Selection of essential medicines for tuberculosis, HIV, oncology and hepatitis C: a case study in ten countries

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Layman's summary

In view of the United Nations' Millennium and Sustainable Development Goals, it is important to achieve universal access to essential medicines. One of the tools to ensure access to medicines is the World Health Organization's (WHO's) model list of essential medicines. The essential medicines list (EML) presents a limited number of carefully selected medicines that are considered essential. Each country should implement the WHO model list into a national essential medicines list (NEML), which can then be used as a resource for advocacy, selection, purchasing and supply of essential medicines within countries. The aim of this study was to analyze how long it takes for medicines on the WHO model list to be included into selected countries' NEMLs as an indicator of access to these medicines. The hypothesis was that high-cost medicines for tuberculosis and HIV/AIDS were quickly adopted into NEMLs, while high-cost medicines for cancer and hepatitis C were either slowly adopted into NEMLs or not at all. NEMLs from ten countries were analyzed for the presence of medicines added to the WHO model list for tuberculosis, HIV/AIDS, cancer and hepatitis C. We found that most medicines were present for tuberculosis and HIV/AIDS compared to the medicines for cancer and hepatitis C. Another finding was that countries in the eastern Mediterranean region and the lower-middle income group added many medicines for cancer and hepatitis C on their NEMLs, despite their lower GDP and burden of disease for these diseases. Moreover, the national burden of disease did not predict how many medicines would be included on the NEML. Finally, almost all cancer medicines were already present on NEMLs before they were added to the WHO model list. The next part of this study was about holding interviews with national policy workers to identify barriers in the selection of medicines on NEMLs with a specific focus on medicines to treat tuberculosis, HIV/AIDS, oncology and hepatitis C. In this part, we found that countries with limited resources for the revision of their NEML were either supported by donors or by voluntary work. Limited resources in a country also resulted in high-cost medicines not being included on NEMLs. Another finding was that not all countries were working with guidelines for the treatment of diseases and that some countries still depended on donors for the provision of HIV/AIDS medicines. The final finding was that the WHO model list was used as a standard and as a guide for the selection criteria to include medicines on NEMLs. In conclusion, this study has shown that most medicines were added on NEMLs for tuberculosis and HIV/AIDS rather than for cancer and hepatitis C. We also found that the biggest barrier in the selection of medicines was limited resources in a country, which prevented the inclusion of high-cost medicines. Therefore, we recommend including high-cost medicines for cancer and hepatitis C that follow the guidelines for their treatment.

Abstract

Introduction & Aim

One of the tools to ensure access to medicines is the World Health Organization's (WHO's) model list of essential medicines. The aim of this study was to analyze how long it takes for a basket of medicines on the WHO model list to be adopted into selected countries' national essential medicines lists (NEMLs) as an indicator of access to these medicines within countries. The hypothesis was that high-cost medicines for acute conditions (tuberculosis and HIV) are quickly adopted into NEMLs, while high-cost medicines for chronic conditions (oncology and hepatitis C) are slowly adopted into NEMLs.

Part 1

WHO model lists between 2007 and 2015 were aligned with NEMLs from ten countries for the presence of essential medicines for tuberculosis, HIV, oncology and hepatitis C. The time period between inclusion of medicines on the WHO model list and inclusion into NEMLs was also noted. In conclusion, most medicines were added for acute conditions over those for chronic conditions. Moreover, countries in the Eastern Mediterranean region and the lower-middle income group included many oncology and hepatitis C medicines, despite their lower GDP and burden of disease for these disease areas. Also for most countries, burden of disease did not correlate with inclusion of medicines. Finally, almost all oncology medicines were already present on NEMLs before their addition to the model list.

Part 2

Next to this, interviews were held with national policy workers to identify barriers in the selection of medicines on NEMLs with a specific focus on medicines to treat tuberculosis, HIV, oncology and hepatitis C. In summary, countries with limited resources were either supported by donors or by voluntary work. Furthermore, not all countries were working with Standard Treatment Guidelines (STGs) and aligned them with their NEML. The most important finding was that high-cost medicines were either not listed on NEMLs, as in the case for hepatitis C medicines, or restricted in their use on another special list, which was the case for oncology medicines. Some countries still depended on donors for the provision of HIV medicines. Finally, the WHO model list was used as a standard for inclusion and a guide for the revision process and for the selection criteria in most countries.

Discussion & Conclusions

This study has shown that most medicines were added on NEMLs for acute conditions (tuberculosis and HIV) over those for chronic conditions (oncology and hepatitis C). The biggest and overarching barrier in the selection of essential medicines is having limited resources in a country, which does not lead to an institutionalized process for the revision of the STGs and also prevents listing of high-cost medicines on NEMLs, especially in the case of new hepatitis C medicines. The recommendation is to include high-cost medicines for chronic conditions with restrictions following the STGs, which is now mostly done for oncology medicines.

Introduction

Background

In 2002, eight Millennium Development Goals (MDGs) were developed by the United Nations (UN) to eradicate extreme poverty by 2015.[1] MDG 6 was developed to combat HIV/AIDS, malaria and other diseases, as target 6B reads: "*Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it*". MDG 8 was aimed at developing a global partnership development, as target 8E reads: "*In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries*". The UN established the Sustainable Development Goals (SDGs) in 2015 to build on the MDGs and by 2030 complete what these did not achieve.[2] SDG 3 was developed to: "*Ensure healthy lives and promote well-being for all at all ages*", by achieving universal health coverage (SDG 3.8) and by supporting research and development (R&D) of medicines for prevalent diseases in developing countries (SDG 3.b).

Affordable access to quality medicines and medical devices is critical for functioning health systems and fundamental for obtaining universal health coverage.[3] Access to medicines depends on several factors such as pricing and reimbursement of a medicine, availability of Standard Treatment Guidelines (STGs), disease burden and prevalence of the disease in a country, and regulatory status of a medicine.[4,5] The existence of an Essential Medicines List (EML) is an important tool that can contribute to access to medicines.

Essential Medicines List

In 1977 the WHO started advocating for the principle that some medicines are more essential than others by publishing the first WHO Essential Drugs List, later named the Essential Medicines List.[6] The WHO defines essential medicines as medicines that should be available within health systems in adequate amounts, in the right dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford.[7] This publication also pointed out that many medicines in developing countries were not useful or did not reach populations at need. Essential medicines are selected by an expert committee from the WHO and its EML is a model list used as a resource for advocacy, selection, purchasing and supply of essential medicines in countries.[6,7] Every two years the model list has been revised and since 2007 a model list for children has been created to include pediatric formulations. In the model list, medicines are divided into two categories: core, which includes efficacious, safe and cost-effective medicines for priority conditions, and complementary, which includes medicines for priority diseases that are efficacious, safe and cost-effective but not necessarily affordable or for which specialized health care facilities or services may be needed. The selection process for medicines has evolved from an experience-based to an evidence-based transparent approach in 2002.[6] A systematic review of the available evidence on efficacy and safety data, public health needs, and availability and costs of a medicine is now an important part of the selection process.[8]

National Essential Medicines List

The implementation of the WHO model list into a National Essential Medicines List (NEML) is a national responsibility.[4,9,10] In practice, the criteria for the selection of essential medicines in NEMLs are the same

as for the WHO model list in addition to quality, ease of use, local manufacture and availability of medicines.[11] Out of the 193 WHO member states, 153 countries have official EMLs, but it is unclear exactly which considerations were made for the selection of essential medicines in countries.[12] An overview of important aspects that influence access to medicines following the post-marketing drug life cycle is shown in **Figure 1**.

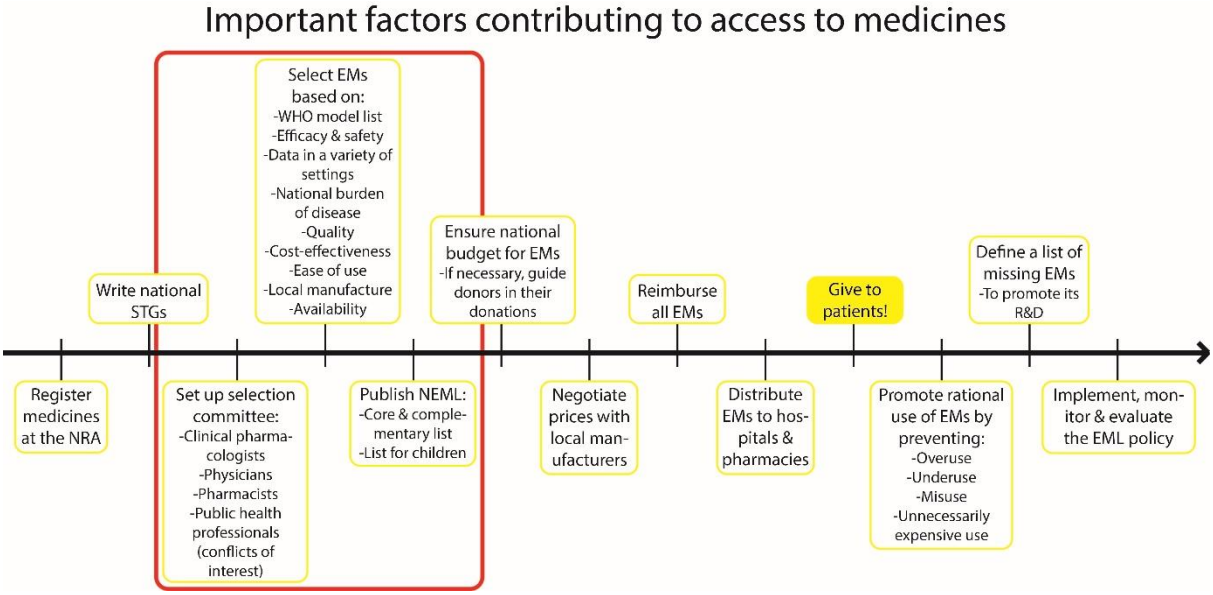

Figure 1: Important factors contributing to access to medicines. The red box indicates the area of focus in this study, which is the selection of essential medicines for the NEML. EM: essential medicine; EML: essential medicines list; NEML: national essential medicines list; NRA: national regulatory authority; R&D: research and development; STG: Standard Treatment Guideline; WHO: World Health Organization.

Burden of disease and access to treatment

Despite all efforts, access to medicines is still suboptimal. A previous study in which they conducted surveys in 40 developing countries found that availability of medicines for chronic conditions is lower than for acute conditions, particularly in the public sector.[13] In the private sector, medicines for chronic conditions are often unaffordable. This raises concerns about access to treatments for chronic conditions in developing countries. This finding also supports the fact that acute conditions, mostly infectious diseases, have traditionally been the focus of health systems. This is also reflected in health and development agendas in developing countries with a low profile for chronic diseases, even though the disease burden is large, since chronic diseases cause 40-70% of all deaths in low- and middle-income countries.[13]

Chronic conditions: oncology & hepatitis C

Cancer is one of the major chronic diseases globally as it was the cause of death for 8 million people in 2010, mostly in high income countries in Asia and Europe.[14] Moreover, lung cancer was the 5th ranked cause of death globally.[14] Due to new advances in cancer treatment there is an increase in cancer survivors living with a chronic condition that requires long term care and support.[15] Despite the finding that cancer was a major cause of death mostly in high income countries,[14] the mortality and morbidity of cancer is increasing more in developing countries, especially since patients in these countries often

present at much later stages of the disease.[16] Selection of oncology medicines in low and middle income countries was explored through investigating NEMLs for cancer treatments.[17,18] Overall, a median of sixteen oncology medicines were present on NEMLs and newer technologies such as targeted therapies were infrequently incorporated.[17] In the case of breast cancer, selection of medicines in NEMLs were inconsistent with guidelines' recommendations for different types of early and advanced breast cancer.[18] This reflects insufficiencies and inequalities in access to cancer treatments in the public sector of these countries.

Another chronic disease which is less recognized and prioritized, is hepatitis C, because it has a smaller disease burden compared to other chronic diseases. As for burden of disease, hepatitis C killed 0.5 million people in 2010, making it the 25th ranked cause of death globally.[14] Fewer persons are living with HCV infection than previously estimated, because presence of anti-HCV antibodies indicates a history of HCV infection, but only HCV-RNA positive people are chronically infected.[19,20] However, deaths due to hepatitis C continue to increase,[21] unless treatment is scaled up considerably.[22] The new direct-acting antivirals (DAAs) for the treatment of hepatitis C are highly effective, have a shorter treatment period and fewer side effects than the previous medicines for hepatitis C.[23] However, the prices for these new DAAs are unaffordable globally, which was found in a study where the prices of these new hepatitis C medicines were compared in 30 countries by calculating the potential total cost of these medicines for different health systems and individual patients.[24] This was supported by another study where the full opportunity costs of treating all infected patients in seven countries were estimated, showing that these new medicines for hepatitis C are still unaffordable for most countries, even with price discounts offered to some low income countries.[25]

Acute conditions: tuberculosis & HIV

On the other hand, acute diseases still have a big impact on the burden of disease in developing countries, as a study showed that tuberculosis (TB) killed 1.2 million people in 2010.[14] Despite efforts to end the global tuberculosis epidemic, there still was a high burden of disease in 2017 and the progress was not fast enough to reach the WHO target of 90% fewer deaths and 80% lower incidence for tuberculosis by 2030.[26] Resistance to rifampicin, a rifamycin which is the current treatment, increased from 31% new and previously treated tuberculosis patients in 2015 to 41% in 2016.[26] Moreover, 153,119 cases of multidrug-resistant TB and rifampicin-resistant TB (MDR/RR-TB) were notified in 2016.[26] Rifabutin is recommended for the treatment of MDR/RR-TB and for patients co-infected with HIV receiving protease inhibitors (PIs).[27–29] Rifapentine is recommended to treat latent tuberculosis infection (LTBI), because of its shorter course, fewer side effects and improved efficacy, adherence, immunity duration and economic influence.[26,30–34] As for access to tuberculosis treatments, in a study in 30 countries they found that only 18% of the estimated MDR-TB cases were enrolled on treatment and in another study in India they found that only 48% MDR-TB patients successfully completed their treatment.[35,36] Access to treatment with rifabutin or rifapentine has not yet been studied.

HIV is still one of the major acute diseases that has an impact on developing countries. The global burden of disease study in 2010 also found that deaths from HIV/AIDS increased from 0.3 million deaths in 1990 to 1.5 million deaths in 2010 and that HIV/AIDS is one of the leading causes of death and life lost due to premature mortality.[14] With the arrival of new antiretroviral therapy (ART) and its success, patient health

and life expectancy is improved.[37] First-line ART consists of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI).[38] Second-line ART consists of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted PI. Heat-stable fixed-dose combinations of azatanavir/ritonavir or lopinavir/ritonavir are the preferred boosted PI options.[38] Unfortunately, ART is not curative, which means that patients have to take expensive and potentially toxic drugs for several decades.[37] In a low income and lower-middle income country, a study found that providing ART can be economically beneficial, despite the high costs.[39,40] Barriers related to access to ART included high financial costs, delays in receiving care from treatment centers, shortage of drugs and fear of side effects.[41] In the last few updates, several new essential medicines were added to the WHO model list for the four disease areas mentioned above.[7,12,42–45]

Aim of the study

To sum up, access to medicines can be improved by using a list of essential medicines to guide selection, procurement or reimbursement of medicines in a country. The model list made by the WHO is a resource for countries to make their NEML, but it is unclear to what extent the model list is used to guide the selection of essential medicines for NEMLs.

The aim of this study was to analyze the time period for a basket of medicines on the WHO model list to be adopted into selected countries' NEMLs as an indicator of access (availability and affordability) to these medicines within countries. This study was split up in two parts: the first part consisted of a quantitative analysis by aligning NEMLs from ten countries with WHO model lists. The objective of this part was to assess if medicines that were added to the WHO model list were included into NEMLs and to determine the time period between inclusion of medicines on the WHO model list and inclusion into NEMLs. In the second part, a qualitative analysis was done by holding interviews with national policy workers to identify the factors that contribute to the selection of these medicines onto NEMLs.

The hypothesis was that high-cost medicines for tuberculosis and HIV are quickly adopted into NEMLs, while high-cost medicines for oncology and hepatitis C are either slowly adopted into NEMLs or not at all. As medicines for acute diseases are more available globally, even high-cost medicines are expected to be more available for tuberculosis and HIV. In contrast, medicines for oncology and hepatitis C are expected to be of lower priority, since they are chronic diseases and cancer is still viewed as a high income country disease, while hepatitis C is less recognized, so their high-cost drugs are expected to be either slowly adopted into NEMLs or not at all.

Part 1: Quantitative

Purpose

This quantitative study was done to align NEMLs from ten countries with WHO model lists to assess if medicines added to the WHO model list for tuberculosis, HIV, oncology and hepatitis C were included into NEMLs and to determine the time period between inclusion of medicines on the WHO model list and inclusion into NEMLs.

Methods

Data collection

Medicines added to the WHO model list for adults between 2007 and 2015 were reviewed to identify medicines included for tuberculosis, HIV, oncology and hepatitis C. The name of the medicine was noted along with its listing on the core or complementary list, in addition to its administration route, dosage, whether it was representative of a therapeutic class, its indication(s) and age or weight restrictions. These were extracted from the WHO Expert Committee Reports (2007-2015).[12,42–45] From the list of added medicines, the ones that were removed from the model list in subsequent years were filtered out. A basket of medicines was selected from this list of all included medicines that still remained on the list. The first criterion for the basket was that the medicines were added for the abovementioned disease areas. The next criterion was addition of the medicine to the core model list, with the exception of oncology medicines, which were only added to the complementary list. For oncology, all these medicines were selected, leaving out the medicines for palliative care. To further characterize the basket of medicines, parts of the WHO Expert Committee reports were reviewed for reasons of addition for these medicines.[12,42,44,45] Each defined daily dose (DDD) was obtained from the ATC/DDD index from the WHO and from the MSH International Medicinal Products Price Guide.[46,47] Their international price was also obtained, as the median supplier price per unit, from the MSH International Medicinal Products Price Guide.[47] The year of international market entry was obtained from the KNMP Kennisbank, which is a Dutch database for pharmacists that includes information on prices, mechanism of action and regulatory status of medicines registered in the Netherlands.[48]

A selection of countries was made based on the language of their NEMLs (English), disease burden for tuberculosis, HIV, oncology and hepatitis C, income group and geographic region (to include a variety of both) and the number of total NEMLs (>1). NEMLs were obtained from the WHO website on National Medicines List/Formulary/Standard Treatment Guidelines.[49] In addition, to complete the collection of NEMLs for each country, national Ministry of Health websites were used to search for NEMLs with the keywords “essential medicines” and “essential drugs”. Also, for this reason national policy workers were contacted through the WHO Country Offices and existing contacts. In South Africa the EMLs for Primary Health Care and at Hospital Level were selected. For high income countries, reimbursement lists were used as an alternative to NEMLs. An online search on their national Ministry of Health website was used to obtain reimbursement lists and their updates. Furthermore, additional information was obtained to characterize the selected countries. The income group and GDP per capita, purchasing power parity

(PPP) based, was obtained from the World Bank to describe national income in 2016, which was the most recent data at the time.[50] The geographic regions were obtained from the WHO website on regional offices.[51] The United Nations' human development index (HDI) rank, a number between 0 and 1, was used as a summary measure for life expectancy, education and per capita income reported in 2015, which was also the most recent data.[52] The burden of disease was obtained from the Institute of Health Metrics and Evaluation (IHME) global burden of disease study, where disability-adjusted life years (DALYs) were used as a measure for morbidity.[53] Links to this data can be found in **Appendix 1.4**.

Data analysis

The NEMLs of the selected countries were analyzed for the presence of the basket of medicines. Generic names of the medicines were searched for in NEMLs and its inclusion was noted as "1" and no inclusion was noted as "0" in an Excel sheet (**Appendix 1.2**). Relevant notes on its administration or dose were noted. In the high income countries, reimbursement lists were checked in the years WHO updated their model list to see if a medicine was added or removed in between two lists. The precise date of addition or removal was determined by looking up the monthly updates to the lists. If a medicine was included on an NEML, the time between its addition to the model list and inclusion on the NEML was also noted.

Most analyses were descriptive, as the sample size of the countries was too small to do any statistical tests. An overview table was made to describe the current state of the included medicines on the NEMLs. The table shows the number and percentage of medicines included overall (median of all countries) and in every country, in total and per disease area. For every country, a table was made to show the inclusion of medicines over time shown in **Appendix 1.3**. To represent the data in a graphical way, bar graphs were made to show percentage inclusion of medicines per disease area in the different income groups and geographic regions. Also, spread graphs were made to show a possible correlation for GDP, HDI and burden of disease with the number of included medicines. If any spread graph seemed to have a correlation, a linear trendline was made to view its R-squared. To show the timing of inclusion in every country, whisker plots were made per disease area against the time between addition of a medicine to the model list and its inclusion on an NEML. In addition, separate graphs were made for each medicine to show inclusion of each medicine over time (**Appendix 1.5**).

Results

Data characteristics

The basket of medicines from the WHO EMLs consists of 40 medicines, out of which two medicines were added for tuberculosis, eleven for HIV, nineteen for oncology and eight for hepatitis C. The selected medicines are listed below in **Table 1** and their full information can be found in **Appendix 1.1**.

Table 1. Basket of medicines.

Name	Year added[1]	Indication[1]	Market year[2]	Price[3]	Notes on its addition[4]
Rifabutin	2009	Tuberculosis in HIV patients receiving PIs	1992	0.85	-
Rifapentine	2015	Latent tuberculosis infection	-	-	-
Zidovudine + lamivudine	2007	HIV	-	0.13	New FDC
Zidovudine + lamivudine +	2007	HIV	-	0.14	New FDC

nevirapine					
Efavirenz	2007	HIV	1998	0.11	New strength: once daily
Emtricitabine + tenofovir	2007	HIV	-	0.20	New FDC
Efavirenz + emtricitabine + tenofovir	2007	HIV	-	0.36	New FDC
Lopinavir + ritonavir	2009	HIV	-	0.13	New heat stable formulation
Atazanavir	2009	HIV	2003	0.41	-
Ritonavir	2009	HIV	1996	0.02	New heat stable formulation
Sulfamethoxazole + trimethoprim	2011	Prevention of *P. jiroveci* in HIV patients	-	0.02	New strength FDC
Abacavir + lamivudine	2015	HIV	-	0.07	Formulation for children
Darunavir	2015	HIV; alternative to ritonavir-boosted PIs	2007	0.76	75 mg for children
Paclitaxel	2011	Early and advanced breast cancer	1993	65.03	New taxane
Docetaxel	2011	Early and advanced breast cancer	1995	30.99	New taxane
All-trans retinoic acid	2015	acute promyelocytic leukemia	1962	-	-
Cisplatin	2015	Cervical, head and neck, nasopharyngeal and non-small cell lung cancer; osteosarcoma; ovarian and testicular germ cell tumor	1979	6.05	Chemotherapy
Fludarabine (powd.)	2015	chronic lymphocytic leukemia	1991	-	-
Fludarabine (tabl.)	2015	chronic lymphocytic leukemia	1991	-	-
Bendamustine	2015	chronic lymphocytic leukemia; follicular lymphoma	2008	-	-
Imatinib	2015	chronic myeloid leukemia; gastrointestinal stromal tumor	2001	-	-
Rituximab	2015	diffuse large B-cell lymphoma; chronic lymphocytic leukemia; follicular lymphoma	1997	-	-
Anastrozole*	2015	early stage and metastatic breast cancer	1995	-	Aromatase inhibitor representative
Leuprorelin*	2015	early stage and metastatic prostate cancer	1985	-	LHRH representative
Capecitabine	2015	early stage colon and rectal cancer; metastatic breast and colorectal cancer	1999	-	Oral fluoro-pyrimidine
Oxaliplatin	2015	early stage colon cancer; metastatic colorectal cancer	1996	-	3rd generation platinum compound
Trastuzumab	2015	early stage & metastatic HER2+ breast cancer	1998	-	-
Gemcitabine	2015	epithelial ovarian, non-small lung cancer	1995	-	-
Irinotecan	2015	metastatic colorectal cancer	1997	-	Type I topoisomerase inhibitor
Bicalutamide*	2015	metastatic prostate cancer	1995	6.74	Oral antiandrogen
Vinorelbine	2015	non-small lung, metastatic breast cancer	1995	-	Chemotherapy; oral formulation is better tolerated
Filgrastim	2015	prophylaxis for febrile neutropenia associated with / following prior myelotoxic chemotherapy; facilitate administration of chemotherapy	1991	-	G-CSF for ovarian & testicular germ cell tumors
Ribavirin (oral)	2007	Hepatitis C	1986	-	-
Ribavirin (inj.)	2007	Hepatitis C	1986	-	-
Daclatasvir	2015	Chronic hepatitis C infection	2014	-	New DAA
Sofosbuvir	2015	Chronic hepatitis C infection	2013	-	New DAA

Dasabuvir	2015	Chronic hepatitis C infection	2014	-	New DAA
Ledipasvir + sofosbuvir	2015	Chronic hepatitis C infection	-	-	New DAA FDC
Ombitasvir + paritaprevir + ritonavir	2015	Chronic hepatitis C infection	-	-	New DAA FDC
Simeprevir	2015	Chronic hepatitis C infection	2013	-	New DAA

*therapeutic equivalence in its pharmacological class; [1] on the WHO model list of essential medicines; [2] on the international market; [3] international median supplier prices per unit in US dollars; [4] from WHO Expert Committee Reports; DAA: direct acting antiviral; FDC: fixed-dose combination; G-CSF: granulocyte colony-stimulating factor; HIV: human immunodeficiency virus; LHRH: luteinizing hormone-releasing hormone; PI: protease inhibitor; WHO: World Health Organization.

A variety of both income group and geographic region was included in the selection. The final selection of countries consisted of ten countries: Australia, Bhutan, Ethiopia, India, Ireland, Jordan, Lebanon, South Africa, Suriname and Uganda (**Table 2**). In the case of Australia and Ireland, reimbursement lists (RLs) were used as NEMLs, since these countries did not have any NEMLs. The high number of total RLs in Australia and Ireland is due to their monthly updates from 2003 and 2008 onwards, respectively.

Table 2. Selection of countries.

#	Country	Income group[1]	Geographic region[2]	GDP per capita[3]	HDI rank[4]	Range of NEMLs/RLs	Total NEMLs/RLs
1	Australia	High	Western pacific	46,790	0.939	2003-2017	133
2	Bhutan	Lower middle	South-east Asia	8,744	0.607	2007-2016	5
3	Ethiopia	Low	African	1,735	0.448	2007-2015	4
4	India	Lower middle	South-east Asia	6,572	0.624	2003-2015	3
5	Ireland	High	European	68,883	0.923	2008-2017*	103
6	Jordan	Lower middle	Eastern Mediterranean	9,050	0.741	2006-2017	4
7	Lebanon	Upper middle	Eastern Mediterranean	13,996	0.763	2010-2014	2
8	South Africa**	Upper middle	African	13,225	0.666	2003-2015	6
9	Suriname	Upper middle	The Americas	14,146	0.725	1990-2014	4
10	Uganda	Low	African	1,849	0.493	2001-2016	4

* first list referred to the date of first addition of medicines before 2008; **EMLs were selected for Primary Health Care and at Hospital Level; [1] as classified by the World Bank; [2] as classified by the WHO; [3] GDP: gross domestic product, per capita, purchasing power parity based, in millions of US dollars; [4] HDI: Human Development Index; NEML: national essential medicines list; WHO: World Health Organization.

Overall results

Each NEML was analyzed for the presence of the medicines in the basket and the time between addition to the model list and their inclusion on the NEML (**Appendix 1.2-1.3**). **Table 3** shows the number of medicines that were included per disease area in each country on the final version of their NEML.

Overall, the most medicines were added for HIV (55%), then for tuberculosis (50%), oncology (37%) and hepatitis C (13%). There were only two medicines in the basket for tuberculosis and five countries added the same one (50%). Almost all countries added some medicines for HIV, except for Ireland. Ethiopia added the most HIV medicines (82%). For oncology most countries added medicines, except for Bhutan and South Africa. Jordan added the most oncology medicines (95%). For hepatitis C five countries added a few medicines and Australia added the most (50%).

Table 3. Number of included medicines per disease area overall and in every country.

Country	Total EMs	Tuberculosis	HIV	Oncology	Hepatitis C

WHO model list	40	2	11	19	8
Overall countries	**15 (38)**	**1 (50)**	**6 (55)**	**7 (37)**	**1 (13)**
Australia	22 (55)	1 (50)	8 (73)	9 (47)	4 (50)
Bhutan	2 (5)	0 (0)	2 (18)	0 (0)	0 (0)
Ethiopia	15 (38)	0 (0)	9 (82)	6 (32)	0 (0)
India	22 (55)	1 (50)	7 (64)	12 (63)	2 (25)
Ireland	10 (25)	1 (50)	0 (0)	7 (37)	2 (25)
Jordan	25 (63)	0 (0)	4 (36)	18 (95)	3 (38)
Lebanon	13 (33)	0 (0)	5 (45)	7 (37)	1 (13)
South Africa	7 (18)	1 (50)	6 (55)	0 (0)	0 (0)
Suriname	5 (13)	0 (0)	3 (27)	2 (11)	0 (0)
Uganda	18 (45)	1 (50)	6 (55)	11 (58)	0 (0)

WHO model list: number of medicines in the basket; **Overall countries**: median of all countries; (in brackets): percentage included medicines; EM: essential medicine; HIV: human immunodeficiency virus; WHO: World Health Organization.

Income groups & Geographic regions

The results for the percentage of medicines included on the final version of the NEMLs per income group are shown in **Figure 2**. The high income countries included around the same percentage medicines for all four disease areas. Out of all income groups, they also included the highest percentage of tuberculosis medicines (50%) and hepatitis C medicines (38%). The upper-middle income countries included most medicines for HIV (45%) and very few or none for other disease areas. The lower-middle income countries include the highest percentage for oncology (63%) and the second highest percentage for hepatitis C medicines (25%) out of all income groups. They include few medicines for HIV (36%). The low income countries included the most medicines for HIV (68%) out of all income groups. They included some medicines for oncology (45%) and tuberculosis (25%) and none for hepatitis C.

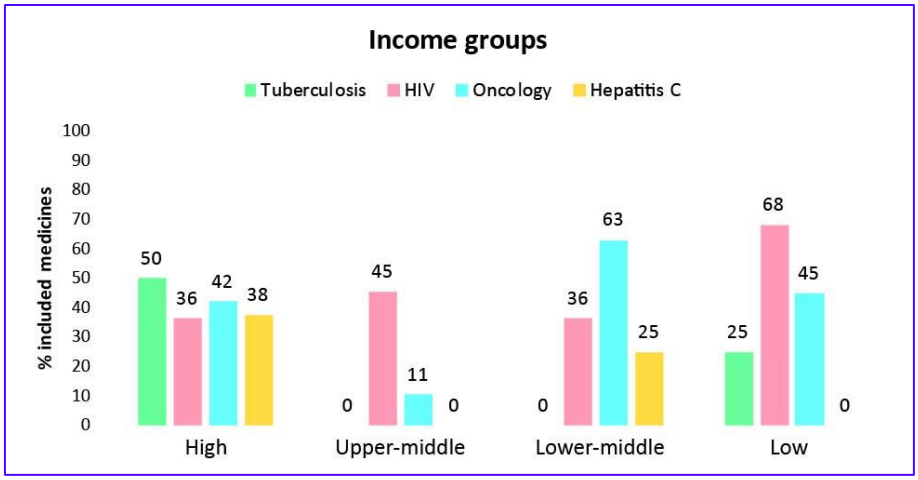

Figure 2. Percentage included medicines per income group on the final version of the NEMLs. HIV: human immunodeficiency virus; NEML: national essential medicines list.

The next bar graph shows the percentage included medicines on the final version of the NEMLs per geographic region (**Figure 3**). Only geographic regions with more than one country in its group are shown. The African region and South-East Asia included a relatively high percentage of medicines for

tuberculosis (25-50%) and HIV (41-55%) and relatively low percentages for oncology (32%) and hepatitis C medicines (0-13%). The Eastern Mediterranean region included the most oncology (63%) and hepatitis C medicines (25%) out of all regions.

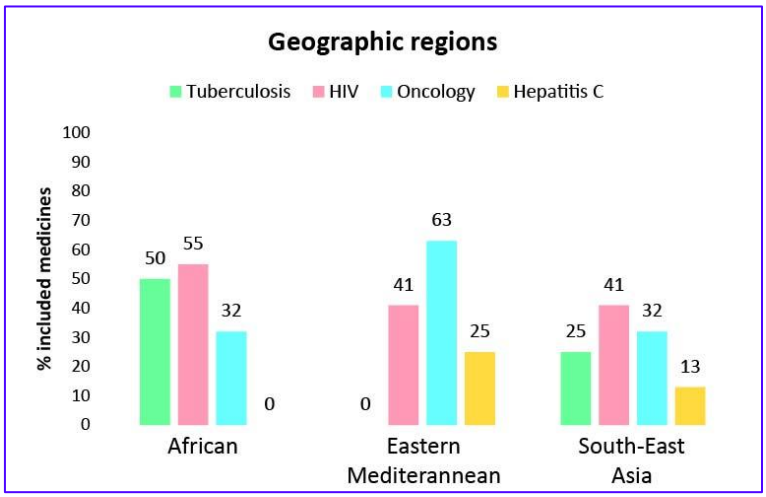

Figure 3. Percentage included medicines per geographic region on the final version of the NEMLs. HIV: human immunodeficiency virus; NEML: national essential medicines list.

Correlations GDP, HDI & Burden of disease

In **Figure 4-9**, spread graphs were made to show a possible correlation between the number of included medicines and GDP, HDI and disease burden. The final version of the NEMLs and the number of included medicines for all disease areas were considered here. Each colored dot on the graph represents a country. In general, there are no clear correlations.

The GDP per capita was plotted against the number of included medicines (**Figure 4**). Four countries with a GDP on the lower side included many medicines (Ethiopia, India, Jordan and Uganda).

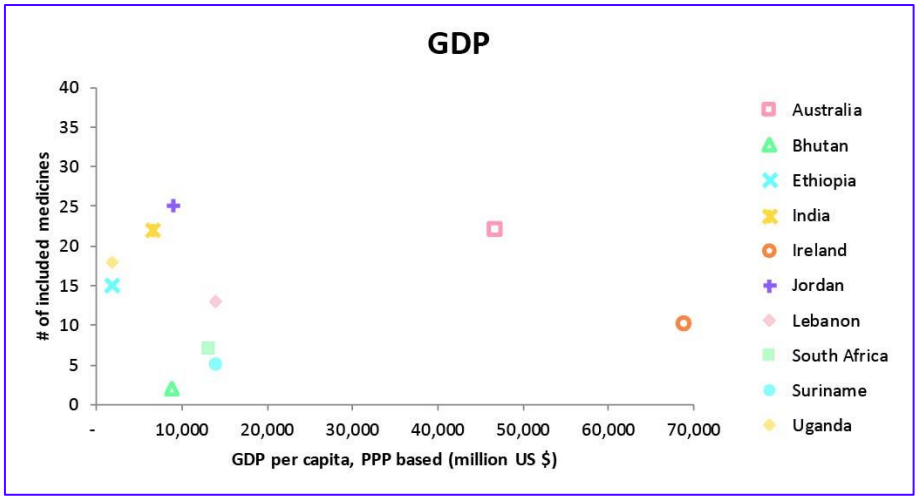

Figure 4. Spread graph for the GDP and number of total included medicines. GDP: gross domestic product; PPP: purchasing power parity; US: the United States.

The HDI rank was plotted against the number of included medicines in **Figure 5**. This graph suggests a pattern, where the higher the HDI, the more medicines are included. However, in this set of data there is

no statistical significant correlation between the two variables, as the R-squared of the linear trendline was only 0.0037 (not shown).

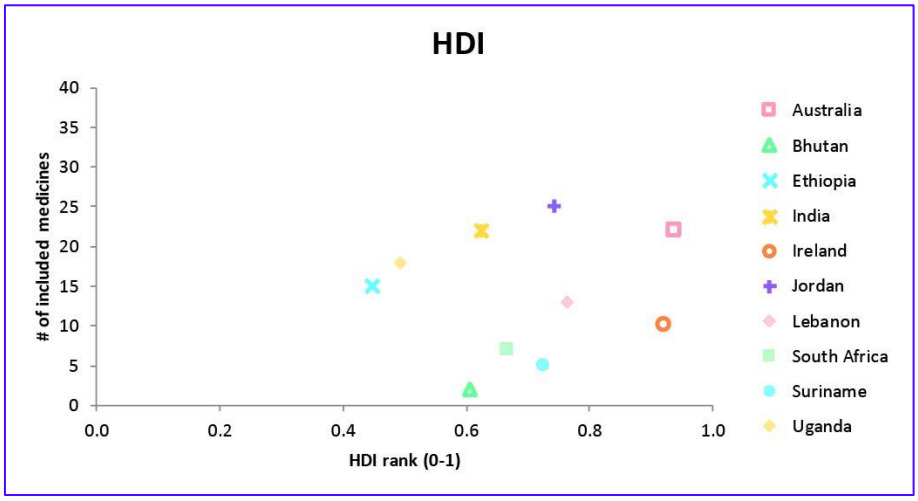

Figure 5. Spread graph for the HDI and number of total included medicines in selected countries. HDI: human development index.

The burden of disease was noted for the four disease areas in percentage DALYs out of total percentage DALYs in that country (**Appendix 1.4**). First, the disease burden for chronic conditions (oncology and hepatitis C) will be discussed and then for acute conditions (tuberculosis and HIV).

The graph for the disease burden of oncology is shown below with nineteen medicines in its basket (**Figure 6**). Countries with lower morbidity (India, Jordan and Uganda) still included many medicines for oncology.

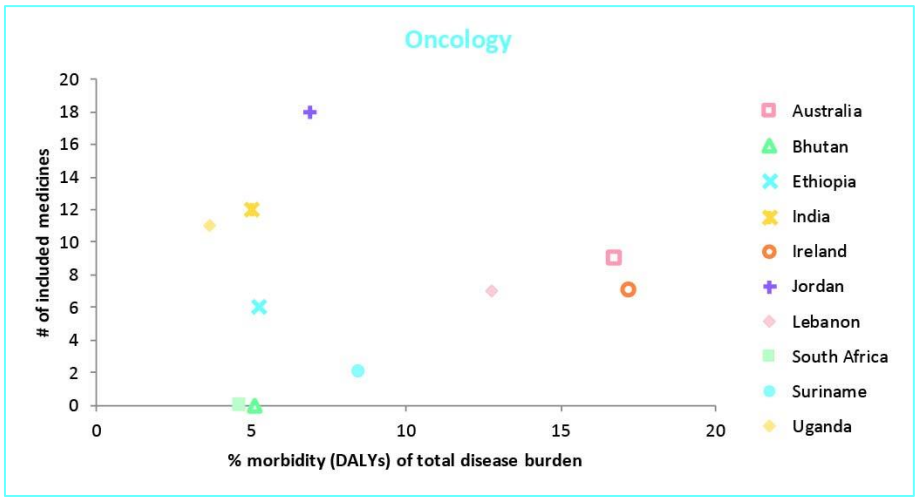

Figure 6. Spread graph for the burden of disease and number of included medicines for oncology. DALY: disability-adjusted life year.

The graph for the disease burden of hepatitis C is shown with eight medicines in its basket (**Figure 7**). Countries with low burden of disease (Australia, Ireland and Jordan) still included some hepatitis C medicines. Countries with high burden of disease (India and Ethiopia) did not include many hepatitis C medicines. However, the range of the percentage DALYs is very narrow within these countries.

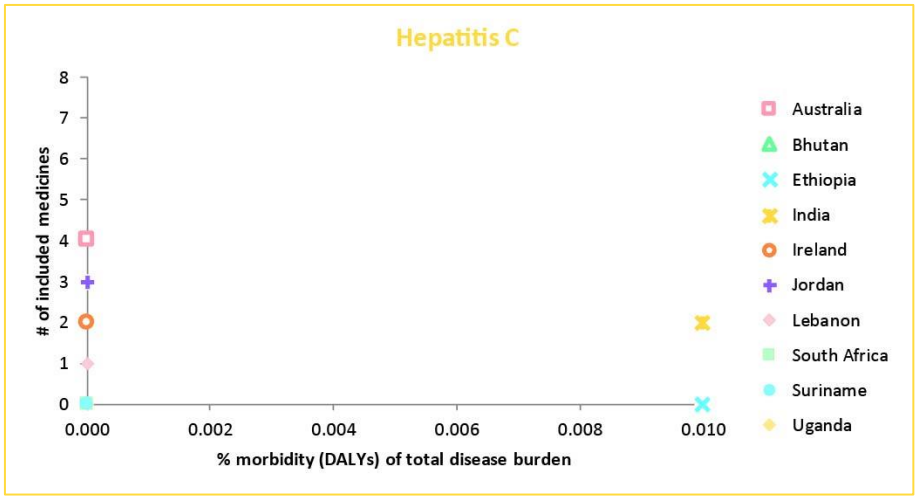

Figure 7. Spread graph for the burden of disease and number of included medicines for hepatitis C. DALY: disability-adjusted life year.

From the scatter plots for disease burden, the one for tuberculosis is shown in **Figure 8** with two medicines in its basket. Australia and Ireland included a tuberculosis medicine even though their disease burden is very small. Ethiopia did not include any tuberculosis medicines, even though its disease burden is large.

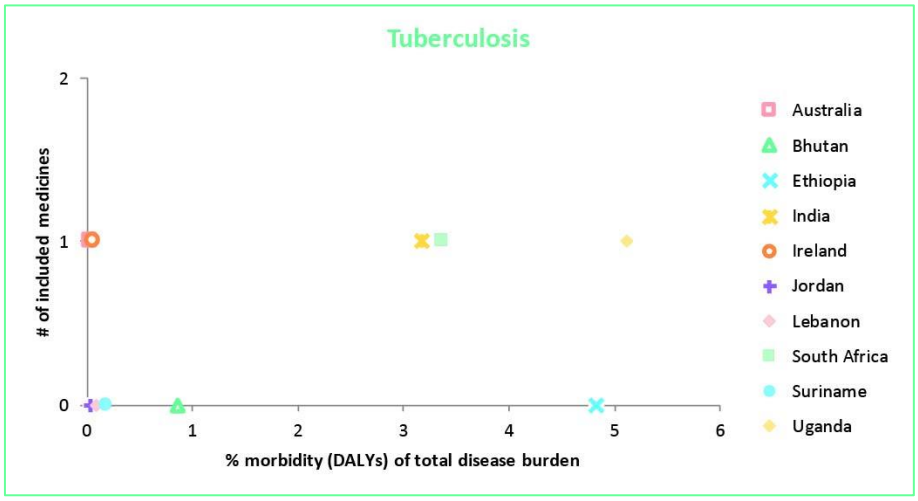

Figure 8. Spread graph for the burden of disease and number of included medicines for tuberculosis. DALY: disability-adjusted life year.

The graph for the disease burden of HIV with eleven medicines in its basket is shown in **Figure 9**. Countries with low burden of disease (Australia, Ethiopia and India) still included many medicines for HIV. The highest burden of disease was in South Africa (on the right side of the graph), where six medicines for HIV were included.

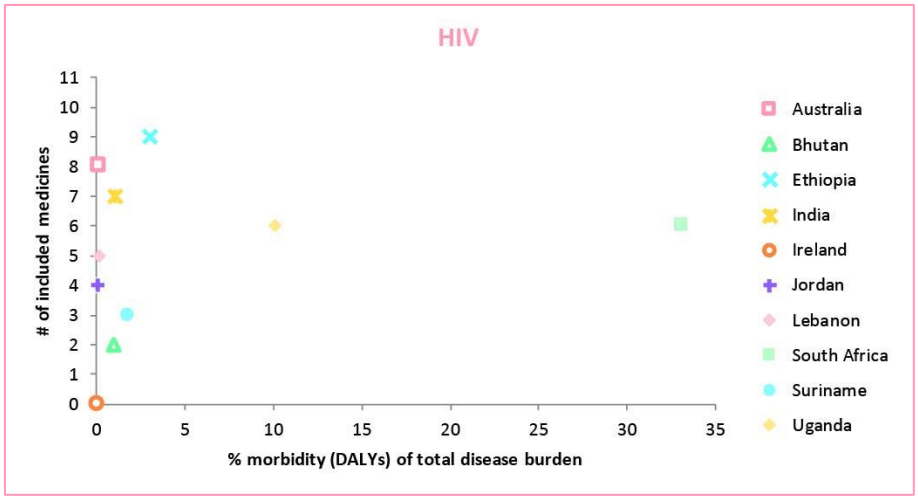

Figure 9. Spread graph for the burden of disease and number of included medicines for HIV. DALY: disability-adjusted life year.

Inclusion per country

In addition to the number of included medicines per disease area in **Table 3**, the (timing of) inclusion of the separate medicines was also noted in a table for each country in **Appendix 1.3**. This information on all countries is discussed below.

Australia added 31 medicines in total to their reimbursement list, out of which nine were removed. One medicine was added for tuberculosis six years before its addition to the WHO model list. Eight medicines were added for HIV either 1-8 years before (n=7) or three years after its addition to the model list (n=1). For oncology, 17 medicines were added, but eight were removed later on. These medicines were all added 7-12 years before their addition to the model list. For hepatitis C, five medicines were added, from which one was removed. They were added either 1-4 years before (n=2) or one year after their addition to the model list (n=3).

Bhutan added two medicines in total to their NEML for HIV in the same year and after their addition to the model list. No medicines were included for tuberculosis, oncology and hepatitis C.

Ethiopia added twenty medicines in total of which five medicines were removed from their NEML. One medicine was included for tuberculosis two years before it was added to the model list, but it was later removed. Ten medicines were included for HIV either 2-7 years before their addition to the model list (n=5), in the same year (n=4) or three years later (n=1). One of these medicines was later removed. For oncology, Ethiopia added eight medicines, either eight years before their addition to the model list (n=3), in the same year (n=4) or four years later (n=1). Two oncology medicines were later removed. Only one medicine was added for hepatitis C in the same year as its addition to the model list, but it was later removed.

India added 22 medicines in total to their NEML. One medicine was added for tuberculosis six years after its addition to the model list. Seven medicines were added for HIV either four years before (n=1), in the same year (n=3) or 4-8 years after their addition to the model list (n=3). For oncology, twelve medicines were added either 4-12 year before (n=6), in the same year (n=5) or four years after their addition to the model list (n=1). Two medicines were included for hepatitis C either in the same year or eight years after its addition to the model list.

Ireland added ten medicines in total to their reimbursement list. One medicine was added for tuberculosis one year before its addition to the model list. No medicines were added for HIV. For oncology, seven medicines were added 7-19 years before their addition to the model list. For hepatitis C, two medicines were added eight either years before or four years after their addition to the model list.

Jordan added 25 medicines in total to their NEML. No medicines were added for tuberculosis. Four medicines were added for HIV either in the same year (n=1) or 2-10 years after their addition to the model list (n=3). For oncology, eighteen medicines were added either 5-9 years before (n=17) or two years after its addition to the model list (n=1). Three medicines were added for hepatitis C either one year before (n=1) or two years after their addition to the model list (n=2).

Lebanon added twelve medicines in total to their NEML. No medicines were added for tuberculosis. Five medicines were added for HIV 3-7 years after their addition to the model list. For oncology, seven medicines were added either one year before (n=5) or three years after their addition to the model list (n=2). No medicines were added for hepatitis C.

South Africa added nine medicines in total of which two medicines were removed from their NEML. One medicine was added for tuberculosis six years after its addition to the model list. For HIV, seven medicines were added either 1-8 years before (n=3) or 1-7 years after their addition to the model list (n=4), out of which one was removed. For oncology, one medicine was added nine years before its addition to the model list, but it was removed later on. No medicines were added for hepatitis C.

Suriname added five medicines in total to their NEML. No medicines were added for tuberculosis and hepatitis C. Three medicines were added for HIV seven years after their addition to the model list. Two medicines were added for oncology 1-18 years before their addition to the model list.

Uganda added 21 medicines in total of which three medicines were removed from their NEML. One medicine was added for tuberculosis seven years after its addition to the model list. Nine medicines were added for HIV, out of which three were removed. They were added three years before their addition to the model list (n=1), in the same year (n=2) or 3-7 years later (n=6). For oncology, eleven medicines were added either three years before their addition to the model list (n=4) or 1-5 years later (n=7). No medicines were included for hepatitis C.

Timing of inclusion

Whisker plots were made for each country to show the time between addition of a medicine to the WHO model list and inclusion into NEMLs (**Figure 10**).

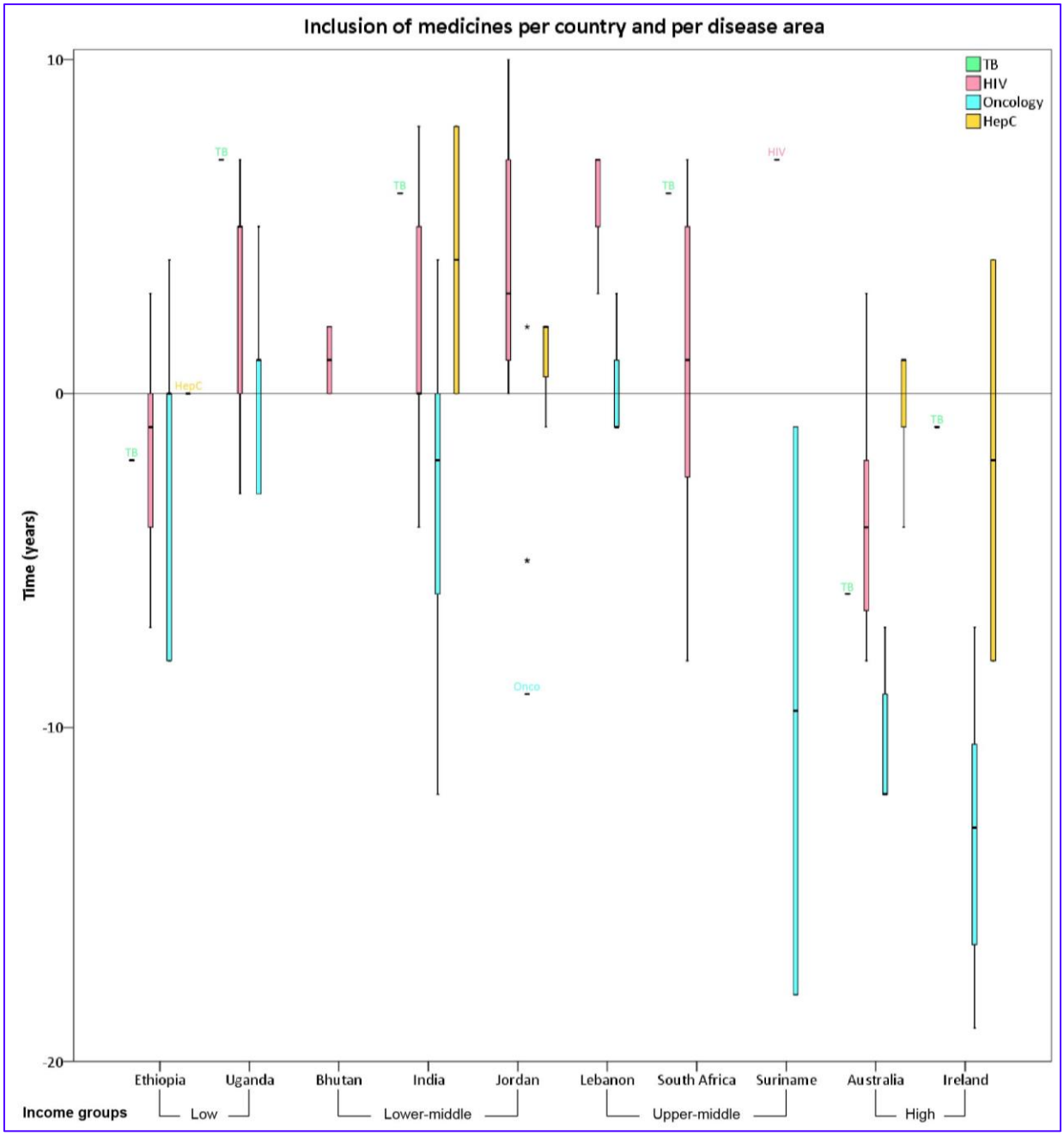

Figure 10. Whisker plots for all countries showing the time between addition to the WHO model list and addition to NEMLs for every disease area. Countries are clustered by income group. TB: tuberculosis; HIV: human immunodeficiency virus; HepC: hepatitis C; WHO: World Health Organization.

Australia included the most medicines in total, often before they were added to the model list and Bhutan included the least medicines, only two for HIV, but none for the other disease areas. Most low- and lower-middle income countries (Ethiopia, India, Jordan and Uganda) already included medicines on their NEMLs before they were added to the model list. More specifically, most included medicines below the line were added for oncology. Many boxes for HIV and hepatitis C are above the line, meaning that these medicines were added to NEMLs after their addition to the model list. High income countries

(Australia and Ireland) added most medicines to their reimbursement lists before their addition to the model list.

Medicines per disease area

Figure 11-20 are graphs that were made for each medicine to show on which NEMLs it was added and in which year. The first black dot labeled as "WHO" shows the year in which the medicine was added to the model list. Each colored dot represents a country. If the medicine was added after its addition to the model list, the colored dot falls above the black line. When the medicine was added before addition to the WHO model list, the dot falls below the black line. When the dot appears at the bottom of the graph, it means that it was never included on the NEML. First, examples are discussed below for chronic conditions (oncology and hepatitis C) and then for acute conditions (tuberculosis and HIV). The graphs for the rest of the medicines that are not mentioned here can be found in **Appendix 1.5**.

Oncology

Taxanes added to the model list for oncology in 2011 were included on many NEMLs. Paclitaxel was already present on some NEMLs (Australia, India and Jordan), added to other NEMLs later (Ethiopia, Lebanon and Uganda) and removed once (**Figure 11**).

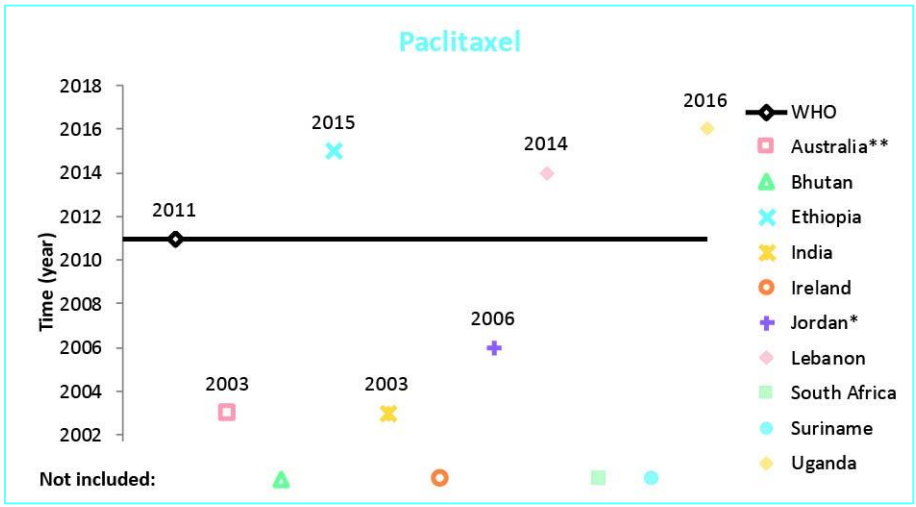

Figure 11. Paclitaxel was included on six NEMLs, some before (Australia, India and Jordan) and some after its addition to the model list (Ethiopia, Lebanon and Uganda). The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. *: left out; **: removed from an NEML.

Oncology medicines added to the model list in 2015 were often already present on NEMLs. Some medicines were included on most NEMLs, such as cisplatin, which was included on seven NEMLs (Australia, Ethiopia, India, Jordan, Lebanon, Suriname and Uganda) before its addition to the model list and removed once (**Figure 12**). Some medicines added to the model list in 2015 were included on fewer NEMLs, such as imatinib, which was included on four NEMLs (Australia, India, Ireland and Jordan) also before its addition to the model list (**Figure 13**).

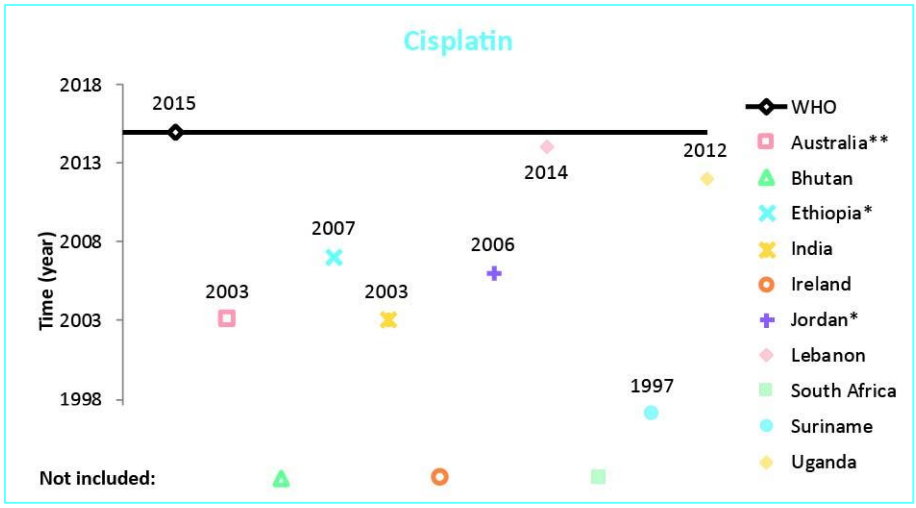

Figure 12. Cisplatin was included on seven NEMLs (Australia, Ethiopia, India, Jordan, Lebanon, Suriname and Uganda) before its addition to the model list. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. *: left out; **: removed from an NEML.

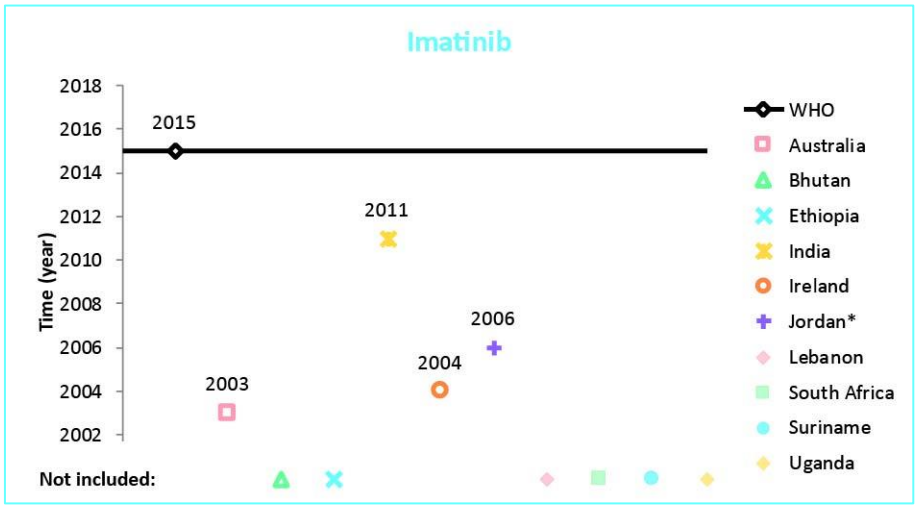

Figure 13. Imatinib was included on four NEMLs (Australia, India, Ireland and Jordan) all before its addition to the model list. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. *: left out from an NEML.

Hepatitis C

The basket contains eight medicines for hepatitis C, from which two formulations of the same medicine were added to the model list in 2007, and six new direct-acting antivirals (DAAs) were added in 2015 as can be found in **Figure 14-16**. Ribavirin was added as oral formulation and as an injection. Since the oral formulation was included on six NEMLs and removed once (**Figure 14**), and the injection was included on only one NEML (**Appendix 1.5**), the oral formulation could be considered more essential.

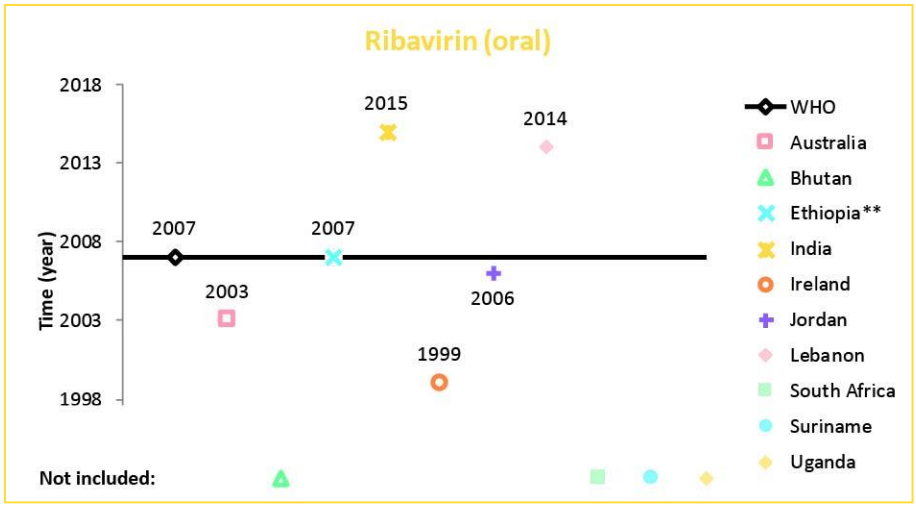

Figure 14. Inclusion of ribavirin (oral formulation) on NEMLs. Ribavirin was included on six NEMLs and removed once. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. **: removed from an NEML.

Moreover, the DAAs that were added to the model list in 2015 were often not included on NEMLs with the exception of one or two countries. They can be found in **Figure 15-16**. Sofosbuvir was included on NEMLs in Australia and India (**Figure 15**) and ombitasvir + paritaprevir + ritonavir combination was only included in Jordan (**Figure 16**).

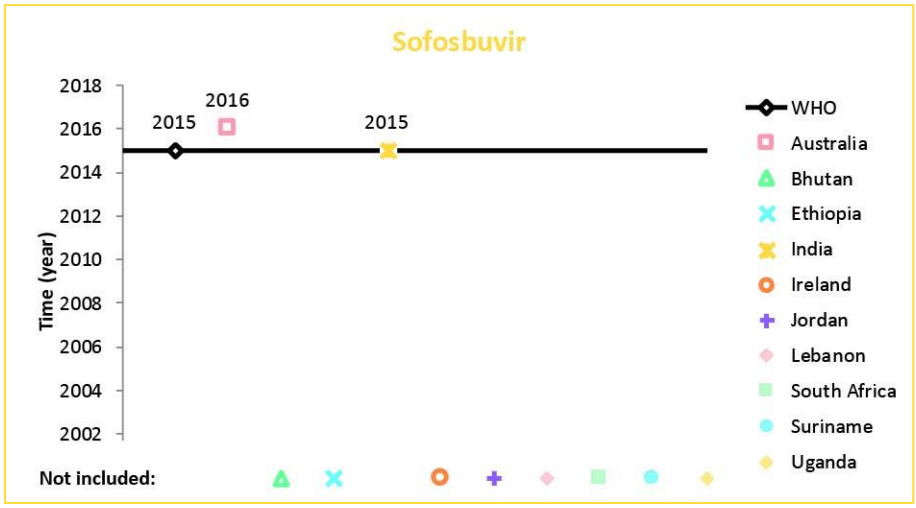

Figure 15. Sofosbuvir, a new DAA, was included on only two NEMLs. The black dot and line represent the year in which the medicine was added to the WHO model list. DAA: direct-acting antiviral; WHO: World Health Organization.

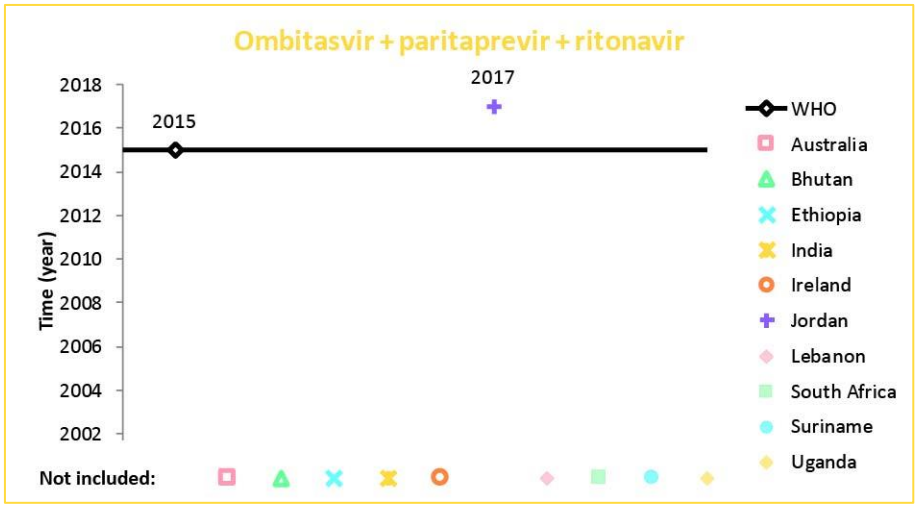

Figure 16. Ombitasvir + paritaprevir + ritonavir combination, a new DAA, was included on the NEML of Jordan. The black dot and line represent the year in which the medicine was added to the WHO model list. DAA: direct-acting antiviral; WHO: World Health Organization.

Tuberculosis

Rifabutin and rifapentine are the two medicines in the basket for tuberculosis. Rifabutin was included on six NEMLs: Australia, Ethiopia, India, Ireland, South Africa and Uganda; it was removed in Ethiopia as can be seen in **Figure 17**. Three countries added the medicine before, and three countries added it after its inclusion to the model list. Rifapentine, however, was not included on any NEMLs (**Appendix 1.5**).

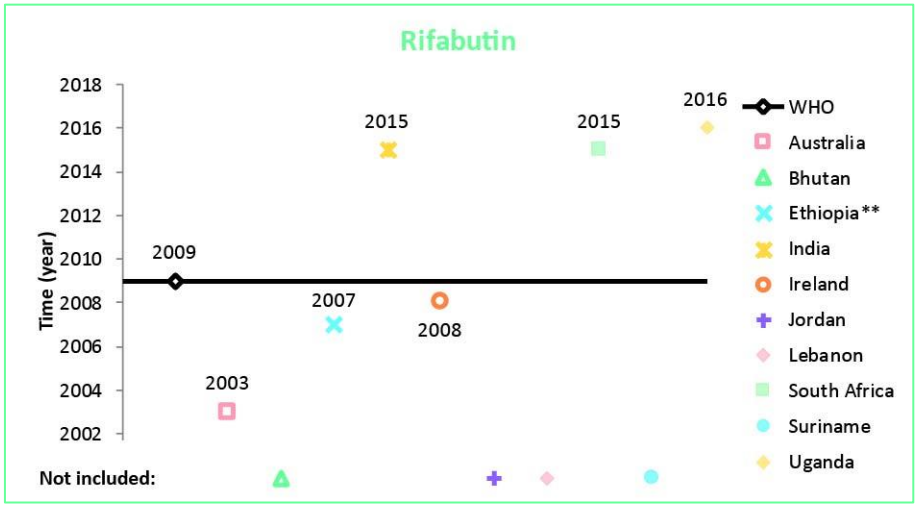

Figure 17. Inclusion of rifabutin on NEMLs. Rifabutin was included on six NEMLs and removed once. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. **: removed from an NEML.

HIV

Medicines for HIV added between 2007 and 2011 were included on many NEMLs, which can be seen in **Figure 18-19**. Lopinavir + ritonavir combination was included in eight countries (Australia, Bhutan, Ethiopia, India, Jordan, Lebanon, South Africa and Uganda) with some before and some after its addition to the model list (**Figure 18**). Efavirenz + emtricitabine + tenofovir combination was included in five

countries (Australia, Ethiopia, Lebanon, South Africa and Uganda), in the same year or after its addition to the model list (**Figure 19**).

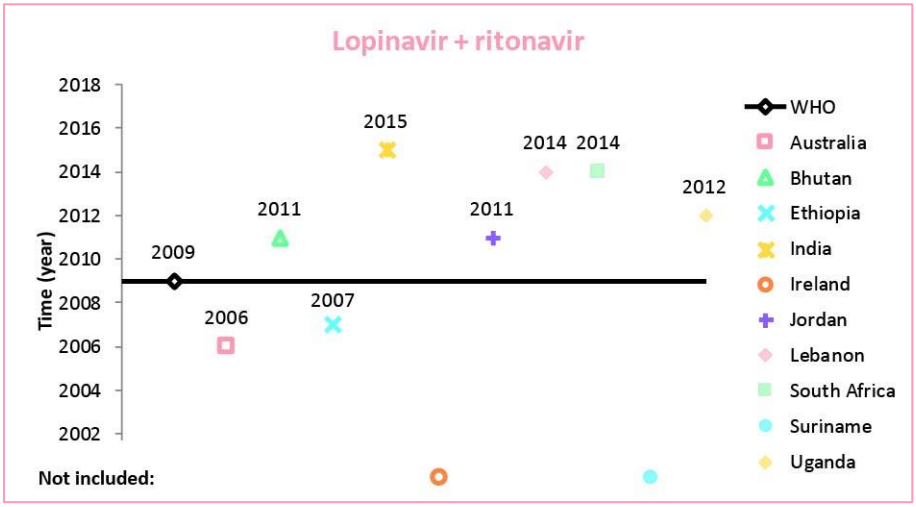

Figure 18. Lopinavir + ritonavir combination was included on eight NEMLs, some before and some after its addition to the model list. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization.

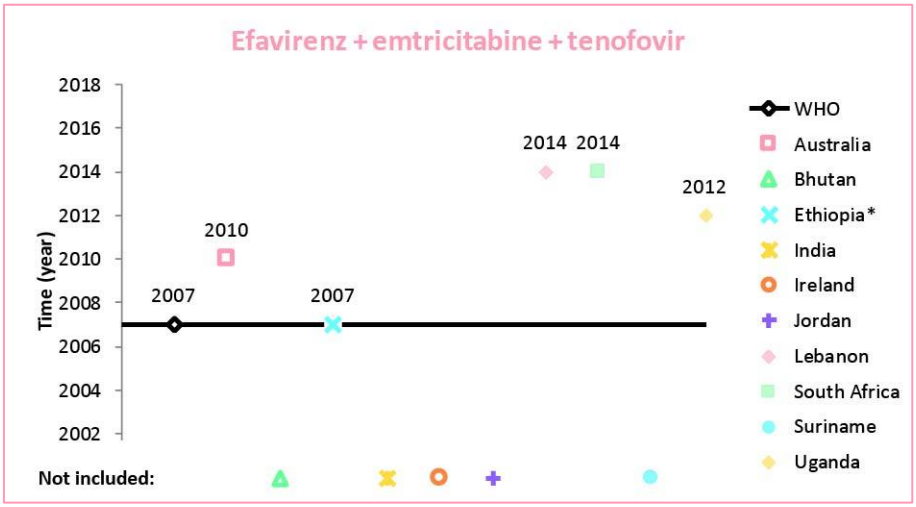

Figure 19. Efavirenz + emtricitabine + tenofovir combination was included on five NEMLs in the same year or after its addition to the model list. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. *: left out from an NEML.

HIV medicines that were added to the model list in 2015 were already present on NEMLs. Abacavir + lamivudine combination was already present on NEMLs in Ethiopia and Uganda and added in the same year in India as its addition to the model list and it was removed once, as can be seen in **Figure 20**.

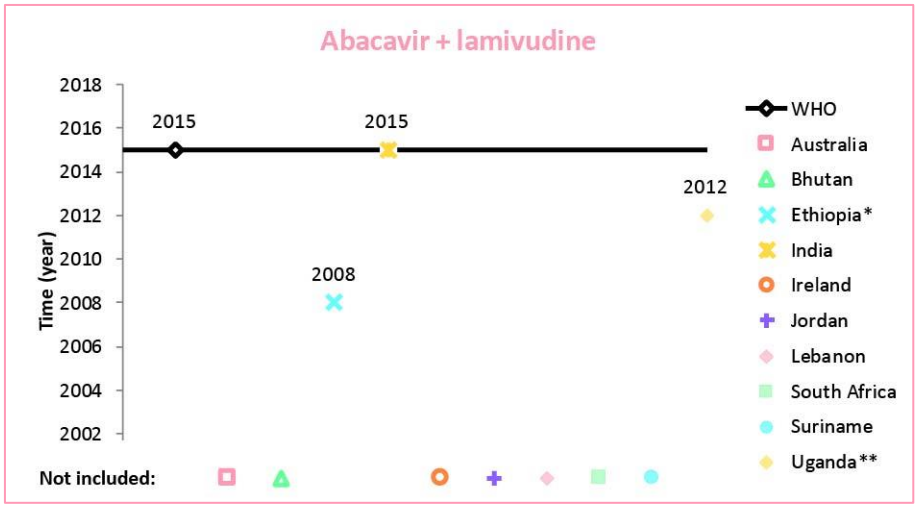

Figure 20. Abacavir + lamivudine combination, a recently added HIV medicine, was either already present on NEMLs (Ethiopia and Uganda) or added in the same year (India) as its addition to the model list. The black dot and line represent the year in which the medicine was added to the WHO model list. WHO: World Health Organization. *: left out; **: removed from an NEML.

Discussion

Overall, most medicines were added for HIV (median: 55%), then for tuberculosis (median: 50%, but n=2), then for oncology (median: 37%) and the least for hepatitis C (median: 13%) on the final version of the NEMLs. These data support the hypothesis, because more tuberculosis and HIV medicines were included on NEMLs versus oncology and hepatitis C medicines. However, it should be noted that most medicines added to the WHO model list for oncology and hepatitis C were added in 2015 (2 out of 19 medicines for oncology and 2 out of 8 medicines for hepatitis C).

As for the different income groups, the upper-middle income countries included most medicines for HIV (45%) and very few or none for other disease areas. Surprisingly, the lower-middle income countries included the highest percentage for oncology and second highest percentage for hepatitis C medicines out of all income groups. These countries also included fewer medicines for HIV and none for tuberculosis. As expected, the low income countries included the most medicines for HIV, some medicines for oncology and tuberculosis, and no medicines for hepatitis C.

Within the geographic regions, the regions of Africa and South-East Asia showed expected results with relatively high percentages for included tuberculosis and HIV medicines and relatively low percentages for included oncology and hepatitis C medicines. The Eastern Mediterranean region was more unexpected with the highest percentage for included oncology and hepatitis C medicines.

Moreover, half of the countries with a GDP on the lower side of the spread graph still included many medicines. Also, a pattern is suggesting that the higher the HDI is in a country, the more medicines are included. More data is needed to confirm this pattern as a correlation.

It was surprising to see that burden of disease did not correlate to the number of included medicines in countries. On the one hand, Australia and Ireland included a tuberculosis medicine even though their disease burden is very small. On the other hand, Ethiopia did not include any tuberculosis medicines, even though its disease burden is large. Furthermore, countries with lower morbidity (India, Jordan and Uganda) still included many medicines for oncology. It was also unexpected to see countries with low burden of disease (Australia, Ethiopia and India) still included many medicines for HIV. South

Africa has a very high burden of disease for HIV, but only included six medicines. Moreover, countries with low burden of disease for hepatitis C (Australia, Ireland and Jordan) still included some medicines, while countries with high burden of disease (India and Ethiopia) did not include many hepatitis C medicines, though the range of the percentage DALYs within these countries is very narrow.

Concerning the timing of inclusion, Australia included the most medicines in total, often before they were added to the model list and Bhutan included the least medicines, only two for HIV during and after their addition to the model list. Some low- and lower-middle income countries (Ethiopia, India, Jordan and Uganda) already included medicines on their NEMLs before they were added to the model list, which was quite surprising. Most included medicines below their addition to the model list were added for oncology. However, many medicines for the other disease areas were added to NEMLs after their addition to the model list.

Medicines added to the WHO model list in 2015 were either already present or not included on NEMLs. Two medicines in the basket for HIV, which were added to the model list in 2015, were mostly already present on NEMLs. Also, seventeen medicines added to the model list for oncology in 2015 were mostly already present on NEMLs. In contrast, one medicine added to the model list in 2015 for tuberculosis was not included on any NEMLs. For hepatitis C, six medicines added to the model list in 2015 were included on NEMLs. This finding was partially unexpected, since we hypothesized that tuberculosis medicines would be included more quickly and oncology medicines would be included more slowly.

Conclusions

In conclusion, the hypothesis was supported by the data that showed most medicines were added for acute conditions (tuberculosis and HIV) over those for chronic conditions (oncology and hepatitis C). Moreover, countries in the Eastern Mediterranean region and the lower-middle income group included many oncology and hepatitis C medicines, despite their lower GDP and burden of disease for these disease areas. Also for most countries, burden of disease did not correlate with inclusion of medicines. Finally, almost all oncology medicines were already present on NEMLs before their addition to the model list.

Part 2: Qualitative

Purpose

The next step of this project was to further analyze the quantitative data presented in Part 1 of the project in a qualitative way by holding interviews with national policy workers. The questions in the interviews were about the factors contributing to the selection of medicines into their NEMLs with a specific focus on medicines for tuberculosis, HIV, oncology and hepatitis C.

Methods

Analytical framework

As preparation for the interviews, literature was read on possible factors that could influence the selection of essential medicines for NEMLs.[6,10,54,55] Based on this, an analytical framework was made (**Figure 21**).

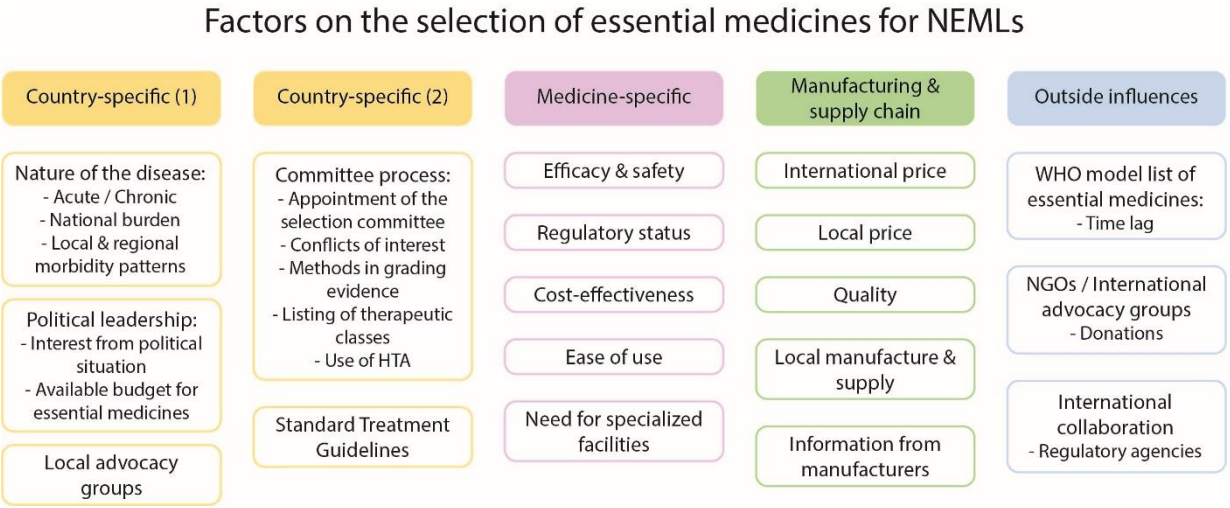

Figure 21. Analytical framework about the factors on the selection of essential medicines for NEMLs, which was used to guide the questions in the interviews.[6,10,54,55]

This analytical framework was used to guide the questions in the interviews and sent approximately two working days in advance to the interviewees as preparation for the interview.

Sample selection

The initial plan was to hold in-depth interviews with twenty participants in total: two persons from the selection committee in each country: the chair or secretary and a member of the committee. Contacts were established during Part 1 of the project, in which additional NEMLs were requested from WHO Country Offices. These persons were contacted again and asked for redirection towards the right persons for the interviews. An official invitation letter (**Appendix 2.1**) was sent to these persons after confirmation of their function in the selection committee, from which six persons responded and agreed to participate in the study. In the end, four participants completed the interview.

Discussion guide

A discussion guide was created as preparation for the interviews, which included all questions to guide the interviewer throughout the interview. The discussion guide was made in accordance with all authors. It was set-up to ask open ended questions in general about the NEML process and the selection of essential medicines, then to discuss focused questions about the inclusion of medicines for tuberculosis, HIV, oncology and hepatitis C into their NEML and finally to prioritize factors from the analytical framework. A draft version of the discussion guide for the in-depth interviews was piloted with a member of the selection committee in South Africa, who was known to one of the authors, but not the interviewer. During this pilot interview, MH held the interview and RvdH sat in to give feedback afterwards. The discussion guide and analytical framework were subsequently fine-tuned based on the recommendations made during this pilot interview. This can be found in **Appendix 2.2**.

Data collection

Prior to each interview, the context of the country was read upon by MH. For this, WHO Country Profiles were read, or if unavailable, the most recent national policy documents or books about the pharmaceutical policy in these countries.[56–59] This was done to increase understanding of the countries' context in their pharmaceutical policies to validate responses from the participants during the in-depth interviews and to further verify information obtained from the literature.

The interviews were carried out from March until May 2018 and were conducted by MH, who had no previous knowledge of the working of the selection other than what was read in preparation of the interviews. The interviews were conducted in English, as all researchers and participants were fluent in the language. All interviews were audio recorded after obtaining consent from the participants.

Data processing and analysis

The recorded interviews were transcribed verbatim. Transcripts were then coded in NVivo, a qualitative software to facilitate analysis of the data, by MH. A thematic analysis approach was used by coding phrases from the interviews into themes. First, old themes were coded from the analytical framework and then new themes were coded based on the answers in the interview. These themes were then verified, confirmed and adapted by RvdH when needed. The included and excluded participating countries were illustrated in a flow chart. The data was represented in hierarchy charts for each country separately. Also, all themes were pooled and listed in a table in order of frequency. The number of times that medicines for tuberculosis, HIV, oncology or hepatitis C were specifically mentioned, was noted. All themes were also listed in a table separately for each country (**Appendix 2.3**). Quotes supporting the six main themes were also noted in a table.

Ethics statement

This study was approved by the Board of Examiners of the Graduate School of Life Sciences at Utrecht University. The participants were ensured anonymity during the study by only stating the name of the country.

Results

Three out of ten originally invited countries participated in the interviews (**Figure 22**). All countries initially responded to the request. Ireland indicated that the decisions for the selection of medicines in

their reimbursement scheme were made by Senior Management and unfortunately, we could not get access to them. From the nine interested countries, in four countries (Ethiopia, India, Jordan and Lebanon) the initial contacts were positive about the study, but they either did not identify the right person for the interview or the proposed persons did not reply to the interview request. In the five remaining countries, the proposed persons agreed to participate in an interview. Two of these countries (Australia and South Africa) did not reply to the call for scheduling the interview, so they did not participate in the end. Bhutan, Suriname and Uganda were the three participating countries. One person was interviewed from Bhutan and one person was interviewed from Suriname. From Uganda, two persons were interviewed, but one of the interviews had to be excluded due to bad recording quality.

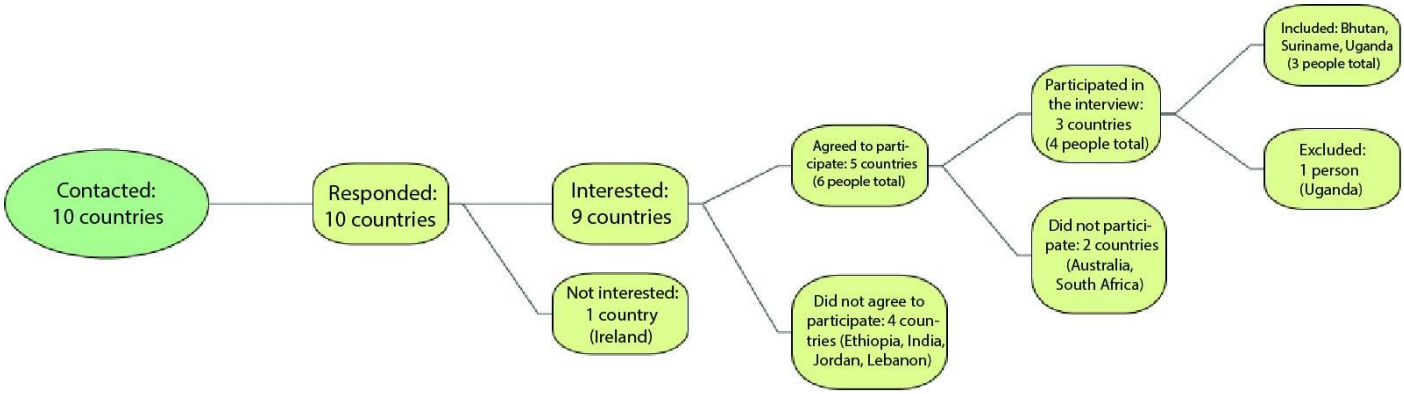

Figure 22. Flow chart of the participants who were included and excluded from the study.

For each interview, a hierarchy chart was made that can be seen in **Figure 23-25**. The bigger the box, the more often the theme was mentioned during the interview. The boxes are also color-coded based on the four pillars in the analytical framework (**Figure 21**). New themes were coded as red boxes.

From the interview in Bhutan, the key themes were: *committee process*, *WHO model list* and *structure of NEML*, as can be seen in **Figure 23**. For Suriname, the key themes were: *WHO model list*, *NEML process* and *STGs* (**Figure 24**). The key themes from the interview with Uganda were: *committee process*, *STGs* and *NGOs/International advocacy groups*, which can be seen in **Figure 25**.

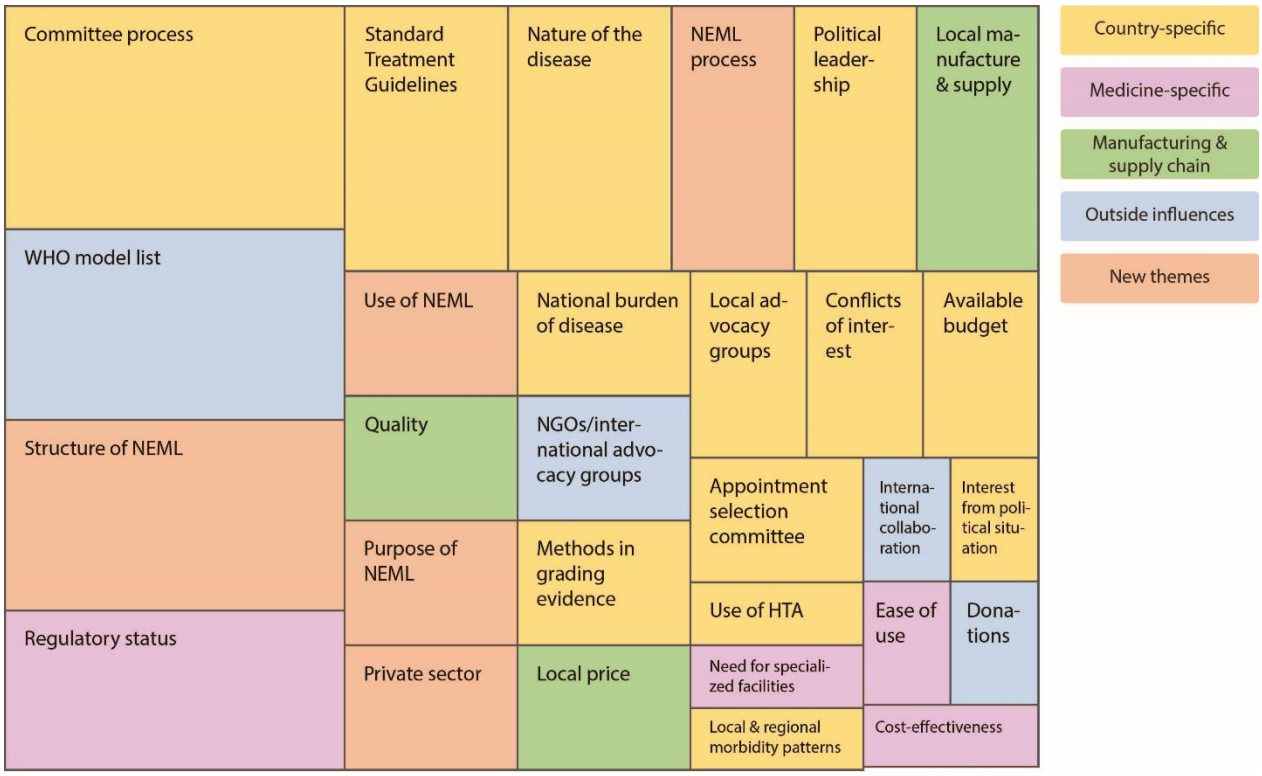

Figure 23. Hierarchy chart made from the interview with a policy worker from Bhutan. The three most important themes were: *committee process*, *WHO model list* and *structure of NEML*. The boxes are color-coded from the four pillars in the analytical framework: yellow = country-specific; purple = medicine-specific; green = manufacturing & supply chain; blue = outside influences; red = new theme.

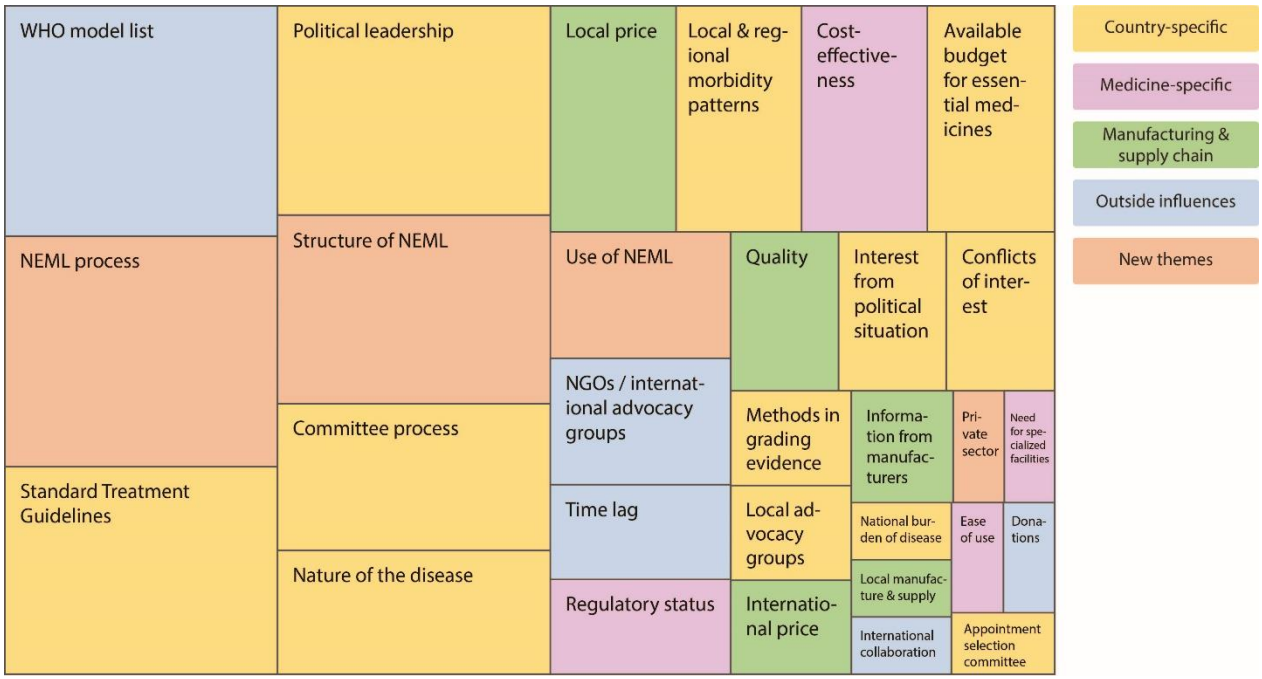

Figure 24. Hierarchy chart made from the interview with a policy worker from Suriname. The three most important themes were *WHO model list*, *NEML process* and *STGs*. The boxes are color-coded from the four pillars in the analytical framework: yellow = country-specific; purple = medicine-specific; green = manufacturing & supply chain; blue = outside influences; red = new theme.

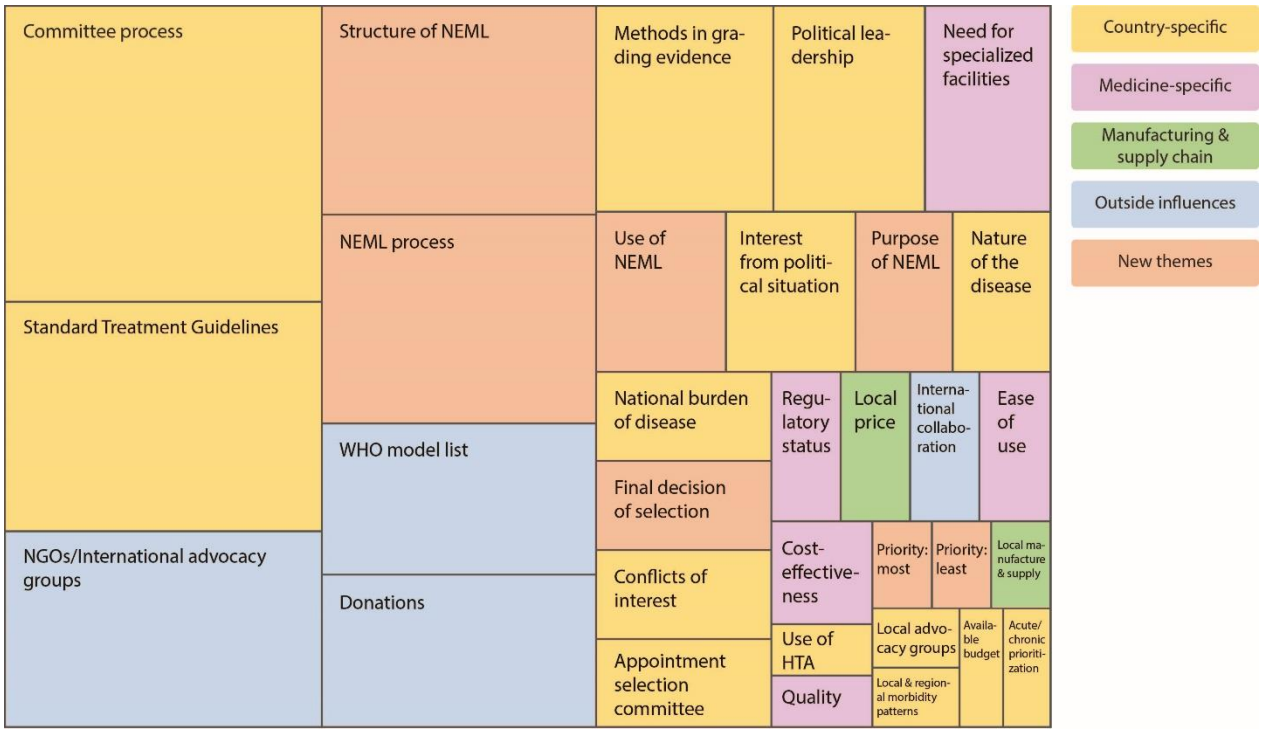

Figure 25. Hierarchy chart made from the interview with a policy worker from Uganda. The three most important themes were *committee process*, *STGs* and *NGOs/international advocacy groups*. The boxes are color-coded from the four pillars in the analytical framework: yellow = country-specific; purple = medicine-specific; green = manufacturing & supply chain; blue = outside influences; red = new theme.

The themes of all interviews together were pooled and arranged by the frequency of their mentions in general and specifically for tuberculosis, HIV, oncology and hepatitis C medicines (**Table 4**). Some new themes emerged while coding the interviews. The themes from the interviews were also arranged separately for each country (**Appendix 2.3**). Overall, *committee process*, *STGs* and *WHO model list* were the key themes during the interviews. These are all old themes from the analytical framework.

Table 4: All themes arranged by how many times they were mentioned in the interviews in general and specifically for tuberculosis, HIV, oncology and hepatitis C. Some new themes emerged while coding the interviews.

Themes	Old/new theme	Interviews	Mentions	Specific mentions*
Committee process	Old	3	32	3
Standard Treatment Guidelines	Old	3	28	3
WHO model list	Old	3	24	4
NEML process	New	3	24	3
Structure of NEML	New	3	23	5
NGOs/international advocacy groups	Old	3	18	5
Political leadership	Old	3	17	2
Nature of the disease	Old	3	12	4
Methods in grading evidence	Old	3	11	0
Donations	Old	3	10	0
Regulatory status	Old	3	10	0
Use of NEML	New	3	10	1

Local price	Old	3	9	3
Interest from political situation	Old	3	8	0
Conflicts of interest	Old	3	8	1
Cost-effectiveness	Old	3	7	2
Available budget for essential medicines	Old	3	7	1
Need for specialized facilities	Old	3	7	1
Local & regional morbidity patterns	Old	3	6	1
Appointment of the selection committee	Old	3	6	0
Quality	Old	3	6	1
Local manufacture & supply	Old	3	5	0
Local advocacy groups	Old	3	5	1
Purpose of NEML	New	2	5	0
International collaboration	Old	3	4	3
Ease of use	Old	3	4	0
Private sector	New	2	3	0
Time lag	Old	1	3	2
Final decision of selection	New	1	3	0
Use of HTA	Old	2	2	0
Information from manufacturers	Old	1	2	1
International price	Old	1	2	2
National burden	Old	3	6	2
Acute/chronic prioritization	Old	1	1	1

* Mentions specifically for the selection of tuberculosis, HIV, oncology and hepatitis C medicines out of total mentions.

Quotes supporting the six main themes have been noted in **Table 5**. These quotes originate from different countries and are randomly ordered in the table.

Table 5. Quotes about the most important themes that emerged from the interviews.

Themes	Quotes
Committee process	"This process had a number of weaknesses. It didn't go as it was planned and it was not planned well. So, many processes were a bit patched and the review of evidence was patchy, different experts worked in different ways. Some, I think, did a real evidence review and some they just started and wrote down what they thought was best. So, really, I'm afraid expert opinion played quite a big role and it should have not."
	"… we form a technical committee and we review the proposals. And only after the revision we put out to our national essential medicines committee for final approval."
	"So, we try to give evidence. Not really like doing a review for every new medicine. We are just with six people […] very busy, so it's way too much for us. We would like to do that, but for that we really need far more people. [...] Because we are all doing this voluntarily aside from our work."
Standard Treatment Guidelines	"Until 2012 the two documents were separated. There was the Clinical Guidelines on one side, and the Essential Medicines List on the other side. They were reviewed and worked upon in different moments and somehow, through different processes […] in 2012 they took the document and revised concurrently and aligned. So, the process focused first on the revision of Standard Clinical Guidelines, so the protocols for treatment, and then the Essential Medicines List was somehow aligned that way."
	"The main problem, I think is the lack of accepted guidelines that are also being checked upon their use […] And it's one of the problems of extending an Essential Medicines List, because you always have to sit, you know, on the financial chair and think "how can this medicine be misused?" and if there's a slight chance, then we have to include restrictions for prescribing the medicine."

WHO model list*	"… the idea is as for the WHO's criteria, like the morbidity, the capacity of the clinicians, diagnostic tests available at that particular level of the health facilities. And I think these are the main criteria for the inclusion." "…medicines that were not on the WHO essential list, I mean, we wouldn't even take into consideration."
	"Usually as in when WHO guidelines are being updated, our program people like HIV and TB programs they put up the proposals [for inclusion]."
	"… all medical specialists, so all physicians for that way or pharmacists can ask us as a Board to include new medicines [...] So, on the contrary, we actively ask them to have a look at the new WHO list and to see what is necessary for us as a country to include in our list."
	Interviewer asked about the addition of two oncology medicines to the NEML before their addition to the model list: "Well, cisplatin, I don't think so, because cisplatin is really like a hundred-year-old medicine […] it's the basic medicine for a lot of cancers. […] I think I have to say that maybe we were way ahead of WHO."
NEML process	"As soon as NEML gets revised, then we look critic[ally] [at] the [Standard] Treatment Guidelines then we incorporate the changes"
	"For me, the guideline is: it has to be scientifically proven, public health-wise very important, but still keeping our budget and being able to have, like normal medicines for the whole year and not run out because I included an expensive medicine. So, that's really our responsibility […] So, as a Board we have to be very, very careful to look what we include in our list."
Structure of NEML*	"Because, we have two kinds of systems actually. Like, one is the Essential Medicines List and another system is that we have this named patient medicines. That named patients medicines is basically, like for those higher, the latest medicines for chemotherapy. So, since we don't have good morbidity data those anticancer drugs are being procured from, either locally or from India as in when a request."
	"HIV medicines are already a little bit included in the Essential Medicines List, but they are paid for by a total different system. So, they are for free and the government is paying for the medicines […] they are very, very cheap and people get them on a special recipe […] and we are now in the process of including all the medicines into the normal Essential Medicines List. But that takes a lot of time, because then we have to know exactly who is allowed to prescribe which ART, etc."
NGOs/international advocacy groups*	"How it would happen [the process of making an NEML], it varied according to the funder, somehow. There is no institutionalized mechanism for the revision of these documents."
	"So, for the HIV drugs, since in the same period the HIV guidelines were being reviewed, they took care of the section of the Essential [Medicines] List. So, the drugs were determined by that group, which is […] quite donor dominated."

* Mentions specifically for the selection of tuberculosis, HIV, oncology and hepatitis C medicines out of total mentions.

At the end of the interview, the interviewees were asked to look at the analytical framework and to prioritize the three most and least important factors on the selection of essential medicines for their NEML. The results of the included countries can be found in **Table 6**.

Table 6. Prioritization of the three most and least important factors in the selection of essential medicines for the NEML.

	Most important factors	**Least important factors**
Bhutan	Nature of the disease	Information from manufacturers
	Standard Treatment Guidelines	International price
	Efficacy & Safety	NGOs/international advocacy groups
Suriname	WHO model list	Information from manufacturers

	Nature of the disease	Local advocacy groups
	Price	NGOs/international advocacy groups
Uganda	Standard Treatment Guidelines	Information from manufacturers
	Cost-effectiveness	Local manufacture & supply
	Local price	Local advocacy groups

In Bhutan, the review of proposals is done by a technical committee first and then approved by the selection committee. Generally, the same criteria as for the WHO model list are used for the selection. The STGs are revised after the NEML. When medicines are too expensive or specialized, such as for oncology, they are categorized as 'named patient medicines', which are only procured for specific patients when necessary. However, medicines for hepatitis C were simply not included due to their costs. The most important factors in Bhutan were the nature of the disease, STGs and efficacy & safety, whereas manufacturers and international price and NGOs/advocacy groups were the least important.

In Suriname, the selection committee is working with limited resources and on a voluntary basis, which makes it hard for the committee members to do a full review on every medicine. The WHO model list is used for the reviews on the medicines and as a standard for inclusion. Specialists can propose new medicines from the WHO model list and the most important consideration for inclusion is the cost-effectiveness and the potential number of patients. The country is in a financial crisis, so the budget for essential medicines is limited. High-cost oncology medicines were added to the list of special essential medicines and medicines for hepatitis C were not included due to their high costs. On the other hand, HIV medicines are paid for by government through a special program. Furthermore, there are no STGs in Suriname, so if a medicine could be misused, then the medicine is put on the special EML with restrictions on its use. The most important factors in the selection were the inclusion of the medicine on the WHO model list, the nature of the disease and the price that the medicine could be procured for. The least important factors were the information from manufacturers, local and international advocacy groups, because Suriname is a small country.

In the interview from Uganda it was mentioned that donors would initiate the revision of the STGs in alignment with the NEML. It was also admitted that there were some weaknesses in the process, because there was no institutionalized mechanism, which led to a more expert opinion based selection. It was also evident that in Uganda STGs and cost of medicines play the biggest role in the selection, while (local) manufacturers and advocacy groups do not influence the selection. When dealing with high-cost medicines, donors would provide HIV medicines.

Discussion

This qualitative study is still a work in progress, because the original plan could not be completed due to low responses and limited time. Ideally, we would have liked to interview at least two members of the committee in each country to cross-check their responses. However, the response rate from the countries was lower than expected. Initially, many countries were positive about participating in our study, but eventually only three countries completed the interview, even though contact was sought out repeatedly.

There are some interesting findings from Bhutan, Suriname and Uganda, the three countries that participated in this study. When prioritizing the most and least important factors on the selection of essential medicines, the least important factors were more or less similar. On the other hand, there was a disagreement between the three countries in the most important factors, as they were different for each country. In Bhutan the efficacy and safety of a medicine was very important, while in Suriname and Uganda the price and cost-effectiveness of a medicine were very important.

In each country, the nature of the disease was considered either with or without the use of STGs. Suriname did not have STGs, so if a medicine could be potentially misused by prescribing it for other diseases, restrictions for its use would be included. In Uganda only the STGs were revised, from which the NEML was extracted. Bhutan only revised the STGs after the new update of the NEML to incorporate important changes.

Countries strive to make their own reviews on efficacy, safety and cost-effectiveness, but this can be difficult with limited resources and without a standard mechanism for the NEML revision process. Uganda was dependent on donors for the revision of the STGs and NEML, which left the country without an institutionalized mechanism for the NEML revision. Suriname depended on voluntary work of the committee members, burdening them with a huge responsibility without being able to provide them with the proper support.

These countries all use different methods to deal with high-cost medicines. In Bhutan, oncology medicines were listed on the 'named patient medicines' list, from which medicines were procured for specific patients only when needed. In Suriname, the cost-effectiveness of the medicine was considered together with the potential number of patients that would use it to estimate the budget impact. The budget impact prevented the listing of hepatitis C medicines and it allowed the listing of oncology medicines on their special list of essential medicines. Uganda depended on donors for HIV medicines.

Surprisingly, the WHO model list was not considered an important factor for the selection of medicines in two out of three countries. For Suriname the WHO model list was an important factor for the selection. The model list was less frequently mentioned in the interview from Uganda and it was also not considered an important factor for the selection of medicines. However, in both countries the model list was the starting point for the selection criteria and it was the standard for inclusion, as very few medicines outside of the model list were included on their NEML. In Bhutan, the model list was the second most mentioned theme, but it was not selected as an important factor for the selection. The model list was mostly used as a guide for the selection criteria.

This study will be expanded by including more interviews. The results will be presented in the existing figures, clustering the countries based on income group. In this way, anonymity can be ensured and specific barriers in the selection of medicines can be identified in countries with varying income groups.

Conclusions

To sum up, it should be considered that countries might not have the resources to support the process of the NEML revision. These resources can either be sought from donors or provided on voluntary basis. Furthermore, not all countries are working with STGs and have aligned them with their NEML. The most important finding was that high-cost medicines were either not listed on NEMLs, such as in the case for hepatitis C medicines, or restricted in their use on another special list, such as in the case for oncology medicines. Some countries still depend on donors for the provision of HIV medicines, which are not

always listed on the NEML. Finally, the WHO model list is used as a standard for inclusion and a guide for the selection criteria in most countries.

Discussion

Summary of main findings

In conclusion, the quantitative part of the study showed that most medicines were added on NEMLs for tuberculosis and HIV over those for oncology and hepatitis C. Eastern Mediterranean countries and the lower-middle income countries included many oncology and hepatitis C medicines, despite their lower GDP and burden of disease for these disease areas. Also for most countries, burden of disease did not correlate with inclusion of medicines. Finally, almost all oncology medicines were already present on NEMLs before the revision of the model list in 2015.

To sum up the qualitative part of the study, barriers in the selection of essential medicines are limited resources in a country, the use of accepted STGs and high-cost medicines. When countries have limited resources, they can depend on donations or voluntary work from the selection committee. Moreover, STGs are not present in all countries and even if they are, they might not be accepted as the standard in the clinic. As for high-cost medicines, countries may find other ways to deal with it other than using the NEML by putting them on a separate list or by restricting their use. In most countries, the WHO model list is used as a standard for inclusion and to guide the selection criteria.

Relation to other studies & recommendations

Inclusion of medicines on NEMLs

The results from this study support our hypothesis that medicines for acute conditions are more quickly adopted into NEMLs over medicines for chronic conditions. This is concerning, since chronic conditions account for a substantial amount of the global burden of disease. They impose a large and growing health burden on developing countries, as 80% of chronic disease deaths occur in low and middle income countries.[60] The WHO has set a target of 80% availability of affordable essential medicines to treat major NCDs by 2025.[61] The WHO is also monitoring the progress of NCDs by indicators to set national targets to among others, generate mortality data, reduce risk factors and strengthen health systems for NCDs.[62] To strengthen health systems, guidelines for the treatment of NCDs should be made, including guidelines for oncology, and providing drug therapy to prevent heart attacks and strokes. Unfortunately, these targets are not including many other chronic diseases such as hepatitis C. Although, this report showed that the selected countries in our study do have guidelines for the treatment of NCDs, but it is unclear if these also include guidelines for oncology and hepatitis C.[62]

There is poor access to essential medicines for chronic conditions in resource-constrained settings. A study on availability of medicines for chronic conditions showed that generic medicines for chronic conditions are less available than generic medicines for acute conditions.[63] Another study, in which access to medicines for chronic conditions was assessed in five low and middle-income countries, found that less than half of the patients had access to medicines in every country, ranging from 16% in Uganda

to 49% in Jordan.[64] They also found that higher household socioeconomic level was the most significant predictor of the availability of medicines for chronic conditions. The WHO baseline data also show low availability and/or poor affordability, which results in few essential NCD medicines meeting the target in low- and middle-income countries.[61] To improve the access to medicines for chronic conditions, more medicines for these conditions should be included on NEMLs. During the interviews, it became clear that medicines for hepatitis C were not included on NEMLs due to their high costs and oncology medicines were included on a special essential medicines list.

This should not take away the fact that acute conditions should be forgotten. In fact, the eradication of tuberculosis is not on track as it remains the top infectious killer in 2016.[26,65] There were an estimated 10.4 million new TB cases worldwide and seven countries accounted for 64% of the total burden including India and South Africa.[66] Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. WHO estimates that there were 600,000 new cases with resistance to rifampicin, the most effective first-line drug. Underreporting and underdiagnosing continues to be a challenge, especially in countries with large unregulated private sectors and weak health systems.[66] Only one in five people needing treatment for MDR-TB in 2016 actually received it and only half of those who started MDR-TB treatment were cured. Tackling the epidemic requires action to close gaps in care and financing, but low- and middle-income countries do not have the resources to provide this. More domestic funding is needed in middle-income countries, and more international donor support is needed to support low-income countries.[26,66] The limited inclusion of new tuberculosis medicines on NEMLs, which are necessary to treat MDR-TB and LTBI, is not contributing to their access. During the interviews it was unclear why these medicines were not included on NEMLs. To improve their access and to finally eradicate tuberculosis, these medicines should be included on NEMLs.

Surprisingly, our results also showed that countries in the eastern Mediterranean region and lower-middle income group included many oncology medicines. Out of the those countries, these results seem to mostly come from Jordan. In literature there are conflicting results. In one study, including Bhutan, India and Jordan among others, they found that in ten eastern Mediterranean countries a median of 17.5 oncology medicines were included and that lower-middle income countries included a median of 18 oncology medicines on their NEMLs compared to the median of 16 medicines in overall countries.[67] These two groups did not include a much higher number of oncology medicines compared to the overall countries, unlike in our study. A similar study, including Jordan, Lebanon, Bhutan and India among others, showed eastern Mediterranean countries included a median of 23.5 oncology medicines out of 25 total oncology medicines, which was the highest number out of all geographic regions.[68] In the same study, lower-middle income countries included a median of 18 oncology medicines, which was not very different from the overall median of 17 medicines. These two studies found different results, which could be due to the fact that the first study was conducted in 2014 and the second in 2016. As the revision of the oncology section on the WHO model list occurred in 2015, this could explain their results. Unfortunately, not many of these countries were interviewed in the second part of this study, so the reason for including many oncology medicines could not be found out.

Another unexpected result was that burden of disease was not correlated with the number of included medicines for that disease area. This could be due to the fact that morbidity data used in this study might not reflect the actual situation due to lack of information, lack of patient registries and

underdiagnoses in low- and middle-income countries.[67] Another reason could be that the data source used in this study is not the same data that is used in countries. In our study, data from the Institute of Health Metrics and Evaluation was used from their global burden of disease study.[53] During the interviews, countries confirmed using their own local data generated from their health facilities. Perhaps their data is a closer representation of reality in terms of disease morbidity.

Barriers in the selection of medicines

The barriers in the selection of medicines for NEMLs were investigated by holding interviews with national policy workers. The overarching barrier in the selection process is having limited resources in a country. Unfortunately, it is a very complex situation that a country cannot easily solve. However, the way to divide the resources should be key to improving access to medicines. One of the main themes from the interviews was the lack of institutionalized support from the government in the NEML process. Countries with limited financial resources or a financial crisis may depend on donors or on voluntary work, but both of these are not sustainable solutions. Next to that, the consequences of the NEML revision could be huge, depending on which medicines are selected for inclusion and also depending on the purpose of the NEML. This can have huge financial implications if the purpose of the NEML is procurement or reimbursement, which is a big responsibility for the said donors or voluntary workers.

The importance of STGs should not be underestimated. First of all, there should be STGs in a country that are accepted by the healthcare workers. The use of STGs should be enforced either by law or by the insurance companies. The next step is to revise the STGs in alignment with the NEML. According to the WHO selection process, the STGs should be revised first and then the NEML should be extracted from them.[10] Included in the STGs should also be the diagnostic criteria for the diseases. Recently, the WHO released its first Essential Diagnostics List, which can be useful to include as well.[70] Diagnosis can be very important in diseases such as hepatitis C and oncology, especially in low- and middle-income countries where patients usually remain undiagnosed until they present with very severe symptoms.[67,71]

The WHO model list of essential medicines serves as a valuable resource for advocacy, purchasing and supply at the country level.[10] The WHO revised the oncology section in the model list in 2015 and added sixteen medicines.[42] One of the findings in the quantitative study was also confirmed during one of the interviews: the WHO was lagging behind with their revision of the oncology section in 2015, as most countries had already added those medicines to their NEML before 2015. This was also confirmed by a study that aligned NEMLs looking for essential oncology medicines, stating that the expert committee's 2015 review of cancer medicines for the WHO model list was long overdue after more than 20 years of limited review of anti-cancer medicines.[68] This shows that before 2015, the WHO model list was a barrier for the selection of oncology medicines, as during the interviews it was also mentioned that the model list was used as a standard and as a guide for the selection criteria of medicines for their NEML.

The final and most significant barrier to the selection is the high cost of medicines. Even if new curative therapies are developed, their high costs can still prevent patients to benefit from them due to their unaffordability. For example, looking back at when the new antiretroviral therapies (ART) were developed, the mortality and morbidity rates of HIV/AIDS patients improved dramatically.[72] Unfortunately, most of the 36 million patients living in developing countries did not have access to these medicines. In 2002, the WHO committed to scaling up ART by guiding its rational use and selection, but

also by improving affordability and sustainability of drug financing.[72] With joint action of many stakeholders, access to ART was achieved for more than five million people in the developing world.[73,74] A similar situation has arisen with the development of the new direct-acting antivirals (DAAs) to treat hepatitis C.[75] These new DAAs are very effective, but also very expensive, which has limited the access to these medicines.[24] These prices threaten the sustainability of health systems in many countries and prevent large-scale provision of treatment. Even high-income countries had to restrict the use of DAAs, negotiate prices or delay reimbursement until prices dropped.[24] Due to the fact that the access to DAAs is unequitable, the WHO has set a target to diagnose 90% of people living with HCV and treat 80% of diagnosed patients.[76] This is also why the WHO added DAAs to the model list of essential medicines in 2015, which can help mobilize international committment.[42] For some low- and middle-income countries, pricing agreements were negotiated and voluntary licensing in India has made it possible to manufacture generics.[24,77] Next steps to improve access to these medicines are to include them on NEMLs and quickly approve them at the national regulatory agencies.[78] From the interviews it was clear that when adding high-cost medicines to NEMLs, they were restricted to prevent misuse and to control the budget impact. This will require transparency in the decision process of the countries in order to assure accountability for reasonableness.[25] Unfortunately, restricting the use of DAAs was still not possible due to their high costs. In the end, joint action of many stakeholders is needed to improve the access to DAAs, which also finally improved the access to ART.

Study strengths and limitations

This is the first study that compared multiple NEMLs from the same country with multiple WHO model lists, which makes it an analysis over time. Moreover, this study was based on a mixed-methods design in which the first part consisted of a quantitative analysis by aligning NEMLs from ten countries with WHO model lists. The second part consisted of a qualitative analysis by holding interviews with national policy workers to identify barriers in the selection of medicines for NEMLs, which has never been studied before either. This design also allowed us to interpret the findings from the first part in a better way with the findings from the second part.

Apart from these strengths, the study had several limitations. It was an exploratory study focused on only ten countries to define problems in access to medicines. The conclusions cannot be directly extrapolated to other countries as the external validity of such a pilot study is not high. Moreover, the sample size of ten countries is low and due to this, only descriptive statistical tests could be performed. There were no NEMLs in Australia and Ireland, so their reimbursement lists were studied instead. Also, the included countries were selected based on having at least one earlier version of their NEML. The WHO recommends the revision of the NEML every few years, which could mean that these countries were more influenced by the WHO model list. The basket of medicines only includes medicines added to the core model list, except for oncology since there were no medicines in the core list. This was decided from a methodological point of view, because these medicines are clinically more important and have a higher chance of inclusion.

In the qualitative study, only three countries from the quantitative study participated in the interviews. Therefore, this qualitative study will be elaborated by holding interviews with more countries, so the results can be aggregated by income group. The assumption in this study is that the interviewee is a

representative of the government of the country and that they are telling the truth. In order to remove this assumption, the original plan was to interview at least two persons from each country to validate their responses, but unfortunately this plan could not have been carried out due to a low response rate and limited time. Another consideration should be that inclusion of a medicine on the NEML does not automatically mean that the medicine is available in the country, so this should be further studied. Another consideration is that this study only aligned NEMLs for the quantitative analysis, but medicines could still be made available by putting them on another list, which was the case for e.g. Bhutan. Finally, the hypothesis was based on comparing acute conditions with chronic conditions. HIV was considered an acute condition, but more recently HIV infection is becoming a chronic disease as patients have access to lifelong treatment.[37]

Follow-up

Already planned for follow-up is the expansion of the qualitative study to interview more countries and to at least two persons from each country to achieve saturation of the data. In this way, the results can also be presented based on income groups instead of individual countries.

One way to elaborate on the impact of the price of medicines is to look at historical prices for which a country can procure the medicine and to see if there is a change in the local price at the timing of inclusion on the NEML. This way the hypothesis can be tested whether cheaper medicines are more quickly adopted into NEMLs. Another important consideration when doing follow-up research on NEMLs, is that it should not be the only thing studied. The reason for this is that from the interviews it became clear that countries also use other ways to ensure access and availability of medicines other than including them on the NEML. So, other possible ways to ensure access to essential medicines should be explored as well. Moreover, to get a better idea about access to medicines, the availability of medicines should also be studied, because inclusion of a medicine on the NEML does not ensure this.

Conclusions

In conclusion, most medicines were added on NEMLs for acute conditions, such as tuberculosis and HIV, over those for chronic conditions, such as oncology and hepatitis C. The biggest and overarching barrier in the selection of essential medicines is having limited resources in a country. This does not lead to an institutionalized process for the revision of the STGs and it also prevents listing of high-cost medicines on the NEML, especially in the case of new hepatitis C medicines. The healthcare budget should not be exhausted, so the recommendation is to include high-cost medicines for chronic conditions with restrictions that follow the STGs, which is now mostly done for oncology medicines. This will require transparency in the decision process to assure accountability for reasonableness. However, in the long run we should aim for universal health coverage to ensure access to medicines to all.

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