alle belanghebbenden noodzakelijk. Dergelijke

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inspanningen moeten niet alleen de toegang bevorderen, maar ook het risico op misbruik beperken.

Toegang tot anesthesie en chirurgische zorg is een groot probleem voor mensen in SSA. In deze regio is ketamine van cruciaal belang voor het verlenen van anesthesie. Pogingen om ketamine internationaal te classificeren als een gereguleerd geneesmiddel kunnen de toegankelijkheid ervan echter aanzienlijk beïnvloeden. In **hoofdstuk 2.3** is daarom getracht een schatting te maken van wat het effect van het reguleren van ketamine zou zijn. Er werden twee methoden gebruikt: een enquête in Rwandese ziekenhuizen en interviews met deskundigen op het gebied van anesthesiezorg in SSA. In 54 ziekenhuizen werden gegevens verzameld over vier anesthesiemiddelen (ketamine, propofol, thiopental en inhalatiemiddelen). Er werden semigestructureerde interviews gehouden met 10 deskundigen.

Uit het onderzoek bleek dat de beschikbaarheid van ketamine en propofol in Rwanda vergelijkbaar zijn (rond de 80%), terwijl thiopental en middelen voor inhalatie zoals halothaan, isofluraan of sevofluraan in ongeveer 50% van de ziekenhuizen beschikbaar waren. Uit de interviews bleek dat er aanzienlijke barrières waren die de toegang tot anesthesiezorg belemmerden, waaronder een algemeen gebrek aan aandacht voor het specialisme door de overheid, een tekort aan anesthesiologen en migratie van opgeleide anesthesiologen en een schaarste aan geneesmiddelen en apparatuur. Als gevolg hiervan beschreven alle deskundigen ketamine als cruciaal geneesmiddel voor het verlenen van anesthesiezorg in SSA en zij gaven aan dat het internationaal reguleren ervan een aanzienlijk negatief effect zou hebben op de kwaliteit van anesthesiezorg die in de regio kan worden verleend. Misbruik van ketamine was volgens de deskundigen geen probleem in SSA.

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Dit onderzoek heeft aangetoond dat ketamine een kritiek geneesmiddel is voor de levering van anesthesiezorg in SSA en dat de toegang tot veilige chirurgische zorg voor miljoenen mensen in gevaar kan komen, indien het wordt gereguleerd op internationaal niveau. Er zijn gecoördineerde inspanningen nodig om de anesthesiezorg in SSA in het algemeen te verbeteren, zodat men in de toekomst minder afhankelijk kan zijn van ketamine.

BEHANDELING VAN SLANGENBETEN

Hoofdstuk 3 richtte zich op slangenbeten. **Hoofdstuk 3.1** had als doel om een algemeen overzicht te geven van de omvang van het probleem en de impact van slangenbeten in vier districten op het platteland van Kenia waar slangenbeten veel voorkomen, om context-specifiek beleid te kunnen creëren. Het gezondheidszorg-zoekend gedrag en de gezondheids-, sociale en economische last van slangenbeten werd bestudeerd door

middel van een enquête onder huishoudens. In de vier districten werden 382 respondenten ondervraagd aan de hand van een gestructureerde vragenlijst.

Uit de bevindingen bleek dat slangenbeten veel voorkwamen in de onderzochte gemeenschappen, aangezien 13% van de deelnemers persoonlijk door een slang was gebeten en meer dan een derde iemand uit de gemeenschap kende die was gebeten. Slachtoffers waren meestal gewoon aan het lopen (38%) of op het land aan het werk (24%), toen ze werden gebeten. De dood van een iemand uit de gemeenschap of een familielid werd gemeld door respectievelijk 9% en 15% van de deelnemers. De meeste mensen die waren gebeten waren tussen de 26 en 45 jaar oud. Het risico op slangenbeten was niet statistisch significant geassocieerd met geslacht, opleidingsniveau of beroep. Verder speelden traditionele geneeswijzen een belangrijke rol bij de behandeling van slangenbeten: terwijl 58% van de gebeten mensen na de beet naar een gezondheidscentrum ging, ging 42% ofwel alleen naar een traditionele genezer ofwel eerst naar een traditionele genezer voordat ze een gezondheidscentrum bezochten. De meest voorkomende eerste-hulpmethoden die mensen gebruikten na een beet, die allemaal ineffectief zijn, waren het gebruik van tourniquets, het gebruik van zwarte stenen en het snijden in de beet. Tot slot hadden slangenbeten zowel sociale als financiële gevolgen voor de slachtoffers.

Om de last die plattelandsgemeenschappen ondervinden van slangenbeten te verminderen is ten eerste de betrokkenheid van de gemeenschap nodig, inclusief die van traditionele genezers, om betere preventieve maatregelen en gezondheidszorg-zoekend gedrag te stimuleren. Ten tweede moet het zorgsysteem worden versterkt zodat slachtoffers van slangenbeten snel en adequaat kunnen worden behandeld met geschikt en betaalbaar tegengif en ondersteunende zorg.

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In **hoofdstuk 3.2** werden de beschikbaarheid, betaalbaarheid en tekorten van geneesmiddelen voor de behandeling van slangenbeten in Kenia beoordeeld. Deze studie werd uitgevoerd omdat er, hoewel er inspanningen worden geleverd om de zorg voor slangenbeten te verbeteren, weinig informatie beschikbaar is over de toegang tot behandeling. De studie maakte gebruik van een aangepaste versie van de WHO/HAI-methodologie. Gegevens over beschikbaarheid, prijzen en tekorten werden verzameld voor 45 geneesmiddelen van publieke (n=85), private (n=36) en private non-profit (PNFP) (n=12) gezondheidscentra in Kenia in juli-augustus 2020. Beschikbaarheid werd gedefinieerd als de aanwezigheid van een geneesmiddel in een vooraf gespecificeerde dosis en formulering ten tijde van de dataverzameling in de gezondheidszorginstelling. Geneesmiddelentekorten werden retrospectief gemeten voor een periode van twaalf maanden. Een geneesmiddel werd als niet op voorraad beschouwd als de instelling het geneesmiddel gewoonlijk op voorraad had, maar de database aangaf dat het middel het afgelopen jaar soms niet op voorraad was. De betaalbaarheid werd berekend aan de hand van het wettelijk loon van een laagstbetaalde overheidswerknemer (LPGW). toegankelijkheid werd vergeleken met het

afkappunt van 80%, zoals vastgesteld door de WHO, en de betaalbaarheid voor een LPGW (<1 dagloon) te combineren.

De algemene beschikbaarheid van geneesmiddelen voor het behandelen van slangenbeten was laag (43%). Tegengif was beschikbaar in 45% van de publieke en 19% van de private gezondheidscentra. Zowel in de publieke (19%) als in de private (12%) sector waren er vaak tekorten van ten minste één van de geneesmiddelen tegen slangenbeten; geneesmiddelen waren gemiddeld ongeveer een maand niet op voorraad in de publieke sector en gemiddeld 24 dagen niet op voorraad in de private sector over een periode van twaalf maanden. Aangezien de meeste geneesmiddelen gratis waren voor de patiënt in de publieke sector, was betaalbaarheid in die sector geen probleem. In de private sector was de betaalbaarheid een groter probleem; de mediane kosten van een ampul tegengif bedroegen 14 dagen loon voor een LPGW. Slechts vijf geneesmiddelen in de publieke sector en twee in de private sector werden als toegankelijk beschouwd.

Om de toegang tot zorg voor slangenbeten te verbeteren, moeten de inspanningen gericht zijn op het garanderen van de beschikbaarheid van geneesmiddelen in alle gezondheidscentra en op het verbeteren van de toeleveringsketen om geneesmiddelentekorten te beperken. Tegengif opnemen in het pakket van vergoede basiszorg die in Kenia op dit moment wordt uitgerold zou de toegang verder kunnen verbeteren.

Hoofdstuk 3.3 onderzocht de capaciteit van gezondheidscentra en zorgpersoneel om slangenbeten te behandelen in Kenia, Uganda en Zambia. Het onderzoek bestond uit een enquête onder zorgpersoneel in gezondheidscentra in Kenia (n=145), Uganda (n=144) en Zambia (n=108) tussen maart 2018 en november 2019.

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Het meeste zorgpersoneel gaf aan dat het aantal gevallen van slangenbeten vergelijkbaar was tussen mannen en vrouwen, dat de meeste patiënten tussen 21 en 30 jaar oud waren en dat de slachtoffers vaak op het land aan het werk waren of aan het wandelen waren toen ze gebeten werden. Ondersteunende behandeling was de meest aangeboden vorm van behandeling voor slangenbeten in de gezondheidscentra. In de drie landen had 85-90% van het zorgpersoneel geen training gehad in het behandelen van slangenbeten. Verder dacht ongeveer 80% van het zorgpersoneel dat hun gezondheidscentrum niet over de nodige uitrusting en geneesmiddelen beschikte om slangenbeten te kunnen behandelen. Zo verklaarde slechts 27% van het zorgpersoneel in Kenia, 4% in Uganda en 8% in Zambia dat ze op het moment van de enquête tegengif op voorraad hadden. Slangenbeten werden bovendien vaak niet systematisch geregistreerd.

Dit onderzoek toont aan dat er nog aanzienlijk veel te verbeteren valt in de zorg voor slangenbeten in de drie landen. Er is een integrale aanpak nodig om meer middelen toe te wijzen voor de versterking van het zorgsysteem, waaronder voorlichting aan

de gemeenschap, opleiding van zorgpersoneel en verbeterde toegang tot behandeling van slangenbeten. Als belangrijk onderdeel van deze aanpak moet er regelgeving komen die ervoor zorgt dat het tegengif dat beschikbaar is in gezondheidscentra voldoet aan kwaliteitsnormen en dat slangenbeten worden opgenomen in gestructureerde rapportagesystemen om de vooruitgang te beoordelen.

SEKSUELE EN REPRODUCTIEVE GEZONDHEIDSZORG

Hoofdstuk 4 onderzocht de toegang tot SRG-diensten en -geneesmiddelen. **Hoofdstuk 4.1** vergeleek Kenia, Uganda, Tanzania en Zambia ten aanzien van de beschikbaarheid, tekorten en betaalbaarheid van SRG-geneesmiddelen. In juli 2019 werden gegevens over de prijs, beschikbaarheid en tekorten voor meer dan vijftig SRG-geneesmiddelen verzameld in publieke, private en PNFP-faciliteiten in Kenia (n=221), Uganda (n=146), Tanzania (n=373) en Zambia (n=245). De beschikbaarheid, betaalbaarheid en tekorten werden berekend volgens de WHO/HAI-methodologie.

De algemene beschikbaarheid van SRG-geneesmiddelen was laag (<50%) in alle sectoren, landelijke en stedelijke gebieden en landen, met de hoogste gemiddelde beschikbaarheid in de publieke sector in Kenia (47%). Geneesmiddelentekorten kwam vaak voor; het gemiddelde aantal dagen per maand in de zes maanden voorafgaand aan de dataverzameling dat er tekorten waren varieerde van drie dagen in de private en PNFP-sectoren in Kenia tot 12 dagen in de publieke sector in Zambia. In de publieke sectoren van Kenia, Uganda en Zambia en in de PNFP-sector van Zambia waren alle SRG-geneesmiddelen gratis voor de patiënt. Magnesiumsulfaat was het minst betaalbare geneesmiddel in de overige sectoren. De toegankelijkheid was laag in alle landen; de publieke sectoren van Kenia en Zambia hadden zes SRG-geneesmiddelen die voldeden aan de toegankelijkheidsmaatstaf van 80% en <1 dag loon. De private sector in Uganda had slechts één SRG-artikel dat aan de maatstaf voldeed.

Uit dit onderzoek blijkt dat de toegang tot SRG-geneesmiddelen een probleem blijft. De lage beschikbaarheid in de publieke sector wordt verergerd door regelmatige geneesmiddelentekorten, waardoor patiënten genoodzaakt zijn om zorg te zoeken in andere sectoren waar er problemen zijn met de beschikbaarheid en betaalbaarheid. Het zorgsysteem zal moeten worden versterkt om de toegang tot deze essentiële geneesmiddelen te garanderen.

In **hoofdstuk 4.2** lag de nadruk op twee belangrijke geneesmiddelen voor de behandeling van postpartum bloedingen: oxytocine en misoprostol. De beschikbaarheid, prijzen en betaalbaarheid werd gemeten in Kenia, Uganda en Zambia. De data werd verzameld bij 376 gezondheidscentra in Kenia, Uganda en Zambia in juli-augustus 2017. De beschikbaarheid en betaalbaarheid werden opnieuw berekend volgens de WHO/HAI-methodologie. Prijzen

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van geneesmiddelen werden vergeleken met internationale referentieprijzen (IRP) en uitgedrukt als mediane prijsverhoudingen.

De beschikbaarheid van oxytocine of misoprostol in gezondheidscentra was hoog: 81% in Kenia, 82% in Uganda en 76% in Zambia. Oxytocine was duidelijk meer beschikbaar dan misoprostol en het was het meest beschikbaar in de publieke sector in alle drie de landen. De beschikbaarheid van misoprostol was het hoogst in de publieke sector in Uganda (88%). Oxytocine en misoprostol werden door patiënten gekocht tegen prijzen die boven de IRP lagen. Beide geneesmiddelen kostten echter minder dan een dagloon en werden daarom als betaalbaar beschouwd. De beschikbaarheid van misoprostol was laag in landelijke gebieden waar het juist meer voorkeur zou hebben vanwege het gebrek aan getraind personeel en goede gekoelde opslagfaciliteiten die nodig zijn voor oxytocine. Hoewel het onderzoek aantoonde dat de beschikbaarheid en betaalbaarheid van oxytocine of misoprostol in gezondheidscentra voldeed aan de WHO-maatstaf van 80%, moeten landen met beperkte middelen mechanismen onderzoeken om de behandeling van postpartum bloedingen te optimaliseren door de toegang tot misoprostol te verbeteren, vooral in landelijke gebieden.

Hoofdstuk 4.3 onderzocht de perspectieven van zorgpersoneel op toegang tot SRG-zorg in de publieke, private en PNFP-sectoren in Kenia, Uganda, Tanzania en Zambia om inzicht te krijgen in de barrières per sector. Er werd gebruik gemaakt van een enquête onder zorgpersoneel dat werkzaam is in gezondheidscentra die SRG-diensten aanbieden in Kenia (n=212), Uganda (n=145), Tanzania (n=371) en Zambia (n=243). De gegevens werden verzameld in juli 2019.

Op basis van de inzichten van het zorgpersoneel uit de verschillende sectoren kwamen enkele significante verschillen naar boven, hoewel over het algemeen veel barrières overkoepelend waren. De meest voorkomende barrière in alle sectoren was een gebrek aan kennis omtrent de SRG van patiënten (37%). Vervolgens werden problemen met de levering van basisgeneesmiddelen (43%) en frequente geneesmiddelentekorten (36%) het vaakst genoemd in de publieke sector, maar ook in de andere sectoren waren dit barrières. Kosten voor de patiënt vormden een belangrijkere barrière in de private sector (33%) en de PNFP-sector (21%) vergeleken met de publieke sector (5%), terwijl religieuze overtuigingen een belangrijkere barrière vormden in de PNFP-sector (45%) vergeleken met de publieke sector (27%). In alle sectoren werd de verlate levering van geneesmiddelen (37%-64%) genoemd als de belangrijkste oorzaak van geneesmiddelentekorten. Het zorgpersoneel was verder van mening dat cliënten vaak terughoudend zijn met het zoeken van SRG-zorg vanwege angst voor stigmatisering, hun gebrek aan kennis, mythen/bijgeloof, religieuze overtuigingen en angst voor bijwerkingen.

6.2

Dit onderzoek toonde aan dat om de toegang tot SRG-zorg te verbeteren, inspanningen zich moeten richten op de voorlichting van cliënten, het gebrekkige logistieke systeem, de hoge kosten in de private sector en de PNFP-sector en religieuze overtuigingen.

GELEERDE LESSEN

Hoofdstuk 5 beschrijft de lessen die uit elk van de onderzoeken zijn getrokken, waarbij aan de hand van de drie casussen wordt aangetoond dat toegang tot geneesmiddelen voor de meerderheid van de mensen in SSA een significant probleem blijft. Hoewel de toegang tot essentiële geneesmiddelen voor specifieke zorggebieden of ziekten onderhevig kan zijn aan specifieke barrières, zijn veel van de barrières transcendent en het resultaat van een samenspel van omstandigheden in het hele zorgsysteem. Door te kijken naar de overeenkomsten tussen zorggebieden en ziekten, en niet naar de verschillen, heeft dit proefschrift aangetoond dat er een systeem-brede aanpak nodig is om de gezondheidszorgstelsels in de Sub-Sahara regio te versterken. Een dergelijke aanpak moet gericht zijn op individuen, huishoudens en de gemeenschap, de uitvoering van de gezondheidszorg en het bestuur op zorgsector-, nationaal en internationaal niveau. Een complex vraagstuk als dit vereist actieve betrokkenheid van alle actoren, waaronder patiënten en gemeenschappen, leiders van gemeenschappen en religieuze leiders, zorgpersoneel, maatschappelijke organisaties, overheden, onderzoekers en internationale actoren. Specifieke beleidsaanbevelingen op basis van dit proefschrift, gecategoriseerd naar de niveaus van het zorgsysteem, zijn:

Individuen, huishoudens en de gemeenschap
› Ontwikkeling en implementatie van bewustmakingsprogramma's, aangepast aan de unieke facetten van elk zorggebied/ziekte, rekening houdend met de sociaal-culturele overtuigingen van de doelgroep. De programma's moeten bestaan uit een combinatie van bewustmakingsmethoden. Het is van cruciaal belang om leiders van de gemeenschap en religieuze leiders hierbij te betrekken, zowel als deelnemers als veranderaars.

Uitvoering van de gezondheidszorg
› De beschikbaarheid van geneesmiddelen verbeteren door het gezondheidszorgniveau waarop ze beschikbaar mogen zijn te verlagen.

› De logistieke keten versterken door:
  » Zorgen voor een goed werkend informatiesysteem voor logistiek beheer;
  » Ervoor zorgen dat er voldoende personeel is opgeleid in logistiek management en forecasting;
  » Voldoende budget toewijzen aan de inkoop van geneesmiddelen.

6.2

› Implementeren van publiek-private partnerschappen en nationale ziektekostenverzekeringen om de toegang tot geneesmiddelen te verbeteren.

› Taakverschuiving en taakverdeling naar kaders van zorgverleners met minder ervaring. Dit kan ook betekenen dat minder gespecialiseerd zorgpersoneel bepaalde geneesmiddelen mogen voorschrijven welke ze normaliter niet voorschrijven. Overheden moeten deze groepen zorgverleners voorzien van de benodigde geneesmiddelen, training, supervisie en programmagelden.

› Evaluatie van medische curricula om de kennis en opleiding van zorgpersoneel te verbeteren, vooral over controversiële en verwaarloosde onderwerpen, zoals ICEMs en slangenbeten.

› Zorgpersoneel meer mogelijkheden bieden voor bijscholing.

› Doorverwijzingstrajecten opzetten tussen PNFP-gezondheidscentra en openbare en private gezondheidscentra om cliënten toegang te geven tot SRG-zorg.

Bestuur op gezondheidssector, nationaal en internationaal niveau

› De overheidsuitgaven voor gezondheidszorg verhogen om te zorgen voor duurzame financiering en voldoende investeringen om een kwalitatief goede dienstverlening te garanderen, zonder afhankelijk te zijn van donoren.

› Herziening van wet- en regelgeving over het voorschrijven van en omgaan met ICEMs door de overheden om te zorgen dat er een balans is tussen toegang tot geneesmiddelen voor medisch gebruik en preventie van misbruik.

6.2

› Aanvullende ondersteuning van het Internationaal Comité van toezicht op verdovende middelen om de kwantificering, schattingen en invoer van ICEMs op nationaal niveau te vergemakkelijken.

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Gaby Ooms was born on December 20, 1993 in Terneuzen, the Netherlands. She obtained her Bachelor's degree in health sciences from the VU University (Amsterdam, the Netherlands) in 2014, during which she undertook a research internship at the Academic Medical Center, University of Amsterdam, on the use of electronic cigarettes in the European Union. In 2017 she finished her Master's degree in Global Health from VU University. During her master programme she undertook research placements at Health Action International (HAI) (Amsterdam, the Netherlands) on internationally controlled essential medicines in Uganda, and at Fundación IFARMA (Bogotá, Colombia) on compulsory licensing of medicines in Colombia and Ecuador.

After graduation, Gaby started working at HAI, where she is currently working as research manager. In this role, she has been responsible for the research activities across HAI's projects on sexual and reproductive health, snakebite envenoming, internationally controlled essential medicines, and antimicrobial resistance. She is also responsible for HAI's capacity-strengthening training on research and leads HAI's internship programme. Currently, Gaby is principal investigator of World Health Organization (WHO)-funded research consultancies on informal markets and substandard and falsified medical products, and separately, access to treatments for substance use disorders. In 2023 she became a member of the WHO STAGE[1] Technical Working Group for WHO Recommended Maternal and Newborn (MNH) Commodities.

Gaby started her PhD research described in this thesis in 2019, at the Utrecht WHO Collaborating Centre for Pharmaceutical Policy and Regulation at Utrecht University, under the supervision of prof. dr. Aukje Mantel-Teeuwisse, dr. Rianne van den Ham and dr. Tim Reed. She combined her research activities with her work at HAI.

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[1] Strategic and Technical Advisory Group of Experts for Maternal, Newborn, Child and Adolescent Health and Nutrition