



A Defined Daily Dose Analysis of Antibiotic Use Trends in Vietnam from 2019-2022

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Local Health System Sustainability Project  
Task Order 1, USAID Integrated Health Systems IDIQ

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## Local Health System Sustainability Project

The Local Health System Sustainability Project (LHSS) under the USAID Integrated Health Systems IDIQ helps low- and middle-income countries transition to sustainable, self-financed health systems as a means to support access to universal health coverage. The project works with partner countries and local stakeholders to reduce financial barriers to care and treatment, ensure equitable access to essential health services for all people, and improve the quality of health services. Led by Abt Associates, the five-year, \$209 million project will build local capacity to sustain strong health system performance, supporting countries on their journey to self-reliance and prosperity.

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## ACRONYMS

ATC	Anatomical Therapeutic Chemical
AWaRe	Access, Watch, Reserve
CH	Central Highlands
DDD	Defined Daily Dose
DDD-BD	DDD/100 bed per days
DDD-LK	DDD/1000 visits with IHC/day
DU75	Drug Utilization 75%
MoH	Ministry of Health
NCC	North Central and Central Coast
NMM	Northern Midlands and Mountains
RRD	Red River Delta
SE	Southeast
Top 10	Top 10 most consumed antibiotics
USAID	United States Agency for International Development



## BACKGROUND

The World Health Organization (WHO), in 2019, declared the global threat of antimicrobial resistance urgent and potentially catastrophic—estimating that multi- and pan-resistant bacteria (also known as superbugs) and associated infections could cause up to 10 million deaths per year by 2050. Many publications about the use of antimicrobials in Vietnam have shown that microbial resistance to multiple antimicrobials, known as multi-drug resistance (MDR) is increasing.

The Vietnam Ministry of Health (MoH) has developed, implemented, and operates the AMR Surveillance System website (<https://kks.kcb.vn>). However, the number of health facilities which have joined and submitted AMR reports is still limited; only 20 out of 54 participating hospitals provided satisfactory data. Therefore, it is not clear if there are extensively drug-resistant (XDR) or pandrug-resistant (PDR) microbes.

The Vietnam MoH issued a 2013–2020 National Action Plan for antimicrobial resistance prevention as well as prescribing guidelines for conditions such as ear-nose-throat infections, chronic obstructive pulmonary disease, joint and bone diseases, oral maxillofacial diseases, and chronic heart failure to ensure best practice in relation to the use of antimicrobials.

The Vietnam Social Security agency (VSS) has put into operation a health insurance claim review system and drug management software (e-LMIS) as part of the data collection system on drug indication and use for insured patients from health facilities nationwide. This allows for the evaluation of trends and levels of drug utilisation and facilitates the evidence-based development of national/regional policies for antibiotic use, production, and distribution.

WHO has created an evidence-based categorisation of agents (AWaRe) to guide appropriate use of antibiotics. The AWaRe Classification divides antibiotics into three groups—Access, Watch, and Reserve antibiotics—based on their risk of developing resistance, along with a fourth category of Not Recommended antibiotics. WHO recommends that 60% of antibiotics used are in the Access group.

The decision on which antimicrobial to prescribe should be based on knowing the infective organism and local microbial sensitivities. However, in the absence of a comprehensive microbial sensitivity monitoring system to identify and track specific micro-organisms, it is not possible for clinicians to make informed decisions.

The Local Health System Sustainability (LHSS) project, in collaboration with the Center for Medical Review and Multiline Payment – Vietnam Social Security (VSS), conducted an analysis of antibiotic use trends (consumption, cost per DDD, and cost) covered by Social Health Insurance (SHI) in the period 2019–2022 nationwide and by economic region, down to level of care. This analysis includes the J01 systemic antibiotics used for patients with health insurance from the MOH's Circular No. 30/2018/TT-BYT dated October 30, 2018. These antimicrobial agents equate to approximately 20% of the total spend on medicines and 16% of the total spend for inpatients.

The data collection period spans the COVID pandemic during which access to services was restricted and prescribing may have necessarily changed. Therefore, the four-year average is used for most parameters.

This summary document is intended to focus on findings which highlight areas for attention.



## 1. METHODOLOGY AND DATA

Data collected via the Vietnam Social Security claim system e-LMIS was analysed through SPSS to evaluate the use of the defined list of antibiotics between 2019 and 2022. This time period includes the exceptional circumstances experienced during the COVID pandemic and may not be indicative of 'normal' practice.

Data was collected at four levels of healthcare defined as central, provincial, district, and commune across all six regions<sup>1</sup> and separately as nationwide.

Drug utilisation of each medicine is expressed as its Defined Daily Dose (DDD), an assumed mean maintenance daily dose, which is a metric for exposure or therapeutic intensity in a defined population. In this study, the denominators per 100 bed days (BD) for inpatients and per 1,000 visits (LK) for outpatients, have been chosen to enable comparison of sectors with different populations, population density, morbidity, and mortality rates.

WHO has created a global reference of DDDs for a wide range of antimicrobial agents defined in groups with similar structures and effects by Anatomical Therapeutic Chemical (ATC) known as the DDD/ATC toolkit, which was used in this study.

The e-LMIS records DDD and spend, and this report looks both at product consumption at each level of care in every region and at the cost per DDD of the defined list of antimicrobial agents. The following indicators were selected for this summary report (detailed parameters are available in the full Vietnamese report and accompanying annexes):

- Highest consumption as DDD/BD and DDD/LK and cost per DDD by region and at all four levels of care in all six regions
- DDD/BD and DDD/LK of antibiotics with highest cost at all four levels of care in all six regions
- Consumption by pharmacological subgroup (DDD/BD and DDD/LK) and costs per DDD focusing on consumption of beta-lactam agents and cost per DDD of these antibiotics
- Consumption of antibiotics in the Reserve group (for restricted use only)
- Oral and parenteral antibiotics that make up 75% of all antibiotic consumption
- Proportional consumption (%) of antibiotics by AWaRe categorisation
- Percentage cost ratio of antibiotics compared to the total cost of antibiotics/medicines covered by health insurance.

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<sup>1</sup> Six regions are included: NCC (North Central and Central Coast), MD (Mekong Delta), RRD (Red River Delta) SE (Southeast), CH (Central Highlands), NMM (Northern Midlands and Mountains)

## 2. FINDINGS

### 2.1 CONSUMPTION: INPATIENT AND OUTPATIENT

#### 2.1.1 APPROPRIATENESS: COMPLIANCE WITH AWARE CATEGORIES

According to WHO's categorization of antibiotics, agents included in the Access list should be first- or possibly second-line, used in primary care settings for empiric management of a wide range of simple bacterial infections. Watch antibiotics should be used in settings where more complex or life-threatening illnesses are likely to present, particularly where intravenous administration is necessary. However, as broad-spectrum agents, these agents are more susceptible to resistance and must be monitored closely. Reserve agents must be retained for last resort, drug-resistant, severe, and complex infections.

There are some agents listed as Other in the data; these agents are not included in the WHO Essential Medicines list or AWaRe categories, which means there is no evidence for their use. One agent listed as Other is explicitly cited Not Recommended by WHO, despite being on the MoH list.

#### Overview of Trends by AWaRe Category

Table 1 summarises the changes over the time period studied as trends in the use of each category. The inpatient use is predominantly Watch agents, whereas outpatient use report more Access agents.

**Table 1. All Regions and Nationwide Trends in Both Inpatients and Outpatients**

AWaRe Group (%) 4 Year Ave.	NCC	MD	RRD	SE	CH	NMM	Nationwide
<b>Inpatient / Outpatient</b>							
ACCESS 31.4% / 59.7%	↑/↑	↑/↑	↑/↑	↑/↑	↔/↑	↔/↑	↑/↑
WATCH 65.8% / 40.2%	↓/↓	↓/↓	↓/↓	↓/↓	↓/↓	↓/↓	↓/↓
RESERVE 0.7% / 0.003%	↑/ZERO	↑/ZERO	↑/↓	↑/↓	↑/↓	↑/ZERO	↑/↓
OTHER 2.1% / 0.1%	↑/↔	↑/↓	↑/↔	↑/↑	↑/↔	↑/↓	↑/↔

Overall, the increase in use of antibiotics in the Access groups and comparative reduction in Watch groups is to be welcomed across the board. The MoH-approved antimicrobials not included in WHO lists and represented in the Other group are oral nalidixic acid, sulphaguanidine, sulfasalazine, and injectable cefoperazone + sulbactam; increasing consumption of these for inpatients must be investigated.

Increases in the use of Reserve agents are concerning, but the actual numbers are low. There is not enough information to assess whether this data implies increasing MDR infections or inappropriate indication.

The Reserve agents used are described in Table 2.

**Table 2. Consumption (trend), Cost, and Cost Ratio of Reserve Agents**

Medication	Consumption DDD/BD (trend)	Cost per DDD/BD (VND)	Cost Ratio (%)
Colistin parenteral	0.11 (↑)	2,748,757	5.1
Doripenem parenteral	0.04 (↑)	1,746,548	1.2
Ertapenem parenteral	0.12 (↑)	552,406	1.2
Fosfomycin oral	0.02 (↔)	119,741	0.03
Fosfomycin parenteral	0.05 (↑)	702,899	0.6
Imipenem + cilastin	0.52 (↑)	683,205	6.1
Linezolid oral	0.03 (↓)	31,305	0.02
Linezolid parenteral	0.12 (↑)	896,569	1.9
Meropenem	0.52 (↑)	977,405	8.5
Teicoplanin parenteral	0.07 (↔)	397,250	0.4
Tigecyclin parenteral	0.008 (↑)	1,461,343	0.1
Vancomycin parenteral	0.43 (↑)	125,077	0.9

Imipenem + cilastin, meropenem, and vancomycin all appear in the Top 10 most consumed antibiotics (Top 10) of Central services in Southeast but not in any other region or level. These agents are intended for use against resistant organisms; therefore, it can be viewed that Southeast has significant problems with resistant microorganisms, or that these agents are being selected inappropriately, which could lead to problematic multidrug resistance. The spend on these agents is significant, particularly considering the high consumption.

Nalidixic acid, a first-generation fluoroquinolone used for urinary tract infections, is the only Other agent which appears in the Top 10 for outpatients at the commune level in Southeast and in the Top 10 for inpatients at the commune level in North Central and Central Coast. It is approved for use by all levels of care in the MoH list despite not being included in the WHO Essential Medicines lists.

Injectable cefoperazone + sulbactam, which is on WHO's Not Recommended list, appears in the Top 10 for inpatients at Central level nationwide, in Southeast, Red River Delta, North Midlands and Mountains, and at Provincial level in Central Highlands. On the MoH list, injectable cefoperazone + sulbactam is approved for specialist, first- and second-level facilities.

### Regional Variation in the Use of AWaRe agents

#### *For Inpatients (Table 3)*

Northern Midland and Mountains has the best balance of AWaRe agents in all six regions, and compared to nationwide data, with the highest Access, lowest Watch and Reserve percentages, and below average Other usage.

Mekong Delta has the largest proportional use of Watch versus Access agents, closely followed by Red River Delta, which may imply different patterns of resistance or poor selection of agents.

The highest use of Reserve agents is in Southeast region, followed by Red River Delta, which also reports the highest use of Other agents and the lowest use of Access agents, a concerning trend.

**Table 3. Regional Variation in Use of AWaRe Agents for Inpatients**

AWaRe Group (%) 4 Year Ave.	NCC	MD	RRD	SE	CH	NMM	Nationwide
ACCESS	32.7%	27.2%	26.8%	31.6%	35.7%	42.8%	31.4%
WATCH	65.5%	71.3%	68.5%	64.5%	62.8%	55.6%	65.5%
RESERVE	0.3%	0.3%	0.9%	1.8%	0.2%	0.2%	0.7%
OTHER	1.6%	1.2%	3.7%	2.1%	1.3%	1.4%	2.1%

*For Outpatients (Table 4)*

The region most compliant with WHO guidelines is Northern Midlands and Mountains with the highest Access to Watch ratio and negligible use of Reserve and Other agents, as would be expected in outpatient settings.

North Central and Central Coast is the second most compliant with no Reserve and few Other prescriptions. Red River Delta also demonstrated above 60% Access prescribing which is good practice but has more Reserve and Other agents use.

Nationwide, there is negligible use of Reserve agents, with use only in Southeast (increasing trend) and a small proportion in Red River Delta, which aligns with use for inpatients. Each occasion should be scrutinised for appropriateness.

Central Highlands has the highest use of Other agents, a finding which warrants further investigation. However, there is relatively low use of Other agents overall. Such a small figure lends itself to tracking individual cases to assess appropriateness.

**Table 4. Regional Variation in Use of AWaRe Agents for Outpatients**

AWaRe Group (%) 4 Year Ave.	NCC	MD	RRD	SE	CH	NMM	Nationwide
ACCESS	61.1%	46.3%	71.6%	49.1%	50%	80.9%	59.7%
WATCH	38.8%	53.7%	28.4%	50.6%	49.7%	19.1%	40.2%
RESERVE	Zero	zero	0.0004%	0.017%	Zero	Zero	0.003%
OTHER	0.017%	0.05%	0.1%	0.2%	0.32%	0.001%	0.1%

**Good Prescribing Practice Indicators Drug Use 75% (DU75)**

European analysis of antimicrobial DU75—those drugs used in the top 75% of reports—observed that the extent of oral use was identified as a quality indicator in hospitals where intravenous agents may be required initially but should be switched to oral as soon as possible. WHO analysis focuses on the number of medicines in the DU75 as a parameter to monitor quality product selection.

**Table 5. DU75 for Inpatient Data – the Number of Antimicrobial Agents in Each AWaRe Category**

AWaRe Group: Number of Agents	Oral	Parenteral	Total
ACCESS	4	7	11
WATCH	6	17	23
RESERVE	0	0	0
OTHER	0	1	1
<b>TOTAL</b>	<b>10</b>	<b>25</b>	<b>35</b>

Table 5 shows that for inpatients, parenteral agents significantly exceed oral agents in the DU75 in the most commonly used groups of antimicrobials, Access and Watch.

Using DU75 four-year average DDD/BD rates, oral amoxicillin + clavulanic acid is the most commonly reported agent (Access = 10.8) followed by oral cefuroxime (Watch = 8.8, reducing over four years) and oral amoxicillin (Access = 6.8). Except injectable cefotaxime (Watch = 5.4, reducing over four years), all other agents average out at less than five, with the majority of DDD/BD coming from four agents: oral amoxicillin + clavulanic acid, cefuroxime, amoxicillin and injectable cefotaxime.

The Other item appearing in the DU75 is cefoperazone + sulbactam, which is included in WHO's Not Recommended list. It has an undesirable four-year average DDD/BD of 2.3.

The outpatient data only includes oral preparations in the DU75; five are Access and four are Watch antibiotics. As with inpatients, in the four-year average DDD/LK for outpatients, the most commonly reported agent is amoxicillin + clavulanic acid (Access = 22.1, increasing over four years), closely followed by amoxicillin (Access = 19.3, also increasing). Oral cefuroxime features highly (Watch = 13.3, reducing over four years) with cephalexin (Access = 13.2, also reducing). This shows an encouraging trend to increasing use of first-line Access agents rather than second-generation cephalosporins (Watch).

The statistical significance of differences is not calculated, so the DDD data is interpreted numerically.

### Fixed Dose Combinations

WHO does not recommend usage of fixed-dose combinations of active agents or second- and third-generation antibiotics with beta-lactamase inhibitors, but combinations of penicillins with beta-lactamase inhibitors such as sulbactam, including combinations like amoxicillin + clavulanic acid, are included in the Access list. Some other beta-lactams inhibitor combinations are in the Watch group, such as piperacillin, which is usually administered with tazobactam to avoid the development of resistance, and similarly imipenem with cilastin.

Table 6 shows the fixed combinations reported in the data. Most are AWARe combinations which may be appropriate in areas of beta-lactamase creating organisms.

**Table 6. Average Consumption and Cost Ratio (%) of Total Antimicrobial Spend**

Antimicrobial Combination	Average % Total Consumption	Cost Ratio (%) Total Spend
Amoxicillin + acid clavulanic Oral (Access)	10.5	1.2
Ampicillin + sulbactam Parenteral (Access)	2.7	6.0
Cefoperazone + sulbactam (not recommended)	2.1	7.8
Amoxicillin + acid clavulanic Parenteral (Access)	2.0	1.6
Imipenem + cilastatin* Parenteral (Watch)	1.1	6.1
Piperacillin + tazobactam Parenteral (Watch)	0.9	2.7
Ticarcillin + acid clavulanic Parenteral (Watch)	0.3	1.8

Cefoperazone + sulbactam, the only WHO Not Recommended combination is reported as the third most commonly used combination at 2.1% of total antibiotic consumption; the cost ratio is the highest of all combinations at 7.8%.

Note: Ticarcillin with clavulanic acid was withdrawn from the U.S. market in February 2015 because of safety concerns. The relevance of this should be considered for Vietnam.

### MoH list of Approved Antimicrobials for Use at Medical Stations and Medical Service Units in Offices (not including Access antibiotics)

Table 7 is a summary of the antimicrobials which currently can be used at the lowest level of primary care. The use of these agents may be inappropriate in relation to the AWaRe list.

**Table 7. Extract from the MoH List of Medicines Approved for Use at Medical Stations and Medical Service Units in Offices**

Antibiotic	Form	ATC Code	AWaRe Classification	DDD g	Notes
Nalidixic acid	Oral	J01MB02	Other	4	Not included by WHO for AWaRe classification 2023
Sulfaguanidine	Oral	A07AB03	Other	4	Not included by WHO for AWaRe classification 2023
Cefaclor	Oral	J01DC04	Watch	1	Second-generation cephalosporin
Cefuroxime	Oral	J01DC02	Watch	0.5	Second-generation cephalosporin
Neomycin (sulfate)	Oral	A07AA01	Watch	5	Aminoglycoside
Clindamycin	Oral	J01FF01	Watch	1.2	Lincosamide
Erythromycin	Oral	J01FA01	Watch	1	Macrolide
Spiramycin	Oral	J01FA02	Watch	3	Macrolide
Ciprofloxacin	Oral	J01MA02	Watch	1	Second-generation fluoroquinolone
Ofloxacin	Oral	J01MA01	Watch	0.4	Second-generation fluoroquinolone

### 2.1.2 CONSUMPTION

Assessment of consumption is based on DDD-BD for inpatients and DDD-LK for outpatients.

#### Top 10 Analyses

*Top 10 nationwide: Inpatient DDD-BD average of 2019-2022 Top 10*

**Table 8. Four-Year Average DDD-BD Inpatient Route/Class, Consumption and Trends of Top 10**

Ranking	Antimicrobial	Route	AWaRe	DDD-BD Ave	Trend over 4 Yrs
1st	Amoxicillin + clavulanic acid	Oral	ACCESS	109.8	Reducing
2nd	Cefuroxime	Oral	WATCH	102.4	Reducing
3rd	Amoxicillin	Oral	ACCESS	64.7	↑
4th	Cefotaxime	Injection	WATCH	60	Reducing
5th	Cefixime	Oral	WATCH	56.4	↑
6th	Ciprofloxacin	Oral	WATCH	46.8	Reducing
7th	Ceftriaxone	Injection	WATCH	36.5	↑
8th	Ceftazidime	Injection	WATCH	27	Reducing
9th	Gentamicin	Injection	ACCESS	24.7	(zero 2022)
10th	Levofloxacin	Injection	WATCH	23.5	↑

The balance of oral and injectable agents (50:50) in the Top 10 is below the WHO 2023 target of 60% oral. There are more Watch agents (7) versus Access agents (3). However, the fact that half of the Top 10 consumption is in the Top 3 (total 277 DDD-BD) where Access agents feature



more than Watch agents and are all oral is positive. It is also important to note that the trend for use of amoxicillin oral is increasing against a reduction in both cefuroxime oral and amoxicillin + clavulanic acid.

Table 9 compares the nationwide Top 10 in order from highest to lowest in six regions. There are some similarities in all regions except Northern Midlands and Mountains where a different range of agents predominates. The Top 3 of all other regions appear amongst the nationwide Top 5.

**Table 9. Analysis of 10 Highest Consumed Antibiotics**

Ranking	Antimicrobial	Route	NCC	MD	RRD	SE	CH	NMM
1st	Amoxicillin + clavulanic acid	Oral	4	1	5	1	3	6
2nd	Cefuroxime	Oral	2	2	3	2	1	
3rd	Amoxicillin	Oral	3		1	9	8	1
4th	Cefotaxime	Injection	1	4	2	10	5	7
5th	Cefixime	Oral		3		3	2	
6th	Ciprofloxacin	Oral	7	5		4	4	10
7th	Ceftriaxone	Injection	5	8	6	5	9	8
8th	Ceftazidime	Injection		5		6		
9th	Gentamicin	Injection	6				7	
10th	Levofloxacin	Injection		7	7	7		

Northern Midlands and Mountains is a significant outlier in the agents reported in the Top 10 and should be investigated more closely, particularly because as mentioned above, this region showed the best Access to Watch ratio.

Cefoperazone injection, a third-generation Watch cephalosporin, appears in Top 10 in five of the six regions. It ranked 11th in nationwide data.

No antimicrobials were used in Mekong Delta or Southeast for commune inpatients, which implies the absence of services to meet the needs of people with infections.

#### *Top 10 Nationwide: Average DDD/LK of Top 10 in 2019-2022*

Table 10 shows that all the Top 10 agents are oral.

**Table 10. Four-Year Average DDD-LK of Top 10 Antimicrobials**

Ranking	Antimicrobial	AWaRe	DDD-LK Ave	Trend over 4 Yrs
1st	Amoxicillin	ACCESS	0.8	↑
2nd	Amoxicillin + clavulanic acid	ACCESS	0.6	No change
3rd	Cefuroxime	WATCH	0.4	↓
3rd	Cefalexin	ACCESS	0.4	↓
5th	Cefixime	WATCH	0.3	↓
6th	Cefadroxil	ACCESS	0.2	No change
6th	Clarithromycin	WATCH	0.2	↓
8th	Cefaclor	WATCH	0.1	No change
8th	Cefradin	ACCESS	0.1	No change
8th	Ciprofloxacin	WATCH	0.1	↓

The Top 4 highest ranking agents (= 2.2 DDD-LK) are mostly Access (3) rather than Watch (1). The figure is small, showing a minor change over time, but there is an increase in use of Access amoxicillin and reduction in use ofno (Watch) Cefuroxime and (Access) Cefalexin. The combination of amoxicillin + clavulanic acid is the second most commonly used oral agent, which may be an empirical choice for prescribing when the organism is not known.

**Table 11. Nationwide Analysis (outpatients) by Region of Top 10s**

Ranking	Antimicrobial	NCC	MD	RRD	SE	CH	NMM
1	Amoxicillin	1	4	1	5	3	1
2	Amoxicillin + clavulanic acid	3	1	4	1	1	4
3	Cefuroxime	5	2	5	2	2	-
4	Cefalexin	2	5	2	9	7	2
5	Cefixime	-	3	6	3	5	6
6	Cefadroxil	4	6	8	-	6	3
7	Clarithromycin	6	7	3	3	8	7
8	Cefaclor	7	-	-	8	4	9
9	Cefradine	7	-	7			5
10	Ciprofloxacin	9	7	9	6	9	9

Overall, prescribing for outpatients varies considerably between regions, but there is some consistency within the national Top 4, with amoxicillin or amoxicillin + clavulanic acid ranked first in the regional Top 10s. Second place in the regions is either cefuroxime (Watch) or cefalexin (Access). For the rest of the antimicrobials, there is no consistency.

### Comparing Top 10s with Level of Care

#### *Agents in the Top 10 in all six regions and nationwide (inpatients)*

The data in Table 12 shows some consistency in the use of essential antibiotics across all regions at all levels except at commune level, where there was significant variability in prescribing. No agents were used in all six regions.

**Table 12. A List of the Top 10 Agents Used for Inpatients in the Different Levels of Care**

Antimicrobial	AWaRe	Central	Provincial	District	Commune	Nationwide
Amikacin	A	Y				
Amoxicillin oral	A		Y	Y		Y
Amox + clav oral	A	Y	Y	Y		Y
Cefalexin oral	A			y		
Levofloxacin inj	W	Y				
Cefixime	W		Y			
Ciprofloxacin oral	W		Y	Y		Y
Cefuroxime inj	W	Y				Y
Cefuroxime oral	W		Y	Y		
Cefotaxime	W	Y	Y	Y		Y
Cefoperazone inj	W	Y	Y			
Ceftazidime	W	Y	Y	Y		
Ceftriaxone	W	Y	Y			
Cefoxitin	W	Y				

Central Highlands (CH) is an outlier as the only Top 10 user of Watch agents; azithromycin, cefaclor, cefipime, netilmicin, ofloxacin. In addition to Access items including cefadroxil and gentamicin, CH also uses Not Recommended cefoperazone+sulbactam, which is not in the Top 10.

*Agents in the Top 10 in all six regions and nationwide (Outpatients)*

**Table 13. A List of the Top 10 Agents Used for Outpatients in the Different Levels of Care**

Antimicrobial	AWaRe	Central	Provincial	District	Commune	Nationwide
Amoxicillin oral	A	Y	Y	Y	Y	Y
Amox + clav oral	A	Y	Y	Y	Y	Y
Azithromycin oral	W				Y	
Cefaclor	W	Y		Y		Y
Cefalexin	A			Y	Y	Y
Cefadroxil	A			Y		Y
Cefixime	W	Y	Y	Y	Y	Y
Ciprofloxacin oral	W	Y	Y	Y	Y	Y
Cefuroxime oral	W	Y	Y	Y	Y	Y
Cefpodoxime	W	Y	Y			Y
Clarithromycin oral	W	Y	Y	Y	Y	Y

This shows that prescribers in every region mostly select a similar range of Access and Watch medicines for outpatients, which predominate in the Top 10. There are no Reserve agents in the Top 10 of consumption across all outpatient settings.

Commune levels in all regions used azithromycin, an additional oral Watch medicine. At the district level, more oral Access and Watch cephalosporins are consistently used than at provincial and central levels. It is important to take these findings in the context of the approved list of antimicrobials shown above.

Four Watch medicines—azithromycin, cefixime, clarithromycin and ciprofloxacin oral—appear in the Top 10 for the commune level in all regions.

From the perspective of rational use of medicines, treatment should be optimised to the most appropriate agent for each condition and the setting in which the patient is being managed. Antimicrobials should be defined in treatment guidelines which restrict the options available, both to reduce inappropriate use which leads to resistant bacteria and to improve cost-effective procurement, storage and handling.

There should not be significant choice or duplication of agents in each category. Also, the higher the DDD-BD or DDD-LK of the total Top 10 items the better, indicating fewer agents used more often which may be linked to compliance with guidelines.

**Comparing DDDs of Top 10s with Level of Care in Each Region**

*DDD/BD at each level in all six regions and nationwide (Inpatients 4-year average)*

Table 14 summarises Top 10 consumption for inpatients at each level of care within each region.

**Table 14. DDD/BD at Each Level in All Regions and Nationwide (Inpatients 4-year average)**

Level of Care	NCC	MD	RRD	SE	CH	NMM	Nationwide
Central	22.1	54.7	23.4	38.5	29	25.4	26.8
Provincial	21.1	40.3	22.2	37.9	30.2	19.7	20.4
District	28	45.9	26.5	40.2	41.7	25.4	30.8
Commune	19.6	0	8.9	0	54.6	16.5	17.2

The data shows there are no antimicrobials used in communes in Mekong Delta or Southeast, possibly due to limited staff capacity or people's non-use of health services at the commune level.

The preferred use of Top 10 agents for inpatients is highest nationwide at the district level. Mekong Delta region's consumption of Top 10 agents at all levels was highest in all regions, with Southeast the second highest in central and provincial levels but not at the district level where Central Highlands is slightly higher.

#### *DDD-LK at each level in all six regions and nationwide (Outpatients 4-year average)*

**Table 15. DDD/LK at Each Level in All Six Regions and Nationwide (Outpatients 4-year average)**

Level of Care	NCC	MD	RRD	SE	CH	NMM	Nationwide
Central	1.8	2.1	1.5	1.9	2.2	2.2	1.8
Provincial	2.9	2.9	2.9	2.4	2.8	3.5	2.7
District	3.7	3.4	4.4	3.0	3.8	4.6	3.6
Commune	5.2	3.0	4.4	2.8	3.1	3.9	3.9

In outpatients, the DDD-LK is small, so the comparison between regions and levels is less clear. The preferred use of Top 10 agents is highest at the commune level nationwide. In comparison with the other regions, Northern Midlands and Mountains has the highest consumption of the Top 10 agents at all levels, except the commune level.

#### **Comparing Consumption by Pharmacological Groups as DDD-BD**

**Table 16. Breakdown of Consumption by Pharmacological Group**

Pharmacological Group	Consumption DDD-BD	Cost per DDD-BD (VND)	Cost Ratio (%)
Beta-lactam J01C	35	43,800	73.1
Quinolones J01M	6.7	120,872	15.3
Aminoglycosides D06A	2.2	132,381	8.9
Macrolides J01F	1.4	632,621	1.7
Other groups	0.8	161,959	0.6
Tetracycline D06A	0.2	10,146	0.2
Lincosamide D10A	0.2	11,323	0.1
Phenicol D06A	0.002	17,424	0.0005
Sulphonamides A07A	0.001	38,092	0.0003

Beta-lactams are the most commonly prescribed pharmacological group and account for approximately 75% of the spend on antibiotics. The list of approved medicines includes 92 individual items, of which 25 are cephalosporins.

Quinolones are the second most widely used, at approximately 20% of the beta-lactams by both DDD-BD and cost ratio, but at almost three times the cost per DDD-BD. Aminoglycosides cost more per DDD-BD but are used only one-third as much as quinolones, therefore representing only 8.8% of total spend on antimicrobials.

Macrolides represent the highest cost per DDD-BD with consumption of only 1.5 DDD-BD, representing less than 2% of the spend on antimicrobials.

Most other groups are minimally used (less than 1.0 DDD-BD).

### Disease Patterns

Table 17 shows the comparison between regions and nationwide for criteria which may affect the use of antimicrobials. The COVID pandemic was declared in March 2020 so the figures collected may reflect the impact on services and disease patterns.

**\*\* Data is taken from MOH Health Statistical Yearbook 2019-2020**

**Table 17. Data from National Epidemiological and Demographic Data**

Regions	Area (*) (km <sup>2</sup> )	Average Population (*) (thousands of people)	Population Density (*) (persons/km <sup>2</sup> )	Infectious and Parasitic Diseases 2019 (**)		Infectious and Parasitic Diseases 2020 (**)	
				Cases (%)	Deaths (%)	Cases (%)	Deaths (%)
North Central and Central Coast (NCC)	9584,8	20584,9	215	9.15	<b>25.91</b>	6.72	12.02
Đồng Bằng Sông Cửu Long (MD)	4092,2	17422,6	426	11.76	7.18	<b>10.58</b>	13.92
Red River Delta (RRD)	21278,5	23224,8	<b>1091</b>	5.22	<b>0.3</b>	<b>3.83</b>	4.03
Southeast (SE)	2355,1	18315,0	778	<b>14.46</b>	5.94	7.1	<b>16.48</b>
Central Highlands (CH)	5454,8	6033,8	<b>111</b>	13.59	10.19	8.42	8.75
Northern Mountains and Midlands (NMM)	9518,4	12925,1	136	<b>4.99</b>	4.97	4.36	<b>2.6</b>
<b>Nationwide</b>	<b>331344,3</b>	<b>98506,2</b>	<b>297</b>	<b>9.25</b>	<b>16.59</b>	<b>6.60</b>	<b>11.37</b>

<b>Lowest figures</b>
<b>Highest figures</b>

Highest population density, which could be seen as a potential risk factor for the increased transmission of infections, is seen in Red River Delta, which is almost 50% more dense than the next highest, Southeast.

However Southeast has gone from having the highest case percentage in 2019 to the highest death percentage in 2020.

Red River Delta had the second lowest percentage of cases reported in 2019 and the lowest percentage of deaths. In 2020, RRD reported the lowest percentage of cases and the second lowest percentage of deaths. The AWaRe data (in Consumption) from RRD showed that for outpatients, almost three-quarters of medicines are Access, and a very small percentage are Reserve and Other. However, for inpatients, RRD has the lowest use percentage of Access medicines and the highest use percentage of Other agents.

The highest percentage of deaths in 2019 was in North Central and Central Coast at 25.91%, more than double the next highest, Central Highlands, and higher than the nationwide figure of 16.59%. In 2020, the highest proportion of deaths was in Southeast at 16.48%, closely followed by Mekong Delta at 13.92% and North Central and Central Coast at 12.02%.

In 2019, Southeast had the highest percentage of reported cases of infectious diseases, which was reduced by approximately half in 2020. However, fatalities increased more than 270% from 5.94% to 16.48% in the same period, maybe in relation to drug resistance.

In 2020, all regions reported a reduction in the percentage of cases of infection compared to 2019. The highest proportion of cases in 2020 was in Mekong Delta, only slightly reduced from the cases in 2019. The proportion of deaths reported in 2020 reduced from 2019 in North Central and Central Coast, Central Highlands, and Northern Mountains and Midlands but increased in the other regions.

## 2.2 SPEND: INPATIENT AND OUTPATIENT

Consumption figures help to compare prescribing practices and describe variation across all levels and regions. However, as prices vary, the spend on these agents is not predictable; there are significant consumption variations across the regions.

The metric used to compare is spend (VND) per DDD/BD or DDD/LK.

### Spend per DDD/BD Inpatients from Top 10 Nationwide from Highest Spend over Four Years

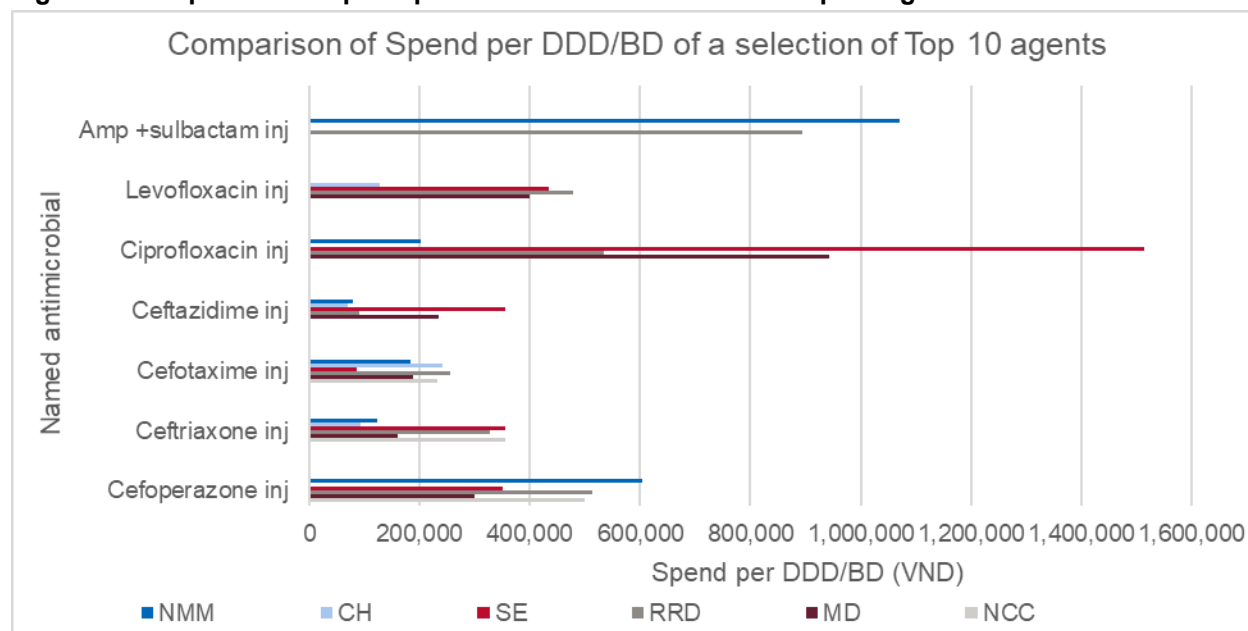
**Table 18. Inpatient Data from Nationwide Top 10 with Highest Average Spend over Four Years**

Ranking by Spend	Antibiotic	Route	Spend (VND)/DDD-BD	Cost Ratio of Total Antibiotic Spend (%)	Ranking Consumption
1	Cefoperazone	Inj	323,910	13.06	11th
2	Levofloxacin	Inj	302,691	10.07	10th
3	Ceftriaxone	Inj	264,072	10.02	7th
4	Cefotaxime	Inj	224,031	8.77	4th

Cefoperazone injection has the highest spend per DDD/BD but is the 11th most consumed agent. The second highest is levofloxacin injection with the 10th highest consumption. All four are Watch agents which are much more expensive than first-line agents.

## Spend per DDD/BD from Top 10 Highest Spend by Region

Figure 1. Comparison of Spend per DDD/BD of a Selection of Top 10 Agents



(Graphical representation of Annex 1)

This overview of the highest spent items across the regions shows variation in spend/DDD-BD up to 750% for ciprofloxacin injection, a Watch antibiotic.

Southeast has the three highest spent medicines and the lowest spent medicine out of the seven items listed. Mekong Delta and Central Highlands spend the least.

## Spend per DDD/LK for Outpatients from Top 10 Nationwide from Highest Spend over Four Years.

Table 19. Comparing Consumption with Spend of the Top 10 Highest Cost Agents for Outpatients

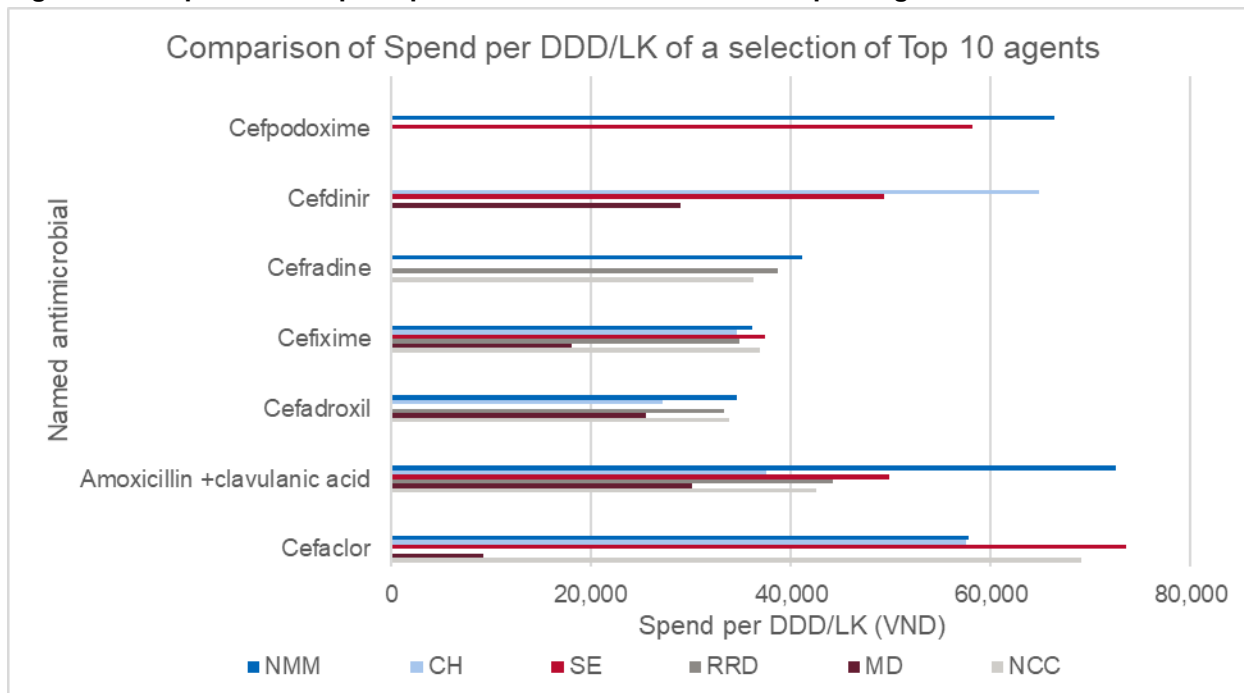
Ranking by Spend	Antibiotic	Route	Spend (VND)/DDD-LK (4 years)	Cost Ratio % Total Antibiotic Spend (4 years)	Ranking Consumption
1	Cefaclor	Oral	65,107	29%	9th
2	Amoxicillin +clavulanic acid	Oral	41,393	99%	2nd
3	Cefadroxil	Oral	31,369	21%	7th
4	Cefixime	Oral	30,890	31%	5th

As for inpatient treatment, the highest spend is associated with agents that are less commonly used such as cefaclor, a Watch medicine which ranked 9/10 in the Top 10 DDD-BD for consumption. However, the second highest spend (99%) is the Access oral medicine, amoxicillin + clavulanic acid which is a good choice for outpatient treatment requiring augmented penicillins in areas of penicillin-resistant organisms; amoxicillin would be a cheaper first-line option where there is no resistance. Cefadroxil would be a suitable first-line option Access medicine but is also one of the costliest nationally.

Cefixime, a third-generation cephalosporin, is also a Watch agent, used more often than cefaclor, second-generation, but costing less.

**Comparisons of Spend/DDD-LK (outpatients) on a Selection of Agents across the Regions**

**Figure 2. Comparison of Spend per DDD/LK of a Selection of Top 10 Agents**

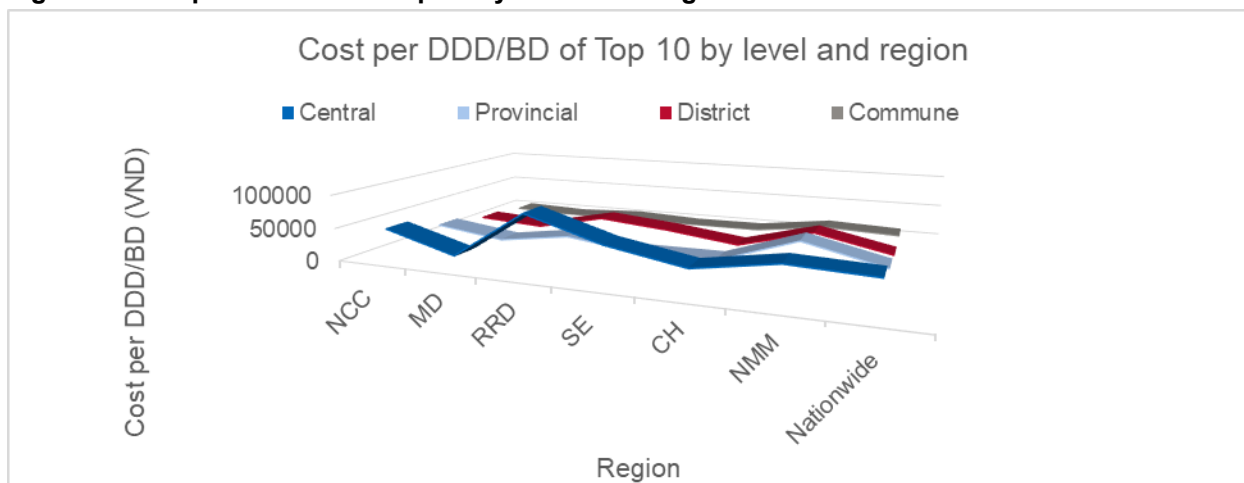


(Graphical representation of Annex 2)

This summary of the highest spend/DDD-LK for outpatients across the regions shows higher variation, up to 822% for cefaclor, a widely distributed Watch antimicrobial permitted for use at all levels. The impact of these price differentials is highlighted by analysis of regional spend at all levels of care. As expected, the cost per DDD and cost ratios of both inpatients and outpatients for the Top 10 in each region vary widely, due to different uses of products in the Top 10 and price variations of the same product across regions.

**Cost per DDD/BD of Top 10 (VND) at Each Level in all Six Regions and Nationwide (Inpatients 4-year average)**

**Figure 3. Cost per DDD/BD of Top 10 by Level and Region**



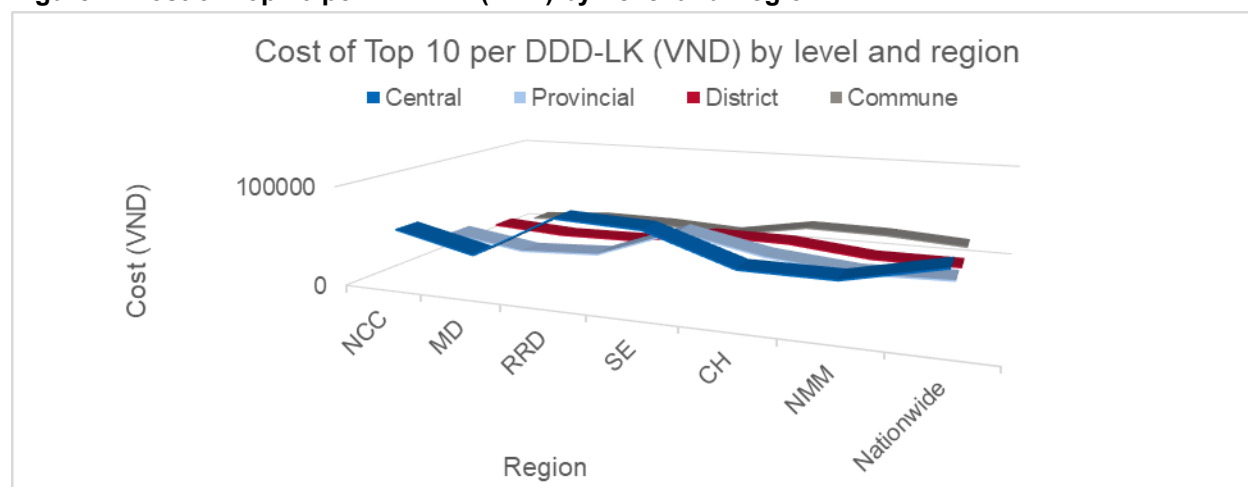


(Representation of Annex 3)

The inconsistent patterns across regions combined with the absence of services in some regions' commune health facilities make it difficult to interpret what "best practice" favors. Higher values may show the increase in service provision capacity or the use of very expensive agents as a result of an ineffective procurement procedure, compared to none, or poor procurement processes leading to very expensive agents being used.

**Cost per DDD/LK of Top 10 (VND) at Each Level in All Six Regions and Nationwide (Outpatients 4-year average)**

**Figure 4. Cost of Top 10 per DDD-LK (VND) by Level and Region**



(Representation of Annex 4)

Top 10 medicines for both inpatients and outpatients in central health facilities in Red River Delta appear to cost more than in other health facilities.

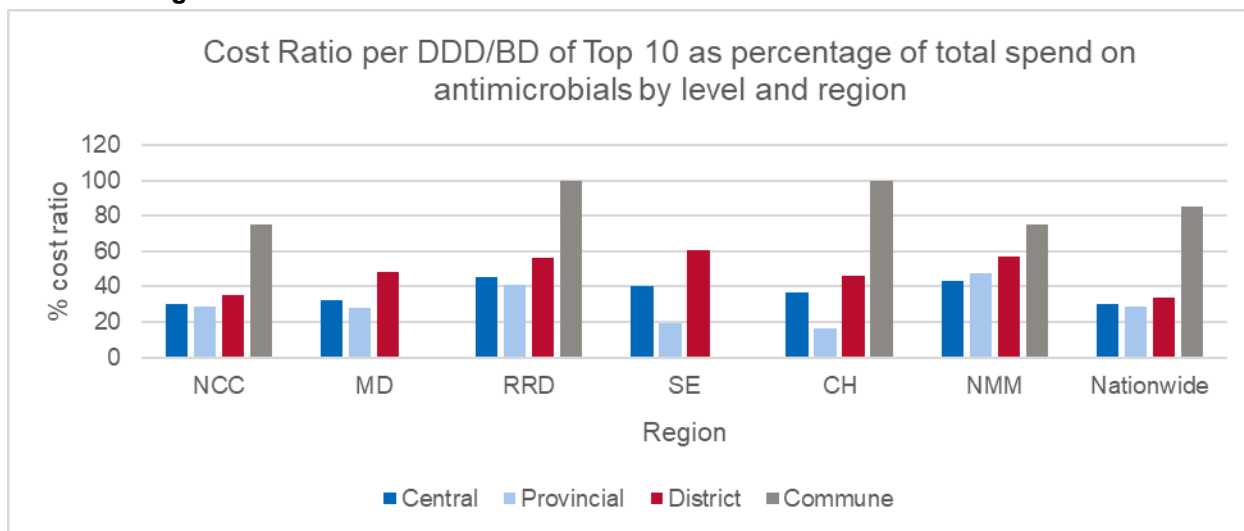
Mekong Delta health facilities pay least at both central and provincial levels for the Top 10 antimicrobials for both inpatients and outpatients.

North Midlands and Mountains pays the most for the Top 10 for inpatient treatment at all levels except the central level. However, the spend for each outpatient in the region is not the highest.

**Cost Ratio**

Cost per DDD/BD of Top 10 as a percentage (%) of total antimicrobial spend at each level in all six regions and nationwide (4-year average for inpatients)

**Figure 5. Cost Ratio per DDD/BD of Top 10 as Percentage of Total Spend on Antimicrobials by Level and Region**

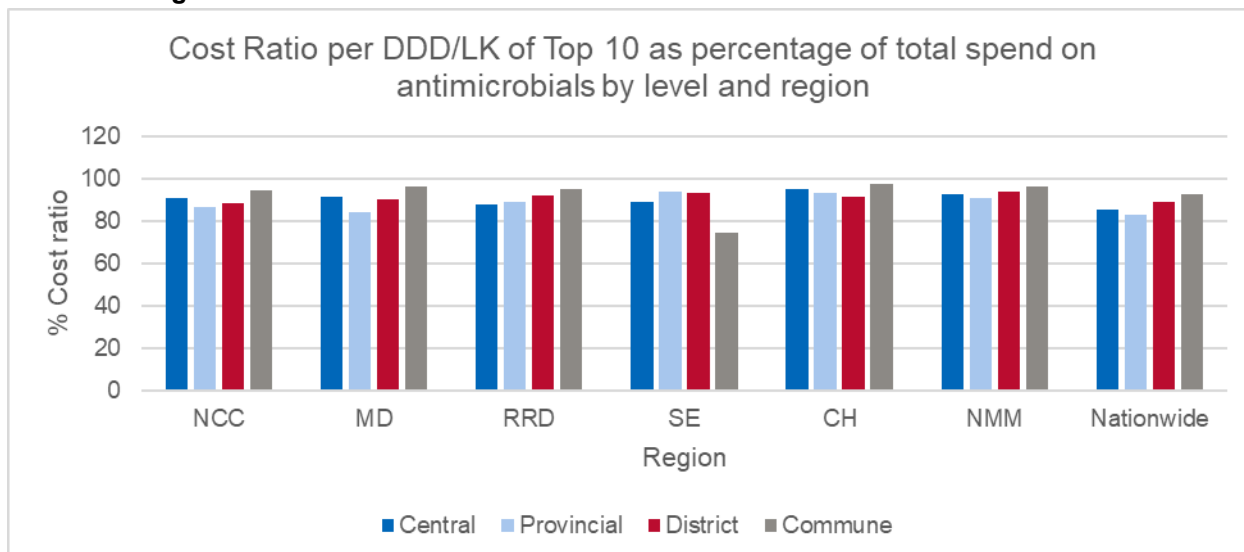


*(Representation of Annex 5)*

The cost ratio of Top 10 agents in the total antimicrobial spend for inpatients ranges from as little as 16.5% in provincial levels of Central Highlands, closely followed by Southeast (19.6%) to 100% in commune levels of Red River Delta and Central Highlands where there are fewer agents in use.

**Cost Ratio per DDD/LK of Top 10 as a Percentage (%) of Total Antimicrobial Spend at Each Level in All Six Regions and Nationwide (Outpatients 4-year average)**

**Figure 6. Cost Ratio per DDD/LK of Top 10 as Percentage of Total Spend on Antimicrobials by Level and Region**



*(Representation of Annex 6)*

There are no clear or consistent patterns across the regions with respect to spend because of the variability in the selection of products which appear in the Top 10 and the wide range of cost/DDD-BD and cost/DDD-LK figures.

The cost ratios show that the Top 10 antimicrobials used for outpatients represent the vast majority of spend on antimicrobials (83.3–97.6%) in all regions and nationwide, at all levels except for the commune level in Southeast which is a significant outlier at only 74.9%. This implies that Southeast has a wide range of high-cost agents in use.

**Table 20. Regional Antimicrobial Spending Trends: Spend on Top 10 over Four Years**

Region	NMM	MD	RDD	SE	CH	NCC
Ave spend/DDD -BD (inpatient)	14,830	4298	14,069	7458	1340	4195
% total antibiotic spend /trend	45.7 ↓	30.8 ↓	25.8 ↑	19.2 ↓	15.8 ↓	17.4 ↑
Ave spend/DDD-LK (outpatient)	25,078	16,741	19,504	41,989	22,809	23,879
% total antibiotic spend /trend	93.9 ↑	88.2 ↑	90 ↑	89.7 ↓	88.8 ↓	87.5 ↓

Lowest spend
Highest spend

### 3. DISCUSSION

Globally, four organisms are known to have developed resistance: (1) *Klebsiella pneumoniae* and *Escherichia coli*, some strains of which are resistant to carbapenems; (2) *Neisseria gonorrhoea* which has become resistant to third-generation cephalosporins; (3) *Staphylococcus aureus* to vancomycin and methicillin; and (4) *Pseudomonas* bacteria, some of which are resistant to fluoroquinolones, beta-lactams, chloramphenicol, and trimethoprim. These lead to untreatable pneumonia, blood infections, urinary tract infections, gonorrhoea, and skin, wound, joint and post-surgical injuries.

In Vietnam, there are reports of multi-drug resistance such as 80% for *Streptococcus pneumoniae*; 30-70% of gram-negative bacteria (eg *K. pneumoniae* and *E coli*) resistant to third- and fourth-generation cephalosporins; and 40-60% resistant to aminoglycosides and fluoroquinolones.

This summary only highlights the most crucial points of the full report. Further analysis will provide more detailed insights at the various levels of healthcare and by region.

In addition to a wide range of products being prescribed, there is clearly significant variation in pricing across the country. However, the connection between price and prescribing decisions has not been analysed.

Limitations of this study is that it only analyses some antimicrobial agents included in the list of medicines covered by health insurance.

- There are many conditions which are treated with a range of antimicrobials which are not included in this report.
- There is known to be considerable self-administration of antimicrobials by patients who chose to buy treatments themselves, even without a prescription. Often this leads to inappropriate selection of antimicrobial, incomplete courses of treatment, or overuse. There is also the possibility of purchasing substandard or counterfeit products on the market which will be sub-therapeutic or can be fatal.

- The data is prescribing information. The health care level corresponds to the health facility where patients receive treatments. Each health facility clearly stipulates the list of drugs used, complying with the list issued by the MoH.
- Insured patients' co-pay for treatment costs depend on their health insurance benefits. Drugs can be procured through bidding at the central, provincial or each health facility, which may affect drug selection and price.

### 3.1 LISTING AND SELECTION OF ANTIMICROBIALS

The WHO EML 2023 contains 48 antimicrobials in total. Only ten of these are cephalosporins—two first-generation, one second-generation, five third-generation, one fifth-generation, and one Other cephalosporin. Two of these ten are Access antibiotics, five are Watch, and the remaining three are Reserve.

The list of antibiotics covered by SHI selected for the DDD analysis includes 92 antimicrobials of which there are 23 cephalosporins. Of these 23, six are Access (three oral and three parenteral) and 17 are Watch (seven are available as oral medicines).

Third-generation cefoperazone + sulbactam injection, a Watch antimicrobial, appears in five of the six regions' Top 10 and ranks 11th nationwide. Overuse of Watch agents, like third-generation cephalosporins, can lead to resistant bacteraemia.

The Vietnam MoH list combines levels 3 and 4 facilities when defining which antimicrobials can be used. This is unhelpful because there will be a difference in competence, and facilities at lower levels of care where more complex agents requiring more technical monitoring and administration may not be suitable.

A range of antimicrobials is used in Medical Stations/Medical Agencies which is the primary health care level. The majority (34) are Access medicines. However, two are Not Recommended—nalidixic acid and sulfaguanidine, and eight are Watch medicines which should be closely monitored to prevent resistance. It is important to ensure that staff working at this level of health service have the tools and skills required to be able to use these agents effectively.

Agents classed Other are included in the list of antimicrobials permitted for use by MoH. Among those are three oral agents, including nalidixic acid and sulfaguanidine, which can be used at all levels of care, and sulfasalazine, which is not included in the WHO 2023 EML and is used at all levels of care except medical stations. Additionally, cefoperazone + sulbactam, a Not Recommended injectable combined preparation is permitted in specialist, first- and second-level services.

Two Other agents appeared in the Top 10, including nalidixic acid, a narrow-spectrum first generation fluoroquinolone antibiotic which is used for urinary tract infections and cefoperazone, a third-generation cephalosporin, broad spectrum injectable antibiotic used in conjunction with a beta-lactamase inhibitor, sulbactam.

Seven Reserve agents intended for drug-resistant infections are analysed, six of which are injectable; all can be used at level 1 and but Tigecyclin at level 2. Injectable minocycline can also be used in levels 3 and 4 hospitals. The data over four years shows an increase in the use of Reserve agents from 0.5 to 0.9% over the period 2019–2022.

### **3.2 CONSUMPTION**

Nationwide, Access agents represent only 31.4% of the agents included in inpatient prescriptions, and 57.9% in outpatient prescribing, lower than WHO criteria point toward optimal prescribing being 60% Access, with no Other and minimal Reserve agents.

The central level in Southeast is the highest user of Reserve agents. This may be reflected in the higher death rates from infections in this region and the presence of resistant microorganisms.

Other agents, those not included on the WHO Essential or Not Recommended list because there is no based evidence, should be avoided where possible. Therefore, the increase in the use of these agents needs to be monitored.

This study shows cefoperazone + sulbactam, in the Not Recommended AWaRe category, is used nationally. Specifically, it is used for inpatients at the central level in three regions, MD, SE, NMM, and at the provincial level in CH.

Consumption data shows a positive trend away from the use of Watch agents to greater use of Access in line with WHO antimicrobial stewardship recommendations.

The outpatient figures approach the WHO 2023 target, with close to 60% of use in the Access group (59.7%). When comparing the average of four years to the 2019 figure, the overall trends are slightly increasing use of Access and decreasing use of Watch agents. This may have resulted from the implementation of the National Action Plan in Vietnam 2013-2020.

However, there are significant exceptions, where both Watch and Reserve agents are being used at a level of care which may not be appropriate because of the monitoring required, or where the degree of consumption implies either high levels of antimicrobial resistance or problematic prescribing.

In the absence of comprehensive antimicrobial resistance monitoring, closer scrutiny of prescribing practices, linked to patient health information records, will be necessary to understand these outliers.

There does not appear to be a correlation between the reported cases of infection and consumption data other than Southeast which uses most Reserve agents, having the highest mortality rate in 2020.

### **3.3 REASONS FOR VARIATION**

There are many reasons why antimicrobials are inappropriately prescribed. Prescribers may not be familiar with MoH guidelines or may be influenced in their selection of a specific agent via marketing efforts by the pharmaceutical industry. Also, concern for the patient or pressure to intervene in their treatment may also lead to the selection of a broader-spectrum agent than necessary. Prescribers also may have limited knowledge of available agents and therefore routinely use the same options. Another reason is that prescribers may not be aware of antimicrobial resistance due to drug procurement challenges.

### **3.4 SPEND**

Issues associated with price management, bidding, and drug supply create great variance in spend and trends in spending, which may stem from the absence of a national level tendering

and procurement process. For example, one product can be sold by a range of pharmaceutical companies and manufacturers with both brand-named drugs and multiple generic drug groups. Listed price and tendering price are not well-managed, hence the cost of one monopolized product can escalate dramatically. Local bidding processes may be constrained by a shortage of competition to drive down prices.

Prescribers may be aware of price when they select a particular agent, and this may influence their prescribing decisions. On the other hand, only a few patients need to co-pay at a limited proportion of drug prices.

Inpatient settings tend to use more parenteral than oral agents as shown in the DU75. However, switching to appropriate oral agents when possible both improves treatment outcomes and reduces the total costs of care.

## **4. CONCLUSIONS**

The analysis identifies priorities for monitoring and improving compliance with antimicrobial usage guidelines, the need to develop more detailed prescribing guidelines, and the consideration and regulation of the list of SHI products in line with international guidelines and recommendations.

Antimicrobials of different generations should be appropriately selected for treatment of different conditions so that antimicrobial use and procurement can be rational and effective.

All AWaRe agents may be necessary in inpatient units, but appropriately trained staff and equipment must be available for administration and monitoring of intravenous or narrow therapeutic range options.

## **5. RECOMMENDATIONS**

Data on SHI drugs is an important source for monitoring and analysis of drug use trends and developing and adjusting the list of SHI drugs. Hence, there is a need to continue the analysis of drug use in each province and, at the same time, update data adequately to evaluate the results of concurrent antibiotic use.

### **5.1 PRODUCT SELECTION**

This report can be a reference for MoH when evaluating and developing the Action Plan in the coming years.

Doctors must be provided all information on patterns of resistance and detailed guidelines on antibiotic use and must comply with them to prevent antimicrobial resistance.

The list of SHI medicines approved for use by the MoH must be revised in compliance with WHO Essential Medicines List and AWaRe categories, particularly at lower levels of care. Watch and Reserve agents must be limited to higher-level facilities with more complex cases.

Ticarcillin + clavulanic acid should be used with caution as it has been associated with an increased incidence of adverse effects and was withdrawn from the U.S. market in 2015.

Aminoglycosides such as gentamicin in the Access category and amikacin in the Watch group require checking of patient's kidney function and antibiotic concentrations when used.

Intravenous administration for agents with good oral bioavailability such as some fluoroquinolones and linezolid should be limited to a minimum extent which reduces inconvenience to the patient such as hospitalisation or the need for trained personnel to administer the doses.

Reserve agents must be restricted for infections which have not responded to other classes of antibiotics or those shown to be resistant to other agents by laboratory analysis, to prevent resistance developing to them. They are expensive, and the consumption report shows use is increasing for inpatients. Further analysis is needed to determine if use increase is due to increases in resistant infections or inappropriately selected agents.

The use of agents described as Other is increasing in all regions' inpatient services and Southeast's outpatient services. Other agents are not included in the WHO Essential Medicines list or AWaRe categories and should not be used unless there is evidence for their effectiveness against resistant organisms in Vietnam. The MoH-approved antimicrobials not included in WHO lists are oral nalidixic acid, sulfaguanidine, sulfasalazine; injectable cefoperazone + sulbactam is included in the Not Recommended list.

Southeast appears to be an outlier region in the use of restricted antimicrobials, and this needs to be clarified. Comparison of patterns of resistance, diseases, and prescribing indicates that Northern Midlands and Mountains use antimicrobials closer to the WHO- proposed optimal practice.

Implementation of prescribing guidelines must be regularly audited by monitoring compliance; a benchmarking exercise may enable more open debate and motivate change. DDD-BD and DDD-LK data from every level of care or region can be compared to others of the same complexity in an anonymised way. This self-reporting motivates change towards a target of 100% compliance with prescribing guidelines.

In parallel it is vital that more organisations participate in and report to the national AMR Surveillance System so that resistance is monitored and treatment is appropriately targeted.

## **5.2 COST**

Once national guidelines have been established, a Formulary of all the agents included can be published. The procurement of medicines must be managed based on central procurement principles or national negotiations on price to ensure that all medicines listed are available to patients in each setting at reasonable prices.

Cost must not have an impact on the availability of the most appropriate antibiotics and must be managed to optimise the use of limited resources.

## RESOURCES

### WHO

<https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis>

ATC-DDD Toolkit. <https://www.who.int/tools/atc-ddd-toolkit/indicators>

Antibiotics in the WHO Essential Medicines List 2023:  
<https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.04>

WHO guideline for carbapenem resistance <https://iris.who.int/handle/10665/259462>

WHO Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in health care facilities.  
<https://www.who.int/publications/i/item/9789241550178>

10 THREATS TO GLOBAL HEALTH <https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>

WHO Health Topics, Vietnam. Global Database of self-report including focus on Antimicrobial Sensitivity Testing (AST) 2021 <https://www.who.int/vietnam/health-topics/antimicrobial-resistance>

### ANTIMICROBIAL RESISTANCE IN VIETNAM

#### Community Acquired Pneumonia

[Outpatient antibiotic prescribing for acute respiratory infections in Vietnamese primary care settings by the WHO AWaRe \(Access, Watch and Reserve\) classification: An analysis using routinely collected electronic prescription data - PubMed \(nih.gov\)](#) Lancet Reg Health West Pac. 2022 Oct 11:30:100611. doi: 10.1016/j.lanwpc.2022.100611. eCollection 2023 Jan.

Drivers of antibiotic use in Vietnam: implications for designing community interventions. BMJ Global Health Volume 6 Issue 7 July 2021 <https://gh.bmj.com/content/6/7/e005875>

A National Survey of Dispensing Practice and Customer Knowledge on Antibiotic Use in Vietnam and the Implications. [Antibiotics \(Basel\)](#). 2022 Aug; 11(8): 1091. Published online 2022 Aug 12. doi: [10.3390/antibiotics11081091](https://doi.org/10.3390/antibiotics11081091)  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9405246/#>

Vietnam in the context of community-acquired respiratory tract infections: links between antibiotic susceptibility, local and international antibiotic prescribing guidelines, access to medicines and clinical outcome *Journal of Antimicrobial Chemotherapy*, Volume 77, Issue Supplement\_1, September 2022, Pages i26–i34,  
<https://doi.org/10.1093/jac/dkac214> Published: 06 September 2022  
[https://academic.oup.com/jac/article/77/Supplement\\_1/i26/6692270](https://academic.oup.com/jac/article/77/Supplement_1/i26/6692270) Country data on AMR in Hospital surveillance predicts community pneumococcal antibiotic resistance in Vietnam 29 July 2020. *Journal of Antimicrobial Chemotherapy*, Volume 75, Issue 10, October 2020, Pages 2902–2906, <https://doi.org/10.1093/jac/dkaa276>



## REGIONAL ACTIVITIES ON AMR

Guidelines on implementing Antimicrobial Stewardship Programs in Korea. *Infect Chemother.* 2021 Sep;53(3):617-659. doi: 10.3947/ic.2021.0098.  
<https://pubmed.ncbi.nlm.nih.gov/34623784/>

Trends of Fixed-Dose Combination Antibiotic Consumption in Hospitals in China: Analysis of Data from the Center for Antibacterial Surveillance, 2013–2019. *Antibiotics (Basel)*. 2022 Jul; 11(7): 957. Published online 2022 Jul 15. doi: [10.3390/antibiotics11070957](https://doi.org/10.3390/antibiotics11070957)  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9312249/>

## GLOBAL ACTIVITIES

Global PPS datasets <https://www.global-pps.com/>

Drug Use 75% (DU75) in 17 European Hospitals 2000- 2005 *Curr Clin Pharmacol.* 2011 Feb;6(1):62-70. doi: 10.2174/157488411794941322.  
<https://pubmed.ncbi.nlm.nih.gov/21235461/>

Commonwealth Pharmacy Association AntiMicrobial Stewardship training and Toolkit. Available to pharmacists who join here: <https://commonwealthpharmacy.org/join-us/>

BNF British National Formulary section on Carbapenems <https://bnf.nice.org.uk/treatment-summaries/carbapenems/>

## PATIENT SAFETY

Withdrawn antimicrobials in the U.S.– combination Ticarcillin and clavulanic acid. 2015 *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury* [Internet]. October 20, 2020.  
<https://www.ncbi.nlm.nih.gov/books/NBK548183/#:~:text=The%20combination%20of%20ticarcillin%20and,infections%20due%20to%20susceptible%20organisms>

## GOVERNMENT PLANS AND GUIDELINES ON THE USE OF ANTIMICROBIALS

1. Ministry of Health. National Action Plan on drug resistance prevention for the period from 2013 to 2020 (<https://kcb.vn/thu-vien-tai-lieu/ke-hoach-hanh-dong-quoc-gia-ve-style-chong-khang-thuoc-giai-.html>)
2. **Guidelines of MOH for the use of antibiotic:**
  - Decision No. 708/QD-BYT dated March 2, 2015 of the Minister of Health on "Guidelines for the use of antibiotics" <https://kcb.vn/thu-vien-tai-lieu/tai-lieu-huong-dan-su-dung-khang-sinh.html>
  - Decision No. 5631/QD-BYT dated December 31, 2020 of the Minister of Health promulgating the document "Guidelines for implementing antibiotic use management in hospitals" <https://thuvienphapluat.vn/van-ban/The-thao-Y-te/Quyết-dinh-5631-QD-BYT-2020-tai-lieu-Huong-dan-quan-ly-su-dung-khang-sinh-trong-benh-vien-461349.aspx>
  - Decision No. 4815/QD-BYT dated November 20, 2020, the Ministry of Health issued the professional document "Guidelines for diagnosis and treatment of community-acquired pneumonia in adults". [https://moh.gov.vn/chuong-trinh-muc-tieu-quoc-gia/-/asset\\_publisher/7ng11fEWgASC/content/bo-y-te-huong-dan-chan-oan-ieu-tri-viem-phoi-o-nguoi-lon-nhan-manh-viec-tiem-phong?inheritRedirect=false](https://moh.gov.vn/chuong-trinh-muc-tieu-quoc-gia/-/asset_publisher/7ng11fEWgASC/content/bo-y-te-huong-dan-chan-oan-ieu-tri-viem-phoi-o-nguoi-lon-nhan-manh-viec-tiem-phong?inheritRedirect=false)

- Decision no. 5643/qd-byt dated December 31, 2015 of the minister of health on diagnosis and treatment guidelines some ENT diseases. <https://kcb.vn/phac-do/huong-dan-chan-doan-va-dieu-tri-mot-so-benh-ve-tai-mui-hong.html>
- Decision No 5642/QD-BYT dated December 31, 2015 issued by the Minister of Health on Guidelines for diagnosis and treatment of some infectious diseases <https://thuvienphapluat.vn/van-ban/The-thao-Y-te/Quy-et-dinh-5642-QD-BYT-2015-Huong-dan-chan-doan-va-dieu-tri-mot-so-benh-truyen-nhiem-379633.aspx>

## GOVERNMENT PROVISION FOR AMR SURVEILLANCE

Vietnam's antibiotic resistance surveillance system: In 2022, the Ministry of Health will have the AMR Surveillance System website (<https://kks.kcb.vn/amr/auth/login>). Currently, there are 54 hospitals participating in surveillance reports, but only 20 hospitals have satisfactory data. AMR information has been compiled into the reports but the reports has not been widely shared.

## PUBLISHED STUDIES ON THE EFFECTIVENESS OF ANTIMICROBIAL AGENTS IN VIETNAM

Ly Ngoc Kinh, Ngo Thi Bich Ha and colleagues. Find out the current situation of antibiotic use in hospital infections in intensive care units in some medical examination and treatment facilities in 2009-2010. <https://vhea.org.vn/tim-hieu-thuc-page-use-of-health-birth-in-patient-patients-at-the-donations-with-the-effects-on-a-number-of-health-care-sufferers-benh-11-10-2011-192.html>

Nguyen Van Kinh and colleagues of GARP-Vietnam National Research Team. Analysis of the current situation: Antibiotic use and antibiotic resistance in Vietnam. [http://bennhietdoi.vn/UploadFiles/2018/12/20/Bao\\_cao\\_su\\_dung\\_khang\\_sinh\\_va\\_khan\\_g\\_khang\\_sinh\\_tai\\_15\\_benh\\_vien\\_nam\\_2008-2009.pdf](http://bennhietdoi.vn/UploadFiles/2018/12/20/Bao_cao_su_dung_khang_sinh_va_khan_g_khang_sinh_tai_15_benh_vien_nam_2008-2009.pdf).

Didem Torumkuney, Subhashri Kundu, Giap Van Vu, Hoang Anh Nguyen, Hung Van Pham, Praveen Kamble, Ngoc Truong Ha Lan, and Nergis Keles. Country data on AMR in Vietnam in the context of community-acquired respiratory tract infections: links between antibiotic susceptibility, local and international antibiotic prescribing guidelines, access to medicines and clinical outcome. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9445855>)

Or ([https://academic.oup.com/jac/article/77/Supplement\\_1/i26/6692270](https://academic.oup.com/jac/article/77/Supplement_1/i26/6692270))

Larsson M, Nguyen HQ, Olson L et al. Multi-drug resistance in *Streptococcus pneumoniae* among children in rural Vietnam more than doubled from 1999 to 2014. *Acta Paediatr* 2021; 110: 1916–23 (<https://pubmed.ncbi.nlm.nih.gov/33544434/>)

Tien Viet Dung Vu, Thi Thuy Nga Do, Ulf Rydell, Lennart E Nilsson, Linus Olson, Mattias Larsson, Håkan Hanberger, Marc Choisy, Tuyet Trinh Dao, H Rogier van Doorn, Van Kinh Nguyen, Vu Trung Nguyen, Heiman F L Wertheim, VINARES consortium. Antimicrobial susceptibility testing and antibiotic consumption results from 16 hospitals in Viet Nam: The VINARES project 2012-2013 (<https://pubmed.ncbi.nlm.nih.gov/31201995/>).

## ANNEX 1. INPATIENT DATA FROM TOP 10 NATIONWIDE SHOWS THE SIGNIFICANT RANGE OF COSTS ASSOCIATED WITH THE TOP 10 AGENTS

Region/ VND/DDD- BD	NCC	MD	RRD	SE	CH	NMM	Range (1000 VND) / % Change
Cefoperazone inj	498,207	<b>298,379</b>	511,960	350,385	Not in top 10	<b>604,099</b>	298k-604k. Increase <b>202%</b> Nationwide 324k.
Ceftriaxone inj	<b>356,098</b>	160,642	326,611	<b>356,098</b>	<b>92,488</b>	123,075	92k-356k. Increase <b>387%</b> Nationwide 264k
Cefotaxime inj	232,483	188,068	<b>255,449</b>	<b>86,194</b>	240,091	181,987	86k-255k. Increase <b>297%</b> Nationwide 224k
Ceftazidime inj	Not in Top 10	233,515	90,609	<b>354,309</b>	<b>70,376</b>	79,484	70k-354k. Increase <b>506%</b> Nationwide 216k
Ciprofloxacin inj	Not in Top 10	943,213	533,193	<b>1,514,254</b>	Not in top 10	<b>202,200</b>	202k-1,514k. Increase <b>750%</b> <b>Not listed nationwide</b>
Levofloxacin inj	Not in Top 10	399,658	<b>477,754</b>	433,652	<b>127,173</b>	Not in Top 10	127k-478k. Increase <b>376%</b> Nationwide 303k
Amp + sulbactam inj	Not in Top 10	Not in Top 10	<b>893,229</b>	Not in Top 10	Not in top 10	<b>1,069,679</b>	893k-1,070k. Increase <b>120%</b> <b>Not listed nationwide</b>

<i>Lowest value</i>
<i>Highest value</i>

## ANNEX 2. OUTPATIENT DATA FROM TOP 10 NATIONWIDE SHOWS THE SIGNIFICANT RANGE OF COSTS ASSOCIATED WITH THE TOP 10 LIST OF AGENTS

Region/VND/ DDD-LK	NCC	MD	RRD	SE	CH	NMM	Range (1000 VND) / % Change
Cefaclor	69,115	9,205	Not on top 10	<b>73,501</b>	57,566	57,816	9k-74k Increase <b>822%</b> Nationwide 65k
Amoxicillin + clavulanic acid	42,563	30,098	44,251	49,788	37,487	<b>72,480</b>	30k-72k Increase <b>240%</b> Nationwide 41k
Cefadroxil	33,767	25,527	33,260	Not on top 10	27,109	<b>34,528</b>	26k-35k Increase <b>135%</b> Nationwide 31k
Cefixime	36,925	18,104	34,876	<b>37,429</b>	34,536	36,187	18k-37k Increase <b>205%</b> Nationwide 31k
Cefradine	36,300	Not on top 10	38,731	Not on top 10	Not on top 10	<b>41,169</b>	36k-41k Increase <b>114%</b> Nationwide 30k
Cefdinir	Not on top 10	28,964	Not on top 10	49,269	<b>64,874</b>	Not on top 10	29k-65k increase <b>224%</b> <b>Not listed nationwide</b>
Cefpodoxime	Not on top 10	Not on top 10	Not on top 10	58,110	Not on top 10	<b>66,308</b>	58k-66k Increase <b>114%</b> Nationwide 15k

**Highest spend**

### ANNEX 3. COST (VND) OF TOP 10 PER DDD-BD BY LEVEL AND REGION

Level of Care	NCC	MD	RRD	SE	CH	NMM	Nationwide
Central	45,885	<b>15,535</b>	<b>88,117</b>	54,387	34,334	53,036	48,287
Provincial	24,309	<b>9,739</b>	25,749	11,196	11,839	<b>51,462</b>	24,324
District	11,403	4,773	28,449	18,122	<b>3,871</b>	<b>34,570</b>	10,232
Commune	3,962	0	5,145	0	876	<b>15,750</b>	11,103

<b>Lowest cost</b>
<b>Highest cost</b>

## ANNEX 4. COST (VND) OF TOP 10 PER DDD-LK OUTPATIENTS BY LEVEL AND REGION

Level of Care	NCC	MD	RRD	SE	CH	NMM	Nationwide
Central	54,664	<b>36,298</b>	<b>79,624</b>	75,991	48,021	47,581	66,653
Provincial	30,461	<b>18,485</b>	22,812	<b>53,689</b>	36,709	28,670	31,141
District	20,416	<b>15,343</b>	16,581	<b>29,331</b>	28,427	19,838	19,842
Commune	<b>9,997</b>	15,913	15,126	10,847	<b>25,503</b>	24,305	18,792
<b>Lowest cost</b>							
<b>Highest cost</b>							

## ANNEX 5. INPATIENT COST RATIO OF TOP 10 BY LEVEL AND REGION AS A PERCENTAGE OF TOTAL ANTIMICROBIAL SPEND

Level of Care	NCC	MD	RRD	SE	CH	NMM	Nationwide
Central	30.3	32.5	45.2	40.5	36.5	43.3	30.1
Provincial	28.7	27.9	41.4	19.6	16.5	47.3	28.9
District	35.0	48.4	56.6	60.4	46.2	56.8	33.9
Commune	74.9	0	100.0	0	100.0	75.0	85.6

## ANNEX 6. OUTPATIENT INFORMATION ON TOP 10 COST RATIO ACROSS ALL LEVELS AND REGIONS

Level of Care	NCC	MD	RRD	SE	CH	NMM	Nationwide
Central	91.1	91.4	88.2	89.1	95.3	93.1	85.8
Provincial	87.0	84.2	89.1	94.2	93.3	90.9	83.3
District	88.6	90.6	92.3	93.3	91.4	94.0	89.1
Commune	94.9	96.5	95.4	74.9	97.6	96.7	93.1