Final version

Testing the robustness of the adapted SDG indicator 3.b.3 methodology to determine access to essential medicines for children

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Date:	4 February 2022

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Abstract

Background

Within Sustainable Development Goal 3, a target is to provide access to affordable essential medicines and vaccines for the entire population on a sustainable basis. Therefore, the SDG indicator 3.b.3 is created to measure the access to essential medicines for the general population. However, there is currently no standardized way to determine the access to essential medicines for children. By adapting the original SDG indicator 3.b.3 to a child specific indicator, a method for assessing access to essential medicine for all children was developed. The purpose of this study is to perform multiple sensitivity analyses on different input parameters that influence the child-specific SDG indicator 3.b.3 methodology to test the robustness of the adapted method.

Method

The historical World Health Organization/Health Action International data from 10 different countries were combined into one dataset with 25 hypothetical facilities which together formed a hypothetical country. The data on 19 of the 22 medicines in the young children medicine basket was matched. In addition to this base case set, another dataset has been created in which more medicine prices were included. With these datasets multiple sensitivity analyses were performed on the input parameters: the national poverty line (NPL), number of units needed for treatment (NUNT) and the burden of disease. The average facility score was calculated to compare outcomes of different sensitivity analysis.

Results

The average facility scores of the multiple sensitivity analyses were compared to the average facility scores of 35,25% (base case dataset) and 68,18% (price dataset). Changing the NPL did not result in a relevant shift (range: 33,62 – 36,62%) of the average facility score. The results showed that using the NUNT instead of units per treatment had little impact on the average facility score (range: 33,33 – 41,21%) and it did not matter whether the minimum, maximum or average NUNT was used. Also, both the base case dataset and the price dataset showed little influence on the average facility score when changing the burden of the disease.

Conclusion

The average facility scores in the sensitivity analyses on the different parameters (NPL, NUNT and burden of disease) do not show a relevant change, so it can be concluded that robustness of the adapted SDG indicator 3.b.3 methodology is proved.

1 | Introduction

Since 2000 death among children before the age of 5 is halved through various initiatives. (1) Unfortunately, in 2019 7,4 billion children, adolescents and young people still died mostly from preventable or treatable causes. (2) The most common causes, such as respiratory infections and diarrheal diseases, could easily be prevented by better access to health care and essential medicines. (1)

1.1 | Sustainable Development Goals

In 2000, eight Millennium Development Goals (MDGs) were developed and had to be achieved by 2015. (3) Although the progress on health-related goals, MDG 4, 5 and 6, was remarkable, several disadvantages with the MDGs were recognized. This led to the introduction of the Sustainable Development Goals (SDGs) by the United Nations in 2015. (4) 17 New goals (figure 1) with 169 associated targets were formulated and are linked together to address several cross-cutting issues. The goals integrate the three dimensions of sustainable development, which are economics, social, and environment, with five themes: people, planet, prosperity, peace, and partnership. (3)

Figure 1 *The Sustainable Development Goals. The health-related goal is SDG 3: "Ensure healthy lives and promote well-being at all ages".* (5)

SDG 3 *"Ensure healthy lives and promote well-being at all ages"* is the only goal related to global health. This goal discusses access to safe, quality, and affordable essential medicines for everyone around the world. (6) The SDG 3 consists of 13 targets (table 1), but for the scope of this research, only target 3.b will be discussed in detail. Target 3.b mentions the importance of access to affordable essential medicines and vaccines. (3) By measuring the access to medicine, the quality of health can be monitored. Therefore, the World Health Organization (WHO) has formulated SDG indicator 3.b.3: "*Proportion of health facilities that have a core set of relevant essential medicines available and affordable on a sustainable basis*". (6) With this indicator the availability and affordability of essential medicines can be calculated.

Table 1 *The nine substantive targets and four additional targets of SDG 3.* (3)

3.1	By 2030, reduce the global maternal mortality ratio to less than 70 per 100 000 live births
3.2	By 2030, end preventable deaths of newborns and children under five years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1000 live births and under-five mortality to at least as low as 25 per 1000 live births
3.3	By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, waterborne diseases and other communicable diseases
3.4	By 2030, reduce by one third premature mortality from noncommunicable diseases through prevention and treatment and promote mental health and well-being
3.5	Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol
3.6	By 2020, halve the number of global deaths and injuries from road traffic accidents
3.7	By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programs
3.8	Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all
3.9	By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination
3.a	Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate
3.b	Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, **provide access to affordable essential medicines and vaccines**, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all
3.c	Substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries, especially in least-developed countries and small island developing States
3.d	Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks

1.2 | Access to essential medicine

Access to essential medicine consists of 2 parts. First, *access* is defined as "the timely use of services according to needs", with a demand and supply side. The demand side is determined by the patients and the supply side by the healthcare sector and associated aspects. More specifically, access to medicine has multiple levels. (7) Bigdeli's framework (figure 2) shows the five levels of the system and involves the associated interactions and relationships. The five levels are: Level 1 - Individuals, households, community; Level 2 - Health service delivery; Level 3 - Health sector level; Level 4 - Public policies cutting across sectors; and Level 5 - International and regional levels. (7) Circular dynamic thinking made it possible to visualize the complexity of the health system. It considers the limitations of the supply side and the re-organization of building blocks of the health system, which are medicines, human resources, financial resources, health information and health infrastructure. On top of that, leadership and governance of the health sector in their local, national, and international context are included. (7)

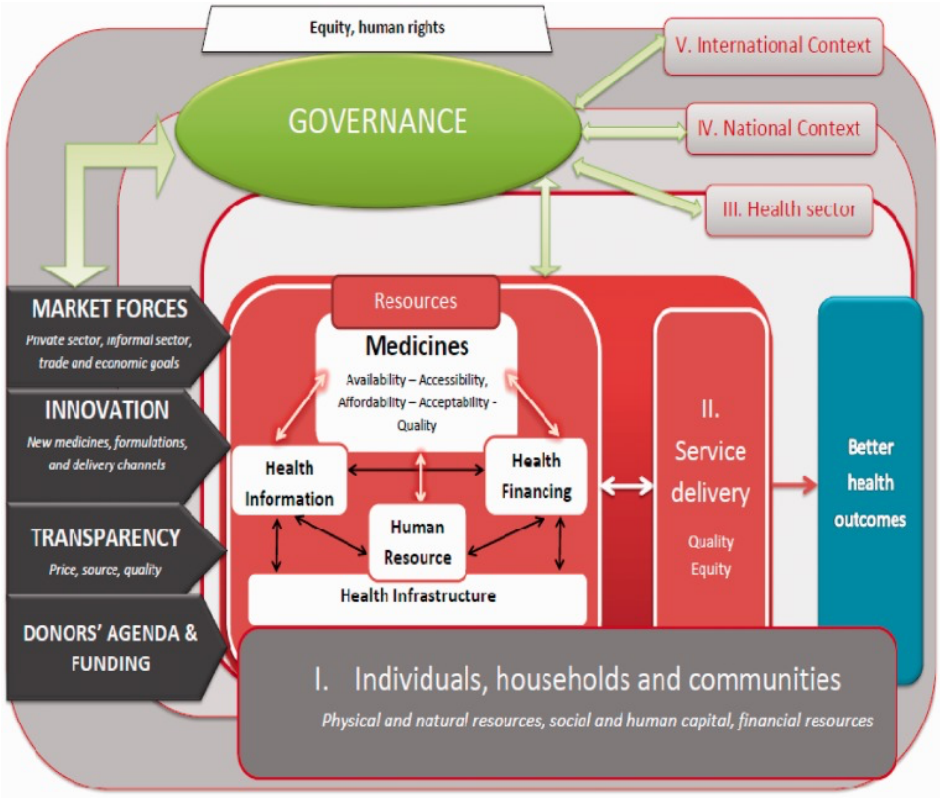

Figure 2 *Bigdeli's framework on access to medicine from a health system perspective.* (7)

Second, the WHO stated that "*essential medicines* are those that satisfy the priority health care needs of the population". (8) The Essential Medicines List (EML) is a list with carefully selected essential medicines that should always be available in the correct dosage forms, of assured quality and at prices that patients and health systems can afford. (8) Essential medicines are based on the prevalence of diseases, the evidence of effectiveness and safety, and whether the medicine is cost-effective. Every 2 years, the WHO publishes a model list that is intended as a guide for countries or regional authorities to formulate their own National EML (NEML). (8) Together with good purchasing and distribution processes, correct prescription of medicines and lower costs for healthcare and patients, the NEML can lead to better access to medicine. (9)

1.3 | Data collection

In 2001 the international non-governmental organization Health Action International (HAI) and the WHO developed a standardized method for measuring the prices and availability of medicines using surveys, because such methodology did not exist before. (10) The first edition of the methodology was published in 2003 and until 2015 55 national and reginal surveys have been carried out by trained data collectors. These surveys are conducted in randomly chosen medicine facilities from the public, private and up to two other sectors in six areas in a country or province. In each facility, up to 50 medicines are surveyed on the price and availability of the medicines from the originator brand and the lowest-priced generic equivalent available. However, this method was time-consuming and the WHO launched a new

pilot tool in 2016. The Price and Availability Monitoring mobile application (WHO EMP MedMon) allows routine collection of medicines and health products data, in a user-friendly, flexible, and cheap way and can be adjusted per country. (11)

1.4 | The SDG indicator 3.b.3

With SDG indicator 3.b.3 access to essential medicine for a general population can be determined. The indicator is a multidimensional index, where a proportion of facilities with available and affordable medicine is divided by the total number of surveyed health facilities, see formula 1 below: (6)

$$SDG_{3.b.3.} = \frac{Facilities\ with\ available\ and\ affordable\ basket\ of\ medicines\ (n)}{Surveyed\ Facilities\ (n)} \qquad \textit{Formula 1}$$

There are three core concepts that are used to measure the indicator: availability of medicines, affordability of medicines and a core set of relevant essential medicines. This combination of availability and affordability is unique and has not been used before. (7) A medicine is *available* when it is present in the right dosage in the reviewed facility on the day of data collection. So, when a formulation is present in the facility, the requirement of availability is met. Availability is expressed with a binary measurement, where 1 = medicine is present and 0 = medicine is not present. (6) A medicine is *affordable* when no extra daily wages (EDW) are needed for the lowest paid unskilled government sector worker (LPGW) wage to purchase a monthly dose treatment of a medicine after fulfilling basic needs. These basic needs are based on the national poverty line (NPL). The EDW and price per treatment can be calculated using the formulas below: (6)

$$Extra\ daily\ wages\ (EDW) = \frac{NPL + price\ per\ treatment}{daily\ wage\ of\ LPGW} \qquad \textit{Formula 2}$$

$$Price\ per\ treatment = \frac{unit\ price * units\ per\ treatment}{365/12} \qquad \textit{Formula 3}$$

The outcome of EDW is a value that can vary from 0 to infinity, however, this is converted to a binary variable for affordability. When a medicine is affordable there are no extra daily wages required to purchase it. So, affordability = 1 when EDW ≤ 1 and in other cases affordability = 0. (6) A medicine is accessible when it is available and affordable. (6)

The original basket of medicines consists of 32 essential medicines selected from the 2017 WHO EML. (6) (12) These medicines are assigned a weight based on the regional burden of disease. The burden is determined by using the Disability Adjusted Life Year (DALY) from the WHO Global Health Estimates (GHE). (13) DALY is a time-based measure which represents the loss of the equivalent

of one year of full health. (14) It is necessary to assign this weight to address the specific regional needs in term of medicines. (6)

In formula 1, the number of facilities that have 80% of essential medicines accessible, are divided by the total number of surveyed facilities. This threshold of 80% is according to the WHO Global Action Plan on Non-Communicable Diseases. The value from formula 1 is a percentage between 0-100%. There is no specific reference value, but over time the $SDG_{3.b.3}$ can be compared with previous values and hopefully improvement can be observed. (6)

1.5 | The pharmacotherapy differences between adults and children

The method explained in the previous section cannot easily be adopted for children, because in pharmacotherapy children are not small adults, but differ in many aspects. (15) For children, the route of administration, dosage form, taste preferences and strength should be considered. (10) Usually, the dose for children is determined with 'bridging', where the dose for adults is divided by a fixed (scaling) factor. It is assumed that the correct efficacy and safety profile can be guaranteed, but it has its pitfalls in practice. (16)

The bridging methods are based on body weight, age, or body surface area (BSA). (16) The most used method is to normalize the adult dose based on body weight (mg/kg), assuming a linear relationship between weight and dose. The pediatric dose is also determined by the age of the patient. However, this method does not consider the changes due to developmental growth (metabolism) that occur within each age group. With the BSA dosage, the assumption is that metabolic processes in humans are constant and can be expressed as a function of the BSA. However, determining a patient's BSA is difficult because of the complexity and inaccuracy of the formulas. In addition, the pharmacokinetic parameters do not change proportionally with the BSA. (16)

For a desired treatment outcome, the acceptability and preferences of formulations is very important. As a child grows, cognitive and motor skills, and their ability to swallow medicines develop. Previously, liquid formulations for (young) children were preferred due to their easy and simple dosing. However, flexible oral solid dosage forms such as orodispersible tablets are now a priority because these forms are more stable and have lower transportation and storage costs. Lastly, taste characteristics are important for the acceptability of medicines for children, since children prefer sweet and salty flavors. (15)

1.6 | The SDG adapted indicator 3.b.3

Previous research proposed an adapted methodology to measure access to essential medicines for children. (17)(18) Table 2 provides an overview of the different changes to the indicator. The biggest changes, compared to the original methodology, are in the basket of medicines surveyed and the units per treatment needed for the calculations of affordability.

Table 2 *An adapted overview of the input variables for the calculation of the original SDG indicator 3.b.3 and the adapted SDG indicator 3.b.3* (17) (18)

Parameter	**The SDG original 3.b.3 methodology**	**The SDG 3.b.3 adapted methodology for children (neonates, 1-59 months, 5-12 years)**
Availability of medicines		
Availability	Medicine is present at the facility on the day of data collection (0 = unavailable / 1 = available)	Medicine is present at the facility on the day of data collection (0 = unavailable / 1 = available)
Affordability of medicines		
EDW ratio (0 - ∞)	- Calculated from the medicine price, DDD, the NPL, and the LPGW. - Transformed to a binary variable (if EDW < 1, medicine is affordable)	- Calculated from the medicine price, NUNT, the NPL, and the LPGW - Transformed to a binary variable (if EDW < 1, medicine is affordable)
Daily dose treatment of a medicine	DDDs, to allow comparison across strengths, quantities, and pack sizes	- NUNT, based on international treatment guidelines, predetermined for the formulation that was surveyed - Calculated from the recommended dosing per age, weight group, or BSA, the transformation of weight-based dosing to age-based dosing and treatment duration
Core set of globally relevant essential medicines		
Selection of medicines	- Defined on a global level - Selected from the EML 2017 - Selection process not described	- Defined on a global level - Selected from the EMLc 2019 - Selection based on the global burden of disease and international treatment guidelines
Baskets*	- One basket for all ages - 32 tracer essential medicines for acute, chronic, communicable, and non-communicable diseases - No specific formulations selected	- Three baskets for different age groups (neonates; young children; school-aged children) - 14 (neonates), 22 (young children), and 22 (school-aged children) tracer essential medicines for acute and chronic, communicable, and non-communicable diseases -Includes specific child-friendly formulations
Burden of disease	- Weighted according to the regional burden of disease (in DALYs) - Based on WHO Global Health Estimates (GHEs) -Pre-defined GHE codes, with overarching GHE code for infectious diseases	- Weighted according to the regional burden of disease (in DALYs) - Based on WHO Global Health Estimates (GHEs) 2016 - Affiliated GHE codes determined according to the uses as described in the EMLc, except for infectious diseases

BSA = Body Surface Area, DALYs = Disability-adjusted life years, DDD = defined daily dose, EDW = extra daily wages, EML = WHO Model List of Essential Medicines, EMLc = WHO Model List of Essential Medicines for children, LPGW = lowest-paid governmental worker, NPL = national poverty line, NUNT = number of units needed for treatment.
**The medicine baskets are currently under review by experts.*

1.6.1 | Young children medicine basket

With the adaptations for the child specific SDG indicator 3.b.3, it is necessary to formulate a basket of medicines that reflects the needs of children. Since there is a high variability of disease prevalence in children, three age groups are created prior to the disease selection. The age groups are: neonates (0-28 days), young children (1-59 months) and school aged children (5-12 years). The starting point for the disease selection per age group is the 2016 GHE. (17) The GHE present the latest available data since 2000 onwards for health-related indicators. They provide insights on mortality and morbidity trends, as well as the burden of disease in DALYs. These two indicators are used to identify the top 10 diseases per age group. (17) Furthermore, the diseases must be treatable with medicines from the EML for Children (EMLc). (2) When both criteria are met, the medicines used for treatment of the disease are included in the basket of medicines. Every medicine has been linked to one or more GHE code (i.e. disease). (17) In contrast, the first-choice disease on the EMLc with corresponding code is used to determine the disease for antibiotics. Using this code limits the disproportionate representation of antibiotics in the medicine basket. An overview of the different medicine baskets per age groups can be found in Appendix 1. The scope of this research is limited to young children (1-59 months), with the related medicine basket shown in table 3 below.

Table 3 *The medicine basket of relevant essential medicines for young children (1-59 months).* (17)(18)

Medicine name	**Affiliated disease (GHE code)**
Oral rehydration salts	Diarrhoeal diseases (110)
Zinc sulphate	
Carbamazapine OR phenobarbital OR phenytoin OR lamotrigine	Epilepsy (970)
Valproic acid	
Diazepam OR lorazepam OR midazolam	
Abacavir + lamivudine + dolutegravir OR Abacavir + lamivudine + lopinavir/ritonavir OR Tenofovir alafenamide + lamivudine + dolutegravir	HIV/AIDS (100)
Ferrous salt	Iron-deficiency anemia (580)
Mebendazole OR albendazole	
Artemether + lumefantrine OR Artesunate + amodiaquine OR Artesunate + mefloquine OR Dihydroartemisinin + piperaquine OR Artesunate + Sulfadoxine-pyrimethamine OR Chloroquine	Malaria (220)
Artesunate	
Retinol	Measles (150) Vitamin A deficiency (570)
Paracetamol	Pain and palliative care (weight = 1/T)
Morphine	
Ibuprofen	
Ethambutol + isoniazid + pyrazinamide + rifampicin	Tuberculosis (30)
Amoxicillin OR Amoxicillin + clavulanic acid	Lower respiratory infections (390) Other infectious diseases (370)
Ampicillin	
Benzylpenicillin	
Gentamicin	
Ceftriaxone	Other infectious diseases (370) Meningitis (170)
Cefotaxime	
Procaine benzylpenicillin	Syphilis (50)

1.6.2 | Units per treatment

Affordability is calculated with the price per treatment (formula 3), where units per treatment is an important component in the calculation. However, the original indicator differs from the adapted indicator for children, where units per treatment in the original indicator 3.b.3 are based on the Defined Daily Dosage (DDD), this cannot be used to determine the dosages of children. The DDD is, according to the WHO, the assumed average maintenance dose per day for a drug used for its main indication in adults. (19) There is no standard dosage that fits all children in the age group. As described in section 1.5, children's dosages often depend on other factors, such as body weight and metabolism. Therefore, the units per treatment for the pediatric medicines must be determined separately. More about the units per treatment is explained in the methods section.

1.7 | Previous research

In a pilot study, this adapted methodology was used for the first time to determine access to essential medicines for children (neonates) in Burundi. (17) The methodology was successfully applied to a historical survey of Burundi. In addition, sensitivity analyses were performed by varying units per treatment and the burden of disease.

The influence of the units per treatment on the mean facility score was minimal. This suggests that the transformation of weight-based to age-based dosing, and the duration of treatment dosing has little effect. The pilot only considered neonates, where the difference between the minimum and maximum units per treatment is relatively small. For the other age groups (young children and school aged children), the number of units needed for treatment (NUNT) may have a much bigger influence since the difference in weight and age is larger. (17) The influence of the burden of disease on the facility score was also examined. There is no significant difference when burden of disease data from different years (2015 vs 2019) are used to determine the facility score. There is, however, a decrease in the facility scores when each medicine is given the same weight burden. This suggests that the burden of disease can have a major influence on the facility score. (17) Lastly, the pilot study suggests that other factors such as the NPL, the LPGW wage and medicine pricing can also have a substantial influence. (17)

The historical WHO/HAI data from Burundi used in this pilot study contained a low number of investigated pediatric medicines. On top of that, medicines surveyed did not directly mean that the medicine was accessible. Combining that with a lack of data made it difficult to perform meaningful sensitivity analysis and thereby made it impossible to determine the accuracy of the adapted indicator.

1.8 | Objective of this study

Based on the findings from the pilot study using data from Burundi, this research is going to perform multiple sensitivity analyses on different parameters that influence the adapted SDG indicator 3.b.3 methodology, using a different dataset. These analyses could determine the accuracy of the adapted indicator.

More specifically, the research question is:
What is the robustness of the adapted SDG indicator 3.b.3 methodology regarding the input parameters: national poverty line, numbers of units needed for treatment, and the burden of disease based on multiple sensitivity analyses?

2 | Methods

2.1 | Data source

Insightful sensitivity analyses of the adapted methodology require enough available data on availability and affordability of pediatric medicines. For this study the historical WHO/HAI datasets of different countries were used. As stated before (section 1.7), these individual datasets contained too little data on the availability and affordability of child-friendly medicines. (17) To increase the volume of available data on the 22 medicines in the young medicine basket, the WHO/HAI data from 10 countries were combined into one new main dataset. This dataset represented a hypothetical country (Hypoland) with 25 hypothetical facilities. Some medicines in the young children medicine basket had been surveyed in several of these countries. For these surveyed medicines, data was available for the same or different formulations. The formulation is important, because a surveyed medicine was only considered available when both the correct formulation and dosage was available. For other medicines, it had only been surveyed in one country or not at all. The HIV/AIDS medicines, tuberculosis medicines and artesunate in the young children medicine basket had not been surveyed.

The Hypoland is based on the WHO/HAI survey dataset from the countries: Bolivia (2008), Burundi (2013), China (2012), Haiti (2011), Mongolia (2004), Sudan (2012 and 2013), Tanzania (2012), Kyrgyzstan (2010 and 2015). In these countries, the surveyed facilities were examined, categorized, and merged based on level of care and health sector (private and public). Private Not For Profit was not included because this health sector was only surveyed in a few countries. During the matching, the health sector was considered as much as possible, but it was not feasible everywhere. Since the minimum number of facilities was 25 in the dataset of Kyrgyzstan 2015, the combined datasets also consisted of 25 hypothetical facilities. After that, the medicines and price data were linked to a facility, resulting in data on 19 of the 22 medicines in the young children medicine basket. Appendix 2 provides an example of the final data for facility 1 used for the analysis.

2.2 | Input parameters

Several parameters were needed for the calculation of the adapted SDG indicator 3.b.3. Each parameter and how its value was established for the Hypoland in Microsoft Excel version 16.56 is explained below.

2.2.1 | The nation poverty line (NPL)

“The NPL is the benchmark for estimating poverty indicators that are consistent with the country's specific economic and social circumstances.” (6) Earning below this level will classify you as poor. The World Bank sets the international poverty line with the aim of applying a common standard for measuring extreme poverty in the world. In October 2015, the World Bank set the international poverty line at $1,90 per day. (20) In this study, $1,90 was adopted as the NPL for the Hypoland.

2.2.2 | The Lowest-Paid Government Worker (LPGW) wage

"The LPGW wage is a minimum living wage that employees are entitled to receive to ensure overcome of poverty and reduction of inequalities." (6) In the WHO/HAI datasets of the countries used in the construction for the Hypoland, the LPGW wage in the local currency per day and the corresponding exchange rates was mentioned. The LPGW wage has been converted to United States Dollar (USD) using this exchange rates and then averages were taken. This gave an LPGW wage of $2,609 per day for the Hypoland.

2.2.3 | The number of units needed for treatment (NUNT)

The units per treatment were needed to calculate the price per treatment (formula 3). In the original method, this was determined by the DDD, but this did not apply to children. The NUNT must therefore be determined differently. Based on various assumptions, a standard method was developed. First, the recommended dosage for young children (age: 1-59 months or weight: 4,3 – 18,1 kg (18)) was examined. This information was taken from the WHO Pocket Book of Hospital care for Children (WHO PB). If the information was not available in the WHO PB, British National Formulary for Children and Supplementary: Standard Treatment Guidelines and Essential Medicines List South Africa were used. (18) Next, the actual dose per medicine was calculated per day or gift. These were rounded off to whole units according to the assumptions shown in table 4. For example, that only 2 tablets per gift per day can be swallowed by a child or that 0,5 mL was the minimum amount for oral drinks and injections. Lastly, the duration of the treatment was taken into account. For chronic treatment, the NUNT was based on 30 days. In addition to the average NUNT, the minimum NUNT and maximum NUNT were also calculated because there is a large age and weight difference in the young children age group. An example of two NUNT calculations is shown in table 5. The NUNT was calculated for all medicines in the medicine basket, considering different dosages and formulations. In Appendix 3 the complete list of the average NUNT, minimum NUNT and maximum NUNT for young children can be found. In summary, the units per treatment in formula 3 has been replaced by the average NUNT in the adapted method.

Table 4 *A list of the assumptions on which the NUNT has been determined.*

Cap/tab	
Range NUNT	0,5 – 2 tab/cap per gift
Minimum NUNT	0,5 tablet
Maximum NUNT	2 tab/cap per gift
Average NUNT	Always rounded to a whole number
Breaking	Gastro-resistant cap/tab does not break, according to the Dutch Farmaceutisch Kompas. With other tablets, breaking to half is possible.
Oral drinks and injections	
Range NUNT	0,5 – 10 mL per gift
Minimum NUNT	0,5 mL per gift
Maximum NUNT	10 mL per gift
Round off	To whole milliliters (1 – 10 mL)
Other dosage forms	
Having	Rectal dosage forms and powder sachets cannot be halved.

Vials and tubes	
Vial	At least 1 vial is used per day.
	No half vial can be given. The vials are always plural.
Tube	No part of a tube can be given: 1 tube per gift.
Comments	
NA	When the minimum, average and maximum NUNT fall outside the established range, and are therefore illogically high or low.
Average NUNT the same as maximum or minimum NUNT	If the average NUNT is already equal to the minimum or maximum per gift, then the minimum or maximum NUNT (respectively) is equal to the average NUNT.

Table 5 *An example of two NUNT calculations: ibuprofen 200 mg cap/tab and gentamicin 40 mg/mL injection.*

Ibuprofen 200 mg cap/tab				
Dosage	5 – 10 mg/kg in 3 – 4 times a day (chronic treatment)			
NUNT	**Age**	**Weight**	**Dose**	**NUNT value**
Minimum NUNT	1 month	4,3 kg	5,0 mg x 4,3 kg = 21.5 mg/gift	0,5 cap/tab * 3 times * 30 days = 45 cap/tab
Average NUNT	30 months	11,2 kg	7,5 mg x 11,2 kg = 84 mg/gift	1 cap/tab * 3 times * 30 days = 90 cap/tab
Maximum NUNT	59 months	18,1 kg	10 mg x 18,1 kg = 181 mg/gift	1 cap/tab * 4 times * 30 days = 120 cap/tab
Gentamicin 40 mg/ml injection				
Dosage	7,5 mg/kg in 1 dose (5 days)			
NUNT	**Age**	**Weight**	**Dose**	**NUNT value**
Minimum NUNT	1 month	4,3 kg	(7,5 mg x 4,3 kg)/ 40 mg/mL = 0,81 mL/day	0,5 mL * 1 time * 5 days = 4 mL
Average NUNT	30 months	11,2 kg	(7,5 mg x 11,2 kg)/ 40 mg/mL = 2,10 mL/day	2,0 mL * 1 time * 5 days = 10 mL
Maximum NUNT	59 months	18,1 kg	(7,5 mg x 18,1 kg)/ 40 mg/mL = 3,39 mL/day	3,0 mL * 1 time * 5 days = 15 mL

2.2.4 | The burden of disease

The burden of disease provides information about premature death, disability and loss of health and is expressed in DALY. (6) The global burden of disease was used on two occasions in the adapted method. First, it was used in the selection of diseases per age group. (17) (18) Second, the global burden of disease was used to assign a weight to each pediatric medicine. The weight was calculated by dividing the burden of disease per medicine by the total number of burden of disease in the medicine basket. This information came from the WHO's GHE, which provides data on death and disability worldwide, by region and country, and by age, gender, and cause. (13) Each medicine in the medicine basket has previously been linked to one or more GHE code, which is explained in section 1.6.1. Next, the number of DALYs belonging to the GHE code of boys and girls (1-59 months) were added together. This was done both globally and separately for the six WHO regions (African Region (AFR), Region of the Americas (AMR), South-East Asian Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR) and Western Pacific Region (WPR)). An overview of the regional burden of diseases can be found in Appendix 4.

The associated weight burden was then linked to the medicines in the basket. Certain medicines fall under two diseases, then both burden of disease values were included for that medicine. An example is retinol which is prescribed for measles and vitamin A deficiency (table 6). (6)

There was no burden of disease for pain and palliative medication (paracetamol, ibuprofen, and morphine). Therefore, in the original method and the adapted method, the weight was calculated as 1/T. Where T was a total number of medicines in the surveyed basket, assuming an equal use of the pain medication compared to the other medicines. (6)

Table 6 *An example calculation of how weight is determined based on the burden of disease.*

Medicine name	Affiliated disease (GHE code)	Burden of disease for both genders	Burden of disease per medicine	Total burden of disease	Weight
Retinol	Measles (150)	11.574.752	12.234.129	640.456.668	0,019102197
	Vitamin A deficiency (570)	659.377			

2.3 | Dataset selection

The main dataset was the set that represented the Hypoland with 25 hypothetical facilities and all surveyed medicine data. Of this dataset two smaller datasets were created: the base case dataset and the price dataset.

2.3.1 | Base case dataset

When creating the base case dataset, the NUNT was taken into account. The medicines and formulations that had a average NUNT were examined in advance and given preference. After that, formulations with associated availability and prices were selected at random, regardless of whether a price was known. Appendix 2 provides an example of the final data for facility 1.

2.3.2 | Price dataset

The price dataset was created with the aim of having as much price data as possible, to be able to study the effects on affordability. Therefore, formulations for which the most price data was available were selected. Subsequently, facilities in countries with the most price data on these formulations were given priority in the rematching and selection of facilities. Appendix 2 also provides an overview of facility 1 for the price dataset.

2.4 | Data analysis

2.4.1 | Base case analysis

The baseline scenario (table 7) was a scenario that most closely resembles the original SDG indicator 3.b.3 methodology in which only necessary adjustments were made (table 3).

Table 7 An overview of the parameters in the base case scenario.

Base case scenario	
The national poverty line	$1,90 per day
The lowest-paid government worker	$2,609 per day
Burden of disease	Based on global 2010
Burden of disease: pain medication	1/medicine basket (1/22 = 0,045454545)
NUNT	Average NUNT

According to the original methodology, the $SDG_{3.b.3}$ value (formula 1) is the endpoint. Only the facilities with a facility score >80% are represented in this outcome, but as already pointed out in the Burundi pilot study, the chance that this would happen with the WHO/HAI data was very small. (17) It was therefore decided to use the average facility score as the endpoint. This endpoint could easily be compared with each other when sensitivity analyses were performed and the difference between facilities were better reflected.

2.4.2 | Sensitivity analyses

Analysis NPL

The NPL was based on the international poverty line, but in reality this line is different for high- and low-income countries. The amount of influence of this parameter on the average facility score was determined in the scenario NPL (table 8). The NPL was varied by 10% ($2,09 - $1,71).

Table 8 An overview of the parameters in analysis NPL.

Analysis NPL		
Scenario NPL maximum	The national poverty line	$2,09 per day
Scenario NPL minimum	The national poverty line	$1,71 per day
The lowest-paid government worker		$2,609 per day
Burden of disease		Based on global 2010
Burden of disease: pain medication		1/medicine basket (1/22 = 0,045454545)
NUNT		Average NUNT

Analysis NUNT

During the calculation of the NUNT, averages were taken of the ages, weights, and dosing ranges. Since averages were taken, it was important to see what the influence of the NUNT was and how the facility score changes by using a different value of the NUNT. The NUNT analysis consisted of four scenarios. A minimum and maximum NUNT has been calculated in two different ways.

- When formulating the average NUNT, a minimum NUNT and a maximum NUNT have also been determined. In Appendix 4 these values can be seen.
    - Maximum NUNT: based on the weight of children of 59 months.
    - Minimum NUNT: based on the weight of children of 1 month.

- The average NUNT was used to calculate a new minimum and maximum value. In this scenario the variation was set on 60% because the difference between the average weight (11,2 kg), the minimum weight (4,3 kg) and the maximum weight (18,1 kg) was approximately 60%. So, this resembles the minimum and the maximum of the dosing range.
    - NUNT +60%: average NUNT + 60%
    - NUNT -60%: average NUNT - 60%

Table 9 *An overview of the parameters in analysis NUNT.*

Analysis NUNT		
The national poverty line		$1,90 per day
The lowest-paid government worker		$2,609 per day
Burden of disease		Based on global 2010
Burden of disease: pain medication		1/medicine basket (1/22 = 0,045454545)
Scenario maximum NUNT	NUNT	Maximum NUNT
Scenario minimum NUNT	NUNT	Minimum NUNT
Scenario NUNT +60%	NUNT	Average NUNT + 60%
Scenario NUNT -60%	NUNT	Average NUNT – 60%

Analysis burden of disease

The burden of disease was an important parameter that may have a relevant influence on the facility score. (17) As indicated before, the burden of disease was used in different ways in the method. Therefore, several scenarios were performed in which the burden of disease was used differently.

First, a sensitivity analysis was performed in which the burden of disease was no longer determined based on the GHE global 2010. In this sensitivity analysis, the burden of disease was determined at regional level. The 10 countries that form the Hypoland came from 5 regions in the world. These 5 regions together (scenario 2) and the regions separately (scenario 2.a to 2.e) were used in different scenarios (table 10).

Table 10 *An overview of the parameters in analysis burden of disease region.*

Analysis burden of disease region		
The national poverty line		$1,90 per day
The lowest-paid government worker		$2,609 per day
Scenario 2	Burden of disease	Based on the 5 regions (AFR, AMR, EU, EMR, WPR) where the data for the Hypoland comes from.
Scenario 2.a	Burden of disease	Based on region: AFR
Scenario 2.b	Burden of disease	Based on region: AMR
Scenario 2.c	Burden of disease	Based on region: EU
Scenario 2.d	Burden of disease	Based on region: EMR
Scenario 2.e	Burden of disease	Based on region: WPR
Burden of disease: pain medication		1/medicine basket (1/22 = 0,045454545)
NUNT		Average NUNT

Second, we looked at which medicines were surveyed from the young children medicine basket. In this scenario (table 11), the main issue was that medicines that have not been surveyed were not considered in the calculation. The medicine basket consisted of 22 medicines, of which only 19 medicines have

been surveyed. The HIV/AIDS medicines, tuberculosis medicines and artesunate have not been surveyed. So, these 3 medicines were taken out, with the result that 2 diseases were also expired. Next to that, the pain medication was determined by 1/19 instead of 1/22. Normally, no distinction was made between medicines that have or have not been surveyed. However, this could certainly influence the facility score.

Table 11 *An overview of the parameters in analysis burden of disease surveyed.*

Analysis surveyed burden of disease		
The national poverty line		$1,90 per day
The lowest-paid government worker		$2,609 per day
Scenario 3	Burden of disease	The medicines that have not been surveyed are not considered. Based on global 2010.
Burden of disease: pain medication		1/surveyed medicines (1/19 = 0,052631578)
NUNT		Average NUNT

Third, a sensitivity analysis was performed in which the burden of disease was not divided based on the diseases but based on the number of medicines per disease. There were several medicines in the medicine basket for every disease. Normally, the burden of disease was included per medicine but in scenario 4 (table 13), the weight (= burden per disease / total burden) was distributed over the number of medicines that were included by diseases. Table 12 shows an example: for diarrheal diseases 2 medicines are included (oral rehydration salts and zinc sulfate), therefore the burden of disease was divided by 2. For the total burden of disease, all burden of disease per medicine were added together.

Table 12 *An example calculation of how weight is determined based on the burden of disease per medicine*

Medicine name	**Affiliated disease**	**Burden of disease**	**Burden of disease per medicine**	**Total burden of disease**	**Weight**
Oral rehydration salts	Diarrheal diseases	56.053.144	28.026.572	251.421.699	0,11147
Zinc sulfate			28.026.572		0,11147

Table 13 *An overview of the parameters in analysis burden of disease per medicine.*

Analysis burden of disease per medicine		
The national poverty line		$1,90 per day
The lowest-paid government worker		$2,609 per day
Scenario 4	Burden of disease	Based on the burden of disease corrected for the number of medicines per disease that occur in the medicine basket.
Burden of disease: pain medication		1/medicine basket (1/22 = 0,045454545)
NUNT		Average NUNT

In addition to scenario 4, two more sub-scenarios were performed, in which more than just the burden of disease was varied. In the first sub scenario (scenario 4.a), the weight for the pain medication was determined by dividing 1 by the number of diseases that were surveyed (weight = 1/9). In the second sub-scenario, in addition to the calculation of the pain medication, the medication not surveyed was also removed from the analysis (scenario 4.b). An overview can be seen in table 14.

Table 14 An overview of the parameters in the additional scenarios of the burden of disease analysis per medicine.

Additional analysis burden of disease per medicine		
The national poverty line		$1,90 per day
The lowest-paid government worker		$2,609 per day
Scenario 4.b	Burden of disease	Based on the burden of disease corrected for the number of **surveyed** medicines per disease that occur in medicine basket.
Scenario 4.a	Burden of disease: pain medication	1/surveyed disease (1/9 = 0,111111111)
NUNT		Average NUNT

For the last sensitivity analysis performed, no difference in the burden of disease was made. This means that the same burden applies to every medicine in the basket. From this scenario 5, additional sub-scenarios have been performed. Several previously mentioned scenarios were combined with scenario 5 (table 15).

Table 15 An overview of the parameters in analysis equal burden of disease.

Analysis equal burden of disease		
The national poverty line		$1,90 per day
The lowest-paid government worker		$2,609 per day
Scenario 5	Burden of disease	Weight is equal to total burden/22 (medicine basket)
Scenario 5.a	Burden of disease	Weight is equal to total burden/19 (surveyed medicine). Non-surveyed medications have been removed.
Scenario 5.b	Burden of disease	Weight is equal to total burden/9 (surveyed diseases). Non-surveyed medications have been removed (scenario 3) Also, adjusted for the number of medicines per disease (scenario 4).
Scenario 5.c	Burden of disease	Weight is equal to total burden/9 (surveyed diseases). Non-surveyed medications have **not** been removed. Also, adjusted for the number of medicines per disease (scenario 4).
Burden of disease: pain medication		Same as the other medicines
NUNT		Average NUNT

All analysis were performed with the help of R Studio version 1.4.1717.

3 | Results

3.1 | General information

3.1.1 | Base case dataset

The base case dataset included 25 facilities in which 19 medicines were surveyed. It differed per facility whether the medicine was available and what the associated price was. Then it was checked whether it was also accessible (available and affordable). An overview of the availability, accessibility, and facility scores of the facilities is shown in Appendix 5. A total of 173 medicines were available, of which 148 medicines were also accessible. In figure 4 the facilities are plotted against their associated facility score. The results showed that the scores were between 7,16 – 50,29% and there was an average facility score of 35,25%.

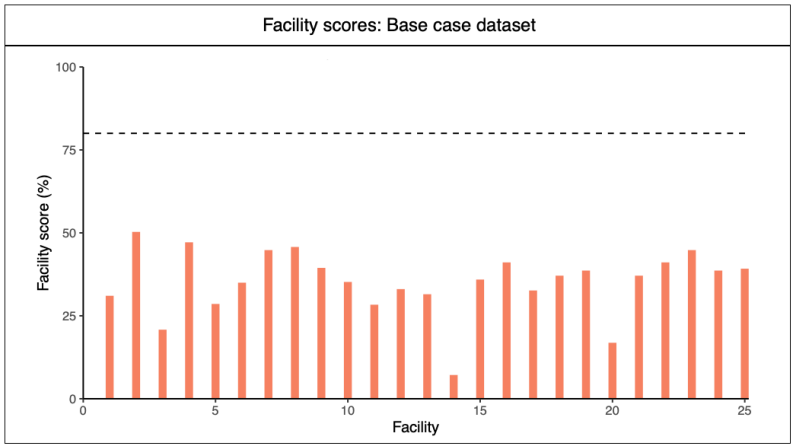

Figure 4 *The facility scores of the 25 facilities of the base case dataset. The dotted line indicates the 80% threshold. The average facility score for the base case dataset is 35,25% (range: 7,16 – 50,29%).*

3.1.2 | Price dataset

In the price dataset a total of 314 medicines with an associated price were available, this is 141 more medicine prices compared to the base case dataset. Of all surveyed medicines, 299 medicines were accessible. The number of surveyed medicines and facilities were the same as the base case dataset. More information about the price dataset can be found in Appendix 5.

The base case scenario that most closely resembled the original method gave an average facility score of 68,18% in the price dataset with a spread of 51,56 – 82,20%. All scenarios performed on the base case dataset, except scenario 2 and its sub-scenarios, were also performed on the price dataset and were compared with the average facility score of 68,18%. Figure 5 shows the facility scores of the individual facilities. Compared to the base case dataset, these scores were much higher in this dataset.

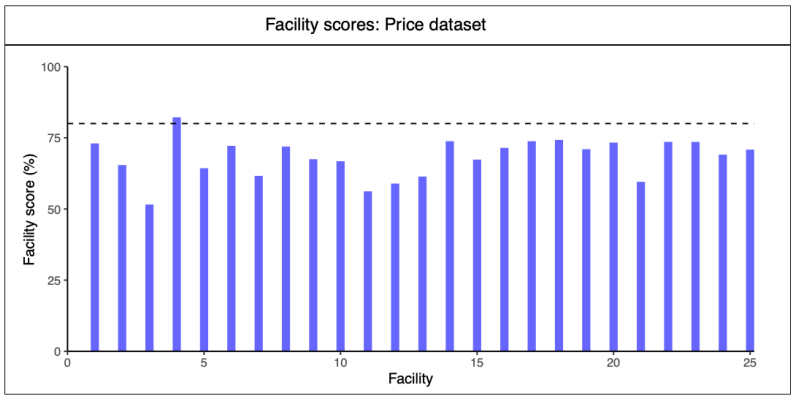

Figure 5 *The facility scores of the 25 facilities of the price dataset. The dotted line indicates the 80% threshold. The average facility score for the price dataset is 68,18% (range: 51,56 – 82,20%).*

3.2 | Sensitivity analysis

Different sensitivity analyses were performed on two datasets. First, the results of the base case dataset are shown using multiple one-dimensional bars (figure 6). In each sub-figure a bar was shown in which the scenarios were compared with the base case average facility score of 35,25%. An important note, in none of the scenarios did the average facility score exceed 80%. Second, the results of the price dataset are presented (figure 7). The scenarios were plotted with their minimum, average and maximum facility scores. The price dataset showed certain scenarios in which a facility had a facility score of >80%. The average facility scores of the various scenarios were all below 80%, with the base case scenario average facility score of 68,18%. An overview of the average facility scores of the different scenarios per dataset can be seen in Appendix 6.

3.2.1 | Base case dataset

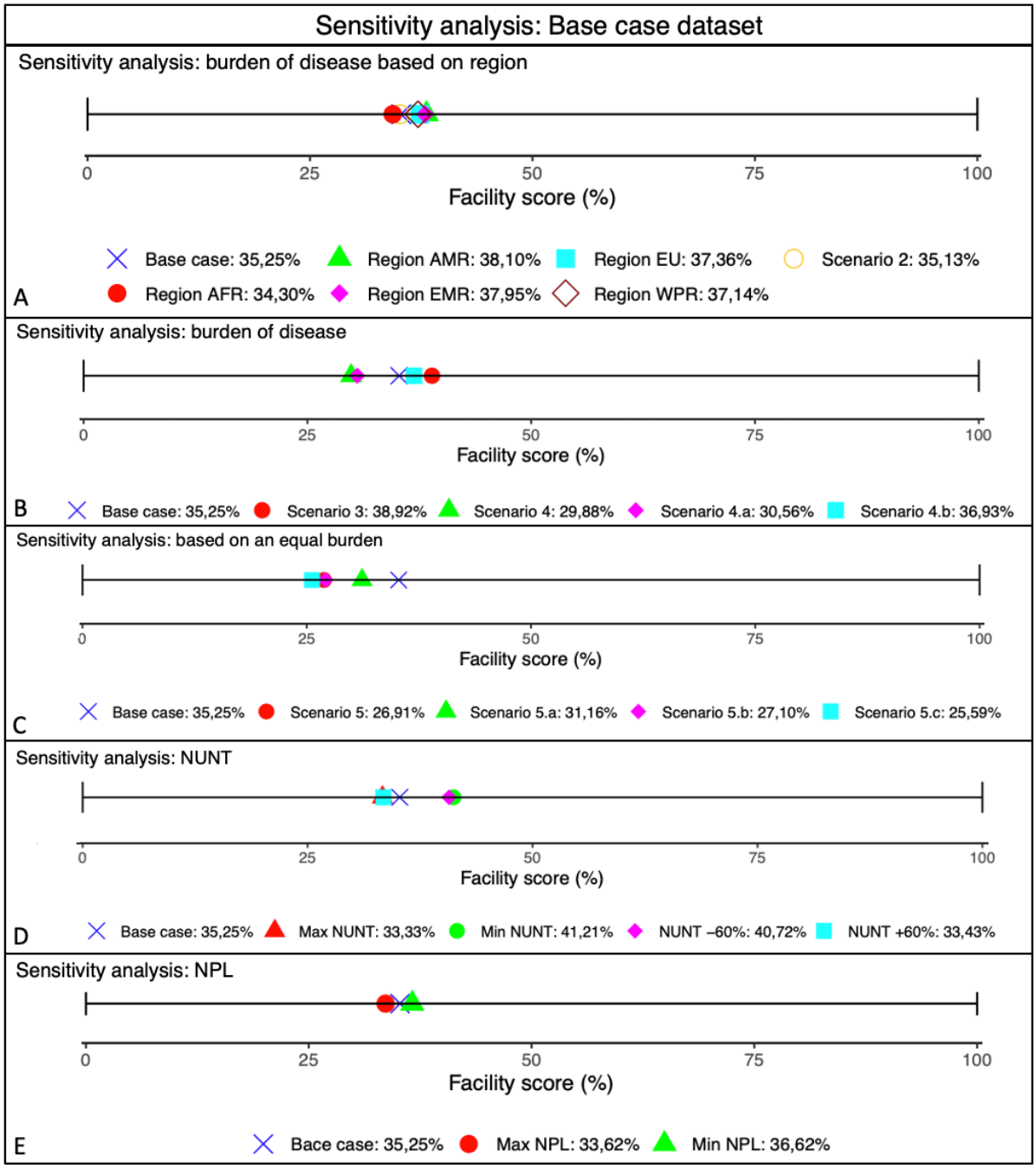

Figure 6 *The results of the sensitivity analyses on the base case dataset in the form of one-dimensional bars.* ***A****: Sensitivity analysis varying global burden for regional burden of disease.* ***B:*** *Sensitivity analysis varying the weight of the burden of disease.* ***C****: Sensitivity analysis based on an equal weight of the burden of disease.* ***D****: Sensitivity analysis varying the average NUNT for the minimum NUNT and maximum NUNT.* ***E****: Sensitivity analysis varying the NPL with 10% ($2,09 - $1,71).*

The burden of disease

The first three bars in figure 6 are about the burden of disease. The top bar (figure 6.a) showed that the region of the burden of disease had little influence on the average facility score. The scores of the scenarios 2 to 2.c were between 34,30 – 38,10%.

Figure 6.b showed the scenarios in which the burden of disease weighting was performed in a different way than in the original methodology. The weight of the burden of disease was distributed over

the number of medicines that were included for the diseases, which had much more influence on the spread of average facility scores. Scenarios 4 and 4.a had a lower average facility score, 29,88% and 30,56% respectively. Scenarios 3 and 4.b had a higher average facility score than the average base case facility score. When the weight of the burden of disease was equal divided (scenario 5 to 5.c), the average facility scores were below 35,25% (Figure 6.c).

The NUNT

Two different maximum and minimum NUNT scenarios have been performed. The two maximum scenarios were below the average facility score, while the minimum scenarios were above it (figure 6.d). The difference between the two maximum average facility scores was 0.1% and the difference between the two minimum average facility scores is 0,49%.

The NPL

When the NPL was varied by 10%, the average facility scores were 33,62% ($2,09) and 36,62% ($1,71). Sub-figure 6.e shows that the spread of the average facility score was very small.

3.2.2 | Price dataset

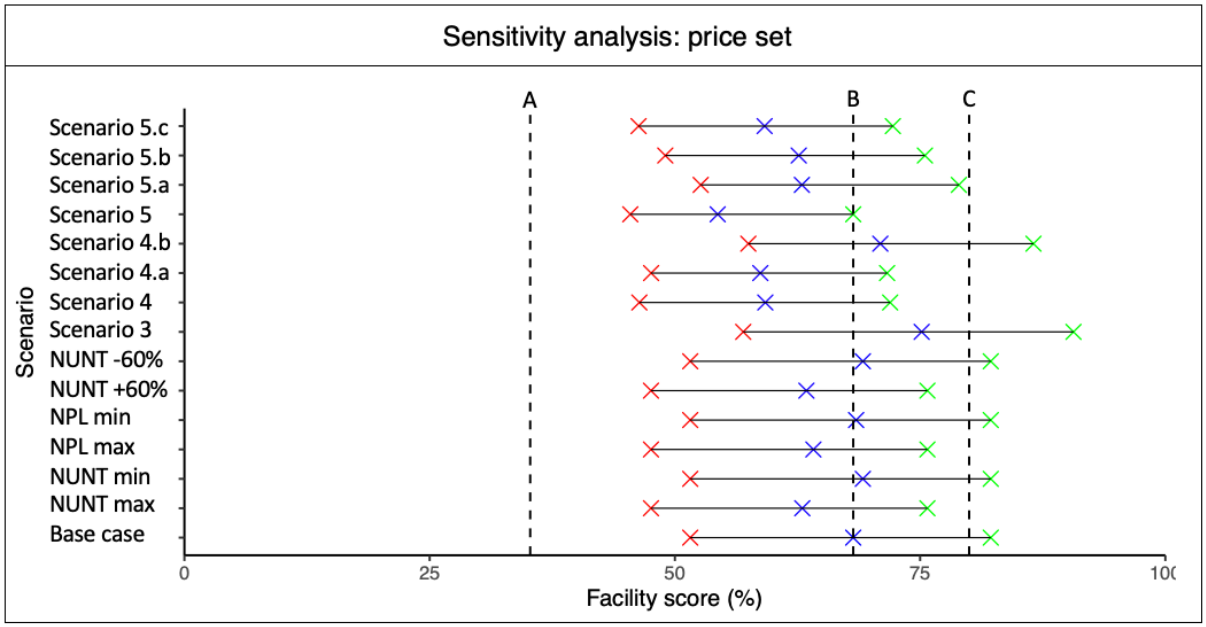

Figure 7 *The results of the sensitivity analyses on the price dataset. There are three dotted lines in the figure: A = 35,25% and is the average facility score of the base case scenario of the base case dataset. B = 68,18% and is the average facility score of the base case scenario of the price dataset. C = 80% and the threshold value from the original SDG indicator 3.b.3 method. Red X = the minimum facility score. Blue X = the average facility score of the scenario. Green X = the maximum facility score. The corresponding facility scores are shown in Appendix 6.*

The burden of disease

In scenario 5 and its sub-scenarios the weight of the burden of disease was equally distributed. In each scenario this happened in a different way, as explained in the methods. The average facility scores for scenarios 5, 5.a, 5.b and 5.c were respectively 54,37%, 62,95%, 62,63% and 59,15%. These values were below the average facility score of 68,18%, just like the base case dataset. The decrease in average facility scores in scenarios 5 and 5.a were larger in the price dataset, but the decrease in average facility scores in scenarios 5.b and 5.c were smaller in this dataset than in the base case dataset.

In scenario 3, scenario 4 and its sub-scenarios, the burden of disease was equally distributed over the medicines. In scenarios 3 and 4.b, the non-surveyed medicines were also removed from the analysis. This resulted in a higher average facility score (75,16% and 70,94% respectively), because the blue crosses appear above the dotted line B, as can be seen in figure 7. The green crosses of these scenarios were also above dotted line C, which shows that at least 1 facility had a facility score above the threshold of 80%. The differences between the average facility scores of scenarios 3, 4, 4.a and 4.b and 68,18% were greater than the differences between the average facility scores of these scenarios in de base case dataset and 35,25%.

The NUNT

Similar variations were seen in average facility score between the price data set and the base case set for the various NUNT scenarios. In the minimum NUNT scenario the minimum facility score was 51,65%, the average facility score was 69,16%, and the maximum facility score was 82,80%. For the maximum NUNT scenario, the facility scores of 47,56%, 63,99% and 75,74% applied to the minimum, average and maximum respectively.

The NPL

The average facility score of the NPL $1,71 was 86,48% with a range of 51,56 – 82,20%. The range of the NPL $2,09 was 47,46 – 75,74% with an average facility score of 64,12%. This was comparable to the NPL scenario values of the base case dataset. The average facility score of the minimum NPL also had a higher value and the maximum NPL had a lower value than the average facility score of the base case dataset.

4 | Discussion

For this study we assessed the robustness of the adapted SDG indicator 3.b.3 methodology. We performed sensitivity analyses on the input parameters; NPL, NUNT and burden of disease. Changing the NPL did not result in a relevant shift of the average facility score and has therefore no influence on the robustness of the adapted method. The results show that using the NUNT instead of units per treatment has little impact on the average facility score and it does not matter whether the minimum, maximum or average NUNT is used. Therefore, using the NUNT as DDD is a reliable way to include the duration of therapy for children in the adapted method. Also, both the base case dataset and the price dataset show little influence on the average facility score when changing the burden of the disease. So, the burden of disease has also no influence on the robustness of the adapted method.

4.1 | Robustness of the adapted method

4.1.1 | The relevance of the average facility score

The results show that the individual facility scores do not reach the 80% threshold that is used in the methodology. To obtain a relevant $SDG_{3.b.3}$ score from formula 1, this threshold of 80% must be reached. This is further explained in section 1.4. If no facility achieves a facility score of 80%, the $SDG_{3.b.3}$ is 0%, meaning that there is insufficient access to essential medicine.

Lowering this threshold is not the solution. As an example out of a previous study, the WHO/HAI data of Haiti (2011) showed $SDG_{3.b.3}$ scores of ~10% and ~40% when the threshold was lowered to 40% and 20% respectively. With the current threshold of 80% this score was 0%. (21) A threshold of 20% means that only 20% of the surveyed medicines is accessible.

However, with the facility score progress can be measured. A facility can have an increase in the facility score from 20% to 60%, which shows an absolute improvement in accessibility, but this is not reflected in the $SDG_{3.b.3}$ score. It does not show in which area (disease area, health sector or geographical) this progress is made. Therefore, to demonstrate the robustness of the adapted method, we did not use the $SDG_{3.b.3}$ score but the average facility score. A change of a few percent in the average facility score does not have a relevant influence. Although, a change of a few precent in the individual facility score can have a relevant influence if it results in the achievement of the 80% threshold.

4.1.2 | The validation of indicators

In March 2015, the United Nations Statistical Commission created the Inter-agency and Expert Group on SDG Indicators (IAEG-SDGs) with the mandate to develop and implement the global indicators framework for the SDGs and targets of the 2030 Agenda. The work of the IAEG-SDGs includes regularly reviewing methodological developments and issues related to the indicators and their metadata, and the sharing of experiences and best practices on SDG monitoring. (22) The IAEG-SDGs created the Tier Classification for Global SDG Indicators to classify the global indicators based on their level of methodological development and the availability of data at the global level. (23) The tier system only supports the development of global implementation strategies and does not favor indicators. The system has three tier levels: (24)

> **Tier I** – Indicator is conceptually clear, has an internationally established methodology and standards are available, and data are regularly produced by countries for at least 50% of countries and of the population in every region where the indicator is relevant.
> **Tier II** – Indicator is conceptually clear, has an internationally established methodology and standards are available, but data are not regularly produced by countries.
> **Tier III** – No internationally established methodology or standards are yet available for the indicator, but methodology/standards are being (or will be) developed or tested.

In December 2020, 130 indicators were classified as Tier I, 97 as Tier II and 4 indicators have multiple tiers (different components of the indicator are identified into different tiers). (25) Within the SDGs, the average tier level of the indicators varies. For example, the goals related to people (SDG 1 to 5) have a higher average tier level, than the goals relating to planet (SDG 6, 12, 13, 14 and 15).

The original SDG indicator 3.b.3 is classified as Tier II. (25) The adapted SDG indicator 3.b.3 is not classified yet, but it could be a valuable addition to the original SDG indicator. Implementation of this adapted method is only considered when "a crucial aspect of a target is not being monitored by the current indicator(s) or to address a critical or emerging new issue that is not monitored by the existing indicators, or when a whole goal has very few Tier I or Tier II indicators for the follow up". (26) For this specific SDG indicator 3.b.3, the crucial aspect (access to essential medicine for children) is not being monitored.

4.2 | Assumptions of accessibility & affordability

Comparing the two datasets shows a large difference in the number of prices. The price dataset contains 314 prices with an average facility score of 68,18%, whereas the base case dataset contains 173 prices with an average facility score of 35,25%. It seems that a large increase in price data also leads to a large increase of the average facility score. Affordability is, amongst others, determined by price, but this is only registered during data collection when the medicine was available at time of data collection. (6) As

the increases in price data and average facility score seem to relate, low access to medicine is not caused by affordability of medicines. Further statistical analysis is necessary to prove this assumption, but this is beyond the scope of this study.

In addition to the NUNT, two other important parameters that affect affordability are the NPL and the LPGW wage. Both parameters are internationally acceptable values, but in practice not always representative. (27) For the adapted method in this study we used the defined international poverty line as the NPL, however, this can vary between individual countries. On the other hand, the LPGW-based metric is easy to apply and to understand. However, this metric can overestimate or underestimate affordability, because a substantial proportion of the population in some countries earns less or more than the LPGW respectively. (28) The costs, expressed in number of daily wages, of a course of medicines for the LPGW cannot be extrapolated to the whole population. (27) Although these arguments could reject the adapted method in this study, it is difficult to set one unique standard of affordability, even though various methods tried to define this concept. It would help if scholars and policy makers discuss and agree upon an international benchmark for the affordability, which ensures intertemporal and international comparison, and transparency. (27) Until then, the assumptions made in this study still substantiate the adapted method.

As the assumption above suggests, the problem of access to medicine may be due to low availability rather than affordability. A review study has examined the availability and affordability of medications for children on a total of 18 multicenter cross-sectional studies. The result of the review study showed that for most pediatric medicines availability was low in the public and private sector. (29) This result seems to be related to the assumption made about the comparison of the two datasets. The low availability in the public sector is associated to insufficient supply, due to the high demand of these free or low costs medicines. Supply side problems are caused by a combination of factors such as predicting and maintaining inventory levels, inefficient distribution systems, insufficient funding, or leakage of medicines for private resale. (29)

4.3 | Strengths and limitations

4.3.1 | Strengths

As indicated in section 1.4, there is currently no standardized way to determine the access to essential medicines for children. By modifying the original indicator 3.b.3 of the general population, it could be possible to say something about access to essential medicine for children in the future. This study shows that the original SDG 3.b.3 indicator was successfully modified to a child-specific indicator. The average facility scores in the different sensitivity analyses do not change with a relevant difference, so for the first time it can be concluded that robustness of the adapted SDG indicator 3.b.3 methodology is proved.

For this study, a list of the NUNT for the young children has been created. This list did not exist before and can be found in Appendix 3. With this list, it is possible to replace the DDD in the adapted methodology. In addition to the list of the NUNT for young children, the list for school aged children is also created. Due to the scope of this study, this list has not been used but could be found in Appendix 3.

4.3.2 | Limitations

For this study, no statistical tests with significant outcomes have been performed on the results of the sensitivity analyses. The conclusions are based on our own experiences, knowledge, and assumptions, which is a relevant knowledge gap for future research on the adapted method.

The findings in this study are difficult to put directly into practice. All findings and conclusions are made on a hypothetical approach to reality. Although, the historical WHO/HAI data used for the Hypoland is real, it was not initially collected for the purpose of this study. We were forced to create our own dataset, based on the low available data of the availability and affordability of child-friendly medicines. (29)

The reason for low availability of data is twofold: there is a lack of surveys on pediatric medicines and the surveys, conducted in the public domain, do not contain enough pediatric medicines. (30) For example, of the 55 WHO/HAI surveys studied, only 17 surveys evaluated medicine accessibility on essential medicines for children. (29) More studies on medicine access for children are needed, because of the unique requirement of children. The access data on adult medicine cannot simply be translated into access data for children. Due to the low available data for children, no barriers can be identified which reduces the potential transition towards better access to medicine for children. (6) (29)

A possible solution could be the use of the WHO EMP MedMon tool. This app allows routine monitoring of medicine prices and determination of availability in a sustainable, cost-effective, and timely manner. (29) Additionally, the tool can be adapted to the needs of each country. It may therefore be possible to provide child-appropriate medicines data collection on a regular basis. Another solution could be the inclusion of a range of child-appropriate medicines in national surveys. (30) The medicine baskets for the different age groups (neonates, young children, and school aged children) and the NUNT lists with the child-friendly formulations and doses can form a good basis for these national surveys.

Another limitation of this study is that the sensitivity analyses are only performed on data that represents the young children medicine basket. The medicine baskets for the other age groups (neonates and school aged children) are not considered in this study. The input parameters (NPL, NUNT and burden of disease) are expected to have an overall comparable influence on the average facility scores of the scenarios as to those of the young children. However, the influence of the NUNT is expected to be less for the neonates, because the weight and age range in this group is smaller than that of the young children. This is also shown in the results of the Burundi pilot study. (17) Despite this presumption, the NUNT is still a reliable replacement for the DDD in the adapted method.

4.4 | Recommendations for future research

4.4.1 | Testing scenarios

As discussed earlier, it is shown that the necessary changes have no relevant influence on the average facility scores, therefore it can be assumed that it does not affect the robustness of the adapted methodology. On top of that, we have tested two scenarios about the use of the burden of disease weighting in the adapted method.

The first scenario focusses on the non-surveyed medicines and what happens when they are removed from the analysis (scenario 3). In the original method, a country is charged when a medicine from the medicine basket is not surveyed. This results in a lower facility score and $SDG_{3.b.3}$ score, which shows an underestimation of access to essential medicine. Therefore, removing the non-surveyed medication from the analyses seems to be reasonable. However, testing this assumption with the adapted method, causes an irrelevant increase in the average facility score.

For the second scenario, I believe that the burden of disease should be adjusted for the number of medicines per disease (scenario 4), or the burden of disease will be overestimated. If a disease has many medicines and the burden of disease is not divided over the number of medicines per disease, then the total burden and weight on that medicine consists for a large part of that disease. This reduces the influence of other diseases, making it less important whether these medicines are accessible. In some cases, this could give an incorrect conclusion of access to essential medicine. This could be prevented by dividing the burden of disease over the number of medicines per disease in the medicine basket. Testing this scenario with the adapted method, causes an irrelevant decrease in the average facility score. Meaning that changing the burden disease based on the above scenarios, although it seems to make sense, does not have a relevant influence on the adapted method. Future research should test this hypothesis on the other age groups (neonates and school aged children) and on the original methodology.

4.4.2 | A complicated method

The original SDG indicator 3.b.3 methodology is a complicated calculation that determines access to essential medicine. It is the first method that incorporates affordability and affordability into one score. (7) However, this results in a very complicated calculation with many different steps, which makes it hard for countries to implement this methodology. It is therefore suggested to create a standard user-friendly model where only survey values and country specific input parameters have to be entered. The model would then perform the calculations itself, so that the $SDG_{3.b.3}$ score is almost immediately calculated.

A basket of core set of relevant essential medicines for primary health care has been determined for the original method, with the number of units and duration per treatment. (6) Using this list, a country knows exactly which medicines, doses and quantities must be surveyed. For the adapted method, we

have formed different baskets of core set of relevant essential medicines for the three age groups with the accompanying NUNT list, which includes the number of units and duration per treatment. These lists could make it easier for a country to conduct surveys and thus implement the adapted methodology. This could potentially narrow the gap in child-specific data regarding availability and affordability of essential medicines.

The goal of the WHO with creating SDG indicator 3.b.3 is to quantify target 3.b to ensure a policy recommendation for (local, regional, or national) governments. Correct identification of the problems in the affordability and availability of medicines can lead to better access to essential medicines for children. (3) With indicator 3.b.3, a value can be attached to the complex SDG 3, so that progress of access to essential medicine becomes visible over time. The indicator also provides more insight in the individual facility scores, with which health sectors and areas in a country can be analyzed separately. So, in the future it could be possible to gain enough insight through research with this validated child-specific method to contribute to achieving the SDG 3 by 2030.

5 | Conclusion

There is currently no standardized way to determine the access to essential medicines for children. By modifying the original SDG indicator 3.b.3 of the general population, it could be possible to say something about access to essential medicine for children in the future. This study shows that the original SDG 3.b.3 indicator was successfully modified to a child-specific indicator. The average facility scores in the sensitivity analyses on the different input parameters (NPL, NUNT and burden of disease) do not change with a relevant influence, so it can be concluded that robustness of the adapted SDG indicator 3.b.3 methodology is proved.

In this study, a list of the NUNT for the young children age group has been created. With this list it can be concluded that using the NUNT instead of the DDD is a reliable way to include the duration of therapy for children in the adapted method.

For future research, it is important that more studies on access to essential medicine for children are done. The access data on adult medicine cannot simply be translated into access data for children. Due to the low available data for children, no barriers can be identified reducing the potential transition towards better access to essential medicine for children.

6 | Glossary

AFR –	African Region
AMR –	Region of the Americas
BSA –	Body Surface Area
DALYs –	Disability-Adjusted Life Year
DDD –	Defined Daily Dosage
EDW –	Extra daily wages
EML –	WHO Model List of Essential Medicines
EMLc –	WHO Model List of Essential Medicines for children
EMR –	Eastern Mediterranean Region
EUR –	European Region
GHE –	Global Health Estimates
HAI –	Health Action International
IAEG-SDGs –	Inter-agency and Expert Group on SDG Indicators
LPGW –	Lowest-paid government sector worker
MDG –	Millennium Development Goals
NEML –	National Essential Medicines List
NPL –	National poverty line
NUNT –	Number units needed for treatment
SDGs –	Sustainable Development Goals
SEAR –	South-East Asian Region
USD –	United State Dollar
WHO –	World Health Organization
WHO EMP Medmon –	WHO Essential Medicines and Health Products Price and Availability Monitoring Mobile Application
WHO PB –	WHO Pocket Book of Hospital care for Children
WPR –	Western Pacific Region

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Appendix

Appendix 1

Table 1 *The medicine basket of relevant essential medicines for school aged children (5-12 years).*

Medicine name	Affiliated disease
Salbutamol or other short-acting beta-agonist inhaler	Asthma (1190)
Budesonide or other corticosteroid inhaler	
Oral rehydration salts	Diarrhoeal diseases (110)
Zinc sulphate	
Carbamazapine or phenobarbital or phenytoin or lamotrigine	Epilepsy (970)
Valproic acid	
Diazepam or lorazepam or midazolam	
Abacavir + lamivudine + dolutegravir OR Abacavir + lamivudine + lopinavir/ritonavir OR Tenofovir alafenamide + lamivudine + dolutegravir	HIV/AIDS (100)
Ferrous salt	Iron-deficiency anemia (580)
Albendazole	
Artemether + lumefantrine OR Artesunate + amodiaquine OR Artesunate + mefloquine OR Dihydroartemisinin + piperaquine OR Artesunate + Sulfadoxine-pyrimethamine OR Chloroquine	Malaria (220)
Artesunate	
Paracetamol	Pain and palliative care (weight = 1/T)
Morphine	
Ibuprofen	Migraine (990)
Ethambutol + isoniazid + pyrazinamide + rifampicin	Tuberculosis (30)
Amoxicillin OR amoxicillin + clavulanic acid	Lower respiratory infections (390) Infectious and parasitic diseases (20)
Ampicillin	
Benzylpenicillin	
Gentamicin	
Ceftriaxone	Infectious and parasitic diseases (20)
Cefotaxime	

Table 2 *The medicine basket of relevant essential medicines for young children (1-59 months).*

Medicine name	**Affiliated disease (GHE code)**
Oral rehydration salts	Diarrhoeal diseases (110)
Zinc sulphate	
Carbamazapine OR phenobarbital OR phenytoin OR lamotrigine	Epilepsy (970)
Valproic acid	
Diazepam OR lorazepam OR midazolam	
Abacavir + lamivudine + dolutegravir OR Abacavir + lamivudine + lopinavir/ritonavir OR Tenofovir alafenamide + lamivudine + dolutegravir	HIV/AIDS (100)
Ferrous salt	Iron-deficiency anemia (580)
Mebendazole OR albendazole	
Artemether + lumefantrine OR Artesunate + amodiaquine OR Artesunate + mefloquine OR Dihydroartemisinin + piperaquine OR Artesunate + Sulfadoxine-pyrimethamine OR Chloroquine	Malaria (220)
Artesunate	
Retinol	Measles (150) Vitamin A deficiency (570)
Paracetamol	Pain and palliative care (weight = 1/T)
Morphine	
Ibuprofen	
Ethambutol + isoniazid + pyrazinamide + rifampicin	Tuberculosis (30)
Amoxicillin OR Amoxicillin + clavulanic acid	Lower respiratory infections (390) Other infectious diseases (370)
Ampicillin	
Benzylpenicillin	
Gentamicin	
Ceftriaxone	Other infectious diseases (370) Meningitis (170)
Cefotaxime	
Procaine benzylpenicillin	Syphilis (50)

Appendix 2

Table 1 *An overview of the analyzed data for the newly formulated facility 1 of the base case dataset.*

New facility	Original Facility	Level of care	Bask.index	Index	Availability	Price (USD)	API	Formulation	Dose	Unit
1	CPub08	1	1	FOR-36	0	*NA*	ORS	Powder sachet	500	ml
1	DPub27	1	2	FOR-51	1	0	Zinc sulphate	Cap/tab	20	mg
1	DPub27	1	3	FOR-43	0	*NA*	Phenobarbital	Oral solution	3	mg/ml
1	EPr01	private	4	FOR-47	1	0.536225738809139	Valproic acid	Cap/tab	150	mg
1	CPub08	1	5	FOR-26	0	*NA*	Diazepam	Injection	5	mg/ml
1	9	9	6	9	9	*NA*	NA	NA	NA	NA
1	JPub20	1	7	FOR-27	0	*NA*	Ferrous salt	Cap/tab	200	mg
1	GPub02	public	8	FOR-32	1	0.13276884324766	Mebendazole	Cap/tab	100	mg
1	JPub20	1	9	FOR-13	0	*NA*	Artemether + lumefantrine	Cap/tab	20/120	mg
1	9	9	10	9	9	*NA*	NA	NA	NA	NA
1	BPub20	1	11	FOR-50	0	*NA*	Vitamin A	Cap/tab	200000	IU
1	DPub27	1	12	FOR-38	1	0.00978511675629183	Paracetamol	Suspension	24	mg/ml
1	DPub27	1	13	FOR-34	0	*NA*	Morphine	Oral solution	2	mg/ml
1	EPr01	private	14	FOR-30	1	0.0489257060957244	Ibuprofen	Cap/tab	200	mg
1	9	9	15	9	9	*NA*	NA	NA	NA	NA
1	HPub21	1	16	FOR-08	1	0.636032589158969	Amoxicillin	Suspension	50	mg/ml
1	GPub02	public	17	FOR-10	0	*NA*	Ampicillin	Cap/tab	500	mg
1	DPub27	1	18	FOR-15	0	*NA*	Benzylpenicillin	Injection	1	MIU/vial
1	EPr01	private	19	FOR-29	1	0.193256539078111	Gentamicin	Injection	40	mg/ml
1	CPub08	1	20	FOR-21	0	*NA*	Ceftriaxone	Injection	250	mg/vial
1	APub02	1	21	FOR-19	1	0.913616442422954	Cefotaxime	Injection	1	g/vial
1	CPub08	1	22	FOR-46	0	*NA*	Procaine benzylpenicillin	Injection	1	MIU/vial

NA = Not Available. Level of care 1 = public sector facility (primary care facility). Level of care 2 = public sector facility (secondary care facility). Level of care 3 = public sector facility (tertiary care facility). 9 = for non-surveyed medication. Price NA = the price was unknown. Price 0 = when a medicine is free.

Table 2 *An overview of the analyzed data for the newly formulated facility 1 of the price dataset.*

New facility	Original Facility	Level of care	Bask.index	Index	Availability	Price (USD)	API	Formulation	Dose	Unit
1	CPub10	1	1	FOR-36	0	*NA*	ORS	Powder sachet	500	ml
1	DPub41	1	2	FOR-51	1	0	Zinc sulphate	Cap/tab	20	mg
1	CPub10	1	3	FOR-44	1	0.00246971112464281	Phenytoin	Cap/tab	50	mg
1	EPr01	private	4	FOR-47	1	0.536225738809139	Valproic acid	Cap/tab	150	mg
1	JPub12	1	5	FOR-26	1	0.115112249353471	Diazepam	Injection	5	mg/ml
1	9	9	6	9	9	*NA*	NA	NA	NA	NA
1	JPub12	1	7	FOR-27	0	*NA*	Ferrous salt	Cap/tab	200	mg
1	BPub23	1	8	FOR-32	1	0.00969303294333019	Mebendazole	Cap/tab	100	mg
1	HPub20	1	9	FOR-14	1	163.085.279.271.531	Artesunate+Sulfadoxine+Pyrimethamine	Cap/tab	50/500/25	mg
1	9	9	10	9	9	*NA*	NA	NA	NA	NA
1	DPub41	1	11	FOR-49	1	0	Vitamin A	Cap/tab	100000	IU
1	IPub22	1	12	FOR-38	1	0.0217447039028707	Paracetamol	Suspension	24	mg/ml
1	DPub41	1	13	FOR-34	0	*NA*	Morphine	Oral solution	2	mg/ml
1	DPub41	1	14	FOR-30	1	0.0260936446834449	Ibuprofen	Cap/tab	200	mg
1	9	9	15	9	9	*NA*	NA	NA	NA	NA
1	BPub23	1	16	FOR-08	1	0.0161544087033541	Amoxicillin	Suspension	50	mg/ml
1	GPub01	public	17	FOR-10	1	0.113801930670526	Ampicillin	Cap/tab	500	mg
1	CPub10	1	18	FOR-15	1	0.0374866867133284	Benzylpenicillin	Injection	1	MIU/vial
1	FPr01	private	19	FOR-29	1	0.28245683293583	Gentamicin	Injection	40	mg/ml
1	GPub01	public	20	FOR-21	0	*NA*	Ceftriaxone	Injection	250	mg/vial
1	APub21	1	21	FOR-19	1	13.826.242.897.202	Cefotaxime	Injection	1	g/vial
1	FPr01	private	22	FOR-46	1	0.56491366587166	Procaine benzylpenicillin	Injection	1	MIU/vial

NA = Not Available. Level of care 1 = public sector facility (primary care facility). Level of care 2 = public sector facility (secondary care facility). Level of care 3 = public sector facility (tertiary care facility). 9 = for non-surveyed medication. Price NA = the price was unknown. Price 0 = when a medicine is free.

Appendix 3

Table 1 *A list of the number of units needed for treatment for the young children.*

Active ingredient	Formulation	Strength	Unit	Average NUNT	Minimum NUNT	Maximum NUNT
ORS	Powder sachet	200	ml	2	2	4
		500	ml	2	1	6
		1	L	1	1	2
Zinc sulphate	Cap/tab	20	mg	14	5	14
Carbamazepine	Cap/tab	100	mg	60	30	90
	Cap/tab	200	mg	NA	NA	NA
	Oral liquid	100	mg/5 ml	180	60	450
Phenobarbital	Cap/tab	30	mg	60	15	120
	Cap/tab	100	mg	30	15	45
	Injection	100	mg/ml	30	60	60
	Injection	200	mg/ml	15	30	30
	Oral liquid	15	mg/5 ml	600	120	600
Phenytoin	Cap/tab	25	mg	90	30	120
	Cap/tab	50	mg	60	30	120
	Cap/tab	100	mg	60	30	60
	Oral liquid	25	mg/5 ml	480	240	600
	Oral liquid	30	mg/5 ml	420	240	600
	Injection	50	mg/ml	60	15	120
Lamotrigine	Cap/tab	2	mg	NA	NA	NA
	Cap/tab	5	mg	NA	NA	NA
	Cap/tab	25	mg	60	15	60
	Cap/tab	50	mg	30	15	60
	Cap/tab	100	mg	30	15	30
	Cap/tab	200	mg	NA	NA	NA
Valproic acid	Oral liquid	200	mg/5 ml	240	90	300
	Cap/tab	100	mg	60	30	60

	Cap/tab	150	mg	60	30	60
	Cap/tab	200	mg	60	15	60
	Cap/tab	500	mg	30	30	30
Diazepam	Rectal solution	5	mg/ml	1	1	1
	Injection	5	mg/ml	1	0,5	1
Lorazepam	Parenteral solution	2	mg/ml	0,5	0,5	2
	Parenteral solution	4	mg/ml	0,5	0,5	1
Midazolam	Oromucosal solution	5	mg/ml	10	2	20
	Oromucosal solution	10	mg/ml	6	1	20
	Ampoule	1	mg/ml	NA	NA	NA
	Ampoule	10	mg/ml	6	1	20
Abacavir + lamivudine	Cap/tab	120/60	mg	60	60	60
Lopinavir/ritonavir	Oral liquid	400/100	mg/5 ml	NA	NA	NA
	Cap/tab	40/10	mg	120	90	120
	Cap/tab	100/25	mg	60	30	120
Ferrous salt	Cap/tab	60	mg	28	28	42
	Cap/tab	200	mg	14	7	14
	Oral liquid	25	mg/ml	56	56	112
Albendazole	Cap/tab	200	mg	2	2	2
	Cap/tab	400	mg	1	1	1
Mebendazole	Cap/tab	100	mg	6	6	6
	Cap/tab	500	mg	NA	NA	NA
Artemether + lumefantrine	Cap/tab	20/120	mg	6	3	12
Artesunate + amodiaquine	Cap/tab	25/67.5	mg	6	3	6
	Cap/tab	50/135	mg	3	3	3
	Cap/tab	100/270	mg	NA	NA	NA
Artesunate + mefloquine	Cap/tab	25/55	mg	6	3	6
	Cap/tab	100/220	mg	NA	NA	NA
Dihydroartemisinin + piperaquine	Cap/tab	20/160	mg	6	3	6

	Cap/tab	40/320	mg	3	3	6
Artesunate + Sulfadoxine-pyrimethamine	Cap/tab	50/500/25	mg	1	1	1
Sulfadoxine-pyramethamine	Cap/tab	500/25		1	1	1
Artesunate	Cap/tab	50	mg	3	3	3
	Injection	60	mg	NA	NA	NA
	Suppository	50	mg	3	3	3
	Suppository	100	mg	NA	NA	NA
	Suppository	200	mg	NA	NA	NA
Chloroquine	Oral liquid	50	mg/5 ml	30	10	45
	Cap/tab	100	mg	5	5	5
	Cap/tab	150	mg	NA	NA	NA
Vitamin A	Cap/tab	25000	IU	4	2	6
	Cap/tab	100000	IU	2	1	6
	Cap/tab	200000	IU	2	1	3
Paracetamol	Cap/tab	100	mg	150	60	360
	Cap/tab	500	mg	NA	NA	NA
	Suppository	100	mg	150	120	180
	Suspension	120 or 125	mg/5 ml	900	240	1800
Morphine	Cap/tab	10	mg	NA	NA	NA
	Injection	10	mg/ampoule	30	30	30
	Oral liquid	10	mg/5 ml	300	60	720
	Cap/tab (slow release)	10	mg	60	60	120
	Cap/tab (slow release)	200	mg	NA	NA	NA
Ibuprofen	Cap/tab	200	mg	90	45	120
	Cap/tab	400	mg	NA	NA	NA
	Cap/tab	600	mg	NA	NA	NA
	Oral liquid	200	mg/5 ml	180	45	600
Ethambutol	Oral liquid	25	mg/ml	9	3	10
	Cap/tab	100	mg	60	15	60

	Cap/tab	400	mg	30	15	30
Isoniazid + pyrazinamide + rifampicin	Cap/tab	50/150/75	mg	60	30	60
Isoniazid + rifampicin	Cap/tab	50/75	mg	60	30	60
Amoxicillin	Cap/tab	250	mg	20	10	20
	Cap/tab	500	mg	10	10	10
	Suspension	125	mg/5 ml	100	70	100
	Suspension	250	mg/5 ml	90	30	100
	Powder for injection	250	mg/vial	20	10	20
	Powder for injection	500	mg/vial	10	10	10
	Powder for injection	1	g/vial	5	5	5
Amoxicillin + clavulanic acid	Cap/tab	100/125	mg	30	8	30
	Cap/tab	250/125	mg	15	8	30
	Cap/tab	500/125	mg	15	8	15
	Oral liquid	125/31.25	mg/5 ml	135	45	150
	Oral liquid	250/62.5	mg/5 ml	60	15	135
	Powder for injection	500/100	mg/vial	8	8	15
	Powder for injection	1000/200	mg/vial	NA	NA	NA
Ampicillin	Cap/tab	250	mg	40	20	40
	Cap/tab	500	mg	20	10	40
	Injection	1	g/vial	10	10	20
	Injection	500	mg/vial	20	10	40
Benzylpenicillin	Injection	1	MIU/vial	5	5	5
	Injection	5	MIU/vial	NA	NA	NA
Gentamicin	Injection	10	mg/ml	40	15	50
	Injection	40	mg/ml	10	4	15
Ceftriaxone	Injection	250	mg/vial	28	7	40
	Injection	500	mg/vial	14	3,5	40
	Injection	1	g/vial	7	4	20
Cefotaxime	Injection	250	mg/vial	NA	NA	NA
	Injection	1	g/vial	18	7	30

Procaine benzylpenicillin	Injection	1	MIU/vial	10	10	10
	Injection	3	MIU/vial	NA	NA	NA

NUNT = number of units needed for treatment. NA = Not Available. Average weight is 11,2 kg, minimum weight is 4,3 kg and maximum weight is 18,1 kg. Cap/tab = capsule/tablet

***Table 2** A list of the number of units needed for treatment for the school aged children.*

Active ingredient	Formulation	Strength	Unit	Average NUNT	Minimum NUNT	Maximum NUNT
Salbutamol or other short-acting beta-agonist inhaler	inhaler (aerosol)	100	mcg/dosis	180	90	240
Budesonide or other corticosteroid inhaler	inhaler (aerosol)	100	ug/dosis	60	30	60
	inhaler (aerosol)	200	ug/dosis	30	30	30
Oral rehydration salts	Power sachet	200	ml	NA	NA	NA
	Power sachet	500	ml	4	3	4
	Power sachet	1	L	2	1	2
Zinc sulphate	Cap/tab	20	mg	14	14	14
Carbamazepine	Cap/tab	100	mg	60	60	60
	Cap/tab	200	mg	60	30	60
	Suspension	20	mg/ml	300	270	300
Phenobarbital	Cap/tab	15	mg	120	90	120
	Cap/tab	30	mg	90	60	120
	Cap/tab	100	mg	30	15	75
	Injection	100	mg/ml	30	15	90
	Injection	200	mg/ml	15	15	30
	Oral solution	3	mg/ml	600	450	600
Phenytoin	Cap/tab	25	mg	120	120	120
	Cap/tab	50	mg	120	60	120
	Cap/tab	100	mg	60	30	120
	Suspension	6	mg/ml	600	450	600
	Suspension	5	mg/ml	600	540	600
	Injection	1	mg/ml	NA	NA	NA

Valproic acid	Cap/tab	100	mg	180	120	240
	Cap/tab	150	mg	120	90	180
	Cap/tab	200	mg	90	60	150
	Cap/tab	500	mg	60	30	60
	Suspension	40	mg/ml	540	360	720
Diazepam	Cap/tab	5	mg	NA	NA	NA
	Cap/tab	10	mg	NA	NA	NA
	Injection	5	mg/ml	2	2	5
	Suspension (oral)	0,4	mg/ml	NA	NA	NA
	Rectal solution	2,5	mg	NA	NA	NA
	Rectal solution	5	mg	NA	NA	NA
	Rectal solution	10	mg	1	1	2
Lorazepam	Injection	2	mg/ml	1	1	2
	Injection	4	mg/ml	0,5	0,5	1
Midazolam	Injection	1	mg/ml	12	9	20
	Injection	5	mg/ml	2	2	4
	Suspension	2	mg/ml	6	5	10
	Cap/tab	7,5	mg	NA	NA	NA
	Cap/tab	15	mg	NA	NA	NA
Abacavir	Cap/tab	60	mg	NA	NA	NA
Lamivudine	Suspension	10	mg/ml	NA	NA	NA
	Cap/tab	150	mg	30	30	60
Abacavir + lamivudine	Cap/tab	120/60	mg	60	60	60
Efivarenz	Cap/tab	200	mg	60	45	90
Zidovudine	Suspension	10	mg/ml	NA	NA	NA
Ferrous salt	Cap/tab	200	mg	NA	NA	NA

	Suspension	25	mg/ml	90	60	240
	Cap/tab	60	mg	30	30	90
Albendazole	Cap/tab	200	mg	2	2	2
	Cap/tab	400	mg	1	1	1
Artemether	Injection	80	mg/ml	60	54	60
Amodiaquine	Cap/tab	153	mg	6	3	6
	Cap/tab	200	mg	6	3	6
Mefloquine	Cap/tab	250	mg	3	3	3
Artemether + lumefantrine	Cap/tab	20/120	mg	12	12	12
Artesunate + amodiaquine	Cap/tab	25/67,5	mg	6	6	6
	Cap/tab	50/135	mg	6	3	6
	Cap/tab	100/270	mg	3	3	6
Artesunate + mefloquine	Cap/tab	25/55	mg	6	6	6
	Cap/tab	100/220	mg	3	3	6
Dihydroartemisinin + piperaquine	Cap/tab	20/160	mg	3	3	6
	Cap/tab	40/320	mg	3	3	3
Sulfadoxine + pyrimethamine	Cap/tab	250/12,5	mg	2	2	2
	Cap/tab	500/25	mg	2	1	2
Artesunate + Sulfadoxine-pyrimethamine	Cap/tab	50/500/25	mg	1	1	1
Artesunate	Cap/tab	50	mg	6	3	6
	Injection					
	Cap rectal	50	mg	1	1	1
	Cap rectal	100	mg	NA	NA	NA
	Cap rectal	200	mg	NA	NA	NA
Chloroquine	Cap/tab	100	mg	5	5	10
	Cap/tab	150	mg	5	5	5
	Suspension	10	mg/ml	50	45	50

Paracetamol	cap/tab	100	mg	240	240	360
	cap/tab	300	mg	120	120	270
	Cap/tab	500	mg	120	60	180
	Suppository (rectal)	100	mg	NA	NA	NA
	Suspension	24	mg/ml	1200	960	1800
	Suspension	25	mg/ml	1200	840	1800
Morphine	Cap/tab	10	mg	120	60	360
	Cap/tab	200	mg	NA	NA	NA
	Injection	10	mg/ml	60	60	180
	Oral solution	2	mg/ml	480	240	1080
Ibuprofen	Cap/tab	200	mg	90	90	150
	Cap/tab	400	mg	90	90	90
	Suspension	40	mg/ml	450	180	720
Ethambutol	Suspension	25	mg/ml	NA	NA	NA
	Cap/tab	100	mg	NA	NA	NA
	Cap/tab	400	mg	30	30	60
Isoniazid	solution	10	mg/ml	NA	NA	NA
	Cap/tab	50	mg	NA	NA	NA
	Cap/tab	100	mg	60	60	60
	Cap/tab	300	mg	30	15	45
Pyrazinamide	Suspension	30	mg/ml	NA	NA	NA
	Cap/tab	150	mg	NA	NA	NA
	Cap/tab	400	mg	60	30	60
Rifampicin	Cap/tab	150	mg	60	30	60
	Cap/tab	300	mg	30	30	60
	Solution	20	mg/ml	300	270	300
Isoniazid + rifampicin	Cap/tab	50/75	mg	NA	NA	NA

Isoniazid + pyrazinamide + rifampicin	Cap/tab	50/150/75	mg	NA	NA	NA
Amoxicillin	Cap/tab	250	mg	NA	NA	NA
	Cap/tab	500	mg	20	20	20
	Suspension	25	mg/ml	NA	NA	NA
	Suspension	50	mg/ml	NA	NA	NA
	Injection	250	mg/vial	NA	NA	NA
	Injection	500	mg/vial	NA	NA	NA
	Injection	1	g/vial	10	10	10
Amoxicillin + clavulanic acid	Cap/tab	500/125	mg	15	15	15
	injection	500/100	mg/vial	15	10	15
	injection	1000/200	mg/vial	5	5	10
	Suspension	25/6,25	mg/ml	NA	NA	NA
	Suspension	50/12,5	mg/ml	120	90	150
Ampicillin	Cap/tab	250	mg	40	40	40
	Cap/tab	500	mg	20	20	20
	Injection	1	g/vial	10	10	10
	Injection	500	mg/vial	20	20	20
Benzylpenicillin	Injection	600	mg/vial	30	15	60
	Injection	3	g/vial	10	5	10
Gentamicin	Injection	10	mg/ml	90	75	120
	Injection	40	mg/ml	30	15	30
Ceftriaxone	Injection	1	g/vial	2	2	3
	Injection	250	mg/vial	NA	NA	NA
Cefotaxime	Injection	1	g/vial	25	20	30
	Injection	250	mg/vial	NA	NA	NA

NUNT = number of units needed for treatment. NA = Not Available. Average weight is 24,975 kg, minimum weight is 18,40 kg and maximum weight is 31,55 kg. Cap/tab = capsule/tablet

Appendix 4

Table 1 *An overview of the burden of disease value associated with the different regions and the global. All values are from the GHE list from 2010 and are based on the men and women (1-59 months).*

Medicine name	Affiliated disease	Both seks_global2010	Both seks_AFR2010	Both seks_AMR2010	Both seks_SEAR2010	Both seks_EU2010	Both seks_EMR2010	Both seks_WPR2010
ORS	Diarrhoeal Diseases	56.053.144	29159814	1185596	15494193	503746	7832833	1877042
Zinc suphate	Diarrhoeal Diseases	56.053.144	29159814	1185596	15494193	503746	7832833	1877042
Carbamazapine OR phenobarbital OR phenytoin OR lamotrigine	Epilepsy	1.776.082	458428	147347	677962	104282	239004	149060
Valproic acid	Epilepsy	1.776.082	458428	147347	677962	104282	239004	149060
Diazepam OR lorazepam OR midazolam	Epilepsy	1.776.082	458428	147347	677962	104282	239004	149060
Abacavir + lamivudine + dolutegravir OR Abacavir + lamivudine + lopinavir/ritonavir OR Tenofovir alafenamide + lamivudine + dolutegravir	HIV/AIDS	13.735.443	12538660	181106	660078	138816	108101	108682
Ferrous salt	Iron-deficiency anemia	5.114.719	1713869	232036	2092779	155395	671680	248961
Mebendazole OR albendazole	Iron-deficiency anemia	5.114.719	1713869	232036	2092779	155395	671680	248961
Artemether + lumefantrine OR Artesunate + amodiaquine OR Artesunate + mefloquine OR Dihydroartemisinin + piperaquine OR Artesunate + Sulfadoxine-pyrimethamine OR Chloroquine	Malaria	40.728.562	39778306	10264	882912	9	246178	107893
Artesunate	Malaria	40.728.562	39778306	10264	882912	9	246178	107893
Retinol	Measles Vitamin A deficiency	12.234.130	5.405.553	19.239	5.553.092	9.720	1.059.361	187.165
Paracetamol	Vitamin A deficiency	0	0	0	0	0	0	0

Morphine	Vitamin A deficiency (570)	0	0	0	0	0	0	0
Ibuprofen	Pain and palliative care (weight = 1/T)	0	0	0	0	0	0	0
Ethambutol + isoniazid + pyrazinamide + rifampicin	Tuberculosis	14.063.261	3742531	57014	7990234	80953	1057021	1135508
Amoxicillin OR Amoxicillin + clavulanic acid	Lower respiratory infections Other infectious diseases	88.566.879	46.562.715	2.306.858	22.122.872	1.067.782	12.121.274	4.385.378
Ampicillin	Lower respiratory infections Other infectious diseases	88.566.879	46.562.715	2.306.858	22.122.872	1.067.782	12.121.274	4.385.378
Benzylpenicillin	Lower respiratory infections Other infectious diseases	88.566.879	46.562.715	2.306.858	22.122.872	1.067.782	12.121.274	4.385.378
Gentamicin	Lower respiratory infections Other infectious diseases	88.566.879	46.562.715	2.306.858	22.122.872	1.067.782	12.121.274	4.385.378
Ceftriaxone	Other infectious diseases Meningitis	17.885.741	11.517.345	399.009	3.226.180	155.279	2.067.616	520.313
Cefotaxime	Other infectious diseases Meningitis	17.885.741	11.517.345	399.009	3.226.180	155.279	2.067.616	520.313
Procaine benzylpenicillin	Syphilis	1.263.738	838350,9462	26680,50464	187674,1953	4888,024225	112404,2291	93740,55332

Appendix 5

Table 1 *An overview of the information of the 25 facilities of the base case dataset.*

Facility	Available	Accessible	Facility score (%)
1	8	6	31,03
2	10	8	50,29
3	5	4	20,82
4	9	8	47,15
5	7	5	28,57
6	7	7	34,98
7	7	7	44,80
8	9	9	45,74
9	7	7	39,44
10	5	5	35,20
11	6	3	28,34
12	7	5	33,04
13	6	5	31,50
14	4	3	7,16
15	8	6	35,92
16	7	7	41,10
17	7	6	32,63
18	7	6	37,10
19	7	6	38,64
20	3	3	16,87
21	7	6	37,10
22	8	7	41,10
23	7	7	44,80
24	8	6	38,64
25	7	6	39,20

Table 2 *An overview of the information of the 25 facilities of the price dataset.*

Facility	Available	Accessible	Facility score (%)
1	15	13	65,41
2	13	13	51,56
3	12	11	82,20
4	15	15	64,31
5	13	11	72,18
6	15	14	61,63
7	12	12	71,94
8	13	13	67,47
9	14	13	66,77
10	12	12	56,19
11	11	10	58,93
12	12	10	61,38
13	11	11	73,80
14	13	13	67,34
15	13	11	71,48
16	13	13	73,80
17	13	13	74,26
18	13	13	70,99
19	11	11	73,31
20	11	11	59,53
21	11	10	73,55
22	12	12	73,55
23	13	12	69,09
24	12	12	70,85
25	11	10	65,41

Appendix 6

Table 1 *An overview of the average facility scores of the different scenarios base case dataset.*

Scenario	Explanation	Mean facility score (%)
Base case	Baseline situation, whereby as much as possible has been taken from the original SDG 3.B.3. method.	35,245
Max NUNT	In addition to the average NUNT, a maximum NUNT has also been determined, this is based on the weight and age of a child of 59 months.	33,327
Min NUNT	In addition to the average NUNT, a minimum NUNT has also been determined, this is based on the weight and age of a child of 1 month.	41,209
NUNT +/- 60%	For the maximum: NUNT = NUNT + 60%	
NUNT_max_60	For the minimum: NUNT = NUNT - 60%	33,426
NUNT_min_60		40,722
NPL_max	Varying the NPL of $1,90 by +10% (NPL = $2,09)	33,622
NPL_min	Varying the NPL of $1,90 by -10% (NPL = $1,71)	36,622
Scenario 2	Situation is based on the 5 regions (AFR, AMR, EU, EMR, WPR) where the data comes from.	35,133
Scenario 2.a	AFR	34,303
Scenario 2.b	AMR	38,096
Scenario 2.c	EU	37,357
Scenario 2.d	EMR	37,949
Scenario 2.e	WPR	37,135
Scenario 3	In this scenario, the main issue is the fact that medicines that have not been surveyed are not considered. In this dataset 19 medicines were surveyed, therefore 1/19 = 0,05263158. The non-surveyed medications have been removed.	38,920
Scenario 4	For every disease there are several drugs in the medicine basket. Normally the burden disease is included per drug. In this scenario, the weight (= burden per disease / total burden) is distributed over the number of medicines that are included by diseases.	29,883
Scenario 4.a	The same as scenario 4, only the burden for pain medication is determined by 1/9 (surveyed diseases) = 0,11111111.	30,560
Scenario 4.b	This scenario is a combination of scenario 4.a and scenario 3. The scenario is based on the burden of disease corrected for the number of medicines per disease that occur in the medicine basket. In addition, the non-surveyed medicines were removed.	36,926
Scenario 5	Everything weights equally, no burden. Weight is equal to total burden/22 (medicine basket). Further base case scenario.	26,909
Scenario 5.a	Weight is equal to total burden/19 (medicine surveyed). Non-surveyed medications have been removed (scenario 3).	31,158
Scenario 5.b	Weight is equal to total burden/9 (surveyed diseases). Non-surveyed medications have been removed (scenario 3) Also, adjusted for the number of medicines per disease (scenario 4).	27,098
Scenario 5.c	Weight is equal to total burden/9 (surveyed diseases). Non-surveyed medications have **not** been removed. Also, adjusted for the number of medicines per disease (scenario 4).	25,593

Table 2 *The minimum, average and maximum facility scores of the scenarios of the base case dataset.*

Scenario	Minimum facility score (%)	Average facility score (%)	Maximum facility score (%)
Scenario 5.c	9,259	25,593	40,74
Scenario 5.b	9,608	27,098	37,255
Scenario 5.a	15,79	31,158	47,368
Scenario 5	4,078	26,909	54,393
Scenario 4.b	9,002	36,926	52,657
Scenario 4.a	7,45	30,56	47,667
Scenario 4	5,845	29,883	48,568
Scenario 3	8,019	38,92	55,413
Scenario 2.e	6,705	37,135	51,278
Scenario 2.d	7,294	37,949	53,384
Scenario 2.c	8,24	37,357	52,564
Scenario 2.b	8,081	38,096	54,206
Scenario 2.a	7,109	34,303	49,445
Scenario 2	7,158	35,133	50,125
NUNT_min_60	16,872	40,722	64,992
NUNT_min_60	16,872	40,722	64,992
NUNT_max_60	4,703	33,426	50,285
NPL_min	7,16	36,622	52,743
NPL_max	4,703	33,622	50,285
min_NUNT	16,872	41,209	64,912
max_NUNT	4,703	33,327	50,285
Basecase	7,16	35,245	50,286

Table 3 *An overview of the average facility scores of the different scenarios price dataset.*

Scenario	Explanation	Mean facility score (%)
Base case	Baseline situation, whereby as much as possible has been taken from the original SDG 3.B.3. method.	68,181
Max NUNT	In addition to the average NUNT, a maximum NUNT has also been determined, this is based on the weight and age of a child of 59 months.	62,990
Min NUNT	In addition to the average NUNT, a minimum NUNT has also been determined, this is based on the weight and age of a child of 1 month.	69,163*
NUNT_max_60	For the maximum: NUNT = NUNT + 60%	63,409
NUNT_min_60	For the minimum: NUNT = NUNT - 60%	69,163*
NPL_max	Varying the NPL of $1,90 by +10% (NPL = $2,09)	64,122
NPL_min	Varying the NPL of $1,90 by -10% (NPL = $1,71)	69,163
Scenario 3	In this scenario, the main issue is the fact that medicines that have not been surveyed are not considered. In this dataset 19 medicines were surveyed, therefore 1/19 = 0,05263158. The non-surveyed medications have been removed.	75,158
Scenario 4	For every disease there are several drugs in the medicine basket. Normally the burden disease is included per drug. In this scenario, the weight (= burden per disease / total burden) is distributed over the number of medicines that are included by diseases.	59,216
Scenario 4.a	The same as scenario 4, only the burden for pain medication is determined by 1/9 (surveyed diseases) = 0,11111111.	58,711
Scenario 4.b	This scenario is a combination of scenario 4.a and scenario 3. The scenario is based on the burden of disease corrected for the number of medicines per disease that occur in the medicine basket. In addition, the non-surveyed medicines were removed.	70,941
Scenario 5	Everything weights equally, no burden. Weight is equal to total burden/22 (medicine basket). Further base case scenario.	54,366
Scenario 5.a	Weight is equal to total burden/19 (medicine surveyed). Non-surveyed medications have been removed (scenario 3).	62,947
Scenario 5.b	Weight is equal to total burden/9 (surveyed diseases). Non-surveyed medications have been removed (scenario 3) Also, adjusted for the number of medicines per disease (scenario 4).	62,627

Scenario 5.c	Weight is equal to total burden/9 (surveyed diseases). Non-surveyed medications have **not** been removed. Also, adjusted for the number of medicines per disease (scenario 4).	59,148

*Price per treatment and EDW are different, but the same number of medicines are accessible (EDW<1). This makes the weighted accessibility equal (accessible * burden).

Table 4 *The minimum, average and maximum facility scores of the scenarios of the price dataset.*

Scenario	**Minimum facility score (%)**	**Average facility score (%)**	**Maximum facility score (%)**
Scenario 5.c	46,30	59,15	72,22
Scenario 5.b	49,02	62,63	75,49
Scenario 5.a	52,63	62,95	78,95
Scenario 5	45,45	54,36	68,18
Scenario 4.b	57,49	70,94	86,56
Scenario 4.a	47,58	58,71	71,63
Scenario 4	46,38	59,22	71,95
Scenario 3	56,97	75,16	90,64
NUNT min 60	51,56	69,16	82,20
NUNT max 60	47,56	63,41	75,74
NPL min	51,56	68,48	82,20
NPL max	47,56	64,12	75,74
Min NUNT	51,56	69,16	82,20
Max NUNT	47,56	62,99	75,74
Base case	51,56	68,18	82,20