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Research Article

Evaluation of rational drug use based on World Health Organization indicators in a tertiary hospital, Thailand

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ABSTRACT

This study aimed to evaluate the rational drug use in a tertiary hospital, Thailand based on World Health Organization (WHO) indicators. This retrospective study was conducted using electronic data from medical records which detailed dispensed prescriptions in the outpatient department (OPD) in a tertiary hospital, Thailand from April 2019 to March 2020. Core rational drug use was determined by the average number of drugs per prescription, percentage of drugs prescribed from the Essential Medicines List (EML) and oral antibiotic consumption using the defined daily dose (DDD). The average number of drugs per prescription in this study was 2.17. The average percentage of the drugs from the national list of essential medicines (NLEMs) in OPD was 66.52%. The DDD from April-September 2019 was 2.51 which increased to 4.61 in the period October 2019-March 2020. In conclusion, this study found the average number of drugs per prescription in outpatients was higher than WHO recommendations. The average percentage of drugs of essential drugs in our study was lower than the expected WHO value. Oral antibiotic consumption measured by DDD had increased. Therefore, policy regarding rational drug use needs to be accelerated as a policy in hospital. Irrational use of medicines is a multidimensional issue and requires interventions at several levels including areas involving health systems, overall organization, doctors, dispensers, patients and community and it remains a challenge in health facilities.

Keywords:
WHO core drug use indicators, Rational drug use, Irrational, Outpatient

1. INTRODUCTION

Rational drug use is an important aspect of the national health policy; it is also an essential tool with regard to improving the quality of basic health. Rational use of medicine has been defined by the World Health Organization (WHO) and requires patients to receive medication appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at lowest cost to them and their community[1]. WHO indicates that more than half of all medicines in the world were prescribed, administered, or sold inappropriately[2]. In Thailand, the Ministry of Public Health (MOPH) is responsible for the issuing of regulatory policies in healthcare. Its policies are designed to ensure facilities comply with safety standards. The MOPH in Thailand published a manual of rational drug use in hospital in 2015 to monitor core indicators facilitating quantitative evaluation of rational drug use in hospitals in Thailand and implementation of rational drug use has been ongoing since 2016. The manual of rational drug use has been used as a guide to rational clinical decision-making. Irrational use of medicines, for example misuse, overdose, underdose, toxicity, adverse drug reaction (ADR), cost, and shortage of drugs at health facilities, is a global issue[3]. Irrational use of medicines contributes not only to a waste of money, but also to high risk for the patient, including possible side effects and drug interaction from polypharmacy[3]. Evaluation using the indicators from WHO showed irrational use of medicines[4-5]. The core

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indicators from the WHO include average number of drugs per prescription, the percentage of drugs prescribed from an EML, and oral antibiotic consumption using the defined daily dose (DDD). Both professionals and patients play an essential role in promoting and strengthening the rational use of drugs. Effective regulation, clinical guidance, supportive incentive structures, training, education and management, are the key components of an effective policy in this area. This study, therefore, aimed to evaluate rational drug use based on the WHO criteria in a tertiary hospital in Thailand, improve practices associated with rational drug use, and provide information for further investigation.

2. MATERIALS AND METHODS

This retrospective study was conducted using electronic medical records in a tertiary hospital in Thailand. The study population included all the prescriptions dispensed to patients in the outpatient department (OPD) in a tertiary hospital in Thailand from April 2019 to March 2020. The information was collated in OPD and was categorized into the following specialisms: obstetrics and gynecology, surgery, internal medicine, pediatrics, orthopedics, psychiatry, ophthalmology, and otolaryngology based on World Health Organization (WHO) indicators. The study was approved by the Institutional Review Board of the Faculty of Medicine Chiang Mai University, Thailand (STUDY CODE: D-PHA-2563-07720) with a waiver for the granting of informed consent.

There were 3 core indicators. Firstly, the average number of drugs per prescription in outpatients was calculated by dividing the total number of different drug products prescribed by the number of encounters surveyed. Secondly, the percentage of drugs prescribed from the essential medicine list in outpatients was calculated. The percentage of drugs prescribed from the essential drug list in outpatients was calculated to measure the degree to which practices conform to the national drug policy as indicated in the national drug list of Thailand. The percentage was calculated by dividing the number of products prescribed from the essential drug list by the total number of drugs prescribed and multiplied by 100. The most frequent diagnostic International Classification of Diseases, 10th revision (ICD-10) in each department was selected and then the top 5 non-essential drugs were ranked. Finally, oral antibiotic consumption was calculated using the defined daily dose (DDD) in the outpatients department. It was calculated by dividing the number of outpatient encounters in which an oral antibiotic was prescribed by the total number of encounters surveyed, and then multiplied by 1,000.

2.1. Statistical analysis

Statistical analyses were performed using IBM SPSS V23.0. Data are presented using descriptive statistics using frequency, percentage, average and standard deviation (SD).

Table 1. Average number of drugs per prescription in the outpatient department from April 2019-September 2019 and October 2019-March 2020.

Department	Average number of drugs per prescription	
	April 2019-September 2019	October 2019-March 2020
Obstetrics and Gynecology	1.78	1.48
Surgery	1.85	1.88
Internal Medicine	3.14	3.33
Pediatrics	1.75	1.78
Orthopedics	1.95	2.25
Psychiatry	2.39	2.58
Ophthalmology	2.33	2.14
Otolaryngology	1.78	2.24
Average number of drugs per prescription	2.17	

Table 2. Percentage of drugs prescribed from the National List of Essential Medicines (NLEM) in the outpatient department from April 2019 -September 2019 and October 2019-March 2020.

Department	Percentage of drugs prescribed from the essential medicines list	
	April 2019-September 2019	October 2019-March 2020
Obstetrics and Gynecology	72.54	76.70
Surgery	75.18	73.09
Internal Medicine	67.43	68.92
Pediatrics	76.75	79.37
Orthopedics	38.13	39.11
Psychiatry	67.63	70.19
Ophthalmology	59.89	53.32
Otolaryngology	81.49	64.62
Average percentage of drugs prescribed from the essential medicines list	66.52	

3. RESULTS

In Thailand, the data encompassed the 271,596 prescriptions and 810,875 drug items dispensed for the 1,083,976 outpatients in a tertiary hospital, between April 2019-March 2020. The average number of drugs per prescription in this study was 2.17. The average number of drugs per prescription in the outpatient department between April 2019- September 2019 and October 2019- March 2020 are shown in Table 1. The lowest and highest average numbers of drugs in OPD were 1.48 in obstetrics and gynecology and 3.33 in internal medicine between October 2019-March 2020. Table 2 shows the percentage of drugs prescribed from the National List of Essential Medicines (NLEMs) in the outpatient department between April 2019-September 2019 and October 2019-March 2020. The average of percentages of the drugs from the national list of essential medicines (NLEMs) of Thailand in OPD was 66.52%. The lowest and highest percentages of the drugs from the national list of essential medicines (NLEMs) were 38.13% in orthopedics and 81.49% in otolaryngology between April 2019 and September 2019. The most frequently used diagnostic codes, ICD-10, in each department were N959 menopausal and perimenopausal disorder, unspecified, C509 malignant neoplasm of breast, unspecified, I10 essential (primary) hypertension, J00 acute nasopharyngitis (common cold), M170 primary gonarthrosis, bilateral, F322 severe depressive episode without psychotic symptoms, H041 other disorders of lacrimal gland and J304 allergic rhinitis, unspecified, respectively. The top 5 prescribed non-essential drugs in obstetrics and gynecology encompassing N959 Menopausal and perimenopausal disorder, unspecified as ICD10 are shown in Table 3. As can be seen, the menatetrenone 15 mg capsule was the most frequent (42.30% in April 2019-September 2019 and 39.17% in October 2019-March 2020) drug prescribed. In surgery, C509 Malignant neoplasm of breast, unspecified, anastrozole 1 mg tablet was the most frequently prescribed drug (61.40% in April 2019-September 2019 and 64.39% in October 2019-March 2020). In internal medicine, for I10 Essential (primary) hypertension, vitamin B1 100 mg, B6 10 mg, B12 100 mcg combination tablet, were the most frequently prescribed drugs (38.43% in April 2019-September 2019 and 34.70% in October 2019-March 2020). In pediatrics, for J00 Acute nasopharyngitis (common cold), acetylcysteine 200 mg sachet was the most frequently prescribed drug (62.67% in April 2019-September 2019 and 53.90% in October 2019-March 2020). In orthopedics, for M170 Primary gonarthrosis, bilateral, mecobalamin (B-12) 500 mcg tablets were the most frequently prescribed drug (30.81% in April 2019-September 2019 and 30.92% in October 2019-March 2020). In psychiatry, for F322 severe depressive episode without psychotic symptoms, escitalopram 10 mg tablets were the most frequently prescribed drug (25.34% in April 2019-September 2019 and 20.96% in October 2019-March 2020). In ophthalmology, H041 other disorders of lacrimal gland, sodium hyaluronate 1.8 mg/ml eye drops, was the most frequently prescribed drug (89.09% in April 2019-September 2019 and 87.90% in October 2019-March 2020). In otolaryngology, J304 allergic rhinitis, unspecified, fexofenadine 180 mg tablet, was the most frequently prescribed drug (56.98% in April 2019-September 2019 and 51.41% in October 2019-March 2020). Figure 1 shows the comparisons of oral antibiotics prescribed in OPD measured by the DDD between April-September 2019 and October 2019-March 2020. Comparisons of oral antibiotic consumption measured by oral DDD between April 2019-September 2019 and October 2019-March 2020 indicated that DDD in April-September 2019 was 2.51, lower than the 4.61 in October 2019-March 2020. Figure 2 shows a summary of antibiotic oral consumption in OPD measured by the DDD between April 2019-September 2019 and October 2019-March 2020. Sulfasalazine and amoxicillin were the most frequently prescribed oral antibiotics in OPD measured by DDD between April 2019-September 2019 and October 2019-March 2020, respectively.

4. DISCUSSION

This study was carried out in a tertiary hospital in Thailand using three core indicators to determine rational drug use based on the WHO guidelines and the rational drug use manual from MOPH in Thailand. The three core indicators include the average number of drugs per prescription, the percentage of drugs prescribed from an essential medicines list and antibiotic consumption using the defined daily dose (DDD). The average number of drugs per prescription in this study was 2.17. The lowest and highest of average number of drugs in OPD were 1.48 in obstetrics and gynecology and 3.33 in internal medicine between October 2019-March 2020. The results were higher than recommended by WHO (1.6-1.8)[6]. However, the average number of medicines per prescription within the acceptable range was suggested by MOPH in Thailand (less than or equal to 3)[7]. The average of drugs per prescription from this study was lower than in a tertiary care hospital in Nepal[8] and India[9] which were 2.55 and 2.53, respectively. According to the one systematic review[10], the average number of drugs prescribed per encounter was higher than the levels recommended by the WHO, specifically the lowest and highest average number of drugs per encounter being

Table 3. Percentage of top 5 drugs prescribed from the non-essential drugs in the outpatient department from April 2019-September 2019 and October 2019-March 2020.

Department	ICD10	Generic name	April 2019 - September 2019 %	October 2019-March 2020 %
Obstetrics and Gynecology	N959 Menopausal and perimenopausal disorder, unspecified	Menatetrenone 15 mg capsule	42.30	39.17
		Vitamin B1 100 mg, B6 10 mg, B12 100 mcg tablet	24.14	24.42
		Mecobalamin(B-12) 500 mcg tablet	15.07	16.38
		Atorvastatin 20 mg tablet	11.62	13.59
		Rosuvastatin 10 mg tablet	6.87	6.44
Surgery	C509 Malignant neoplasm of breast, unspecified	Anastrozole 1 mg tablet	61.40	64.39
		Ferrous Fumarate 200 mg Folic acid 0.5mg, Vitamin B6 5mg tablet	17.69	10.96
		Vitamin B1 100 mg, B6 10 mg, B12 100 mcg tablet	10.00	10.49
		Lapatinib 250 mg tablet	5.78	6.49
		Paracetamol 300 mg, Codeine Phosphate 15 mg tablet	5.13	7.67
Internal Medicine	I10 Essential (primary) hypertension	Vitamin B1 100 mg, B6 10 mg, B12 100 mcg tablet	38.43	34.70
		Mecobalamin (B-12) 500 mcg tablet	22.70	24.59
		Ezetimibe 10 mg tablet	16.28	18.56
		Bisoprolol fumarate 5 mg tablet	11.69	11.62
		Pitavastatin 2 mg tablet	10.90	10.53
Pediatrics	J00 Acute nasopharyngitis [common cold]	Acetylcysteine 200 mg sachet	62.67	53.90
		Bromhexine HCl 8 mg tablet	20.53	26.25
		Multivitamin (MTV) syrup	9.62	8.50
		Carbocysteine 100 mg/5ml syrup	7.18	5.68
		Perampanel 4 mg tab	0.00	5.67
Orthopedics	M170 Primary gonarthrosis, bilateral	Mecobalamin (B-12) 500 mcg tablet	30.81	30.92
		Diacerein 50 mg capsule	26.32	25.90
		Paracetamol 500 mg , Orphenadrine 35 mg tablet	19.50	17.95
		Paracetamal 325 mg,Tramadol 37.5 mg tablet	15.97	17.17
		Celecoxib 200 mg capsule	7.40	8.06
Psychiatry	F322 Severe depressive episode without psychotic symptoms	Escitalopram 10 mg tablet	25.34	20.96
		Vitamin B1 100 mg, B6 10 mg, B12 100 mcg tablet	22.28	13.78
		Venlafaxine 75 mg tablet	20.42	29.01
		Quetiapine 25 mg tablet	17.52	25.44
		Mirtazapine 30 mg tablet	14.44	10.81
Ophthalmology	H041 Other disorders of lacrimal gland	Sodium Hyaluronate 1.8 mg/ml eye drops	89.09	87.90
		Carboxymethylcellulose sodium, Glycerin sol 0.4 ml eye drops	9.52	10.45
		Sodium hyaluronate Eye Drops 0.3 % (5 ml) eye drops	0.74	0.67
		Pilocarpine HCl 5 mg tablet	0.35	0.55
		Ascorbic acid 500 mg tablet	0.30	0.43
Otolaryngology	J304 Allergic rhinitis, unspecified	Fexofenadine 180 mg tablet	56.98	51.41
		Levocetirizine 5 mg tablet	18.15	19.60
		Acetylcysteine 200 mg sachet	11.96	6.81
		Desloratadine 5 mg tablet	6.59	13.96
		Brompheniramine Maleate, Phenyle-phrine HCl tablet	6.32	8.22

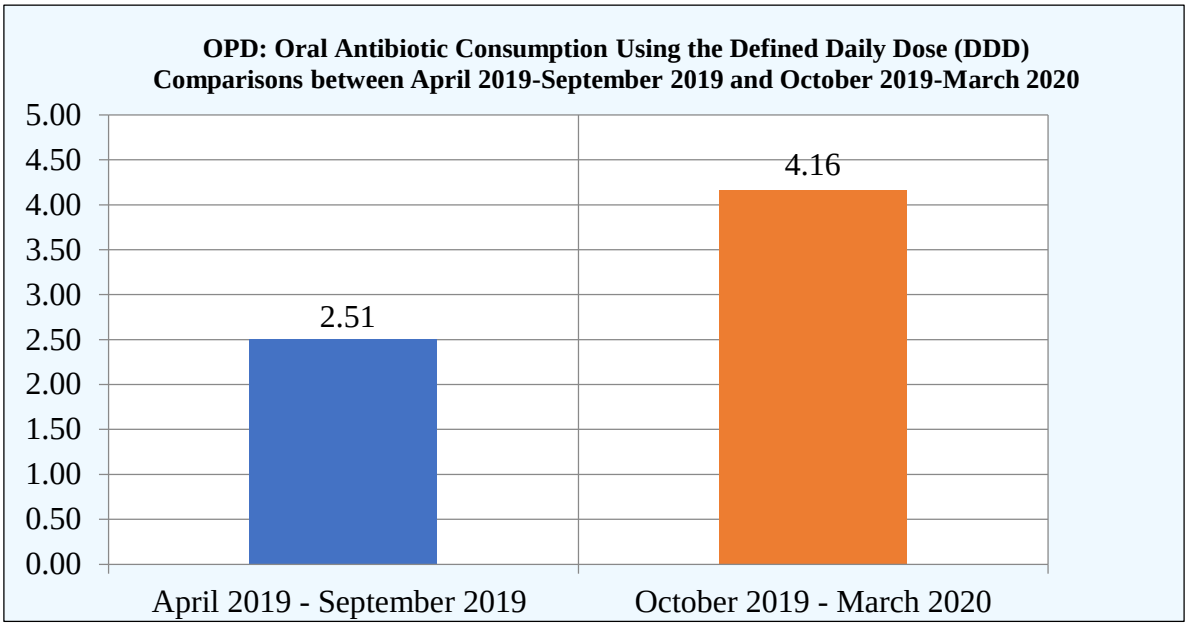

Figure 1. Comparison of oral antibiotic consumption in OPD measured by the DDD between April 2019-September 2019 and October 2019-March 2020.

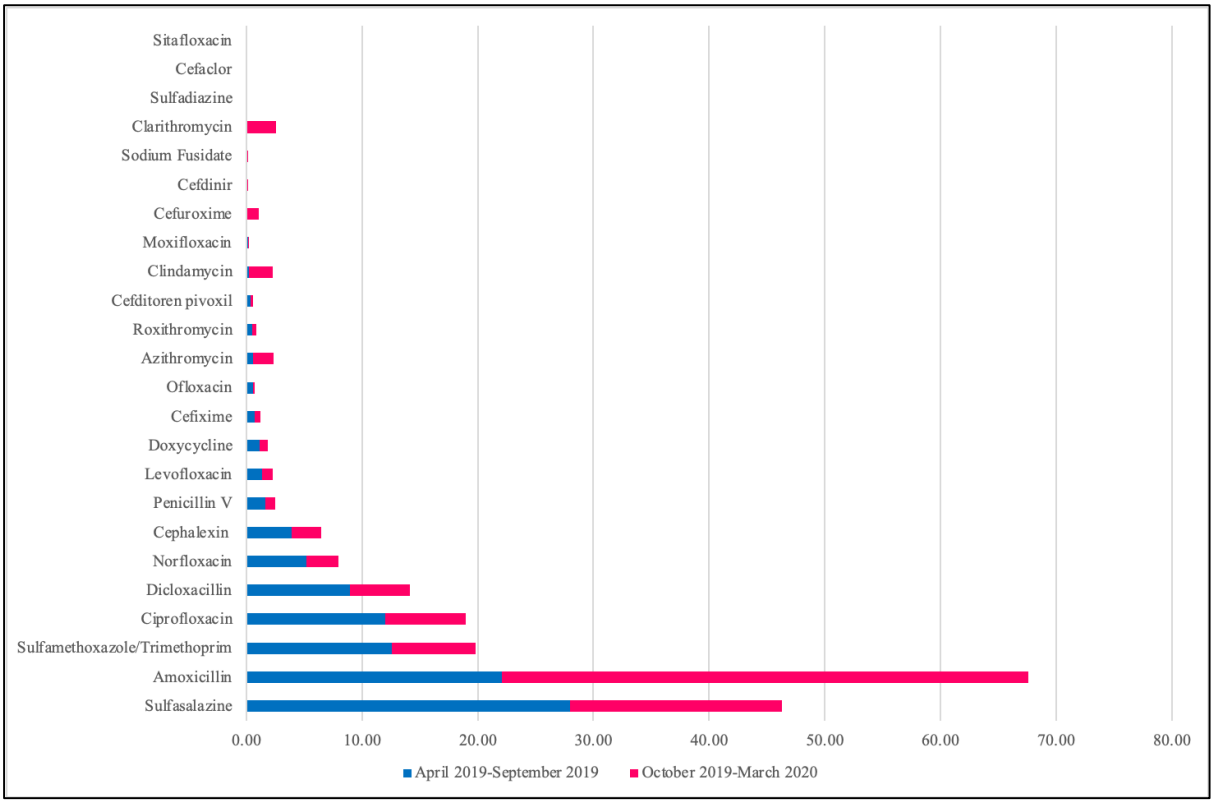

Figure 2. Lists of antibiotics prescribed for oral consumption in OPD measured by the DDD between April 2019-September 2019 and October 2019-March 2020.

0.98 and 2.50 respectively. Gandhi et al.[11] showed the adverse drug events per patient increased by 10% for each additional medication. ADE prevalence was significantly higher with each additional drug used (1.12, 1.09, and 1.10 fold in all patients, the outpatient group, and the inpatient group, respectively)[12]. Use of multiple drugs was associated with an increasing risk of adverse drug reactions[13]. A study by Matsuyama et al.,[12] found the reducing the number of drugs through interventions such as moderation of prescription drugs might reduce ADE prevalence. A study into prescription of potentially inappropriate medications in elderly outpatients found that inappropriate medications increased among patients with ≥5 medications and those chronically prescribed ≥4 medications had a systemic effect[14]. As can be seen, polypharmacy was found to be abundant and likely to

be harmful in elderly people[15].

The average percentage of drugs from the essential drug lists, prescribed from the national list of essential medicines (NLEMs) of Thailand in OPD was 66.52%. This was similar to that found in a study in tertiary care in Nepal[8] which was 65.80%. The lowest and highest percentages of drugs from the essential drug lists, prescribed from the national list of essential medicines (NLEMs) were 38.13% in orthopedics and 81.49% in otolaryngology between April-September 2019. Prescribed percentage of drugs on the essential drug lists from the national list of essential medicines (NLEMs) in orthopedics was comparable with those reported by Özdamar et al.[16] 33.8%. The average percentage of drugs from the essential drug lists in our study was lower than the expected WHO value (100%) and MOPH in Thailand (more than or equal to 85%)[7]. Since the 1980s, the Thai government has released the National Lists of Essential Medicines (NLEM) of essential drugs, which has been officially implemented with regard to the management of drugs in public hospitals. EML use is evidence-based and provides information regarding cost-effective medicines that can lead to better health care, enhanced long-term supply of medicines, and reasonability[17]. This study found that the adherence to prescription from the national list of essential medicines (NLEMs) was low, therefore, there is a need of authority policy to ensure that the drugs prescribed from NLEM are promoted in hospital. A restrictive reimbursement policy implemented in Thailand in October 2012 required prescribers to base the prescription of non-essential drugs on one of six reasons[18]. Firstly, if there are adverse events regarding drugs or allergies listed in NEMLs. Secondly, effectiveness of treatment didn't reach the goals even when using drugs in the NEMLs according to the standard treatment. Thirdly, there is no group of drugs in NEMLs available for use; however, patients need to use these drugs in accordance with indications registered with the Thailand Food and Drug Administration (Thai FDA). Fourthly, patients have a state or disease that absolutely contraindicates the use of drugs on the NEMLs or patients have a contraindication to using those drugs. Fifthly, there is a major drug interaction between NEMLs and other drugs. Finally, patients are more willing to pay for drugs on the non-essential drugs.

The percentage of the top 5 drugs prescribed from non-essential drugs in outpatients are shown in Table 3. The most prescribed medicine in obstetrics and gynecology, N959 Menopausal and perimenopausal disorder, unspecified was menatetrenone given as a 15 mg capsule. Menatetrenone (vitamin K2) may play an essential role to the prevention of fractures in postmenopausal women with osteoporosis[19]. It reduces the incidence of vertebral fractures but has only modest effects on bone mineral density (BMD) and a minor effect on bone quality in postmenopausal women with osteoporosis[20]. The most prescribed non-essential drugs in surgery, for C509 malignant neoplasm of breast, unspecified was anastrozole given as a 1 mg tablet. Hormonal therapy is mandatory for all patients with hormone receptor-positive breast neoplasms and is active both in adjuvant and metastatic disease[21]. The aromatase inhibitors: anastrozole, letrozole, exemestane are only used in postmenopausal cases[21]. Currently, anastrozole and letrozole are NLEMs in Thailand. The most prescribed non-essential drugs in internal medicine, given for I10 essential (primary) hypertension were combination of vitamin B1 100 mg, B6 10 mg, and B12 100 mcg tablets. The essential drug list of vitamin B complex capsules or tablets were prescribed as formulations of vitamin B1 ≥1.2 mg, vitamin B2 ≥1.3 mg, vitamin B6 ≥1.3 mg, vitamin B12 ≥2.4 mcg, folic acid 300-1000 mcg, niacinamide ≥16 mg, pantothenic acid ≥5 mg, and biotin ≥3 mcg. The most prescribed non-essential drug in pediatrics, given for J00 acute nasopharyngitis (common cold) was acetylcysteine prescribed as a 200 mg sachet. Mucolytics are perceived as non-essential drugs because there's some benefit regarding their treatments for acute upper and lower respiratory tract infections[22]. The most prescribed non-essential drugs in orthopedics, given for M170 Primary gonarthrosis, bilateral was mecobalamin (B-12) as a 500 mcg tablet. As a result, there was a limitation of this study with regard to the evaluation of rational use of mecobalamin because cyanocobalamin is in NLEMs in Thailand; however, it's not included in the hospital formulary. Both mecobalamin and cyanocobalamin can be used to treat vitamin B12 deficiency. The most prescribed non-essential drug in psychiatry, given for F322 severe depressive episodes without psychotic symptoms, was escitalopram as a 10 mg tablet. Selective serotonin reuptake inhibitors (SSRIs) have advantages regarding tolerability over antidepressants such as the tricyclics[23]. The three most widely prescribed SSRIs are paroxetine, sertraline, and escitalopram[23]. Sertraline is in the NLEMs in Thailand. The most prescribed non-essential drugs in ophthalmology, used to treat H041 other disorders of the lacrimal gland, was sodium hyaluronate given as 1.8 mg/ml eye drops. It is beneficial not only to patients with aqueous tear-deficient dry eye for increasing tear volume but also to patients with dry eye due to lipid tear deficiency because the treatment improves tear film stability and symptoms[24]. The most prescribed non-essential drug in otolaryngology, given for J304 allergic rhinitis, unspecified, was fexofenadine as a 180 mg tablet. Second-generation histamine H1 receptor antagonists provide efficacious treatment of allergic rhinitis and chronic idiopathic urticaria[25]. Second-generation nonsedating antihistamines, such as loratadine, desloratadine, and fexofenadine, cause little or no sedation and were recommended over older first-line antihistamines for treatment of allergic rhinitis[25]. Cauwenberge et al.[26] found fexofenadine HCl and loratadine that are

administered once daily are effective and well tolerated in treatment of seasonal allergic rhinitis. Fexofenadine HCl was significantly more effective than loratadine in relieving eye symptoms and nasal congestion[26]. Loratadine is in NLEMs in Thailand.

Antibiotic consumption is the main root of antibiotic resistance and a cause of morbidity and mortality globally[27-29]. In Thailand, the prevalence and mortality attributable to MDR are high[29]. Between April 2019 September 2019 and October 2019-March 2020, oral antibiotic consumption measured by DDD was found to be 2.51 and 4.16, respectively, an increase of 66%. In our study, the most frequently used oral antibiotics in outpatients were amoxicillin, then sulfasalazine followed by trimethoprim/sulfamethoxazole. A study in Thailand by Waleekhachonloet et al.[30] examined the effects of a national policy encouraging rational antibiotic prescribing rates in OPD and found that the policy was effective in decreasing antibiotic prescription for questionable cases. The study by Hashimoto et al.[31] found that outpatient antibiotic prescription in Japan were high for acute respiratory or gastrointestinal infections, for which the prescription of antibiotics is generally not indicated, but intervention should be by antimicrobial stewardship. More than half of oral antibiotic prescriptions were given inappropriately in the United States, with most antibiotics being prescribed with no indication[32]. Interventions to improve antibiotic prescription for inappropriate indications, combining physician, patient and public education in a variety of venues and formats were the most successful[33]. To improve compliance with guidelines for the use of antimicrobial drugs in our hospital, we will continue to promote rational drug use through Pharmacy and Therapeutics Committee (PTC), meetings and feedback to physicians. Irrational use of medicines is challenging in numerous health systems across the world[17]. The key factors contributing to inappropriate use of medicines are likely to change over time and policy makers need to be up-to-date with current trends[17].

There were limitations of this study. The study evaluated a single tertiary hospital and the findings may not be transferable in demonstrating the situation of the whole country. In addition, these results may not reflect the trend of prescription across all seasons as it was conducted from April 2019 to March 2020.

5. CONCLUSION

This study found that the average number of drugs per prescription in outpatients was higher than that recommended by the WHO. The average percentage of essential drugs was lower than the expected WHO value. However, oral antibiotic consumption measured by DDD was higher. Therefore, the implementation of rational drug use is an important feature necessitating advancement in policy application in this hospital. Irrational use of medicines is a multidimensional issue and requires interventions at several levels including health systems, organization, doctors, dispensers, patients and community and it remains a challenge in health facilities.

Conflict of interest
There is no conflict of interest.

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Ethics approval
Ethical Approval was given by the Institution Review Board of the Faculty of Medicine Chiang Mai University, Thailand (STUDY CODE: D-PHA-2563-07720).

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