Journal of Clinical Pharmacology and Therapeutics

ISSN: 2766-8347

Research Article

Differential Global Prioritization of Access to Molecularly Identical Medicines: Cross-Sectional Study

Camila Heredia[1], Moizza Zia Ul Haq[1] and Navindra Persaud[1,2]*

[1]MAP Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Unity Health Toronto, Canada

[2]Department of Family and Community Medicine, Faculty of Medicine, University of Toronto, Canada

Abstract

Background: Medicines with the same molecular structure have similar clinical effects but can have different societal impacts including those related to drug spending and access. This study examined how countries prioritize access to such medicines using national essential medicines lists as a metric.

Methods: In May 2023, we reviewed 158 national essential medicines lists to identify molecularly and clinically equivalent medicine pairs, defined by identical active ingredients known to have similar or identical clinical effects.

Results: Among 2084 unique medicines from 158 national lists, 31 pairs of molecularly and clinically equivalent medicines were identified, including enantiomers, prodrugs, active metabolites, and other molecular modifications. Countries listed a median of 18 of these medicines, with a range from 1 in Spain to 38 in Slovenia. Most countries listed more older than newer medicines. Countries listing the highest number of newer agents, such as Latvia and Spain, tended to have higher GDP per capita and health expenditure.

Conclusion: Some countries prioritize newer medicines despite the availability of molecularly identical older ones. Many of these countries are high-income European nations. The inclusion of newer, expensive medicines over older, cost-effective ones on essential medicines lists raises concerns about potential influence of marketing on national essential medicines lists.

Keywords: Biosimilar; Clinically equivalent; Cost-effective alternatives; Essential medicines; Molecular structure

Abbreviations

ATC: Anatomical Therapeutic Chemical Classification; FDA: Food and Drug Administration; EMA: European Medicines Agency; GDP: Gross Domestic Product; WHO: World Health Organization

Introduction

The same molecule can be used to make different medicine products with same clinical effects but different societal effects including drug spending and access. Similar products are sometimes released and promoted after a patent is set to expire for business reasons although the clinical effects of newer agents may be similar or identical to older products such as the citalopram enantiomer, escitalopram, the omeprazole enantiomer, esomeprazole, and the filgrastim pegylated version, pegfilgrastim [1-3]. Ketoprofen and its S(+)-enantiomer dexketoprofen produce similar analgesia and pain relief [4]. The marketing of long-acting oxycodone fueled the opioid crisis in North America although the clinical effects of oxycodone products are similar [5]. Studies of enantiomers, prodrugs, and metabolites of different medicines, evaluating efficacy, adverse events, and pharmacokinetics, generally show no substantial differences efficacy or safety outcomes [6-8].

Policies and regulations have been established globally to oversee the evaluation, production, distribution, and utilization of new medicines that may be similar to already marketed medicinal products. Notable examples include the World Health Organization (WHO) International Reference Standards for Biological Products, [9] the Directive 2001/83/EC of the European Parliament and of the Council in the European Union, [10] and the New Drug Application process regulated by the Food and Drug Administration in the United States of America [11]. These regulations emphasize the importance of clearly defining the circumstances under which the results of toxicological, pharmacological, or clinical studies may be required when seeking authorization for a new medicine that is fundamentally equivalent to an already approved one. The WHO international standards and reference reagents for calibrating bioassays ensure uniformity in reporting the activity or potency of medicines [9]. This common system includes guidelines on evaluation of biosimilars, and facilitates effective communication among healthcare providers, regulators, and manufacturers.

National Essential Medicines Lists (NEMLs) are created to help countries address the most pressing healthcare needs of their populations [12]. The WHO maintains a model list, and over 150 countries have established their own lists to guide the provision and accessibility of medicines for billions worldwide [13]. Modern NEMLs are shaped by clinical factors and practical considerations, including population demands, effectiveness, safety, quality, cost, and availability. These lists are generally revised each year, with medicines being removed if superior alternatives are identified or if a medicine is found to be unsafe or ineffective. NEMLs are commonly used, though their presence alone does not ensure improved access to or use of

Citation: Heredia C, Ul Haq MZ, Persaud N. Differential Global Prioritization of Access to Molecularly Identical Medicines: Cross-Sectional Study. J Clin Pharmacol Ther. 2025;6(1):1066.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Mar 26th, 2025

***Corresponding author:** Navindra Persaud, Department of Family and Community Medicine, Faculty of Medicine, University of Toronto, 80 Bond Street, Toronto, Ontario, M5B 1X2, Canada, Tel: 416-360-4000 ext. 77578

medicines [14].

The purpose of this study was to determine how countries prioritize access to newer and older agents that are molecularly and clinically equivalent. We used listing with national essential medicines as our metric of prioritization.

Materials and Methods

Searching for NEMLs

We searched for NEML documents in May 2023 and abstracted medicines listed for each country [14]. We conducted extensive online searches to locate NEMLs and relevant government resources, such as Ministry of Health websites. We also reached out to technical officers listed as responsible for healthcare access in all countries where the WHO has country offices. Additionally, we reviewed studies on NEML use available on Medline, examined cited references to track sources, and consulted with regional experts and technical officers specializing in the selection and application of essential medicines. These efforts aimed to obtain 158 NEML documents for both outpatient and inpatient care across all healthcare levels (primary, secondary, tertiary, and quaternary). We included NEMLs written in any language and excluded documents that served as prescribing guidelines but were not actual lists.

Extracting medicines from NEMLs

For every included NEML, we compiled a catalog of individual medicines using their International Nonproprietary Names (INNs). Medicines listed in non-English languages were translated using tools like Google Translate or web searches. Combination medicines were broken down into their individual components, while information about salts (e.g., pantoprazole-sodium and pantoprazole-magnesium) was disregarded, and the medicines were recorded using their base names (e.g., pantoprazole).

We utilized a combination of automated processes and manual methods, depending on the formatting of the documents. Regardless of the method used, two members of the research team reviewed every listed medicine for accuracy. To validate the automated extraction, we manually reviewed 400 randomly selected data points (each representing whether a particular medicine was listed by a specific country) and compared them to the original documents. The process had an error rate of 0.75% (3 errors out of 400), which was well below our predefined 3% threshold for discontinuing the algorithm's use.

We did not extract details on medicine usage instructions, recommended indications, dosing, settings for use, or specific formulations. Instead, we collected general information about each list, including publication date, stated objectives, and the type of guidance provided (e.g., advice for community or hospital procurement). Diagnostic agents, disinfectants, antiseptics, saline solutions, and naturopathic medicines were excluded.

We sought medicine pairs where two medicines were both molecularly and clinically equivalent. We defined molecular equivalence as having active ingredients with the same molecular structure and this could include enantiomers, prodrugs, active metabolites, and other additions (methylation, hydroxylation, etc.). We defined clinical equivalence as randomized controlled trial evidence indicating no clinically meaningful difference in clinical effects (benefits and harms), regardless of whether differences in pharmacokinetics or recommended dosing schedules differed [15-20].

Country characteristics, such as life expectancy and real GDP (Gross Domestic Product) per capita were released from the Central Intelligence Agency, [21] population size from the United Nations, [22] and health expenditure data was obtained from the Global Health Observatory, [23] except for Somalia and the Democratic People's Republic of Korea [23,24]. The income level was extracted from the World Bank, [25] and the WHO region was released from the WHO classification [26]. Most of the data pertained to the year 2023; if 2023 records were unavailable, information from the nearest available year to 2023 was accessed.

Results

Among 2084 unique medicines listed by at least one of 158 countries, we identified 31 medicine pairs of molecularly and clinically equivalent medicines: 15 enantiomers, 4 active metabolites, 6 prodrugs, and 6 medicines with specific additions (3 polyethylene glycol additions, 1 hydroxylation, 1 methylation, and 1 hydrogenation) (Table 1).

Of these total 59 medicines, one (licarbazepine) was not listed by any country. Countries listed a median of 18 (IQR: 15.25 - 22) of these medicines. The range of these medicines listed by countries was between 1 (Spain only lists hydrochlorothiazide) and 38 (Slovenia lists acyclovir, aminophylline, amitriptyline, amlodipine, aprepitant, bupivacaine, cetirizine, chloroquine, chlorpromazine, citalopram, desloratadine, ergometrine, escitalopram, esketamine, esomeprazole, filgrastim, fosaprepitant, hydrochlorothiazide, hydroxychloroquine, ibuprofen, ketamine, ketoprofen, lansoprazole, levobupivacaine, levocetirizine, levomepromazine, lipegfilgrastim, loratadine, methylergometrine, omeprazole, oxcarbazepine, paracetamol, pegfilgrastim, phenytoin, sulpiride, theophylline, valaciclovir, and venlafaxine).

We categorized medicines within each pair as being either older or newer agents. 157 countries listed at least one older agent, and 153 countries listed at least one newer agent. Countries listed a median of 15 (IQR: 13 - 16) older medicines. Spain listed no older medicine, while Greece listed 24 older medicines. Japan, Portugal, Romania, Uganda, and Ukraine listed no newer agents, while Oman listed 16 newer agents, with a median of 4 (IQR: 2 - 6) newer agents listed by each country.

We sought to identify countries that listed a disproportionate number of newer agents. 11 countries listed the highest number of newer medicines, ranging from 12 (Croatia) to 16 (Oman) agents in each country list (Table 2). 18 countries listed the highest number of older agents, ranging from 19 (China, Malta, Republic of Moldova, Trinidad and Tobago, United Republic of Tanzania, and Uruguay) to 24 (Greece) medicines each country (Table 3). The difference (newer minus older medicine) in listing a disproportionate number of newer medicines ranged from 1 (Iceland listing 5 new agents and 4 old agents, Latvia listing 9 new and 8 old agents, and Spain listing 1 new and 0 old medicines), to -16 (Republic of Moldova listing 3 new and 19 old agents) (Figure 1). All the countries that listed the highest number of newer agents also listed some of the highest number of older agents, like Oman, Czechia and Ireland.

When considering each pair of newer and older medicines, some countries were more likely to list only the newer agent (e.g. Benin and Guatemala with 6 newer agents each) while many were more likely to list only the older agents (e.g. Ethiopia listing 20 and Republic of Moldova listing 19 older agents). For most pairs, the older agent

Table 1: Pair of similar medicines [27-29].

Medicines	ATC code and use	First year approved FDA/EMA	Chemical structure	Comments
Medicine-enantiomer				
Amfetamine-dexamfetamine	N06BA01- N06BA02 Attention deficit hyperactivity disorder treatment	1955-1955	Dexamfetamine: (S)- enantiomer of amfetamine	
Amlodipine-levamlodipine	C08CA01- C08CA17 Antihypertensives	1987-2019	Levamlodipine: (S)-enantiomer of amlodipine	Levamlodipine FDA discontinued
Bupivacaine-levobupivacaine	N01BB01- N01BB10 Anesthetics	1972-1998	Levobupivacaine: S(-)-enantiomer of bupivacaine	Levobupivacaine FDA discontinued
Cetirizine-levocetirizine	R06AE07- R06AE09 Antihistamines	1995-2007	Levocetirizine: active enantiomer of cetirizine. It binds to the H1-receptor more strongly than cetirizine	
Chlorpheniramine-dexchlorpheniramine	R06AB04- R06AB02 Antihistamines	1972-1986	Dexchlorpheniramine: (S)-enantiomer of chlorpheniramine	
Chlorpromazine-levomepromazine	N05AA01- N05AA02 Antipsychotics	1954-1982	Levomepromazine: (S)-(-) enantiomer of chlorpromazine	Levomepromazine FDA discontinued
Citalopram-escitalopram	N06AB04- N06AB10 Antidepressants	1998-2002	Escitalopram: (S)- enantiomer of citalopram	
Ibuprofen-dexibuprofen	M01AE01- M01AE14 Antiinflammatories	1974-No FDA approval, 1997 EMA	Dexibuprofen: S(+) enantiomer of ibuprofen	
Ketamine-esketamine	N01AX03- N01AX14 Anesthetics	1970-2019	Esketamine: (S)- enantiomer of ketamine	
Ketoprofen-dexketoprofen	M01AE03- M01AE17 Antiinflammatories	1986-No FDA/EMA approval	Dexketoprofen: (S)+ enantiomer of ketoprofen	Dexketoprofen approved in some European countries
Lansoprazole-dexlansoprazole	A02BC03- A02BC06 Peptic ulcer and reflux treatment	1995-2009	Dexlansoprazole: (R)-*enantiomer* of *lansoprazole*	
Licarbazepine-eslicarbazepine	No ATC code-N03AF04 Antiepileptics	No commercialized-2013	Eslicarbazepine: **(S)-enantiomer** of licarbazepine	Licarbazepine not in essential medicine list
Omeprazole-esomeprazole	A02BC01- A02BC05 Peptic ulcer and reflux treatment	1989-2001	Esomeprazole: (S)- enantiomer of omeprazole	
Sulpiride-levosulpiride	N05AL01- N05AL07 Antipsychotics	No FDA/EMA approval	Levosulpiride: *(S)-(−)-enantiomer of sulpiride*	Both approved in some countries
Zopiclone-eszopiclone	N05CF01- N05CF04 Hypnotics, sedatives	No FDA/EMA approval-2004	Eszopiclone: (S)- enantiomer of zopiclone	Zopiclone approved in some countries
Medicine-metabolite				
Amitriptyline-nortriptyline	N06AA09- N06AA10 Antidepressants	1961-1964	*Nortriptyline:* has two carbon atoms attached to its nitrogen atom, *while amitriptyline has three*	
Aminophylline-theophylline	R03DA05-R03DA04 Obstructive airway disease treatment	1940-1947	Aminophylline: **complex** of theophylline combined with **ethylenediamine**	
Loratadine-desloratadine	R06AX13- R06AX27 Antihistamines	1993-2001	Desloratadine: contains a pyridine nitrogen atom and a piperidine nitrogen atom (loratadine lacks it) as its basic centers	
Venlafaxine-desvenlafaxine	N06AX16 -N06AX23 Antidepressants	1993-2008	Desvenlafaxine: **O-demethylated** active metabolite of venlafaxine	
Medicine-prodrug				
Aciclovir-valaciclovir	D06BB03- J05AB11 Antivirals	1982-1995	**Valaciclovir: L-valine ester prodrug of aciclovir**	
Aprepitant-fosaprepitant	A04AD12 Antiemetics	2003-2008	Fosaprepitant: **phosphorylated prodrug** of aprepitant	
Dexamfetamine-lisdexamfetamine	N06BA02-N06BA12 Attention deficit hyperactivity disorder treatment	1955-2007	Lisdexamfetamine: dexamfetamine bonded to the amino acid **L-lysine**	
Paracetamol-propacetamol	N02BE01- N02BE05 Analgesics	1968-No FDA/EMA approval	Propacetamol: paracetamol combined with **diethylglycine**	Propacetamol approved in some countries
Phenytoin-fosphenytoin	N03AB02- N03AB05 Antiepileptics	1953-1996	Fosphenytoin: includes a **phosphate group** attached to phenytoin	
Oxcarbazepine-eslicarbazepine	N03AF02- N03AF04 Antiepileptics	2000-2013	Eslicarbazepine: has a hydroxy group in the 10th position of the ring, while ixcarbazepine has a ketone group	
Medicine-hydroxylated agent				
Chloroquine-hydroxychloroquine	P01BA01- P01BA02 Antimalarials	1949-1955	Hydroxychloroquine: has a hydroxyl group attached to the ethyl group of its amine. Chloroquine lacks it	
Medicine-hydrogenated agent				

Chlorothiazide-hydrochlorothiazide	C03AA04- C03AA03 Diuretics	1958-1959	Hydrochlorothiazide: has an extra hydrogen atom on a nitrogen atom in the sulfonamide ring of the chlorothiazime molecule	
Medicine-methylated agent				
Ergometrine-methylergometrine	G02AB03- G02AB01 Uterotonics	No FDA/EMA approval-1946	Methylergometrine: has a **methyl group** added to the nitrogen atom of the side chain in the ergometrine molecule	
Medicine-pegylated agent				
Filgrastim-empegfilgrastim	L03AA02- L03AA16 Colony stimulating factors	1991- No FDA/EMA approval	Empefilgrastim: is a **pegfilgrastim biosimilar, and has a polyethylene glycol molecule covalently attached to the filgrastim molecule**	Empegfilgrastim commercialized in Russian Federation
Filgrastim-lipegfilgrastim	L03AA02- L03AA14 Colony stimulating factors	1991- No FDA approval, 2013 EMA	Lipegfilgrastim: has a **longer polyethylene glycol chain** conjugated to the filgrastim molecule	
Filgrastim-pegfilgrastim	L03AA02- L03AA13 Colony stimulating factors	1991-2002	Pegfilgrastim: has a **polyethylene glycol molecule covalently attached to the filgrastim molecule**	

Table 2: Countries listing the highest number of newer agents.

Country	List: n° medicines-year	Newer agents listed	Older agents listed	Population size (2021) [22]	Income level* [25]	WHO region [26]	Life expectancy (2023 est.) [21]	Health expenditure U$S per capita (2021) [23]	Real GDP per capita (2021 est.) [21]
Oman	793-2020	16	21	45,20,471	High	Eastern Mediterranean	77.2	853	34,300
Slovenia	931-2023	15	23	21,19,410	High	European	82	2,775	40,000
Maldives	853-2021	15	21	5,21,458	Upper middle	South-East Asia	77.2	1,039	18,800
Czechia	834-2012	15	20	1,05,10,751	High	European	78.3	2,499	40,700
Ireland	740-2023	15	20	49,86,526	High	European	82.2	6,764	1,02,500
Iran (Islamic Republic of)	955-2017	14	21	8,79,23,433	Upper middle	Eastern Mediterranean	75.4	393	15,000
Slovakia	764-2023	14	20	54,47,622	High	European	76.6	1,685	31,900
Greece	918-2007	13	24	1,04,45,365	High	European	81.7	1,846	29,500
Colombia	594-2019	13	20	5,15,16,562	Upper middle	The Americas	74.9	558	14,600
Australia	787-2023	13	18	2,59,21,089	High	Western Pacific	83.3	7,055	49,800
Croatia	756-2022	12	12	40,60,136	High	European	77.5	1,384	31,600

*Income level extracted from website in July 2024.

was more frequently listed by itself than the newer one. However, there were four pairs where the newer agent was more commonly listed alone, compared to the older agent alone: dexamfetamine (newer) over amfetamine (older), hydrochlorothiazide (newer) over chlorothiazide (older), escitalopram (newer) over citalopram (older), and eslicarbazepine (newer) over licarbazepine (older). The pair aprepitant (older agent) and fosaprepitant (newer agent) was unique in that countries either listed both agents or neither, but never listed just the newer agent alone or just the older agent alone.

The characteristics of countries that listed the highest number of newer agents vary significantly in terms of their essential medicine lists' lengths, which range from 594 medicines in Colombia to 955 medicines in Iran, and the years of their lists, spanning from Greece in 2007 to Australia, Ireland, and Slovakia in 2023. Half of these countries are European with high income levels, and their populations range from 521,458 in the Maldives to over 87 million in Iran.

Countries with a highest difference between newer and older agents (number of newer agents minus number of older agents listed) tend to have higher real GDP per capita and higher per capita US$ health expenditure (like Spain), and higher population size (like Japan) (Figures 2-4).

Discussion

We found that some countries (such as Latvia, Panama and Spain) prioritize access to certain newer agents when there are other agents with identical or very similar clinical effects also available, and other countries (such as Oman, Slovenia, Maldives, Czechia, Ireland, Islamic Republic of Iran and Slovakia) list a large number of newer agents together with clinically equivalent older agents. Half of those countries belong to the European continent and have high income level, like Slovenia, Czechia, Ireland, Slovakia, and Greece.

While essential medicines lists are supposed to include medicines that meet the priority needs of populations, they sometimes include medicines for questionable reasons such as medicines that have been withdrawn for good reason. [27-30]. The preferential listing of newer and more expensive medicines with similar clinical effects to older and less expensive medicines raises the possibility that profit by drug manufacturers could indirectly influence national essential medicines [31-33]. Other studies have identified the potential influence of business decisions on medicine prioritization decisions [34,35]. Essential medicines list processes could be similarly influenced.

Strengths and Limitations

We included many countries in this analysis. We did not assess for the actual use of the listed medicines and inclusion in a national essential medicines list does not always lead to better access, although our finding would still raise questions about why newer agents were added to essential medicines lists even if access was not promoted.

Table 3: Countries listing the highest number of older agents.

Country	List: n° medicines-year	Older agents listed	Newer agents listed	Population size (2021) [22]	Income level* [25]	WHO region [26]	Life expectancy (2023 est.) [21]	Health expenditure U$S per capita (2021) [23]	Real GDP per capita (2021 est.) [21]
Slovenia	931-2023	23	15	21,19,410	High	European	82	2,775	40,000
Oman	793-2020	21	16	45,20,471	High	Eastern Mediterranean	77.2	853	34,300
Maldives	853-2021	21	15	5,21,458	Upper middle	South-East Asia	77.2	1,039	18,800
Iran (Islamic Republic of)	955-2017	21	14	8,79,23,433	Upper middle	Eastern Mediterranean	75.4	393	15,000
Belarus	659-2021	21	11	95,78,168	Upper middle	European	74.6	468	19,800
Czechia	834-2012	20	15	1,05,10,751	High	European	78.3	2,499	40,700
Ireland	740-2023	20	15	49,86,526	High	European	82.2	6,764	1,02,500
Slovakia	764-2023	20	14	54,47,622	High	European	76.6	1,685	31,900
Colombia	594-2019	20	13	5,15,16,562	Upper middle	The Americas	74.9	558	14,600
Croatia	756-2022	20	12	40,60,136	High	European	77.5	1,384	31,600
Mexico	794-2017	20	11	12,67,05,138	Upper middle	The Americas	73.5	611	19,100
Uruguay	542-2020	19	9	34,26,260	High	The Americas	78.7	1,620	22,800
Malta	645-2022	19	8	5,26,748	High	European	83.4	3,642	44,700
Trinidad & Tobago	467-2019	19	6	15,25,663	High	The Americas	76.2	1,125	23,000
China	385-2018	19	5	1,42,58,93,465	Upper middle	Western Pacific	78.2	671	17,600
United Republic of Tanzania	452-2021	19	5	6,35,88,334	Lower middle	Africa	70.5	37	2,600
Republic of Moldova	506-2021	19	3	30,61,507	Upper middle	European	69.7	410	13,300

*Income level extracted from website in July 2024.

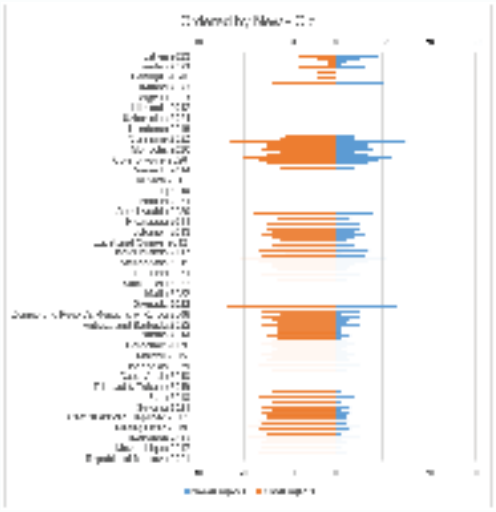

Figure 1: Two-sided bar chart of all country's listings, ordered by the number of newer agents minus the number of older agents.

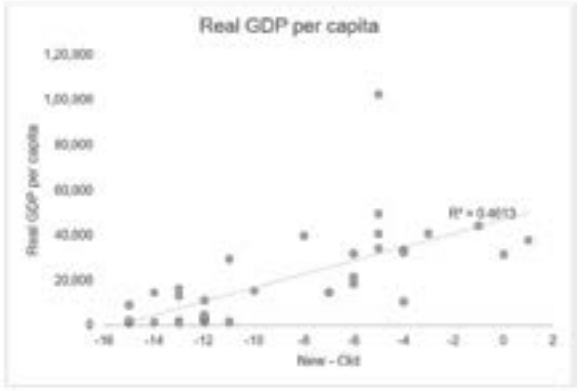

Figure 2: Real GDP per capita ordered by the number of newer agents minus the number of older agents [21].

In some medicine pairs, there may be differences in clinical effects for specific conditions. There may be other reasons that countries decide to list newer agents such as related to local production or other concessions from manufacturers or distributors. We did not assess the processes for updating essential medicines lists.

Conclusion

Some countries should revisit their listing of certain medicines that may be poor value as they are molecularly or clinically equivalent to older and less expensive alternatives. Countries may also examine how the medicine selection policies and procedures led to preferentially listing more expensive agents that may be equivalent to others, with particular attention to whether marketing may influence drug prioritization decisions.

Funding

The work was supported by funding from the World Health Organization. NP was supported by funding from the Canada Research Chairs program and the Canadian Institutes of Health Research.

References

1. Fantino B, Moore N, Verdoux H, Auray JP. Cost-effectiveness of escitalopram vs. citalopram in major depressive disorder. Int Clin Psychopharmacol. 2007;22(2):107-15.

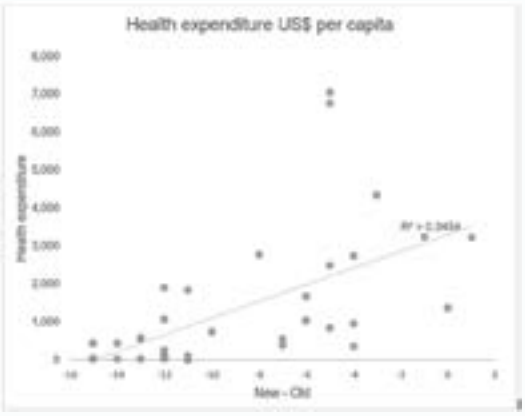

Figure 3: Health expenditure per capita ordered by the number of newer agents minus the number of older agents [23].

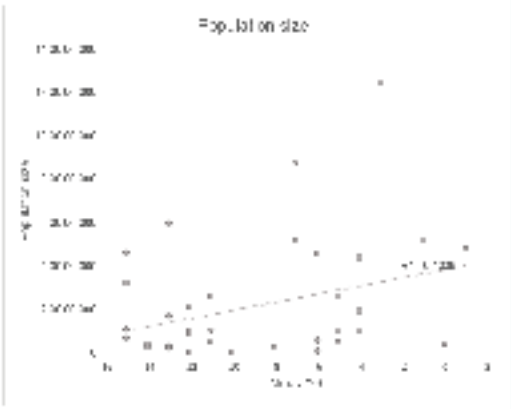

Figure 4: Population size ordered by the number of newer agents minus the number of older agents [22].

2. Wahlqvist P, Junghard O, Higgins A, Green J. Cost Effectiveness of Esomeprazole Compared with Omeprazole in the Acute Treatment of Patients with Reflux Oesophagitis in the UK. Pharmacoeconomics. 2002;20(4):279-87.

3. Gebremariam GT, Fentie AM, Beyene K, Sander B, Gebretekle GB. Cost-effectiveness of pegfilgrastim versus filgrastim for prevention of chemotherapy-induced febrile neutropenia in patients with lymphoma: a systematic review. BMC Health Serv Res. 2022;22(1):1600.

4. Barden J, Derry S, McQuay HJ, Moore RA. Single dose oral ketoprofen and dexketoprofen for acute postoperative pain in adults. In: The Cochrane Collaboration, editor. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2009 p. CD007355.pub2.

5. Zee AV. The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy. Am J Public Health. 2009;99(2):221-7.

6. Tansley R, Lotharius J, Priestley A, Bull F, Duparc S, Möhrle J. A Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Safety, Tolerability, and Pharmacokinetics of Single Enantiomer (+)-Mefloquine Compared with Racemic Mefloquine in Healthy Persons. Am J Trop Med Hyg. 2010;83(6):1195-201.

7. Long AS, Zhang AD, Meyer CE, Egilman AC, Ross JS, Wallach JD. Evaluation of Trials Comparing Single-Enantiomer Drugs to Their Racemic Precursors: A Systematic Review. JAMA Netw Open. 2021;4(5):e215731.

8. Geisslinger G, Menzel S, Wissel K, Brune K. Pharmacokinetics of ketoprofen enantiomers after different doses of the racemate. Br J Clin Pharmacol. 1995;40(1):73-5.

9. WHO. Providing International biological reference preparations.

10. Official Journal of the European Communities. DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 November 2001 on the Community code relating to medicinal products for human use.

11. Drugs@FDA: FDA-Approved Drugs. New Drug Application (NDA): 207078. 2024.

12. WHO. WHO Model Lists of Essential Medicines.

13. Laing R, Waning B, Gray A, Ford N, 't Hoen E. 25 years of the WHO essential medicines lists: progress and challenges. Lancet. 2003;361(9370):1723-9.

14. Persaud N, Jiang M, Shaikh R, Bali A, Oronsaye E, Woods H, et al. Comparison of essential medicines lists in 137 countries. Bull World Health Organ. 2019;97(6):394-404C.

15. Teng M, Khoo AL, Zhao YJ, Lin L, Lim BP, Wu TS, et al. Meta-analysis of the effectiveness of esomeprazole in gastroesophageal reflux disease and Helicobacter pylori infection. J Clin Pharm Ther. 2015;40(4):368-75.

16. Roder L, Konrardy K, Grauer D, Hoffmann M. Effects of filgrastim versus pegfilgrastim on outcomes of DA-R-EPOCH for non-Hodgkin's lymphoma. Support Care Cancer. 2021;29(9):5075-82.

17. Lee R, Seligman A, Clark M, Rousseau P. A comparison of the side effects and hypertensive potency of hydrochlorothiazide and chlorothiazide. N Engl J Med. 1960;262:1066-8.

18. Kim MG, Han N, Lee EK, Kim T. Pegfilgrastim vs filgrastim in PBSC mobilization for autologous hematopoietic SCT: a systematic review and meta-analysis. Bone Marrow Transplant. 2015;50(4):523-30.

19. O'Riordan TG, Mao W, Palmer LB, Chen JJ. Assessing the Effects of Racemic and Single-Enantiomer Albuterol on Airway Secretions in Long-term Intubated Patients. Chest. 2006;129(1):124-32.

20. Ziakas PD, Kourbeti IS. Pegfilgrastim vs. filgrastim for supportive care after autologous stem cell transplantation: can we decide? Clin Transplant. 2012;26(1):16-22.

21. CIA, US. Country Comparisons. The World Factbook. CIA.

22. United Nations. Population Division. 2022.

23. The World Health Organization. Global Health Observatory (GHO). WHO. 2023.

24. Amnesty International Press Release. North Korea's crumbling health system in dire need of aid. 2010.

25. The World Bank. The World Bank. Income level classification, 2023.

26. World Health Organization. Geographic regions. WHO.

27. U.S. Food & Drug Administration. Food & Drug Administration-Approved drugs.

28. European Medicines Agency. European Medicines Agency-Approved drugs.

29. Drug bank.

30. Charles O, Onakpoya I, Benipal S, Woods H, Bali A, Aronson JK, et al. Withdrawn medicines included in the essential medicines lists of 136 countries. PLoS ONE. 2019;14(12):e0225429.

31. IMS Institute for Healthcare Informatics. Understanding the Role and Use of Essential Medicines Lists. Essential Medicines Report. 2015.

32. Hill AM, Barber MJ, Gotham D. Estimated costs of production and potential prices for the WHO Essential Medicines List. BMJ Glob Health. 2018;3(1):e000571.

33. Morgan SG, Bathula HS, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. BMJ. 2020;368:l4627.

34. Piggott T, Moja L, Akl EA, Lavis JN, Cooke G, Kredo T, et al. Decision criteria for selecting essential medicines and their connection to guidelines: an interpretive descriptive qualitative interview study. J Clin Epidemiol. 2023;154:146-55.

35. Moucheraud C, Wirtz VJ, Reich MR. Evaluating the quality and use of economic data in decisions about essential medicines. Bull World Health Organ. 2015;93(10):693-9.