

Relation between opioid consumption and inclusion of opioids in 137 national essential medicines lists

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ABSTRACT

Introduction Opioids are deemed essential medicines by the World Health Organization (WHO). However, many countries have inadequate access to them. Whether including opioids in national essential medicines lists (EMLs) influences national opioid consumption has not been evaluated.

Methods We conducted a cross-sectional study to determine whether the listing of opioids in national EMLs was associated with consumption. We quantified the numbers and types of all opioids included in 137 national EMLs, for comparison with opioids in the WHO's Model List of Essential Medicines. Using the International Narcotics Control Board (INCB) consumption statistics for 2015–2017, we assessed the relation between annual mean opioid consumption (mg/person) and the numbers of opioids included in EMLs, controlling for region, population, healthcare expenditure, life expectancy, gross domestic product, human development and corruption.

Results Five opioids were included in the 20th edition of the WHO's Model List of Essential Medicines: codeine, fentanyl, loperamide, methadone and morphine. On average, countries' lists included significantly ($p<0.05$) more opioids than the WHO's Model List. However, there were wide variations in the numbers (median 6 opioids; IQR: 5–9) and types ($n=33$) of opioids included in national EMLs. Morphine (95%), fentanyl (83%) and codeine (69%) were the most commonly included opioids. Most national EMLs were out of date (median publication date: 2011, IQR: 2009–2013). After adjusting for country characteristics, there was no relation between mean opioid consumption and the number of opioids in EMLs.

Conclusions Including opioids in national EMLs was not associated with consumption. National EMLs should be regularly updated to reflect the availability of opioids and the populations' needs for managing pain.

INTRODUCTION

Opioids are essential in managing pain, and other symptoms frequent in palliative care, opioid dependence and diarrhoeal diseases.¹ Since the publication of its first list in 1977, WHO has included opioids in its Model List of Essential Medicines.² Medicines selected by the WHO for inclusion in its Model List are of

Key questions

What is already known?

- WHO deems opioids as essential for managing pain, palliative care, anaesthesia and opioid dependence.
- WHO encourages countries to adopt and adapt the WHO's Model List of Essential Medicines to identify national essential medicines lists (EMLs) to meet the priority health needs of their populations.
- Studies have not explored the relation between listing opioids in EMLs and consumption.

What are the new findings?

- National EMLs included a median of 6 (IQR: 5–9) opioids.
- Lists included significantly more opioids than the five opioids (ie, codeine, fentanyl, loperamide, methadone and morphine) in the WHO's Model List of Essential Medicines.
- Morphine, fentanyl, codeine, pethidine and tramadol were the most commonly included opioids in lists.
- After adjusting for country characteristics, there was no relation between the number of opioids in EMLs and mean opioid consumption.

What do the new findings imply?

- Simply putting an opioid in an EML may not increase supply or change prescribing habits, which questions the usefulness of current EMLs in extending the accessibility of the most important medicines such as opioids.
- Revisions of current lists to reflect the availability of opioids and the populations' needs for managing pain, palliative care, anaesthesia and opioid dependence would be timely.

'utmost importance, and are basic, indispensable and necessary for the health needs of the population.'² WHO encourages governments to adopt and adapt the WHO's Model List to meet the needs of their populations.

Currently, 137 countries (70% of 195 countries) serving more than 5 billion people have essential medicines lists (EMLs).³ Countries that implement the WHO's EMLs policies have improved the quality of usage

of medicines.⁴ However, studies have highlighted considerable variation in the numbers and types of medicines included in EMLs.^{5 6} Researchers have evaluated the inclusion of medicines for neuropathic pain in national EMLs.⁶ However, this analysis only included four opioids (ie, tramadol, morphine, methadone and oxy-codone) and focused on low-income and middle-income countries.⁶ It is now recognised that adoption of a list of essential medicines could be beneficial in high-income countries, to reduce suboptimal prescribing and improve the affordability of essential medicines.^{7 8} However, the numbers and types of all opioids included by all countries with national EMLs have not been investigated. Nor is it known how the number of opioids included in a list is related to consumption.

The central aim of this study was to determine whether the listing of opioids in national EMLs is associated with consumption, as a proxy measure of accessibility, where consumption refers to the medical use of opioids and excludes recreational use. We also quantified the numbers and types of opioids in 137 national EMLs, for comparison with the WHO's Model List of Essential Medicines.

METHODS

Study design and data sources

We designed and conducted a cross-sectional observational study following the publication of the Global Essential Medicines (GEM) database⁹ and on receiving updated data from the International Narcotics Control Board (INCB)¹⁰ in August 2019. The protocol for our study is openly available on the Open Science Framework (OSF; <https://osf.io/385hx/>).¹¹

The International Narcotics Control Board (INCB), an independent body of the United Nations (UN), monitors implementation of international drug control conventions, including the Single Convention on Narcotic Drugs of 1961, which requires governments to report annual statistics on narcotic consumption relating to controlled drugs.¹² Consumption refers to the total amount of a narcotic that is distributed for medical purposes at the retail level (ie, to institutions and programmes that are licensed to dispense to a patient). We received data from 2015 to 2017 in kg and removed 27 non-opioid substances (eg, cannabis, coca leaf and cocaine) to create a dataset of all opioids consumed. The included and excluded substances are listed in online supplemental box S1. We calculated a 3-year annual mean for each country with an EML. We adjusted for population size using 2016 data from the WHO Global Health Observatory¹³ to create a rate (ie, mean consumption in mg per person), see online supplemental box S2 for a sample calculation.

The GEM database was developed by Persaud *et al* in June 2017, by extracting all medicines listed by all countries with a national EML from the WHO's repository, as previously described,⁵ and all medicines listed in the 20th edition of the WHO's Model List of Essential Medicines¹,

which was the most up to date list published at the time the GEM database was created. In June 2019, WHO published the 21st edition of their Model List but there were no opioids added to the list,¹⁴ and thus, we used the 20th edition to be consistent with the GEM database. The medicines included in the database are coded using the Anatomical Therapeutic Classification (ATC) index. Two authors (GCR and JKA) independently searched the ATC index to create a list of opioids, compared their lists, discussed discrepancies and agreed on a master list of ATC codes for opioids; see online supplemental table S1. We used the ATC codes and medicine names in the master list to search for opioids in the GEM database for every country (n=137) with an EML.

Opioids included in EMLs

We identified the numbers and types of opioids included in the 20th edition of the WHO's Model List of Essential Medicines,¹ which was current when we began this study. We summed the number of opioids and identified the types of opioids for all countries with a national EML (n=137, 70% of 195 countries as defined by the UN¹⁵). We calculated the median and IQR for the number of opioids in EMLs. We calculated the percentage of opioids listed as a total of all included medicines, and compared countries' lists with the WHO's Model list using a one-sample z-test and a significance level of 0.05. For each country, we calculated the numbers of opioids that were the same as or different from the WHO's Model List to create percentages of similarities and differences.

Relation between opioid consumption and listing opioids in EMLs

We extracted geographical region, population, health-care expenditure per capita (US\$), life expectancy at birth (in years) for all sexes, gross domestic product (GDP) per capita, the human development index and the corruption perception scores for each country with an EML from web pages outlined in online supplemental table S2. The assumptions for untransformed linear regression were not met. Thus, we used a square root transformation of the dependent variable (ie, opioid consumption in mg/person), which improved the model. We conducted two multivariable analyses. In the first, we adjusted for GDP per capita and health expenditure per capita, as these variables had the least amount of missing data (n=133). In the second analysis we adjusted for all country characteristics. We conducted a sensitivity analysis by removing extreme outliers.

Statistical software and data access

We used Stata V.16¹⁶ for all statistical analyses and pandas and plotly modules in Jupyter Notebooks with Python v3 for choropleth maps. Our protocol, study materials, data and statistical code are all openly available on the OSF (<https://osf.io/385hx/>)¹¹ and GitHub (https://github.com/georgiarichards/opioid_emls_maps). We used The Strengthening the Reporting of Observational Studies in

Epidemiology (STROBE) reporting guidelines to write our manuscript; see the online supplemental 1 for the completed checklist.

Protocol deviations

We used INCB data from 2015 to 2017 instead of 2014 to 2016, as we obtained the most up-to-date data before we started the analysis (August 2019). We could not convert consumption from volume (ie, kg) to morphine equivalents, because potency ratios are not available for all types of opioids included in our analysis. We did not conduct regression analyses for individual types of opioids as there were missing data; for example, only 73 countries (53%) with EMLs reported consumption data for oxycodone; see online supplemental table S3.

Patient and public involvement

We involved three patients who have chronic pain and experience of taking opioids and other medicines for pain at the analysis phase of our research. Lead author (GCR) presented the preliminary findings to the patients during a formal face-to-face patient and public involvement meeting in December 2019. Patients provided suggestions for final analyses, the presentation of results, and the dissemination plans for our research. Preliminary findings were also presented to stakeholders at the inaugural Global Essential Medicines Meeting in November 2019 in Toronto, Canada, which included members of the WHO's Expert Committee on the Selection and Use of Essential Medicines. All stakeholders will be involved in the dissemination of our research.

RESULTS

Opioids listed in the WHO's Model List of Essential Medicines

The 20th edition of the WHO's Model List of Essential Medicines included five opioids: codeine, fentanyl,

loperamide, methadone and morphine; see online supplemental table S4. The included opioids account for 1.4% of all medicines listed in the WHO's Model List.

Opioids listed in national EMLs

EMLs included a median of six opioids (IQR: 5–9). Slovakia included the most opioids (n=19) while Cambodia did not include any (see [figure 1](#) and online supplemental table S5). There were 33 different opioids included in national EMLs (see [figure 2](#) and online supplemental table S6). The most commonly included opioid was morphine (95%), followed by fentanyl (83%), codeine (69%), pethidine (65%) and tramadol (62%) (see [figure 2](#)). The median publication date for EMLs was 2011 (IQR: 2009–2013; range: 2001–2017); (see online supplemental table S5).

Comparison of national EMLs with the WHO's Model List

Countries with EMLs included significantly more opioids ($z=6.33$, $p<0.05$) as a percentage of all medicines than the WHO's Model List. Ninety-five per cent of countries included morphine, 83% listed fentanyl, 69% codeine, 61% loperamide and 41% methadone (see [figure 3](#)). Most countries (98.5%) included at least one opioid recommended by the WHO, except for Cambodia, which listed no opioids, and Somalia which only listed pethidine. Eighteen per cent of countries (25 of 137) included all five opioids (ie, codeine, fentanyl, loperamide, methadone and morphine) included in WHO's Model list (see online supplemental figure S1). There were also a number of opioids included in national EMLs that were not included in the WHO Model Lists (see online supplemental figure S2).

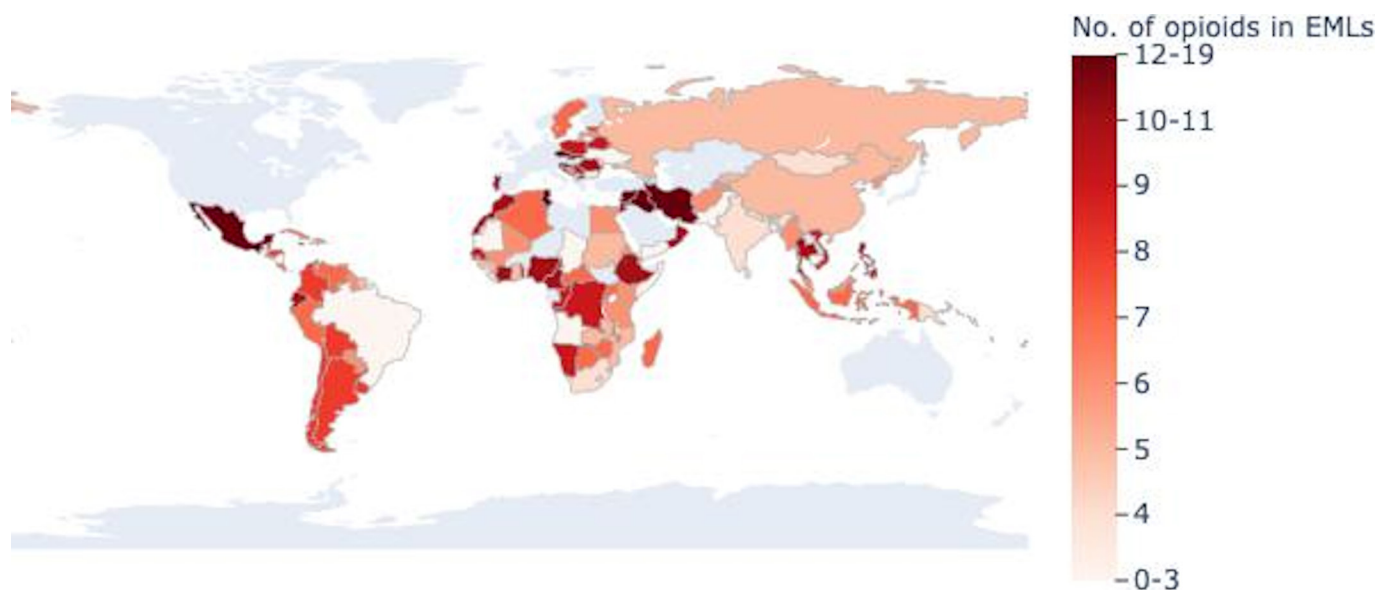


Figure 1 Number of opioids included in national essential medicines lists (EMLs) grouped by nine quantiles. There were 137 countries with EMLs; countries in light grey did not have an EML.

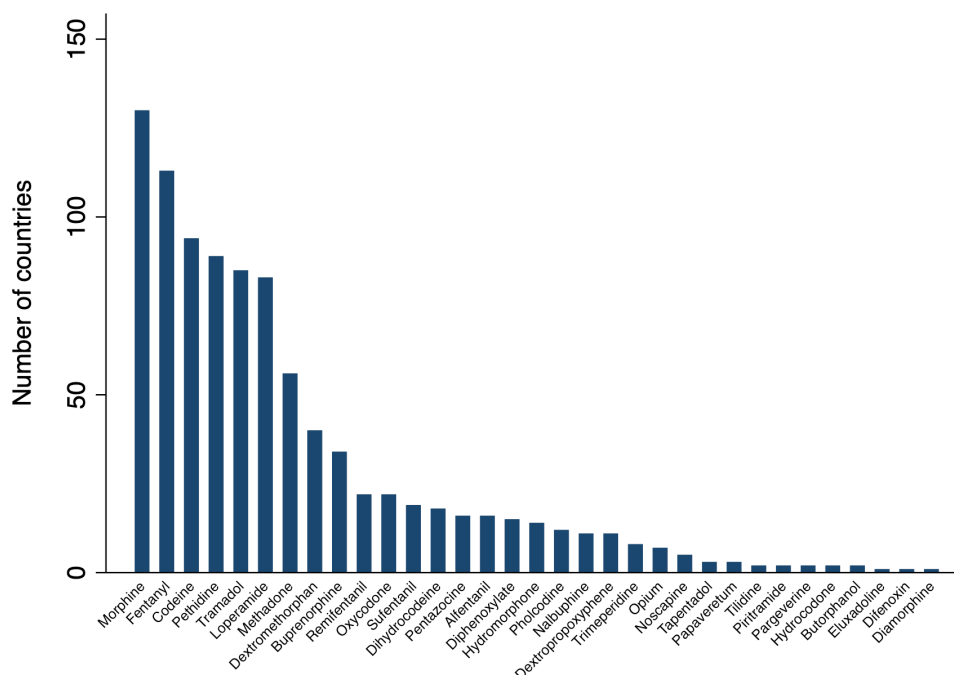


Figure 2 Types of opioids (n=33) included in 137 national essential medicines lists ordered from most common to least.

Relation between consumption and the number of opioids in EMLs

Countries with EMLs consumed a median of 2mg/day (IQR: 0.13–6.8mg/day) of opioids between 2015 and 2017. There was a wide range in consumption (range: 0–97.9mg/day) with most countries (93%, 128 of 137) consuming less than 20mg/person of opioids, and 17% of countries (23 of 137) reporting no opioid consumption. Countries that did not report consumption included a median of 5 opioids (IQR: 3–7; range: 0–12 opioids)

in their national EML. In the univariable analysis, there was a positive and significant association between mean opioid consumption and the number of opioids listed in national EMLs (unadjusted coefficient: 0.172, 95% CI 0.086 to 0.258, $p<0.0001$, [table 1](#)) but not after adjusting for GDP and healthcare expenditure (adjusted coefficient: 0.045, 95% CI –0.022 to 0.111, $p=0.187$, [table 1](#)) or all country characteristics as summarised in online supplemental table S7 (coefficient: 0.0109, 95% CI –0.0087 to 0.0305, $p=0.271$, [table 1](#)). In a sensitivity

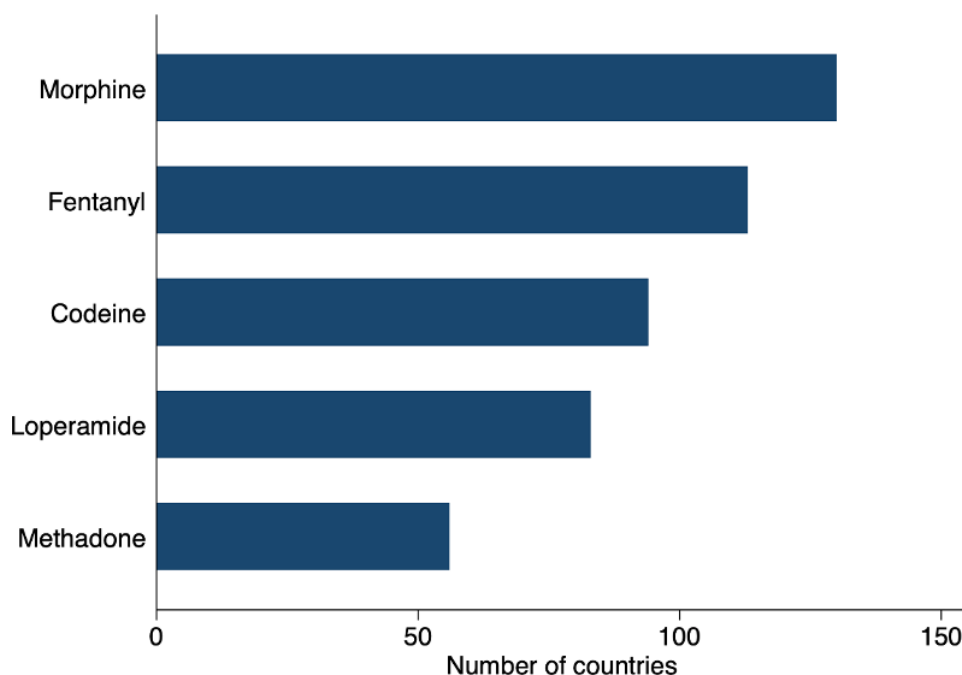


Figure 3 The five opioids in the WHO's Model List of Essential Medicines and the number of countries that included the five opioids in their national essential medicines lists.

Table 1 Regression models for the relation between the square rooted annual mean opioid consumption and the listing of opioids in national essential medicines lists (EMLs)

	Univariate (n=137)			Multivariable* (n=133)			Multivariable (n=117)		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Consumption versus number of opioids in EMLs	0.17	0.09 to 0.6	0	0.05	-0.02 to 0.11	0.19	0.01	-0.009 to 0.03	0.27
GDP/100 per capita				0.006	0.003 to 0.009	0	0.00005	-0.0012 to 0.0013	0.93
Healthcare expenditure per capita				0.0001	0.0007 to 0.002	0	0.0004	0.0002 to 0.0005	0
Population							-1.35e-10	-5.05e-10 to 2.35e-10	0.47
Life expectancy							-0.009	-0.03 to 0.01	0.38
Human development index							1.33	0.012 to 2.64	0.48
Corruption perception score							0.007	0.0007 to 0.01	0.03
Region (Africa)									
America							-0.065	-0.3 to 0.17	0.59
Asia							0.12	-0.09 to 0.33	0.27
Europe							0.32	0.04 to 0.59	0.03
Oceania							0.16	-0.3 to 0.6	0.48

The assumptions for untransformed linear regression were not met. Thus, we used a square root transformation of the dependent variable (ie, opioid consumption in mg/person), which improved the model.

*we conducted this multivariable analysis first as it had the least amount of missing data and the variables had the strongest predictors of opioid consumption. GDP, gross domestic product.

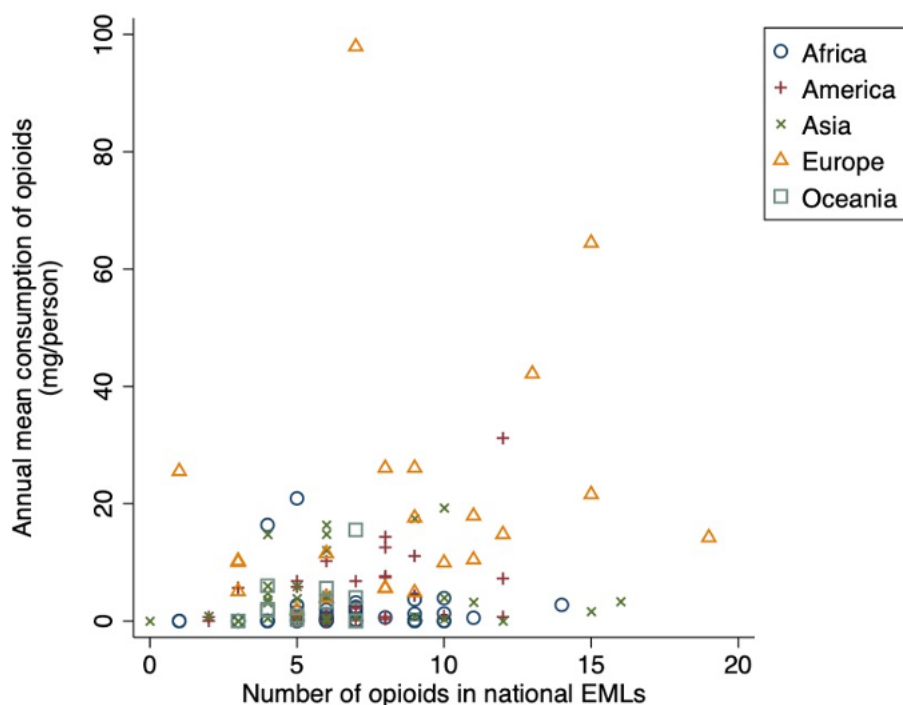


Figure 4 Scatter plot of the relation between annual mean opioid consumption (mg/person) for 2015–2017 and the number of opioids included in national essential medicines lists (EMLs) for 137 countries. Each country is represented by a symbol for its geographical region. After adjusting for country characteristics, there was no relation between consumption and the number of opioids in EMLs (coefficient: 0.0109, 95% CI: –0.0087 to 0.0305, $p=0.271$).

analysis, removing the highest income country Sweden, the relation did not change. [Figure 4](#) illustrates the relation between opioid consumption and the number of opioids included in EMLs before transformation; online supplemental figure S3 illustrates the relation after the transformation.

DISCUSSION

After adjusting for country characteristics, the number of opioids included in EMLs was not associated with the consumption of opioids. There are wide variations in the numbers and types of opioids included in national EMLs. Countries included significantly more opioids than the WHO Model List of Essential Medicines, which included five opioids: morphine for anaesthesia; codeine, fentanyl, methadone and morphine for pain and palliative care; loperamide for diarrhoeal symptoms; and methadone for opioid use disorders. In national EMLs, morphine, fentanyl and codeine were the most common opioids included.

The purpose of EMLs, as originally stated by WHO in 1977, was to improve health, reduce costs of medicines, and extend the accessibility of the most necessary medicines to populations whose basic health needs could not be met by the existing supply system.² The absence of a relation between the number of opioids in EMLs and consumption questions the usefulness of current EMLs in enabling access ‘at all times, in adequate amounts, and in the proper dosage forms’, as originally stated.² However, most lists were out of date and most countries had low or no consumption of opioids. There may be other factors which influence this relation, such as cost implications

imposed by EMLs, patchy implementation of lists, pharmaceutical interests that push more medicines into EMLs and restraints in the healthcare system on where and how medicines are prescribed, and by whom.^{17–21} However, these factors have not been explored in relation to opioids. Thus, future research should evaluate the function of EMLs in extending the accessibility of essential medicines like opioids in practice.

After the development of the first Model List of Essential Medicines, WHO encouraged countries to select medicines that meet the health priorities of their populations. Therefore, variations between countries is expected. However, including 19 different opioids, all with complex pharmacology, as found in Slovakia’s EML, or not including any opioids as found in Cambodia’s EML, may not adequately reflect differences in the health needs of those populations. Importantly, Cambodia has experienced recent outbreaks of HIV due to unsafe use of recreational opioids,²² and is a major transit route for exporting heroin,²³ which may impact policies, access to pharmaceutical opioids, and health services in these regions. Future research could explore reasons for wide variations in the numbers and types of opioids included in national EMLs, and the reasons for adding or removing opioids in individual countries and regions.

Many advantages to using a central list of essential medicines have been identified. These include a reduction in the number of pharmaceutical products to be purchased, stored, analysed and distributed; an improvement in the quality of medicine utilisation, management, information and monitoring; stimulation of local

pharmaceutical companies; assistance to low-income and middle-income countries in urgent need of high-priority medicine programmes to extend their primary health-care provisions.^{2 4} WHO encourages countries to make the selection of essential medicines to be a continuing process that takes into account changing public health priorities, epidemiological conditions, progress in pharmacological and pharmacovigilance systems.² We found that many lists were a number of years out of date based on the available information. Thus, revision of current EMLs to reflect such changes would be timely.

Limitations

The INCB and GEM databases do not specify formulations or dosage, and it is not possible to elucidate the clinical use of opioids consumed or included in EMLs. Thus, we recognise that medicines included in EMLs indicate nominal availability and thus caution is warranted when interpreting medicines on or absent from EMLs. Many high-income countries who consume most of the world's opioids²⁴ do not have EMLs, and therefore our regression model is not generalisable to all countries. Although our regression model was adjusted for a number of country characteristics, it is possible we may have missed some other important confounders. Consumption statistics are not reported to the INCB for opioids that are not regulated as internationally controlled substances (eg, tramadol and buprenorphine). Data reported to the INCB may also be late, unreported, or submitted inaccurately, as previously described.^{25 26} The effects of different types of opioids vary by weight, which morphine equivalent conversion would account for, if accurate conversion were possible. We measured consumption using weight in mg adjusted for country population, as conversion factors for morphine equivalents, and defined daily doses (DDDs) are not available for all opioid substances included in our analysis. Thus, our findings may be less comparable to most previous research on opioid consumption that uses DDDs.

CONCLUSIONS

The number of opioids in lists was not associated with consumption, which questions the usefulness of current EMLs. The numbers and types of opioids included in 137 national EMLs differ from the WHO's Model List and vary between countries. Governments should consider updating their lists to reflect national availability of opioids and their population's needs for managing pain, symptoms frequent in palliative care, opioid dependence and diarrhoeal diseases.

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Contributors GCR devised the research question, designed the methods, wrote the protocol, conducted data screening, data cleaning and management, analysed the data, conducted the literature review and wrote the original manuscript. JKA conducted secondary data screening for the master list of opioids, reviewed preliminary findings, critically revised the manuscript and provided supervisory support. CH, KRM and NP reviewed the protocol and preliminary findings, critically revised the manuscript and provided supervisory support. NP provided access to the Global Essential Medicines Database and was the catalyst for conducting this study. CK provided statistical advice, reviewed the statistical model and preliminary findings and critically revised the manuscript. All authors read, reviewed and approved the final manuscript.

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Patient and public involvement statement We involved three patients who have chronic pain and experience of taking opioids and other medicines for pain at the analysis phase of our research. Lead author (GCR) presented the preliminary findings to the patients during a formal face-to-face PPIpatient and public involvement meeting in December 2019. Patients provided suggestions for final analyses, the presentation of results, and the dissemination plans for our research. Preliminary findings were also presented to stakeholders at the inaugural Global Essential Medicines Meeting in November 2019 in Toronto, Canada, which included members of the WHO's Expert Committee on the Selection and Use of Essential Medicines. All stakeholders will be involved in the dissemination of our research.

Patient consent for publication Not required.

Ethics approval Not required

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Our protocol, study materials, data and statistical code are all openly available on the Open Science Framework (<https://osf.io/385hx/>) and GitHub (https://github.com/georgiarichards/opioid_emls_maps).

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Supplement 1: Additional tables and figures

Box S1: Substances included and excluded from the International Narcotic Control Board (INCB) data on narcotic consumption, in alphabetical order.

Opioids **included** in the opioid consumption calculation:

- | | |
|------------------------------------|----------------------------------|
| 1. (+)-cis-3-methylfentanyl | 35. Bezitramide |
| 2. 3-Acetylmorphine | 36. Butyrfentanyl |
| 3. 3-Methylfentanyl | 37. Carfentanil |
| 4. 3-Methylthiofentanyl | 38. Carfentanyl |
| 5. 3-Monoacetylmorphine | 39. Clonitazene |
| 6. 4-Fluoroisobutyrfentanyl | 40. Codeine |
| 7. 6-Acetylmorphine | 41. Codeine-6GLUC |
| 8. 6-Monoacetylmorphine | 42. Codeine-6-glucuronide |
| 9. Acetorphine | 43. Codeine-Methyl |
| 10. Acetyl-alpha-methylfentanyl | 44. Codeine-N-oxide |
| 11. Acetyldihydrocodeine | 45. Codoxime |
| 12. Acetylfentanyl | 46. Conc. of poppy straw (C) ACA |
| 13. Acetylmethadol | 47. Conc. of poppy straw (C) AMA |
| 14. Acetylmorphine | 48. Conc. of poppy straw (C) AOA |
| 15. Acrylfentanyl | 49. Conc. of poppy straw (C) ATA |
| 16. AH-7921 | 50. Conc. of poppy straw (C) GW |
| 17. Alfentanil | 51. Conc. of poppy straw (M) ACA |
| 18. Allylprodine | 52. Conc. of poppy straw (M) AMA |
| 19. Alphacetylmethadol | 53. Conc. of poppy straw (M) AOA |
| 20. Alphameprodine | 54. Conc. of poppy straw (M) ATA |
| 21. Alphamethadol | 55. Conc. of poppy straw (M) GW |
| 22. alpha-Methylfentanyl | 56. Conc. of poppy straw (N) GW |
| 23. alpha-Methylthiofentanyl | 57. Conc. of poppy straw (O) |
| 24. Alphaprodine | 58. Conc. of poppy straw (O) ACA |
| 25. Anileridine | 59. Conc. of poppy straw (O) AMA |
| 26. Benzethidine | 60. Conc. of poppy straw (O) AOA |
| 27. Benzoylmorphine | 61. Conc. of poppy straw (O) ATA |
| 28. Benzylmorphine | 62. Conc. of poppy straw (O) GW |
| 29. Betacetylmethadol | 63. Conc. of poppy straw (O)-AOA |
| 30. beta-Hydroxy-3-methyl fentanyl | 64. Conc. of poppy straw (T) |
| 31. beta-Hydroxyfentanyl | 65. Conc. of poppy straw (T) ACA |
| 32. Betameprodine | 66. Conc. of poppy straw (T) AMA |
| 33. Betamethadol | 67. Conc. of poppy straw (T) AOA |
| 34. Betaprodine | 68. Conc. of poppy straw (T) ATA |

69. Conc. of poppy straw (T) GW	103. Etorphine-3metheth
70. Conc. of poppy straw (T)-ATA	104. Etoxidine
71. Conc. of poppy straw (total) anhydrous codeine alkaloid	105. Fentanyl
72. Conc. of poppy straw (total) anhydrous morphine alkaloid	106. Furanylfentanyl
73. Conc. of poppy straw (total) anhydrous oripavine alkaloid	107. Furethidine
74. Conc. of poppy straw (total) anhydrous thebaine alkaloid	108. Heroin
75. Concentrate of poppy straw (M)	109. Hydrocodone
76. Concentrate of poppy straw (M)AMA	110. Hydromorphanol
77. Concentrate of poppy straw (M)- ATA	111. Hydromorphone
78. Desomorphine	112. Hydromorphone-3GLUC
79. Dextromoramide	113. Hydromorphone-N-oxide
80. Dextropropoxyphene	114. Hydroxypethidine
81. Diampromide	115. Isomethadone
82. Diethylthiambutene	116. Ketobemidone
83. Difenoquin	117. L-Alphaacetylmethadol
84. Dihydrocodeine	118. Levo-A-acetylmethadol
85. Dihydroetorphine	119. Levomethorphan
86. Dihydroisomorphin-6GLUC	120. Levomoramide
87. Dihydromorphine	121. Levophenacymorphan
88. Dihydromorphine-6GLUC	122. Levopropoxyphene
89. Dihydrothebaine	123. Levorphanol
90. Dimenoxadol	124. L-Isomethadone
91. Dimepheptanol	125. L-Methadol
92. Dimethylmorphine	126. L-methadone
93. Dimethylthiambutene	127. Metazocine
94. Dioxaphetyl butyrate	128. Methadone
95. Diphenoxylate	129. Methadone intermediate
96. Dipipanone	130. Methyl-desorphine
97. D-Isomethadone	131. Methyl-dihydromorphine
98. Drotebanol	132. Metopon
99. Ethylmethylthiambutene	133. Monoacetylmorphine
100. Ethylmorphine	134. Moramide intermediate
101. Etonitazene	135. Morpheridine
102. Etorphine	136. Morphine
	137. Morphine-3,6DGLUC
	138. Morphine-3BD, GLUC
	139. Morphine-3-B-D-glucuronide
	140. Morphine-3GLUC
	141. Morphine-3-PROP
	142. Morphine-6BD, GLUC

143.	Morphine-6-B-D-glucuronide	183.	Phenomorphan
144.	Morphine-6GLUC	184.	Phenoperidine
145.	Morphine-DIMETETH	185.	Pholcodine
146.	Morphine-METHYBRO	186.	Piminodine
147.	Morphine-METHYIOD	187.	Piritramide
148.	Morphine-N-oxide	188.	Poppy straw (C) GW
149.	MPPP	189.	Poppy straw (M)
150.	MT-45	190.	Poppy straw (M) GW
151.	Myrophine	191.	Poppy straw (M) GW-ACA
152.	Nicocodine	192.	Poppy straw (M) GW-AMA
153.	Nicodicodine	193.	Poppy straw (M) GW-AOA
154.	Nicomorphine	194.	Poppy straw (M) GW-ATA
155.	Noracymethadol	195.	Poppy straw (M)-ACA
156.	Norcodeine	196.	Poppy straw (M)-AMA
157.	Norlevorphanol	197.	Poppy straw (M)-AOA
158.	Normethadone	198.	Poppy straw (M)-ATA
159.	Normethadone intermediate	199.	Poppy straw (N) GW
160.	Normorphine	200.	Poppy straw (T)
161.	Normorphine-3GLUC	201.	Poppy straw (T) GW
162.	Norpipanone	202.	Poppy straw (T) GW-ACA
163.	Ocfentanyl	203.	Poppy straw (T) GW-AMA
164.	OLD Morphine-6GLUC	204.	Poppy straw (T) GW-AOA
165.	Opium	205.	Poppy straw (T)-ACA
166.	Opium - non medical use	206.	Poppy straw (T)-AOA
167.	Opium marc	207.	Poppy straw (T)-ATA
168.	Opium, prepared	208.	Poppy straw (total)
169.	Oripavine		anhydrous codeine alkaloid
170.	Oxycodone	209.	Poppy straw (total)
171.	Oxycodone-N-oxide		anhydrous morphine alkaloid
172.	Oxymorphone	210.	Poppy straw (total)
173.	Papaver bracteatum		anhydrous thebaine alkaloid
174.	para-Fluorofentanyl	211.	Proheptazine
175.	PEPAP	212.	Properidine
176.	Pethidine	213.	Propiram
177.	Pethidine intermediate A	214.	Racemethorphan
178.	Pethidine intermediate B	215.	Racemoramide
179.	Pethidine intermediate C	216.	Racemorphin
180.	Phenadoxone	217.	Remifentanyl
181.	Phenampromide	218.	Sufentanyl
182.	Phenazocine	219.	Tetrahydrofurfanylfentanyl

220.	Thebacon	223.	Tilidine
221.	Thebaine	224.	Trimeperidine
222.	Thiofentanyl	225.	U-47700

Substances **excluded** from our opioid consumption calculation:

- | | |
|-----------------------------------|-------------------------------|
| 1. ??? | 15. Ecgonine-Bezprest |
| 2. Cannabis | 16. Ecgonine-Cinmeest |
| 3. Cannabis (non-medical use) | 17. Ecgonine-Diflbene |
| 4. Cannabis oil | 18. Ecgonine-Ethylest |
| 5. Cannabis resin | 19. Ecgonine-Methyest |
| 6. Cannabis resin-non medical use | 20. Ecgonine-M-Hydrox |
| 7. Coca leaf | 21. Not covered substances |
| 8. Coca leaf - non medical use | 22. Other |
| 9. Coca paste | 23. Schedule III preparations |
| 10. Cocaine | 24. Special C.P.S |
| 11. DUMMY | 25. Unknown (ND019---) |
| 12. Ecgonine | 26. Unspecified sources |
| 13. Ecgonine-Benetest | 27. Blank |
| 14. Ecgonine-Bezest,4 | |

Box S2: Calculations for global, regional and national consumption of opioids

INCB recommends using a three-year mean to display the data, and previous studies have used this to account for annual variation in reporting, providing more stable data (Bosetti et al., 2018). To calculate the annual mean consumption of opioids, we summed data for each year (2015-17) in kgs for each country, divided by three to determine the average, converted to mg and divided by 2016 population data from the WHO Global Health Observatory for each country (WHO, 2019). Here we provide an example using Sweden's data:

$$944.88 \text{ kg (2015)} + 949.176 \text{ kg (2016)} + 996.128 \text{ kg (2017)} = \mathbf{2890.18 \text{ kg}}$$

$$((2890.18/3) * 1000000) / 9838000 = \mathbf{97.93 \text{ mg per person in Sweden}}$$

Table S1: Master list of Anatomical Therapeutic Classification (ATC) chemical substance codes for opioids

Drug name	ATC code
Acetyldihydrocodeine	R05DA12
Alfentanil	N01AH02
Anileridine	N01AH05
Bezitramide	N02AC05
Buprenorphine	N02AE01, N07BC01, N07BC51
Butorphanol	N02AF01
Codeine	R05DA04, N02AJ07, N02AJ08, N02AJ09, N02AJ06, N02AA59, N02AA79
Dextromethorphan	R05DA09
Dextromoramide	N02AC01
Dextropropoxyphene	N02AC04, N02AC54, N02AC74
Dezocine	N02AX03
Diamorphine	N07BC06
Difenoxin	A07DA04
Dihydrocodeine	N02AA08, N02AJ02, N02AJ03, N02AJ01, N02AA58
Dimemorfan	R05DA11
Diphenoxylate	A07DA01
Eluxadoline	A07DA06
Ethylmorphine	R05DA01, S01XA06
Fentanyl	N01AH01, N02AB03, N01AH51, QN02AB03
Hydrocodone	R05DA03
Hydromorphone	N02AA03, N02AA53, N02AG04
Ketobemidone	N02AB01, N02AG02
Levacetylmethadol	N07BC03
Levomethadone	N07BC05
Lofexidine	N07BC04

Loperamide	A07DA03, A07DA05, A07DA53
Meptazinol	N02AX05
Methadone	N07BC02, N02AC52
Morphine	N02AA01, N02AG01, A07DA52, N02AA51
Nalbuphine	N02AF02
Nicomorphine	N02AA04
Normethadone	R05DA06
Noscapine	R05DA07
Opium	A07DA02, N02AA02, R05DA05, R05DA20, R05FA02, R05FA01
Oxycodone	N02AA05, N02AA55, N02AA56, N02AJ018, N02AJ019, N02AJ017
Papaveretum	N02AA10
Pentazocine	N02AD01
Pethidine	N02AB02, N02AG03, N02AB52, N02AB72
Phenazocine	N02AD02
Phenoperidine	N01AH04
Pholcodine	R05DA08
Piritramide	N02AC03
Remifentanyl	N01AH06
Sufentanyl	N01AH03
Tapentadol	N02AX06
Thebacon	R05DA10
Tilidine	N02AX01
Tramadol	N02AX02, N02AJ013, N02AJ014, N02AJ015

Table S2: Sources of data for country characteristics used in the regression model

Country characteristics	Source
Geographical region	WHO. (2019). Global Health Observatory data repository. World Health Statistics; World Health Organization. Retrieved May 18, 2019: http://apps.who.int/gho/data/node.main.1?lang=en
Population (in 2016)	
Healthcare expenditure per capita (US\$, 2015)	
Life expectancy at birth (in years) for all sexes (in 2016)	
Gross domestic product (GDP) per capita (July 2017 to June 2018)	Central Intelligence Agency. (2018). GDP - per capita. The World Factbook. Retrieved May 18, 2019: https://www.cia.gov/library/publications/resources/the-world-factbook/fields/211rank.html
Human development index (2016)	United Nations Development Programme. Human Development Data (1990-2017). Human Development Reports. Retrieved May 18, 2019: http://hdr.undp.org/en/data
Corruption perception score (2016)	Transparency International. Corruption Perceptions Index 2016. Transparency International. Retrieved May 18, 2019: https://www.transparency.org/news/feature/corruption_perceptions_index_2016

Table S3: Availability of opioid consumption data for countries with national EMLs by type of opioid

Type of opioid	No. of countries with consumption data (%)	No. of countries with consumption not equal to 0 kg (%)
Morphine	137 (100)	111 (81)
Fentanyl	134 (98)	107 (78)
Codeine	129 (94)	38 (28)
Pethidine	117 (85)	91 (66)
Methadone	83 (61)	62 (45)
Oxycodone	73 (53)	58 (42)
Remifentanyl	62 (45)	48 (35)
Sufentanyl	55 (40)	31 (23)
Alfentanyl	47 (34)	21 (15)
Diamorphine	47 (34)	7 (5)
Hydromorphone	38 (28)	20 (15)
Pholcodine	37 (27)	3 (2)
Dihydrocodeine	36 (26)	5 (4)
Hydrocodone	34 (25)	6 (4)
Dextropropoxyphene	30 (22)	2 (1)
Diphenoxylate	28 (20)	0 (0)
Opium	27 (20)	11 (8)
Tilidine	20 (15)	8 (6)
Trimeperidine	13 (9)	10 (7)
Piritramide	6 (4)	3 (2)

Table S4: Opioids listed in the 20th edition of the WHO Model List of Essential Medicines

Drug	Dose & route of administration	Additional notes
Anaesthetics, preoperative medicines & medical gases: Preoperative medication & sedation for short-term procedures		
morphine	Injection: 10 mg (sulfate or hydrochloride) in 1 mL ampoule	
Medicines for pain and palliative care: opioid analgesics		
codeine	Tablet: 30 mg (phosphate)	
fentanyl	Transdermal patch: 12 µg/hr; 25 µg/hr; 50 µg/hr; 75 µg/hr; 100 µg/hr	cancer pain
methadone	Tablet: 5 mg; 10 mg (as hydrochloride); Oral liquid: 5mg/5mL; 10mg/5mL (as hydrochloride); Concentrate for oral liquid: 5 mg/mL; 10mg/mL (as hydrochloride)	complementary* list; cancer pain
morphine	Granules (slow-release; to mix with water): 20 mg to 200 mg (morphine sulfate); Injection: 10 mg (morphine hydrochloride or morphine sulfate) in 1 mL ampoule; Oral liquid: 10 mg (morphine hydrochloride or morphine sulfate)/5 mL; Tablet (slow release): 10 mg to 200 mg (morphine hydrochloride or morphine sulfate); Tablet (immediate release): 10 mg (morphine sulfate).	Alternatives limited to hydromorphone and oxycodone
Medicines for pain and palliative care: medicines for other common symptoms in palliative care		
loperamide	Solid oral dosage form: 2 mg	
Medicines for mental and behavioural disorders: medicines for disorders due to psychoactive substances		
methadone	Concentrate for oral liquid: 5 mg/mL; 10 mg/mL (hydrochloride). Oral liquid: 5 mg/5 mL; 10 mg/5 mL (hydrochloride).	complementary* list; buprenorphine is an alternative; should only be used alongside an established support programme

*complementary list: presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. In case of doubt, medicines may also be listed as complementary on the basis of consistent higher costs or less attractive cost-effectiveness in a variety of settings.

Table S5: Summary of opioid consumption and national essential medicines lists (EMLs) data by country (n=137) in alphabetical order.

Country	Mean opioid consumption (mg/person)	Year of list	Number of opioids in EMLs (% of all drugs)	Type of opioids in EMLs	Similarity with WHO list, no. (%)	Differences from WHO list, no. (%)
Afghanistan	0.555	2014	6 (2.31)	methadone, morphine, buprenorphine, opium, pethidine & tramadol	2 (40)	4 (67)
Albania	5.057	2011	3 (1.40)	codeine, morphine & pethidine	2 (40)	1 (33)
Algeria	0.164	2016	7 (1.56)	codeine, loperamide, buprenorphine, dextromethorphan, dextropropoxyphene, pholcodine & tramadol	2 (40)	5 (71)
Angola	0.002	2008	1 (1.56)	fentanyl	1 (20)	0 (0)
Antigua & Barbuda	0	2007	6 (2.04)	codeine, fentanyl, methadone, morphine, pethidine & tramadol	4 (80)	2 (33)
Argentina	14.329	2011	8 (1.69)	codeine, fentanyl, loperamide, morphine, dextromethorphan, dextropropoxyphene, remifentanyl & tramadol	4 (80)	4 (50)
Armenia	3.636	2010	4 (1.48)	fentanyl, loperamide, morphine & trimeperidine	3 (60)	1 (25)
Bahrain	12.055	2015	6 (1.09)	fentanyl, loperamide, methadone, morphine, pethidine & remifentanyl	4 (80)	2 (33)
Bangladesh	0.826	2008	2 (1.07)	morphine & pethidine	1 (20)	1 (50)
Barbados	31.185	2011	12 (1.89)	codeine, fentanyl, loperamide, morphine, dextromethorphan, dextropropoxyphene, dihydrocodeine, diphenoxylate, papaveretum, pentazocine, pethidine & tramadol	4 (80)	8 (67)
Belarus	4.852	2012	9 (2.42)	fentanyl, loperamide, morphine, buprenorphine, butorphanol,	3 (60)	6 (67)

				hydromorphone, opium, tramadol & trimeperidine		
Belize	4.331	2008	9 (2.40)	codeine, fentanyl, loperamide, methadone, morphine, buprenorphine, hydromorphone, oxycodone & pethidine	5 (100)	4 (44)
Bhutan	0.247	2016	5 (1.70)	codeine, fentanyl, morphine, pethidine & tramadol	3 (60)	2 (40)
Bolivarian Rep. of Venezuela	0.129	2011	7 (2.26)	codeine, fentanyl, morphine, dextromethorphan, oxycodone, pethidine & tramadol	3 (60)	4 (57)
Bolivia	0.303	2011	8 (2.25)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan, pethidine & remifentanyl	5 (100)	3 (38)
Bosnia & Herzegovina	3.921	2009	6 (3.30)	codeine, loperamide, methadone, buprenorphine, pholcodine & tramadol	3 (60)	3 (50)
Botswana	3.165	2012	7 (2.06)	codeine, fentanyl, loperamide, morphine, dihydrocodeine, pethidine & tramadol	4 (80)	3 (43)
Brazil	5.663	2014	3 (0.74)	codeine, methadone & morphine	3 (60)	0 (0)
Bulgaria	25.534	2011	1 (0.28)	fentanyl	1 (20)	0 (0)
Burkina Faso	0.054	2014	9 (3.28)	codeine, fentanyl, loperamide, methadone, morphine, buprenorphine, nalbuphine, remifentanyl & sufentanyl	5 (100)	4 (44)
Burundi	0.049	2012	4 (1.36)	codeine, fentanyl, morphine & tramadol	3 (60)	1 (25)
Cabo Verde	0.6	2009	8 (1.41)	codeine, fentanyl, loperamide, methadone, morphine, alfentanyl, pethidine & tramadol	5 (100)	3 (38)
Cambodia	0	2003	0 (0)	0	0 (0)	-
Cameroon	0	2010	10 (2.83)	codeine, fentanyl, loperamide, morphine, buprenorphine, dextromethorphan, pethidine, sufentanyl & tramadol	4 (80)	6 (60)
Central African Republic	0	2009	7 (2.37)	codeine, loperamide, morphine, noscapine, opium, pentazocine & pethidine	3 (60)	4 (57)

Chad	0.006	2007	3 (1.24)	codeine, fentanyl & morphine	3 (60)	0 (0)
Chile	12.537	2005	8 (2.29)	codeine, fentanyl, loperamide, methadone, morphine, pargerverine, pethidine & tramadol	5 (100)	3 (38)
China	3.853	2012	5 (1.71)	codeine, fentanyl, morphine, diphenoxylate & pethidine	3 (60)	2 (40)
Colombia	7.658	2011	8 (2.14)	fentanyl, loperamide, methadone, morphine, dihydrocodeine, hydromorphone, oxycodone & pethidine	4 (80)	4 (50)
Cook Islands	5.608	2007	6 (2.50)	loperamide, morphine, dextromethorphan, diphenoxylate, pethidine & tramadol	2 (40)	4 (67)
Costa Rica	6.788	2014	7 (1.80)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan & tramadol	5 (100)	2 (29)
Côte d'Ivoire	3.898	2014	10 (1.98)	codeine, fentanyl, methadone, morphine, buprenorphine, oxycodone, pethidine, remifentanyl, sufentanyl & tramadol	4 (80)	6 (60)
Croatia	14.785	2010	12 (1.99)	codeine, fentanyl, loperamide, methadone, morphine, alfentanil, buprenorphine, hydrocodone, oxycodone, pentazocine, pethidine, sufentanyl & tramadol	4 (80)	8 (67)
Cuba	2.214	2012	7 (1.37)	codeine, fentanyl, morphine, diphenoxylate, nalbuphine, pethidine & tramadol	3 (60)	4 (57)
Czechia	21.582	2012	15 (1.86)	codeine, fentanyl, morphine, alfentanil, buprenorphine, dihydrocodeine, hydromorphone, nalbuphine, oxycodone, pentazocine, pethidine, piritramide, remifentanyl, sufentanyl & tramadol	3 (60)	12 (80)
Democratic People's Republic of Korea	4.475	2012	6 (2.71)	codeine, methadone, morphine, opium, papaveretum & pethidine	3 (60)	3 (50)
Democratic Republic of the Congo	0.026	2010	9 (2.87)	codeine, fentanyl, loperamide, morphine, buprenorphine, dextromethorphan, remifentanyl, sufentanyl & tramadol	4 (80)	5 (56)

Djibouti	0	2007	4 (1.99)	fentanyl, looperamide, morphine & pethidine	3 (60)	1 (25)
Dominica	6.788	2007	5 (1.75)	fentanyl, methadone, morphine, pethidine & tramadol	3 (60)	2 (40)
Dominican Republic	1.022	2015	6 (1.68)	codeine, fentanyl, looperamide, morphine, nalbuphine & tramadol	4 (80)	2 (33)
Ecuador	0.859	2013	10 (2.71)	codeine, fentanyl, looperamide, methadone, morphine, buprenorphine, hydromorphone, oxycodone, remifentanyl & tramadol	5 (100)	5 (50)
Egypt	0.377	2012	6 (1.85)	fentanyl, methadone, morphine, dextromethorphan, pethidine & tramadol	3 (60)	3 (50)
El Salvador	4.481	2009	6 (1.66)	fentanyl, looperamide, morphine, nalbuphine, pethidine & tramadol	3 (60)	3 (50)
Eritrea	0	2010	6 (1.78)	codeine, looperamide, morphine, dextromethorphan, pethidine & tramadol	3 (60)	3 (50)
Estonia	26.066	2012	8 (1.98)	codeine, fentanyl, looperamide, methadone, morphine, diphenoxylate, oxycodone & tramadol	5 (100)	3 (38)
Ethiopia	0.539	2014	11 (1.55)	codeine, fentanyl, looperamide, methadone, morphine, dextromethorphan, diphenoxylate, pentazocine, pethidine, pholcodine & tramadol	5 (100)	6 (55)
Fiji	3.277	2015	6 (2.02)	codeine, fentanyl, methadone, morphine, diphenoxylate & pethidine	4 (80)	2 (33)
Gambia	0	2001	5 (3.03)	codeine, looperamide, morphine, dihydrocodeine & pethidine	3 (60)	2 (40)
Georgia	14.79	2007	4 (1.61)	fentanyl, looperamide, morphine & dextromethorphan	3 (60)	1 (25)
Ghana	2.672	2010	5 (1.65)	codeine, fentanyl, morphine, pethidine & tramadol	3 (60)	2 (40)
Grenada	0	2007	5 (1.76)	fentanyl, methadone, morphine, pethidine & tramadol	3 (60)	2 (40)
Guinea	0	2012	5 (2.09)	codeine, looperamide, morphine, pentazocine & pethidine	3 (60)	2 (40)

Guyana	10.216	2010	6 (2.14)	codeine, fentanyl, loperamide, methadone, morphine & pethidine	5 (100)	1 (17)
Haiti	0.028	2012	2 (1.02)	fentanyl & morphine	2 (40)	0 (0)
Honduras	0.734	2009	8 (2.17)	codeine, fentanyl, loperamide, morphine, dextromethorphan, oxycodone, pethidine & tramadol	4 (80)	4 (50)
India	0.527	2015	4 (1.09)	fentanyl, morphine, pentazocine & tramadol	2 (40)	2 (50)
Indonesia	0.708	2011	7 (2.51)	codeine, fentanyl, methadone, morphine, dextromethorphan, pethidine & sufentanil	4 (80)	3 (43)
Iraq	0	2010	12 (2.08)	codeine, fentanyl, loperamide, morphine, dextromethorphan, dextropropoxyphene, dihydrocodeine, diphenoxylate, oxycodone, pentazocine, pethidine & tramadol	4 (80)	8 (67)
Islamic Republic of Iran	3.325	2014	16 (1.79)	codeine, fentanyl, loperamide, methadone, morphine, alfentanil, buprenorphine, dextromethorphan, diphenoxylate, hydromorphone, oxycodone, pentazocine, pethidine, remifentanil, sufentanil & tramadol	5 (100)	11 (69)
Jamaica	7.241	2012	12 (2.61)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan, diphenoxylate, oxycodone, pethidine, pholcodine, remifentanil & tramadol	5 (100)	7 (58)
Jordan	3.98	2011	10 (1.69)	codeine, fentanyl, loperamide, methadone, morphine, alfentanil, dihydrocodeine, pethidine, remifentanil & tramadol	5 (100)	5 (50)
Kenya	1.927	2016	6 (1.44)	codeine, fentanyl, loperamide, methadone, morphine & buprenorphine	5 (100)	1 (17)
Kiribati	0.288	2009	5 (2.29)	codeine, fentanyl, loperamide, morphine & pethidine	4 (80)	1 (20)
Kyrgyzstan	5.936	2009	5 (1.58)	fentanyl, methadone, morphine, buprenorphine & trimeperidine	3 (60)	2 (40)
Latvia	11.521	2012	6 (1.95)	fentanyl, morphine, dihydrocodeine, tilidine, tramadol & trimeperidine	2 (40)	4 (67)

Lebanon	4.123	2014	6 (2.11)	fentanyl, loperamide, morphine, dextromethorphan, pethidine & tramadol	3 (60)	3 (50)
Lesotho	0	2005	3 (1.54)	morphine, pethidine & diamorphine	1 (20)	2 (67)
Liberia	0	2011	4 (1.86)	loperamide, morphine, buprenorphine & pethidine	2 (40)	2 (50)
Lithuania	10.013	2012	3 (0.88)	fentanyl, morphine & tramadol	2 (40)	1 (33)
Madagascar	0.037	2008	7 (2.77)	fentanyl, loperamide, morphine, dextromethorphan, dextropropoxyphene, noscapine & pethidine	3 (60)	4 (57)
Malawi	1.485	2015	7 (2.16)	codeine, fentanyl, loperamide, morphine, dihydrocodeine, pethidine & tramadol	4 (80)	3 (43)
Malaysia	16.407	2014	6 (1.94)	loperamide, methadone, morphine, dihydrocodeine & diphenoxylate	3 (60)	3 (50)
Maldives	0.763	2011	9 (1.67)	codeine, fentanyl, loperamide, morphine, dextromethorphan, pentazocine, pethidine, pholcodine & tramadol	4 (80)	5 (56)
Mali	0	2012	6 (211)	codeine, fentanyl, loperamide, morphine & tramadol	4 (80)	2 (33)
Malta	42.147	2008	13 (2.12)	codeine, fentanyl, loperamide, methadone, morphine, buprenorphine, dextromethorphan, dextropropoxyphene, dihydrocodeine, pethidine, pholcodine, remifentanil & tramadol	5 (100)	8 (62)
Marshall Islands	0	2007	7 (3.26)	codeine, fentanyl, loperamide, morphine, nalbuphine, pethidine & tramadol	4 (80)	3 (43)
Mauritania	0	2008	3 (1.40)	loperamide, morphine & buprenorphine	2 (40)	1 (33)
Mexico	0.709	2011	12 (1.69)	codeine, fentanyl, loperamide, morphine, buprenorphine, dextromethorphan, dextropropoxyphene, hydromorphone, nalbuphine, oxycodone, remifentanil & tramadol	4 (80)	8 (67)
Mongolia	3.134	2009	4 (1.55)	codeine, fentanyl, morphine & tramadol	3 (60)	1 (25)

Montenegro	5.659	2011	8 (1.77)	fentanyl, loperamide, methadone, morphine, alfentanil, pethidine, remifentanil & tramadol	4 (80)	4 (50)
Morocco	1.289	2012	10 (2.91)	codeine, fentanyl, loperamide, methadone, morphine, buprenorphine, dextromethorphan, pholcodine, sufentanil & tramadol	5 (100)	5 (50)
Mozambique	0.223	2016	5 (1.93)	codeine, fentanyl, loperamide, morphine & tramadol	4 (80)	1 (20)
Myanmar	14.821	2010	6 (1.90)	codeine, fentanyl, methadone, morphine, pethidine & tramadol	4 (80)	2 (33)
Namibia	3.66	2016	9 (2.34)	codeine, fentanyl, loperamide, methadone, morphine, alfentanil, pethidine, tilidine & tramadol	5 (100)	4 (44)
Nauru	0	2010	7 (3.03)	codeine, fentanyl, loperamide, morphine, diphenoxylate, pethidine & pholcodine	4 (80)	3 (43)
Nepal	0.521	2011	4 (1.33)	methadone, morphine, buprenorphine & pethidine	2 (40)	2 (50)
Nicaragua	0.677	2011	2 (0.73)	fentanyl & morphine	2 (40)	0 (0)
Nigeria	0.012	2010	10 (3.27)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan, dihydrocodeine, diphenoxylate, pentazocine & pethidine	5 (100)	5 (50)
Niue	6.001	2006	4 (1.26)	fentanyl, loperamide, morphine & pethidine	3 (60)	1 (25)
Oman	19.292	2009	10 (1.73)	codeine, fentanyl, loperamide, methadone, morphine, hydromorphone, nalbuphine, pethidine, remifentanil & tramadol	5 (100)	5 (50)
Pakistan	0.033	2016	3 (0.80)	loperamide, methadone & morphine	3 (60)	0 (0)
Palau	15.53	2006	7 (2.59)	codeine, fentanyl, loperamide, morphine, hydrocodone, pethidine & tramadol	4 (80)	3 (43)
Papua New Guinea	1.782	2012	4 (1.48)	codeine, fentanyl, morphine & pethidine	3 (60)	1 (25)

Paraguay	0	2009	6 (1.95)	codeine, fentanyl, morphine, alfentanil, dextromethorphan & pethidine	3 (60)	3 (50)
Peru	2.271	2012	7 (1.64)	codeine, fentanyl, morphine, dextromethorphan, oxycodone, pethidine & tramadol	3 (60)	4 (57)
Philippines	0.36	2008	10 (1.93)	codeine, fentanyl, loperamide, morphine, butorphanol, dextromethorphan, nalbuphine, oxycodone, pethidine & tramadol	4 (80)	6 (60)
Poland	17.594	2017	9 (2.03)	fentanyl, loperamide, methadone, morphine, buprenorphine, dihydrocodeine, oxycodone, tapentadol & tramadol	4 (80)	5 (56)
Portugal	17.931	2011	11 (1.21)	codeine, fentanyl, loperamide, methadone, morphine, buprenorphine, dextromethorphan, dextropropoxyphene, hydromorphone, pargerverine & tramadol	5 (100)	6 (55)
Romania	10.459	2012	11 (1.73)	codeine, fentanyl, methadone, morphine, buprenorphine, dextromethorphan, dihydrocodeine, oxycodone, pentazocine, pethidine & tramadol	4 (80)	7 (64)
Russian Federation	1.812	2014	5 (0.96)	fentanyl, loperamide, morphine, tramadol & trimeperidine	3 (60)	2 (40)
Rwanda	0.597	2010	6 (2.08)	codeine, fentanyl, morphine, pentazocine, pethidine & tramadol	3 (60)	3 (50)
Saint Kitts & Nevis	0	2007	5 (1.72)	fentanyl, methadone, morphine, pethidine & tramadol	3 (60)	2 (40)
Saint Lucia	0	2007	5 (1.72)	fentanyl, methadone, morphine, pethidine & tramadol	3 (60)	2 (40)
Saint Vincent & the Grenadines	5.834	2010	5 (1.87)	codeine, fentanyl, methadone, morphine & pethidine	4 (80)	1 (20)
Senegal	1.241	2013	9 (2.65)	codeine, fentanyl, methadone, morphine, alfentanil, buprenorphine, nalbuphine, sufentanil & tramadol	4 (80)	5 (56)

Serbia	9.93	2010	10 (2.11)	fentanyl, loperamide, methadone, morphine, alfentanil, hydromorphone, pethidine, remifentanil, sufentanil & tramadol	4 (80)	6 (60)
Seychelles	20.909	2010	5 (1.68)	codeine, fentanyl, morphine, pethidine & tramadol	3 (60)	2 (40)
Slovakia	14.229	2012	19 (1.92)	codeine, fentanyl, loperamide, morphine, buprenorphine, dextromethorphan, difenoxin, dihydrocodeine, diphenoxylate, eluxadoline, hydromorphone, opium, oxycodone, pentazocine, pethidine, sufentanil, tapentadol, tramadol & trimeperidine	4 (80)	15 (79)
Slovenia	64.451	2017	15 (1.88)	codeine, fentanyl, loperamide, methadone, morphine, alfentanil, buprenorphine, hydromorphone, oxycodone, pethidine, pholcodine, piritramide, remifentanil, tapentadol, tramadol & trimeperidine	5 (100)	10 (67)
Solomon Islands	0.91	2017	5 (1.92)	codeine, fentanyl, morphine, oxycodone & pethidine	3 (60)	2 (40)
Somalia	0	2006	1 (1.20)	pethidine	0 (0)	1 (100)
South Africa	16.377	2014	4 (2.08)	loperamide, morphine, pethidine & tramadol	2 (40)	2 (50)
Sri Lanka	6.003	2013	4 (1.26)	fentanyl, loperamide, methadone & tramadol	3 (60)	1 (25)
Sudan	0.242	2014	5 (1.66)	loperamide, morphine, dextromethorphan, diphenoxylate & pethidine	2 (40)	3 (60)
Suriname	0.293	2014	5 (1.75)	codeine, fentanyl, loperamide, morphine & sufentanil	4 (80)	1 (20)
Sweden	97.926	2016	7 (2.42)	codeine, fentanyl, loperamide, morphine, buprenorphine, hydromorphone & oxycodone	4 (80)	3 (43)
Syrian Arab Republic	1.642	2008	15 (1.54)	codeine, fentanyl, morphine, buprenorphine, dextromethorphan, dextropropoxyphene, diphenoxylate, hydrocodone, noscapine, oxycodone,	3 (60)	12 (80)

				pentazocine, pethidine, remifentanyl, sufentanil & tramadol		
Tajikistan	0.113	2009	6 (2.20)	codeine, fentanyl, loperamide, morphine, tramadol & trimeperidine	4 (80)	2 (33)
Thailand	3.221	2013	11 (2.00)	codeine, fentanyl, loperamide, methadone, morphine, buprenorphine, dextromethorphan, nalbuphine, opium, pethidine & tramadol	5 (100)	6 (55)
The Congo	0	2013	9 (2.97)	codeine, fentanyl, loperamide, morphine, buprenorphine, dextromethorphan, remifentanyl, sufentanil & tramadol	4 (80)	5 (56)
The Republic of Moldova	5.537	2011	8 (1.68)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan, tramadol & trimeperidine	5 (100)	3 (38)
The Republic of North Macedonia	26.076	2008	9 (2.30)	codeine, fentanyl, methadone, morphine, alfentanil, pentazocine, remifentanyl, sufentanil & tramadol	4 (80)	5 (56)
Timor-Leste	4.746	2015	4 (1.67)	codeine, fentanyl, morphine & tramadol	3 (60)	1 (25)
Togo	0.111	2012	9 (3.03)	codeine, fentanyl, loperamide, morphine, alfentanil, buprenorphine, dihydrocodeine, sufentanil & tramadol	4 (80)	5 (56)
Tonga	4.003	2007	7 (3.06)	codeine, fentanyl, loperamide, morphine, alfentanil, pethidine & pholcodine	4 (80)	3 (43)
Trinidad & Tobago	11.087	2010	9 (1.82)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan, pethidine, pholcodine & tramadol	5 (100)	4 (44)
Tunisia	2.739	2012	14 (1.93)	codeine, fentanyl, loperamide, morphine, alfentanil, buprenorphine, dextromethorphan, dextropropoxyphene, opium, pethidine & pholcodine	4 (80)	10 (71)
Tuvalu	2.03	2010	4 (2.23)	codeine, fentanyl, morphine & pethidine	3 (60)	1 (25)
Uganda	2.034	2012	7 (1.92)	codeine, fentanyl, loperamide, morphine, papaveretum, pethidine & remifentanyl	4 (80)	3 (43)

Ukraine	10.253	2009	3 (1.07)	methadone, morphine & buprenorphine	2 (40)	1 (33)
United Republic of Tanzania	1.159	2013	6 (1.66)	codeine, loperamide, methadone, morphine, pethidine & tramadol	4 (80)	2 (33)
Uruguay	7.419	2011	8 (1.52)	codeine, fentanyl, loperamide, methadone, morphine, dextromethorphan, pethidine & tramadol	5 (100)	3 (38)
Vanuatu	0	2006	3 (1.69)	codeine, fentanyl & morphine	3 (60)	0 (0)
Viet Nam	17.481	2008	9 (1.14)	codeine, fentanyl, loperamide, morphine, dextromethorphan, dextropropoxyphene, pethidine, sufentanil & tramadol	4 (80)	5 (56)
Yemen	0	2009	3 (1.20)	fentanyl, morphine & pethidine	2 (40)	1 (33)
Zambia	1.55	2013	5 (1.74)	codeine, loperamide, morphine, dihydrocodeine & pethidine	3 (60)	2 (40)
Zimbabwe	2.407	2011	7 (2.02)	codeine, fentanyl, loperamide, morphine, alfentanil, pethidine & tramadol	4(80)	3 (43)

- no consumption reported to the International Narcotics Control Board (INCB);

opioids in **bold** are listed in the 20th edition of the WHO Model List of Essential Medicines.

Table S6: Opioids included in national essential medicines lists in descending order for each Anatomical

Therapeutic Classification (ATC) subgroup

Medicine (alternative name)	No. of countries list, n=137 (%)
Analgesics	136 (99%)
Morphine	130 (94.9)
Fentanyl	113 (82.5)
Codeine	94 (68.6)
Pethidine (Meperidine)	89 (65.0)
Tramadol	85 (62.0)
Oxycodone	22 (16.1)
Dihydrocodeine	18 (13.1)
Pentazocine	16 (11.7)
Dextropropoxyphene	11 (8.0)
Nalbuphine	11 (8.0)
Trimeperidine	8 (5.8)
Opium	7 (5.1)
Papaveretum	3 (2.2)
Tapentadol	3 (2.2)
Piritramide	2 (1.5)
Butorphanol	2 (1.5)
Pargerverine	2 (1.5)
Tilidine	2 (1.5)
Hydrocodone	2 (1.5)
Antidiarrheals	87 (64%)
Loperamide	83 (60.6)
Diphenoxylate	15 (11.0)
Eluxadoline	1 (0.7)
Difenoxin	1 (0.7)
Opioid substitution therapies	71 (52%)
Methadone	56 (40.9)
Buprenorphine	34 (24.8)
Diamorphine	1 (0.7)

Cough suppressants	34 (25%)
Dextromethorphan	40 (29.2)
Hydromorphone	14 (10.2)
Pholcodine	12 (8.8)
Noscapine	5 (3.7)
Anesthetics	36 (26%)
Remifentanyl (Remifentanyl)	22 (16.1)
Sufentanil (Sufentanyl)	19 (13.9)
Alfentanil	16 (11.7)

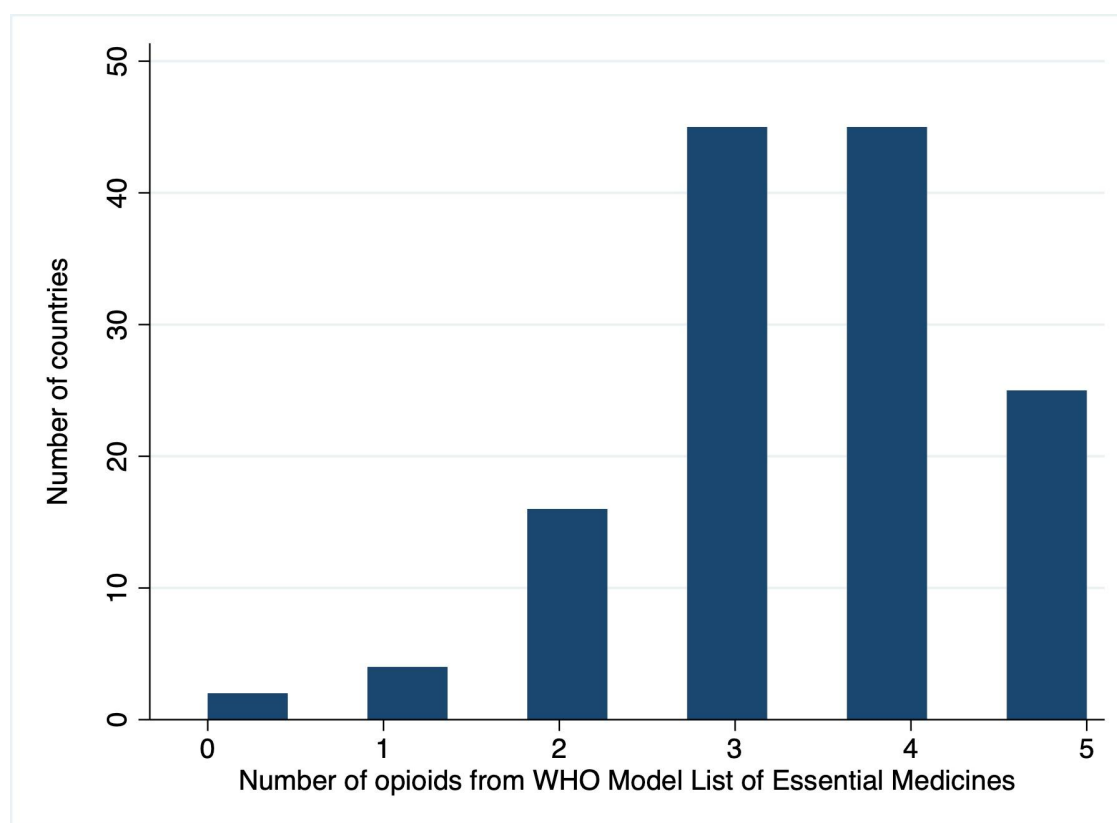


Figure S1: Similarities with the WHO's Model List of Essential Medicines for opioids.

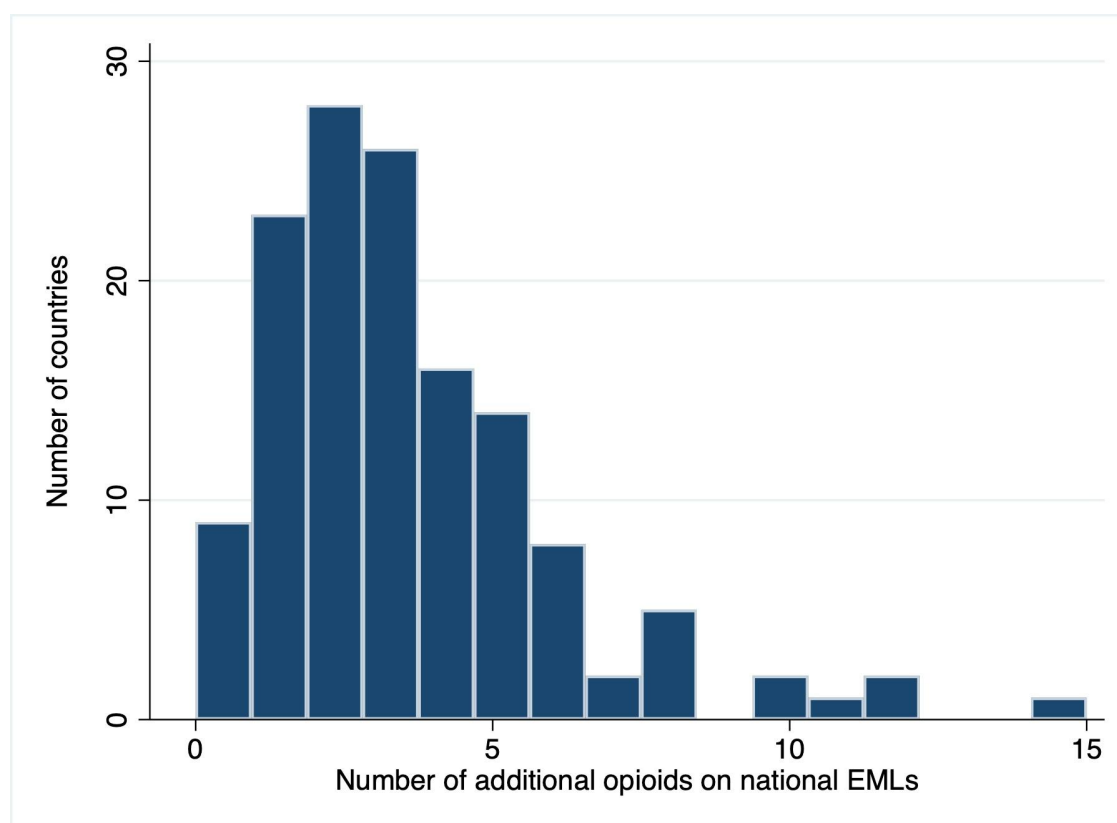


Figure S2: Differences from the WHO's Model List of Essential Medicines for opioids.

Table S7: Descriptive statistics of included variables for countries (n=137) with essential medicines lists

Variable	Median	IQR
Annual mean consumption of opioids (mg per person) (n=137)	2.03	0.13 - 6.79
Number of opioids on EMLs (n=137)	6	5 - 9
Population, 2016 (n=137)	9456000	2078000 - 28800000
Gross domestic product divided by 100 (GDP, \$, USD) per capita, 2017-18 (n=135)	92	36 - 170
Health expenditure (\$, USD) per capita, 2015 (n=134)	239.4	71.7 - 530.1
Human development index, 2016 (n=130)	0.706	0.553 - 0.776
Life expectancy (years), 2016 (n=129)	71.9	65.1 - 75.7
Corruption perception score, 2016 (n=122)	35	28 - 45
Region (n=137)	Count	%
Africa	42	30.7
Americas	30	21.9
Asia	31	22.6
Europe	22	16.1
Oceania	12	8.8

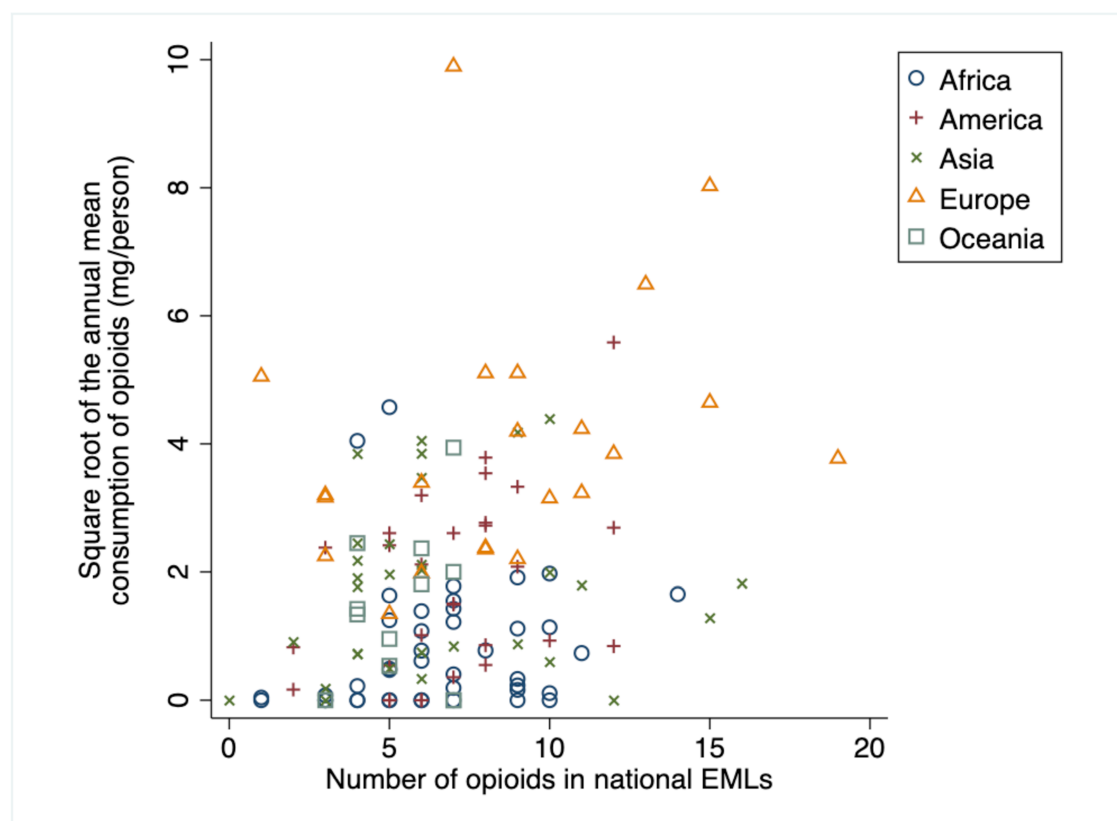


Figure S3: Scatter plot of the relation between the square rooted annual mean opioid consumption (mg/person) for 2015-2017 and the number of opioids included in national essential medicines lists (EMLs) for 137 countries. Each country is represented by a symbol for its geographical region.

References for Supplement

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