

# A Case Study of the Registration of Essential Medicines in the East African Community

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## Research

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# Abstract

**Objective:** To quantify the essential medicine status of registered medicines in the East African Community (EAC) for antimicrobial medicines and medicines for non-communicable diseases.

**Methods:** The National Drug Registers (NDRs) of Kenya, Tanzania, and Uganda (February 2018) were compared with their respective national Essential Medicine Lists (EMLs) to determine the registration status of essential medicines as an indicator of their availability. The number of registered products was analysed for essential medicines and selected non-essential medicines.

**Findings:** Many essential medicines in the EAC are not registered: Kenya 28% (175/632), Tanzania 50% (400/797), Uganda 40% (266/663). Approximately, only one-third of products on the NDRs are essential medicines: Kenya (29%), Tanzania (36%), and Uganda (42%). 23% to 42% of registered essential medicines only have 1 or 2 products. 42 medicines accounted for over 4100 medical products, half of which were non-essential products.

**Conclusions:** This novel analysis provides insight into how registration of medicines is likely to be a major barrier to accessing essential medicines. The under registration of essential medicines and the over registration of non-essential medicines demonstrates a mismatch between the market of medicines being produced and registered and the health needs of the East African Community. Joint regional medicine authorisation programs such as the EAC Medicines Registration Harmonization Project have potential to improve access to key medicines if essential medicines are prioritised.

## Introduction

### Essential Medicines

Access to health care is a fundamental human right and medicines are enshrined in the UN sustainable development goal 3.8 as “...access to safe, effective, quality, and affordable essential medicines” and yet one third of the world’s population lacks reliable access to essential medicines. The WHO has revised its *model list of essential medicines* biannually since 1977, and 137 countries have developed national essential medicines lists to address priority health care need of their population.

Although WHO & Health Action International (HAI) surveys found that selected essential medicines are more available than non-essential medicines [1, 2], low- and middle-income countries (LMICs) struggle to ensure access to a broader set of essential medicines as specified by their national essential medicine lists [3]. Moreover, shortages of essential medicines have been reported in many countries across the world particularly affecting older off-patent, commonly used medicines such as anti-infectives and cardiovascular medicines [4, 5]. Reported reasons for drug shortages include both market factors, such as non-prioritisation of generics and changes in demand, and manufacturing factors, such as disrupted supply chains and consolidation of manufacturing [6, 7].

## Medicine Registration

Generally, before a medical product can be publicly or privately procured it must be assessed for standards of quality, safety, and efficacy; once it has been registered it can be made available. Low- and Middle-Income countries can lack the financial and administrative power required to prioritise, assess, and register products [20–22]. A number of regional and sub-regional programs have been developed whereby countries share common funding, standards, procedures, and regulatory decisions towards the registration of medicines. This reduces workload and costs to individual countries and incentivises producers to have their products registered regionally. These initiatives include the Pharmaceutical Product Working Group of South-East Asian Nations, the European Medicines Agency, the Caribbean Regulation System, and the Pacific Island Countries. In 2012, the East African Community (EAC) launched an initiative, the Medicines Registration Harmonisation Project (MRH), to promote access to affordable quality essential medicines [11].

Despite this global focus on improving registration of medicines, it remains an under researched area. Previous analysis of medicine registration in Uganda, an EAC member, has shown only 51% of medicines listed as essential had a product registered with the national regulatory authority [8]. Alongside the under-registration of essential medicines there may be over-registration of non-essential medicines with an estimated 70% of marketed medicines being duplicate or non-essential [9]. Both, under-registration of essential medicines and over-registration of non-essential medicines are highly problematic. The former for the non-availability of basic medicines to meet public health needs and the later for diverting regulatory and financial resources to non-priority, and in some cases inferior, treatments.

A technical consultation meeting organised by the WHO Department of Essential Medicines and Health Products noted that at least three different manufacturers are “generally considered desirable” to ensure a viable market and stable supply of medicines [5]. Similarly, in response to drug shortages and unprecedented price increases for drugs with just one or two different manufacturers in the US [6] it has been proposed that the US FDA should prioritise market applications related to generics with three or fewer generic products registered [10].

The aim of this study is to examine the extent of registration in the EAC of all essential medicines and to provide an audit of national drug registers to ascertain essential medicine status of highly registered medicines to treat infections and non-communicable diseases.

## Methods

### Countries

Kenya, Uganda, and the United Republic of Tanzania are members of East African Community. Other EAC members – Burundi, Rwanda, and South Sudan – were excluded from the analysis due to unavailability of online national drug registries.

## Data Sources

- i. **The essential medicines lists:** Kenya and Uganda (2016) and United Republic of Tanzania (2017).

Non-pharmacological products such as antiseptic solutions, dialysis solutions and medical devices were excluded. Following exclusions there were 632, 663, and 797 respectively [12–14]. The following information on medicines from the essential medicines lists was extracted: generic name of the medicine, strength, and formulation.

- ii. **The national drug registers:** Kenya, Uganda, and United Republic of Tanzania, accessed on 26th February 2018, listed 6151, 3896 and 3590 products respectively [15–17]. Non-medicinal and veterinary products were excluded. Medicines were collated and named consistently where spellings or formatting of the same medicinal product varied.

## Analysis

### Essential Medicine Status of Registered Medicines

Medicines from each national drug registry were compared with the respective country EML for generic name, strength, and formulation and where half doses (or otherwise divisible) were also considered as essential. Registered Medicines in an inappropriate dose, wrong preparation (e.g., IV instead of oral) or both the wrong dose and preparation, or with missing information were excluded.

The EML of each country lists medicines by class which differ across countries. The number of unregistered essential medicines in each class was analysed. Blood products of human origin, disinfectants and antiseptics, diagnostic agents, nutrition supplements, dialysis solutions, barrier contraceptives, and other non-pharmaceuticals were excluded.

### Number of Products Registered for Essential Medicine

The national drug registries were searched for the number of products (which meet EML criteria) for each essential medicine active ingredient. Convenient sub-analysis of the drug registries is limited due to many inconsistencies in formatting therefore essential medicines with multiple doses and forms are considered as one medicine with a unique active medicine / ingredient (or combination). The number of registered products for each unique essential medicine was counted and grouped into 1–2, 3–15 and over 15 products. These groups were as selected as they indicate an effective market according to Berndt et al, Wiggins and Mannes and the WHO Department of Essential Medicines and Health Products [5, 18, 19]. We calculated the number and proportion of essential medicines belonging to these groups to determine the proportion of essential medicines that are unavailable or at risk of drug shortages

### Essential Medicine Status of Highly Registered Medicines

Medicines with more than 10 registered products in each of the three countries were extracted to give an impression what proportion of the registry contains well registered medicines. Those with more than fifty

products across the three countries, an arbitrary cut-off that produces a manageable number of examples, were identified. This allowed for analysis of essential medicines status of highly (arguably excessively) registered medicines. These were grouped as being antimicrobials or for non-communicable diseases.

## Results

### Essential Medicine Status of Registered Medicines

In Kenya, Tanzania, and Uganda, 72%, 50% and 60% of essential medicines had one or more registered products, respectively (see Table 1A). However essential medicine products accounted for only 29% (1801/6161) of all registered products in Kenya, 37% (1312/3590) in Tanzania, and 42% (1628/3896) in Uganda, with non-essential medicines comprising 4350, 2278 and 2268 registered products, respectively (see Table 1). The essential medicines that were not registered are described by class in Table 2.

43%, 33% and 23% of registered essential medicines Kenya, Tanzania and Uganda respectively had either one or two products only as shown in Table 1C and Fig. 1.

**Table 1** The proportion of essential medicines with and without registered products. Indented are the reasons for which essential medicines did not correspond with any registered (n, %). B) The proportion registered medicines which are essential (Following exclusions). C) Number of products registered for each essential medicine (by key medicine).

	Kenya	Republic of Tanzania	Uganda
<b>A) Total Number of EML Medicines (n)</b>	<b>632</b>	<b>797</b>	<b>663</b>
Registered Essential Medicines ( <i>n, %</i> )	457 (72%)	397 (50%)	397 (60%)
Non-registered Essential Medicines ( <i>n, %</i> )	175 (28%)	400 (50%)	266 (40%)
No Named Products	90	197	170
Wrong Dose	49	93	46
Wrong Preparation	12	50	31
Wrong Dose and Preparation	19	6	0
Incomplete Information	5	54	19
<b>B) Total Number of Registered Products (n)</b>	<b>6151</b>	<b>3590</b>	<b>3896</b>
Essential Medicines ( <i>n, %</i> )	1801 (29%)	1312 (37%)	1628 (42%)
Non-Essential Medicines ( <i>n, %</i> )	4350 (71%)	2278 (63%)	2268 (58%)
<b>C) Registered Essential Medicines group by number of registered products (n)</b>	<b>263</b>	<b>220</b>	<b>245</b>
1–2 products	112 (43%)	72 (33%)	57 (23%)
3-15 products	122 (46%)	130 (59%)	163 (67%)
More than 15 products	29 (11%)	18 (8%)	25 (10%)

**Table 2** The proportion of essential medicines without registered products (*n, %*) shown by “Class” as defined by each country’s EMLS (Following exclusions). Highlighted rows indicate examples of >50% non-registration.

Class of Essential Medicine	Kenya			Republic of Tanzania			Uganda		
	Total	Not Registered (%)		Total	Not Registered (%)		Total	Not Registered (%)	
Anaesthetics	21	3	14%	48	33	69%	32	17	53%
Anti-Allergics And Medicines Used In Anaphylaxis	8	0	0%	14	1	7%	9	0	0%
Antidotes And Other Substances Used In Poisoning	19	14	74%	10	9	90%	17	12	71%
Anti-epileptics/Anticonvulsants	18	5	28%	17	7	41%	14	5	36%
Anti-infective Medicines	160	33	21%	185	55	30%	162	45	28%
Anti-migraine Medicines	5	0	0%	8	2	25%	9	4	44%
Anti-neoplastic And Immunosuppressive Medicines	85	22	26%	64	39	61%	53	31	58%
Anti-parkinsonism Medicines	5	4	80%	5	4	80%	1	1	100%
Cardiovascular Medicines	38	9	24%	55	23	42%	39	11	28%
Dermatological Medicines (Topical)	23	4	17%	29	11	38%	21	10	48%
Diuretics	10	2	20%	7	3	43%	5	0	0%
Ear, Nose And Throat Medicines	7	3	43%	10	4	40%	15	3	20%
Gastrointestinal Medicines	19	2	11%	34	19	56%	26	5	19%
Hormones, Other Endocrine Medicines And Contraceptives	33	7	21%	70	31	44%	39	17	44%
Immunologicals and Vaccines	20	2	10%	20	19	95%	22	13	59%
Medicines Acting On The Respiratory Tract	10	1	10%	13	6	46%	12	4	33%
Medicines Affecting The Blood	24	16	67%	21	15	71%	11	6	55%
Medicines For Diseases Of Joints	7	2	29%				5	3	60%
Medicines For Mental And Behavioural Disorders	21	12	57%	35	17	49%	33	11	33%
Medicines For Neurosurgical Use							3	3	100%
Medicines For Pain And Palliative Care	36	9	25%	45	19	42%	34	7	21%
Muscle Relaxants (Peripherally-Acting) And Cholinesterase Inhibitors	6	1	17%	1	1	100%	8	3	38%
Ophthalmological Preparations	16	5	31%	68	38	56%	39	19	49%
Oxytocics And Anti-Oxytocics	7	2	29%	8	1	13%	4	1	25%
Solutions Correcting Water, Electrolyte And Acid-Base Disturbances	13	1	8%	17	9	53%	12	6	50%
Specific Medicines For Neonatal Care	7	4	57%				4	1	25%
Vitamins and Minerals	9	5	56%	21	18	86%	12	8	67%

## Essential Medicine Status of Highly Registered Medicines

There were 222 unique medicines (and fixed dose combinations) with more than 10 registered products. These accounted for 59% (8056/13637) of all products across the three countries. 42 unique medicines

had over 50 registered products totalling 30% (4153/13637) of regional products. 21 of these were for non-communicable diseases and the remaining 21 were antimicrobials.

## Antimicrobials

There were 21 unique antimicrobial medicines with over 50 registered products each, representing a total of 2310 products. 54% (1173/2310) were registered in a country where the medicine, including dose and formulation, appears on the essential medicine list (Table 3).

Of the total 2310 products 678 were non-antibiotic medicines such as antimalarial, antifungals and antiparasitic medicines. 64% (432/678) of non-antibiotic antimicrobials were present on national essential medicine lists. The remaining 1632 products were antibiotics. 45% (741/1632) of the antibiotics are essential medicines. When subdivided by WHO AWaRe classification, 42% (260/620) of Access antibiotics were essential and 50% (470/939) of Watch antibiotics were essential. No Reserve antibiotics had over 50 products. Combined Ampicillin and Cloxacillin is no longer recommended by the WHO but there are 73 registered products between the 3 countries. The combination is considered essential by Tanzania's EML and 54% (13/24) of Ampicillin with Cloxacillin products registered in Tanzania met the EML specifications.

Many, sometimes the majority, of the highly registered antimicrobials were not essential. There were between 75 and 119 registered products for Amoxicillin and Clavulanic acid, also known as Co-Amoxiclav, in each country. 77% of these were not essential as they were the wrong dose, or formulation. Similarly, there were between 27 and 85 products for Cefuroxime and only 11% of these were considered essential, as it is not listed on either Tanzania's or Kenya's EML.

**Table 3** Shows the number of antimicrobials registered in Kenya, Uganda, and Republic of Tanzania which have over 50 registered products. (EML = Product conforming to EML specification, NonEML = Non-conforming to EML specifications,  $\Sigma$  = Total (n), EAC = East African Community

\* = Medicine does not appear on at least one national EML, n/a = not an antibiotic therefore no AWaRE category). Highlighted sections indicate examples of > 50% non-essential products.

Medicine	AWaRE Category	Kenya					Uganda					Tanzania					EAC				
		Σ	EML	%	Non EML	%	Σ	EML	%	Non EML	%	Σ	EML	%	Non EML	%	Σ	EML	%	Non EML	%
Amoxicillin & Clavulanic acid	Access	119	27	23%	92	77%	90	21	23%	69	77%	75	17	23%	58	77%	284	65	23%	219	77%
Azithromycin	Watch	81	30	37%	51	63%	62	31	50%	31	50%	30	29	97%	1	3%	173	90	52%	83	48%
Cefuroxime*	Watch	85	0	0%	85	100%	44	17	39%	27	61%	27	0	0%	27	100%	156	17	11%	139	89%
Amoxicillin	Access	62	41	66%	21	34%	38	19	50%	19	50%	53	26	49%	27	51%	153	86	56%	67	44%
Ciprofloxacin	Watch	58	12	21%	46	79%	47	44	94%	3	6%	43	38	88%	5	12%	148	94	64%	54	36%
Ceftriaxone	Watch	52	39	75%	13	25%	41	38	93%	3	7%	47	43	91%	4	9%	140	120	86%	20	14%
Clotrimazole	n/a	51	34	67%	17	33%	34	29	85%	5	15%	38	26	68%	12	32%	123	89	72%	34	28%
Albendazole	n/a	64	25	39%	39	61%	28	19	68%	9	32%	27	26	96%	1	4%	119	70	59%	49	41%
Fluconazole	n/a	56	29	52%	27	48%	25	17	68%	8	32%	28	25	89%	3	11%	109	71	65%	38	35%
Artemether & Lumefantrine	n/a	37	29	78%	8	22%	32	17	53%	15	47%	38	20	53%	18	47%	107	66	62%	41	38%
Levofloxacin	Watch	56	31	55%	25	45%	33	11	33%	22	67%	15	3	20%	12	80%	104	45	43%	59	57%
Cefixime	Watch	55	29	53%	26	47%	32	14	44%	18	56%	11	5	45%	6	55%	98	48	49%	50	51%
Metronidazole	n/a	30	14	47%	16	53%	34	21	62%	13	38%	23	16	70%	7	30%	87	51	59%	36	41%
Aciclovir	n/a	37	17	46%	20	54%	24	10	42%	14	58%	18	17	94%	1	6%	79	44	56%	35	44%
Ampicillin & Cloxacillin*	Not Recommended	24	0	0%	24	100%	25	0	0%	25	100%	24	11	46%	13	54%	73	11	15%	62	85%
Erythromycin*	Watch	35	0	0%	35	100%	13	6	46%	7	54%	21	18	86%	3	14%	69	24	35%	45	65%
Sulfamethoxazole & Trimethoprim*	Access	34	22	65%	12	35%	10	0	0%	10	100%	20	15	75%	5	25%	64	37	58%	27	42%
Chloramphenicol	Access	16	0	0%	16	100%	23	19	83%	4	17%	22	13	59%	9	41%	61	32	52%	29	48%
Clarithromycin*	Access	36	30	83%	6	17%	10	0	0%	10	100%	12	10	83%	2	17%	58	40	69%	18	31%
Quinine	n/a	17	12	71%	5	29%	23	19	83%	4	17%	14	10	71%	4	29%	54	41	76%	13	24%
Moxifloxacin	Watch	21	14	67%	7	33%	15	9	60%	6	40%	15	9	60%	6	40%	51	32	63%	19	37%

## Medicines for Non-Communicable Diseases

Highly registered medicines for non-communicable disease are shown in Table 4. The most commonly registered medicines can broadly be described as one of six classes: analgesics, cardiovascular medicines, anti-diabetic medicines, proton pump inhibitors, respiratory medicines, and steroidal medicines. The most commonly registered medicine (with 219 products in the EAC) is Diclofenac which in some forms is considered essential in The Republic of Tanzania and Uganda but not in Kenya. Other

non-essential medicines are highly registered such as telmisartan, rosuvastatin and pregabalin with a total of 65, 65 and 77 products in the EAC.

**Table 4** Shows the total number of non-communicable disease medicines registered in Kenya, Uganda, and Republic of Tanzania with more that 50 registered products of the same medicine and number of products. (EML= Product conforming to EML specification, NonEML= Non-conforming to EML specifications,  $\Sigma$ =Total (n), \* = Medicine does not appear on at least one national EML, \*\*= Medicines does not appear on any National EML in the EAC). Highlighted section indicate examples of >50% non-essential products.

Indication	Medicine	Kenya					Uganda					Tanzania					EAC				
		$\Sigma$	EML	%	Non EML	%	$\Sigma$	EML	%	Non EML	%	$\Sigma$	EML	%	Non EML	%	$\Sigma$	EML	%	Non EML	%
Analgesia	Diclofenac*	85	0	0%	85	100%	80	47	59%	33	41%	54	45	83%	9	17%	219	92	42%	127	58%
	Paracetamol	55	29	53%	26	47%	67	35	52%	32	48%	46	31	67%	15	33%	168	95	57%	73	43%
	Tramadol*	38	0	0%	38	100%	31	29	94%	2	6%	20	14	70%	6	30%	89	43	48%	46	52%
	Ibuprofen	46	22	48%	24	52%	24	12	50%	12	50%	17	7	41%	10	59%	87	41	47%	46	53%
	Pregabalin**	39	0	0%	39	100%	11	0	0%	11	100%	27	0	0%	27	100%	77	0	0%	77	100%
Cardio-vascular	Amlodipine	51	22	43%	29	57%	32	32	100%	0	0%	27	26	96%	1	4%	110	80	73%	30	27%
	Atorvastatin*	58	43	74%	15	26%	31	31	100%	0	0%	19	0	0%	19	100%	108	74	69%	34	31%
	Sildenafil*	37	0	0%	37	100%	17	0	0%	17	100%	21	12	57%	9	43%	75	12	16%	63	84%
	Telmisartan**	27	0	0%	27	100%	14	0	0%	14	100%	24	0	0%	24	100%	65	0	0%	65	100%
	Rosuvastatin**	40	0	0%	40	100%	13	0	0%	13	100%	12	0	0%	12	100%	65	0	0%	65	100%
	Atenolol*	22	0	0%	22	100%	17	8	47%	9	53%	18	8	44%	10	56%	57	16	28%	41	72%
	Losartan	24	22	92%	2	8%	15	13	87%	2	13%	18	12	67%	6	33%	57	47	82%	10	18%
Anti-Diabetic	Metformin	58	31	53%	27	47%	40	23	58%	17	43%	34	12	35%	22	65%	132	66	50%	66	50%
	Glimepiride*	28	0	0%	28	100%	15	9	60%	6	40%	23	20	87%	3	13%	66	29	44%	37	56%
Proton Pump Inhibitors	Esomeprazole*	57	0	0%	57	100%	13	0	0%	13	100%	14	10	71%	4	29%	84	10	12%	74	88%
	Omeprazole	30	26	87%	4	13%	18	18	100%	0	0%	23	19	83%	4	17%	71	63	89%	8	11%
Respiratory	Montelukast*	33	32	97%	1	3%	23	0	0%	23	100%	30	0	0%	30	100%	86	32	37%	54	63%
	Cetirizine	36	32	89%	4	11%	24	14	58%	10	42%	11	11	100%	0	0%	71	57	80%	14	20%
	Salbutamol	22	5	23%	17	77%	20	10	50%	10	50%	21	15	71%	6	29%	63	30	48%	33	52%
	Betamethasone	16	13	81%	3	19%	16	16	100%	0	0%	20	9	45%	11	55%	52	38	73%	14	27%
Steroidal	Hydrocortisone	26	25	96%	1	4%	28	24	86%	4	14%	12	3	25%	9	75%	66	52	79%	14	21%

## Discussion

Essential Medicines Lists are a crucial tool for prioritising medicines and ensuring their availability. However, we found a lack of registration of these essential medicines (28% in Kenya, 50% in Republic of Tanzania and 40% in Uganda). WHO and HAI surveys have found that selected essential medicines are more available than non-essential medicines [2]. Our study suggests accessibility of *all* essential medicines is likely to be much less than previously estimated. The Republic of Tanzania's could not have more than 50% of its essential medicine available to the public as the other 50% are not registered. Furthermore, many of the registered products are non-essential. It would appear regulatory approval has taken a market approach, whereby medicine producers prioritised medicines that move in the market rather than those selected by health experts as essential in addressing public health needs.

### Non-Essential Medicines

There is excessive registration of medicines, including many which are neither essential nor clinically optimal, such as Diclofenac and fixed dose combinations of Ampicillin and Cloxacillin. There are excessive numbers of products for some antibiotics and pain relief medicines registered across the three countries indicating high market potential and consumption. However, a minority of these are essential. This suggests that regulatory resources and household pharmaceutical expenditures are predominantly used on non-essential medicines. As previously demonstrated more than half (51–64%) of registered antimicrobials are non-essential particularly penicillins, cephalosporins and macrolides [9]. This study further demonstrates that market is filled with many versions of these non-essential antimicrobials which is likely to worsen the burden of anti-microbial resistance.

### Market Factors

Examinations of regulatory barriers to registering generic medicines and new essential medicines and vaccines concluded that regulatory fees do not hinder access to medicines but acknowledged that some low-income countries markets are less attractive to producers of low volume generic medicines [10, 20]. Where government funding is lacking, even high-volume essential medicines are not prioritised by producers (eg in India generic producers are not interested in producing iron supplements). The recent Lancet commission on essential medicines for universal health coverage estimated that between \$13 and \$25 per capita is required to cover a basic package of 201 essential medicines while the majority of LICs and more than one quarter of MICs spent less in 2010 [3].

Some LMICs lack sufficient regulatory capacity to conduct full assessments of market applications [20–22]. The WHO has recommended that regulatory authorities in LMICs accept approval decisions made by well-established regulatory authorities and the WHO Prequalification Project [23–25]. Regional regulatory harmonisation such as the East African Community Medicines Registration Harmonisation (EAC MRH) project was established to create a shared and strengthened regulatory capacity to make the registration of medicines simpler and allow more essential medicines to be available [11]. A common larger market should be also more attractive for generic manufacturers due to economies of scale.

### Non-Communicable Diseases

The access to anti-hyperglycaemics (including metformin, gliclazide, glipizide and glibenclamide) alongside other cardiovascular medicines such as statins form the evidence-based treatment protocols of the WHO HEARTS initiative [1, 26]. Metformin is an essential medicine and has 132 products in the EAC. However, 101 (77%) of these are not essential, due to being inappropriate doses or combined with other, often non-essential, medicines. Gliclazide is regarded as an essential medicine by both the Republic of Tanzania and Kenya and yet is not registered at an appropriate dose in either country. Glipizide is also considered essential in Tanzania and there are no registered products. Glibenclamide is considered essential and does have 4–5 registered products in each country.

The consideration of statins as essential medicines is slowly improving. Atorvastatin is the only statin to appear on both Kenya's and Uganda's EML. The Republic of Tanzania does not list a statin at all. And yet, between the three countries there are 65 version of Rosuvastatin alone, which is not essential. Rosuvastatin does not appear on the WHO model EML, in part for its inferior benefits and increased risks, despite a global uptake of the product [27]. There is clear scope for the rationalising of non-essential medicines and perhaps also for essential medicines; nearly a third of the 108 Atorvastatin products registered do not meet the dose or form requirements to be considered essential.

Diclofenac, an analgesic non-steroidal anti-inflammatory, has been removed from the WHO model EML due to significant cardiovascular risks and there are safer alternatives. Despite this, Diclofenac remains on the national EML of almost 90% of countries [28, 29]. We found 219 different Diclofenac products registered for use across the three countries; of these 127/219, (58%) do not meet national standards for essential as they are unsuitable doses, form or in combination with other medicines.

Medicines for NCDs such as Parkinson's Disease remain relatively neglected. Despite Co-Careldopa being the gold-standard treatment for Parkinson's disease, and being considered universally essential, there were no Co-Careldopa products registered in the EAC at the time of analysis but has been added since. Other medicines such as Biperiden and Pramipexole which are named in the national standard treatment guidelines and EMLs for Parkinson's disease but are not registered. "Even when PD patients are able to be diagnosed, treatment is often non-existent or irregular" [30].

## Future Work

This analysis could assist in the auditing and the prioritising of essential medicines for registration and so this process can be expanded to low- and middle-income countries where access to essential medicines remains sub-optimal. In order to assess the impact of registering essential medicines on improving accessibility, data on availability, cost, and consumptions will be required. Future work should assess regional or global effects of registering essential medicines and the excessive registration of non-essential medicines.

## Limitations

The essential medicines lists and national drug registries were accessed before March 2018. Recent additions or amendments have not been considered. Inconsistencies in formatting within the registers may have produced inaccuracies within the central spreadsheet. These have been subjected to multiple checks and corrections however some errors may be persist.

## Conclusion

The lack of registration of essential medicines is a barrier to achieving “access to safe, effective, quality and affordable essential medicines”. The under registration of essential medicines and the over registration of non-essential medicines demonstrates a mismatch between the market of medicines being produced and registered and the health needs of the East African Community. The East African Community Medicines Registration Harmonisation Project has a potential to improve access to essential medicines by prioritising registration and investment in the production of essential medicines. We believe these results are useful for the monitoring the registration status of essential medicines by policy makers in Kenya, Tanzania and Uganda and the EAC MRH project.

## List Of Abbreviations

<b>AWaRe</b>	<b>Access Watch and Reserve</b>
EAC	East African Community
EML	Essential Medicines List
FDA	Food and Drug Administration
HAI	Health Action International
IV	Intravenous
LIC	Low-Income Country
LMIC	Low- and Middle-Income Country
NCD	Non Communicable Disease
NDR	National Drug Registry
MRH	Medicine Registrations Harmonization
UN	United Nations
WHO	World Health Organisation

## Declarations

## Ethics Approval

Not Applicable. No human subjects were involved in this study.

## Consent for Approval

Not Applicable. No individual's data was collected.

## Availability of Data and Materials

The datasets used and analysed during the current study are available in this published article and its supplementary file or can be made available from the corresponding author on request. All data is available from the original open access sources as referenced.

## Competing Interests

The authors declare that they have no competing interests

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## Author's Contributions

All author's contributed to the formulation of the research question, data collection, data analysis and writing of the manuscript.

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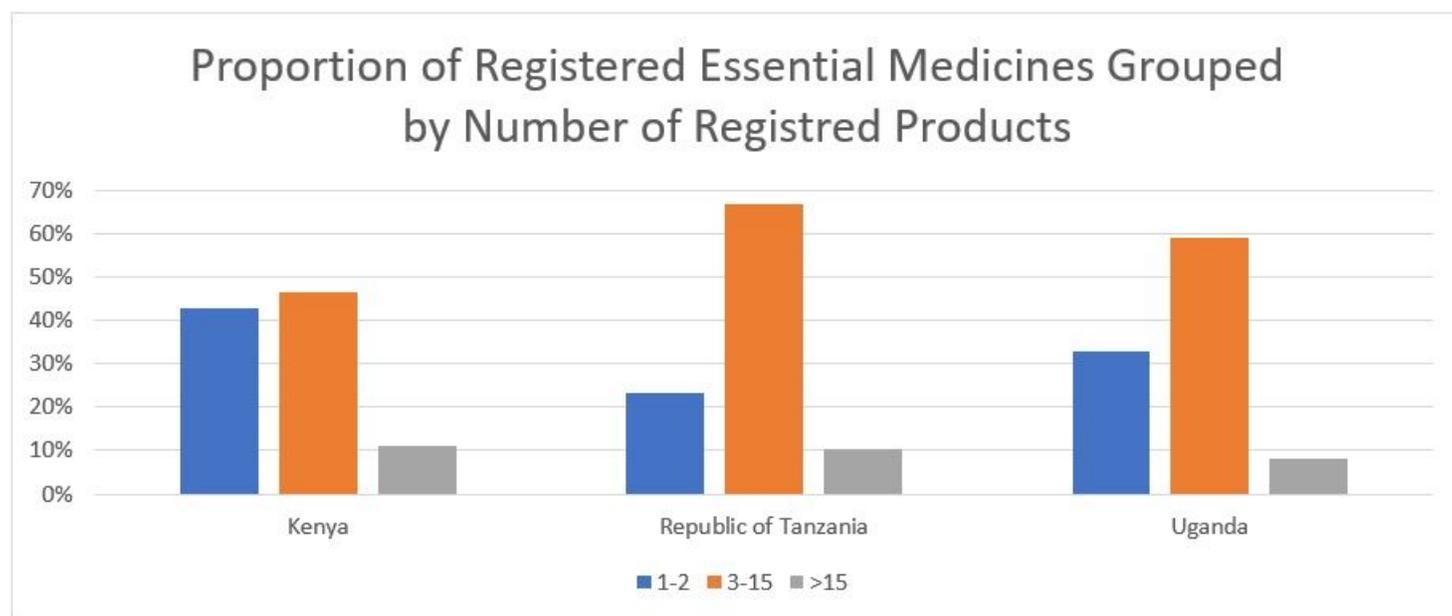
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## Figures



**Figure 1**

Proportion of registered essential medicines by number of registered products in Kenya, Republic of Tanzania, and Uganda

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementalData.xlsx](#)