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Assessing variation among the national essential medicines lists of 21 high-income countries: a cross-sectional study

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ABSTRACT

Objective Essential medicines lists have been created and used globally in countries that range from low-income to high-income status. The aim of this paper is to compare the essential medicines list of high-income countries with each other, the WHO's Model List of Essential Medicines and the lists of countries of other income statuses.

Design High-income countries were defined by World Bank classification. High-income essential medicines lists were assessed for medicine inclusion and were compared with the subset of high-income countries, the WHO's Model List and 137 national essential medicines lists. Medicine lists were obtained from the Global Essential Medicines database. Countries were subdivided by income status, and the groups' most common medicines were compared. Select medicines and medicine classes were assessed for inclusion among high-income country lists.

Results The 21 high-income countries identified were most like each other when compared with other lists. They were more like upper middle-income countries and least like low-income countries. There was significant variability in the number of medicines on each list. Less than half (48%) of high-income countries included a newer diabetes medicines in their list. Most countries (71%) included naloxone while every country including at least one opioid medicine. More than half of the lists (52%) included a medicine that has been globally withdrawn or banned.

Conclusion Essential medicines lists of high-income countries are similar to each other, but significant variations in essential medicine list composition and specifically the number of medications included were noted. Effective medicines were left off several countries' lists, and globally recalled medicines were included on over half the lists. Comparing the essential medicines lists of countries within the same income status category can provide a useful subset of lists for policymakers and essential medicine list creators to use when creating or maintaining their lists.

INTRODUCTION

Essential medicines lists (EMLs) contain medicines deemed necessary in addressing the priority healthcare needs of a population.[1] The WHO has created and maintained a Model List of Essential Medicines as a guide for developing national EMLs with an aim of improving access, quality and rational use of medicines globally.[1] To date, at least 137

Strengths and limitations of this study

► This is the first study to evaluate and compare the essential medicines lists of a subset of countries based on income status.
► The Global Essential Medicines database was published in 2019 and is the most up-to-date repository of essential medicines lists publicly available.
► The analysis is subject to the database's limitations, including outdated information, coding errors and information limited to medication name, country and WHO List of Essential Medicines inclusion.
► The analysis performed does not account for national or subnational drug coverage policies, the utilisation of essential medicines lists within those policies nor the conflict-of-interest policies in developing the respective essential medicine lists.

countries worldwide have developed their own national EMLs, aiming to include medicines that are efficacious, safe and sustainable.[2] Substantial numbers of differences between countries in the included medicines are only partially explained by country characteristics.[1 2] Perhaps it should be expected given the unique challenges faced in each respective country, but it may represent the inclusion of inappropriate medicines or exclusion of essential medicines on national essential medicines lists around the globe.

Countries can be divided into four income status categories per World Bank classification: high income, upper middle income, lower middle income and low income.[3] Countries that fall in the high-income category face different medicine access challenges when compared with countries in the low-income category. For example, the availability of insulin in pharmacies across countries with different income status ranged significantly. Insulin was available in 94% of pharmacies in high-income countries, 40% in upper middle-income countries, 29% in lower middle-income countries and 10% of pharmacies in lower income countries.[4]

The essential medicines concept is relevant to high-income countries and may help to both ensure appropriate medicine selection and, when combined with broader policies, better medicine access.[5][6] For example, the number of high-cost patented medicines on the market in Canada increased more than 200% from 2006 to 2017, all while 1 in 10 Canadians (approximately 3.5 million people) could not afford their prescription drugs.[7][8] This paper aims to analyse and compare high-income countries with national EMLs to evaluate differences between this group, the WHO Model's List of Essential Medicines and other countries with national EMLs. Beyond the broad evaluation, specific medicine classes and medicines were assessed for inclusion and exclusion among the high-income EMLs.

METHODS

Inclusion criteria for the analysis were: (1) the country meets the World Bank definition of a high-income country and (2) the country has a national essential medicines list documented in the Global Essential Medicines database of 137 national essential medicines lists.

High-income countries were defined according to the 2019 World Bank criteria that indicate high-income countries are those with a gross national income per capita, calculated using the World Bank Atlas method, greater than $12 376.[3] The gross national income per capita obtained from the World Bank is calculated using the Atlas Method.[3]

The Global Essential Medicines database was published in 2019 and is a freely accessible repository of 137 national essential medicines lists registered with the WHO. The database provides a list of countries with an EML, the medicines on each EML, the most recent year of the EML's publication and indicates if a medication is included on the WHO List of Essential Medicines.[2]

Patient and public involvement

Given the research design focusing on an analysis of a publicly available database, patients and the public were not involved in the design, conduct or analysis of this research.

Data collection process

Twenty-one countries met both inclusion criteria. The medicines for each countries' EML were extracted from the database into an Excel spreadsheet for comparison.

The following characteristics of each included country were collected: WHO region; population size; life expectancy; infant mortality; gross domestic product (GDP) per capita; gross national income per capita; the current health care expenditure per capita; and the Healthcare Access and Quality (HAQ) Index Score. Data on WHO Regions and per capita healthcare expenditure was obtained from the WHO Global Health Observatory.[9] We extracted data on population, life expectancy, infant mortality and GDP per capita from the Central

Intelligence Agency's World Factbook.[10] We extracted the gross national income per capita from the World Bank.[11] The HAQ Index Score for each country was extracted from the original manuscript.[12]

Data analysis

Essential medicine list comparisons by country

The EMLs of each country were compared with the 2017 WHO's Model List of Essential Medicines to identify the number of medicines on the WHO's Model List not included on a country's list and to identify the number of medicines on a country's list not included on the WHO's Model List.[13]

High-income countries were also compared with each other for differences in commonly included and excluded medicines. Lists were reviewed to identify the number of medicines on a country's EML that less than 50% of high-income countries included on their EMLs and the number of medicines not on a country's EML that greater than 50% of high-income countries included on their EMLs.

Similarity scores were calculated to compare the EMLs. The methodology described by Persaud *et al*[2] was used: 'To calculate a similarity score, we divided medicines into those that are commonly listed (by at least 50% of countries) and those that are uncommonly listed (by less than 50% of countries). For each country's list we calculated the score by counting the medicines on that list that are commonly listed and subtracting the number of uncommonly listed medicines. This calculation provides a similarity integer score for each country; positive scores indicate that most medicines in the country's list are commonly listed in other countries' lists, and negative scores indicate that most medicines are uncommonly listed in other countries' lists'. The similarity scores for each high-income country were calculated using the subset of 21 high-income countries and the database's repository of 137 countries.

High-income countries compared with countries of other income status

We compared the most commonly included medicines on high-income countries' EMLs with those of upper middle income, lower middle income and low income. The gross national income per capita of upper middle, lower middle and low income countries were $3996–$12 375, $1026–$3995 and <$1026, respectively.[3] Common medicines were defined as those included on greater than 80% of countries' EMLs within a specific income status category.

Select medicines and medicine class analysis

To better understand the trends, similarities and differences among the EMLs, we compared select medicines and medicine classes. Additionally, the EMLs of each high-income country were assessed for the inclusion of any of 11 globally recalled medicines.[14]

Table 1 Country characteristics of high-income countries with national essential medicines lists

Country	National EML year of publication	Total medications on list	WHO region	Population	Life expectancy (years, 2016)	Infant mortality (deaths/1000 live births)	Healthcare access and quality index	GNI per capita US$ (2018)	GDP per capita US$ (2018)	Current health expenditure per capita US$ (2016)
Antigua and Barbuda	2008	292	The Americas	94 731	76.7	12.1	67	15 810	16 727	623
Bahrain (Kingdom of)	2015	550	Eastern Mediterranean	1 410 942	79	29.6	79	21 890	24 051	1099
Barbados	2011	625	The Americas	292 336	75.5	10.2	67	15 410	17 949	1164
Chile	2005	349	The Americas	17 789 267	78.9	6.6	76	14 670	15 923	1191
Croatia	2010	599	Europe	4 292 095	76.1	9.3	82	13 830	14 910	884
Czech Republic	2012	802	Europe	10 674 723	78.8	2.6	85	20 250	23 079	1322
Estonia	2012	405	Europe	1 251 581	76.9	3.8	81	20 990	23 266	1185
Latvia	2012	304	Europe	1 944 643	74.7	5.2	78	16 880	17 861	874
Lithuania	2012	339	Europe	2 823 859	75	3.8	77	17 360	19 153	988
Malta	2008	607	Europe	416 338	80.5	3.5	85	26 220	30 098	2328
Oman	2009	576	Eastern Mediterranean	4 613 241	75.7	12.8	77	15 110	16 415	648
Palau	2006	268	Western Pacific	21 431	73.4	10.6	N/A	16 910	15 859	1674
Poland	2017	441	Europe	38 476 269	77.8	4.4	80	14 150	15 421	809
Portugal	2011	905	Europe	10 839 514	79.4	4.3	85	21 680	23 408	1801
Saint Kitts and Nevis	2007	290	The Americas	52 715	75.9	8.4	N/A	18 640	19 275	931
Seychelles	2010	294	Africa	93 920	74.9	10	66	15 600	16 434	597
Slovakia	2012	983	Europe	5 445 829	77.3	5.1	79	18 330	19 443	1179
Slovenia	2017	787	Europe	1 972 126	78.3	3.9	87	24 670	26 124	1834
Sweden	2016	289	Europe	9 960 487	82.1	2.6	90	55 070	54 608	5711
Trinidad and Tobago	2010	493	The Americas	1 218 208	73.1	22.3	62	16 240	17 130	1064
Uruguay	2011	518	The Americas	3 360 148	77.4	8.3	72	15 650	17 278	1379

EML, essential medicines list; GDP, gross domestic product; GNI, Gross National Income.

Table 2 High-income country EMLs compared with the who model list and with high-income countries commonly included medications

Country	Total medications on list	Medications on country EML but not WHO model list	Medications on WHO model list but not country EML	Total differences between country and WHO EML	Medications on country EML but on <50% of high-income EMLs	Medications on >50% of high-income EMLs but not on country EML	Total differences between country EML and high-income majority
Antigua and Barbuda	292	99	176	275	63	180	243
Bahrain	550	300	119	419	212	71	283
Barbados	625	389	124	513	264	48	312
Chile	349	140	162	302	96	156	252
Croatia	599	346	114	460	260	70	330
Czech Republic	802	568	133	701	434	41	475
Estonia	405	267	233	500	137	141	278
Latvia	304	193	256	449	81	186	267
Lithuania	339	201	232	433	77	147	224
Malta	607	385	144	529	278	80	358
Oman	576	303	96	399	231	64	295
Palau	268	114	215	329	83	224	307
Poland	441	287	214	501	169	137	306
Portugal	905	674	136	810	546	50	596
Saint Kitts and Nevis	290	100	180	280	61	180	241
Seychelles	294	102	176	278	67	182	249
Slovakia	983	722	103	825	601	27	628
Slovenia	787	524	97	621	418	40	458
Sweden	289	159	241	400	98	218	316
Trinidad and Tobago	493	247	123	370	163	79	242
Uruguay	518	298	142	440	181	72	253

EMLs, essential medicines lists.

RESULTS

Of the 79 countries that had a gross national income per capita that met the definition of high-income status, 21 (26.6%) had an EML documented in the Global Essential Medicines database.[3] Most of these countries were in the European and Americas WHO region. The included countries had similar life expectancies but varied significantly with respect to their population size, infant mortality, gross domestic product and current health expenditure per capita (table 1). The HAQ Index scores ranged from 62 to 90 among countries, with European countries averaging the highest score of 82.6, Eastern Mediterranean countries averaging 78, countries from the Americas with 68.8 and one African country scoring 66. The correlation between HAQ scores and number of medications on an EML was poor with a R^2 value of 0.1186. The countries also varied in their EML's publication year, with the most recent list updated in 2017 and the oldest list published in 2005.

EMLs comparisons by country

There were large differences among many high-income EMLs when compared directly to the WHO's Model List of Essential Medicines (table 2). Four countries had more than 500 medicines added to their lists not on the WHO's Model List (Czech Republic, Portugal, Slovakia and Slovenia). Six countries had more than 200 medicines excluded from their list recommended by the WHO (Estonia, Latvia, Lithuania, Palau, Poland and Sweden). High-income countries ranged from 275 to 825 difference from the WHO's Model List. The number of differences decreased when comparing individual high-income EMLs with medicines included on more than half of the high-income country lists. Only two countries had more than 500 less common medicines added to their list (Portugal and Slovakia), and two had greater than 200 medicines excluded from their list that were include on more than half of other high-income EMLs (Palau and Sweden).

Table 3 Similarity scores of high-income countries calculated by subset of 21 high-income countries and full database of 137 countries

Countries	Total medications on list	Medications on >50% of high income lists	Medications on <50% of high income lists	Similarity score among 21 high income countries	Similarity score among 137 countries[2]	Delta similarity score between high income group and all countries
Antigua and Barbuda	292	229	63	166	140	26
Bahrain	550	338	212	126	−106	232
Barbados	625	361	264	97	−159	256
Chile	349	253	96	157	67	90
Croatia	599	339	260	79	−151	230
Czech Republic	802	368	434	−66	−398	332
Estonia	405	268	137	131	−141	272
Latvia	304	223	81	142	−96	238
Lithuania	339	262	77	185	−77	262
Malta	607	329	278	51	−201	252
Oman	576	345	231	114	−94	208
Palau	268	185	83	102	70	32
Poland	441	272	169	103	−179	282
Portugal	905	359	546	−187	−497	310
Saint Kitts and Nevis	290	229	61	168	140	28
Seychelles	294	227	67	160	114	46
Slovakia	983	382	601	−219	−553	334
Slovenia	787	369	418	−49	−359	310
Sweden	289	191	98	93	−61	154
Trinidad and Tobago	493	330	163	167	−41	208
Uruguay	518	337	181	156	−106	262

The similarity scores of every high-income country increased when compared with only high-income countries rather than the 137 countries included in the database (table 3). Whereas only 5 of the 21 high-income countries had positive similarity scores when comparing to all 137 countries, 17 had positive scores when comparing to the 21 high-income countries. Similarity scores increased an average of 208 points, with a minimum increase of 26 and maximum increase of 334.

High-income countries compared with countries of other income levels

There were 136 medicines that were listed on greater than 80% of the group of 21 high-income countries' EMLs (table 4). The 48 upper middle-income, 40 lower middle-income and 28 low-income countries had 114, 128 and 134 medicines on over 80% of the lists within their respective income status categories. Comparing the high-income countries list with the other income status categories showed that the upper middle-income countries list had 66.9% of the medicines included on the high-income list, the lower middle-income countries had 58.8% of the medicines included on the high-income list and the low-income countries had 55.1% of the medicines included on the high-income list. The high-income country medicines that were present on the other income country lists represented 79.8%, 62.5% and 56.0% of the total number of medicines on the upper middle, lower middle and low-income country lists, respectively.

Selected medicine and medicine class analysis

Select medicines and medicine classes were assessed for inclusion or exclusion on each high-income country's EML as well as the WHO's Model List. Among newer diabetes medicines, 9 of 21 countries had a DPP4 inhibitor and 8 of 21 had a GLP1 agonist. No countries included an SGLT2 inhibitor, although only four lists had been revised since SGLT2 inhibitors became available in 2012.[15] Despite being listed on the WHO's Model List, only 11 of 21 countries included hepatitis C medicines. Since the availability of direct oral anticoagulants in 2008, only 9 of 16 countries have added them to their lists.[16] For higher cost medicines, 11 countries included a Tumor Necrosis Factor (TNF) inhibitor (eg, infliximab, brand name Remicade) and nine included a monoclonal antibody (eg, adalimumab, brand name Humira).

With respect to medicines used in the management of substance use disorders, 8 countries included alcohol cessation medicines and five included smoking cessation medicines. All 21 countries had an opioid on their list, but only 16 had opioid cessation medicines listed. 15 high-income countries had the opioid overdose reversal agent naloxone included on their lists.

Table 4 Most common medicines included on high-income countries' lists of essential medicines

Medication (alternative name)	No. of countries list (%) n=21	Medication (alternative name)	No. of countries list (%) n=21	Medication (alternative name)	No. of countries list (%) n=21	Medication (alternative name)	No. of countries list (%) n=21
Acetylcysteine	17 (81)	Clozapine	19 (90)	Insulin, short acting	21 (100)	Phenobarbital	18 (86)
Acetylsalicylic acid	19 (90)	Cyclophosphamide	19 (90)	Ipratropium	21 (100)	Phenoxymethylpenicillin (penicillin V)	17 (81)
Acyclovir	19 (90)	Cyproterone	17 (81)	Isoniazid	17 (81)	Phenylephrine	17 (81)
Allopurinol	20 (95)	Desferroxamine (deferoxamine)	17 (81)	Isosorbide dinitrate	18 (86)	Phenytoin	19 (90)
Aminophylline	17 (81)	Dexamethasone	20 (95)	Ketoconazole	18 (86)	Pilocarpine	20 (95)
Amiodarone	21 (100)	Diazepam	21 (100)	Lamivudine	19 (90)	Potassium	19 (90)
Amitriptyline	21 (100)	Diclofenac	19 (90)	Lamotrigine	17 (81)	Prednisolone	20 (95)
Amlodipine	19 (90)	Digoxin	19 (90)	Levodopa	21 (100)	Prednisone	18 (86)
Amoxicillin	21 (100)	Diltiazem	17 (81)	Levothyroxine	21 (100)	Propranolol	20 (95)
Ampicillin	17 (81)	Doxycycline	21 (100)	Lidocaine (lignocaine and xylocaine)	19 (90)	Pyridostigmine	18 (86)
Atenolol	20 (95)	Efavirenz	18 (86)	Lithium	18 (86)	Ranitidine	19 (90)
Atorvastatin	20 (95)	Enalapril	17 (81)	Loratadine	17 (81)	Rifampicin	18 (86)
Atropine	17 (81)	Epinephrine (adrenaline)	18 (86)	Magnesium	18 (86)	Risperidone	21 (100)
Azathioprine	20 (95)	Erythromycin	19 (90)	Medroxyprogesterone	19 (90)	Salbutamol	21 (100)
Azithromycin	19 (90)	Erythropoietin	20 (95)	Melphalan	20 (95)	Salicylic acid	17 (81)
Beclometasone (Beclomethasone)	19 (90)	Ethambutol	17 (81)	Mesalazine	17 (81)	Salmeterol	18 (86)
Betamethasone	20 (95)	Ethinylestradiol	17 (81)	Metformin	21 (100)	Simvastatin	17 (81)
Betaxolol	17 (81)	Fentanyl	21 (100)	Methotrexate	20 (95)	Spironolactone	20 (95)
Bromocriptine	18 (86)	Ferrous fumarate (iron)	19 (90)	Methylprednisolone	21 (100)	Sulfamethoxazole	21 (100)
Budesonide	19 (90)	Fluconazole	20 (95)	Metoclopramide	18 (86)	Sulfasalazine (salazosulfapyridine)	18 (86)
Calcium	20 (95)	Fluorouracil	17 (81)	Metronidazole	20 (95)	Tamoxifen	20 (95)
Carbamazepine	21 (100)	Fluoxetine	21 (100)	Miconazole	17 (81)	Terbinafine	17 (81)
Carbidopa	21 (100)	Folic acid	18 (86)	Midazolam	17 (81)	Timolol	20 (95)
Carvedilol	18 (86)	Furosemide	21 (100)	Morphine	21 (100)	Tramadol	19 (90)
Ceftazidime	17 (81)	Gabapentin	17 (81)	Mycophenolate	18 (86)	Triamcinolone	17 (81)
Cefuroxime	18 (86)	Gentamicin	19 (90)	Neomycin	17 (81)	Trimethoprim	21 (100)
Chlorambucil	18 (86)	Gliclazide	17 (81)	Nifedipine	18 (86)	Valproic acid (sodium valproate, valproate, valproate semisodium)	21 (100)

Continued

Table 4 Continued

Medication (alternative name)	No. of countries list (%) n=21	Medication (alternative name)	No. of countries list (%) n=21	Medication (alternative name)	No. of countries list (%) n=21	Medication (alternative name)	No. of countries list (%) n=21
Ciclosporin (Ciclosporin, Cyclosporine)	17 (81)	Haloperidol	20 (95)	Nitroglycerin (glyceryl trinitrate)	17 (81)	Verapamil	21 (100)
Ciprofloxacin	21 (100)	Heparin	17 (81)	Norethisterone (norethindrone)	19 (90)	Vitamin B12 (cobalamin)	19 (90)
Cisplatin	18 (86)	Hydrochlorothiazide	19 (90)	Nystatin	18 (86)	Vitamin D (cholecalciferol, ergocalciferol)	21 (100)
Clarithromycin	20 (95)	Hydrocortisone	21 (100)	Olanzapine	18 (86)	Vitamin K (menadione, phytomenadione, phytonadione)	18 (86)
Clavulanic Acid	20 (95)	Hydroxyurea (hydroxycarbamide)	17 (81)	Omeprazole	21 (100)	Warfarin	20 (95)
Clindamycin	18 (86)	Ibuprofen	18 (86)	Ondansetron	20 (95)	Zidovudine (retrovir)	18 (86)
Clonazepam	20 (95)	Insulin, long acting	19 (90)	Paracetamol (acetaminophen)	19 (90)	Zuclopenthixol	17 (81)

Of the eleven globally withdrawn medicines, six were present on at least one of the high-income countries' EMLs and 11 of the 21 high-income countries had at least one globally withdrawn medicine on their essential medicines list. The only medicine present on more than one list was thioridazine, which was withdrawn globally in 2005. It was present on a third of the high-income countries' EMLs. The specific medicines withdrawn are presented in table 5.

DISCUSSION

Only about one-quarter of high-income countries had a national EML, despite the associated improvements seen with EML use in prescribing practices and medication access.[5 6] The countries also demonstrated a large range in publication year with a median publication year of 2011. Some of these countries may not have updated their EML because they do not use it in their national drug policy. Alternatively, the database may have included an outdated list.

The national EMLs of the 21 high-income countries differed greatly from the WHO's Model List of Essential Medicines. The individual high-income countries were more similar to each other when compared with countries with smaller economies. However, four countries (Czech Republic, Portugal, Slovakia and Slovenia) stood out with negative similarity scores when comparing among high-income countries, indicating the presence of outliers within the high-income group. A negative similarity score indicates that the majority of a country's EML is made up of medicines not on included on at least 50% of its high-income peer countries' EMLs. These four countries had the four largest EMLs within the high-income group and each included at least 50% more medicines than the high-income country average of 510 medicines. Each country has unique needs and is encouraged by the WHO to adapt their EMLs to address those needs, but outliers within similar income classes may represent opportunities for further evaluation and list refinement.[1] These outlier EMLs are likely a result of overinclusion of medicines that other high-income countries do not deem essential. All countries, and specifically the four outlier countries, should reassess the medicines on their EMLs frequently and remove any medicines found to be ineffective, inappropriate or unsafe.

The income group analysis demonstrated that a relationship exists between income class and the medicines included on a country's EML. High-income countries were most similar to upper middle-income countries, somewhat similar to low middle-income countries and least similar to low-income countries. This may be explained by the differing medical needs of those living in developed and developing nations. For example, 95% of high-income countries include atorvastatin to treat high cholesterol, whereas only 60% of upper middle-income, 38% of low middle-income and 25% of low-income countries include it. Conversely, the antiparasitic medicine niclosamide is

Table 5 Medicines withdrawn worldwide included in one or more high-income country list

Country	Total medications on list	EML year of publication	Total number of withdrawn medications on country EML	Medications withdrawn worldwide (Year of withdrawal)					
				Astemizole (1999)	Drotrecogin (2011)	Laropiprant (2013)	Nebacumab (1993)	Terodiline (1992)	Thioridazine (2005)
Antigua & Barbuda	292	2008	1						Included
Bahrain	550	2015	1				Included		
Barbados	625	2011	1						Included
Chile	349	2005	1						Included
Croatia	599	2010	0						
Czech Republic	802	2012	0						
Estonia	405	2012	0						
Latvia	304	2012	0						
Lithuania	339	2012	0						
Malta	607	2008	0						
Oman	576	2009	2		Included				Included
Palau	268	2006	0						
Poland	441	2017	0						
Portugal	905	2011	1			Included			
Saint Kitts and Nevis	290	2007	1						Included
Seychelles	294	2010	0						
Slovakia	983	2012	1	Included					
Slovenia	787	2017	1					Included	
Sweden	289	2016	0						
Trinidad and Tobago	493	2010	1						Included
Uruguay	518	2011	1						Included

included on more than 80% of the low-income countries' EMLs but on only 10% of high-income country lists. Comparing countries with similar resources as measured through their income status categorisation may allow for more granular comparisons that can better identify areas for improvement. The similarity seen among the high-income countries suggests that income status categorisation defined by World Bank standards can be used for further subset analysis countries with essential medicines lists.

Although high-income EMLs are similar on broad review, potential areas for improvement can still be identified within the group. The newest oral diabetes medicine, SGLT2 inhibitors, has clinical evidence indicating its use reduces the risk of major cardiovascular events and slows the progression of renal disease.[17] However none of the four countries with recently revised EMLs have added it their lists, nor has the WHO added it to the Model List of Essential Medicines as of 2019.[18] Similarly, only 9 of the 16 countries with updated EMLs since 2008 include direct oral anticoagulants that do not require ongoing bloodwork for therapeutic monitoring like warfarin.[19] Aside from clinical efficacy, there were safety concerns within some high-income EMLs. Despite the inclusion of opioid medicines on all 21 lists, the opioid antidote naloxone that can reverse overdoses was only present on

15, representing a deficiency in public health efforts to respond to an increase in opioid-related deaths. Additionally, over half of high-income countries included globally recalled medicines with significant safety concerns, illustrating the importance of ongoing evaluations of EMLs for removal of unsafe or ineffective medicines.[14] These findings underscore the need to update EMLs regularly. The WHO updates the Model List of Essential Medicines every 2 years and countries could update their own EMLs at a similar frequency.[13]

Comparing high-income countries by medicine or medicine class highlights the differences that can be present among the EMLs of similar countries. These differences may be intentional to address specific country needs, or they may represent decisions that should be re-evaluated. It is not the purpose of this paper to focus on a specific country but instead aims to encourage countries to refine their list using all available data, including peer countries' EMLs.

The medication coverage policies of each high-income country with an EML were sought out from publicly available information. Policies ranged from free medicines on the EML at the point of service to fixed or percentage-based copays.[20–22] However, many countries did not specify the role of EMLs in their policy and others did not have any publicly available information describing

their national drug coverage policy. Given the incomplete information, it was not further analysed.

Beyond potential influence on national and subnational medication coverage policies, clinical benefits can be derived from EML use. Sweden, for example, has used their Wise List EML to improve prescribing practices of commonly used medications.[23] Over a 15-year period, Wise List recommendations aimed at improving clinical decision making and cost-effective prescribing in Stockholm improved to 84% recommendation adherence, representing a 9% improvement. Strategic use of an evidence-based and transparently constructed EML can have major impacts on downstream prescribing practices.

To our knowledge, this is the first study comparing the essential medicines lists of high-income countries. The analysis depended on medicine data from the Global Essential Medicines database and thus is subject to the database's limitations, including outdated information and coding errors. The database includes only medication name, country's name and inclusion on the WHO List of Essential Medicines, and thus more robust data including generic status, dosages and prescribing patterns were unavailable. Expanding the database to include this information as well as a country's EML changes over time would be beneficial in providing more detailed analysis. Furthermore, the analysis performed does not account for national or subnational drug coverage policies or the utilisation of EMLs within those policies. We did not have information about potential conflict of interest for EML selection committee members or about procedures for handling conflicts of interest in EML development, and such conflicts could have negatively influenced medicine selection.[24] We attempted to obtain the drug coverage policies and use of EMLs of the 21 high-income countries but that information was not publicly available for many countries. Future research is needed to compare EML drug coverage policies and evaluate the impact of factors that can influence which medicines are included or excluded on a given country's EML. Conflict-of-interest policies and generic availability likely play a significant role in EML list construction and further work to characterise their respective influence is warranted. We focused on national EML, but subnational medicines lists are also important.[23]

EMLs of high-income countries are relatively similar to each other when comparing with countries of other income status. However, specific EML and medicine level analysis of high-income countries allowed for relevant differences to be identified and areas for improvement highlighted. Countries can improve their EMLs by using the global database to compare their list with the lists of their peer countries. By doing so they can identify medicines that should be added to or removed from their own lists. Grouping countries by income status proved to provide a cohort of similar countries that had notable differences and areas for improvement. Future subgroup analysis of the other income groups should be performed to provide more specific insight as those countries continue to revise and improve their own lists. Furthermore, countries without national essential medicines lists should use the Global Essential Medicines database in conjunction with the WHO's Model List of Essential Medicines to construct a list for use in their national medicine coverage policy.

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