Original article

The Normative Cost of Twenty Most Prominent Diseases in Yogyakarta, Indonesia: A Delphi Consensus Study

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Abstract :

Objective: To formulate a convergent and consensus expert panel to calculate normative drug cost in the top twenty diseases in primary care. ***Method:*** In the first round, the expert panel define a list of consensus statements based on data derived from non-systematic reviews of treatment standard for the top twenty disease in primary care. In the second round, experienced doctors in treatment at primary care were involved to express individual consent to the statements using questionnaire. Face-to-face meeting were held simultaneously with filling questionnaire. Consensus was defined as 75% agreement. ***Result:*** Delphi process at the first round, the expert panel consisting of 11 doctors in primary care defined a list of 60 statements from 20 diseases on the treatment standard calculated the normative cost of acute and chronic disease in primary care. The second round involved 11 doctors who are experienced in primary care with more than 6 years' experience in doing treatment in primary care. ***Conclusion:*** The identified consensus statement can help doctors to apply the normative cost calculation results on the top 20 diseases in primary care as evidence based policy study material for calculating the percentage of drug cost in the capitation system in Indonesia.

Keywords: Delphi method; drug cost; primary care; capitation; Indonesia

Introduction

World Health Organization (WHO) determines that Universal Health Coverage(UHC) is ankey problem for developed and developing country, so it is important for the countries to develop a health financing system with the aim of ensuring health for all people[1]. National Health Insurance (NHI) in Indonesia has been implemented since January 1st, 2014. Health insurance according to Ministry of Health Regulation Number 71 of 2013 is defined as insurance in the form of health protection so that the participant receive healthcare benefit and protection in fulfilling basic health needs provided to everyone who have pair the dues or contribution are paid by the government[2].All insurance participant are registered at the First Level Health Facility and provide non-specialized care and they can visit without a prior appointment[3].

Canada incurred 29% for the cost of hospital care and the Western Europe countries incurred less than 40%while in Indonesia, the cost of hospital care is very high, it reach around 60%[4]. The concept of capitation system, in the form of prevention and promotion, intrinsically changes the orientation of health services from curative to preventive[5]. In 2016, a new regulation set the standard for the implementation of capitation system in primary services on capitation rates. The allocation for health

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service payment for each first level health facility is determined to be at least 60% of the capitation fund and the rest is used for operational cost, one of them is for medicine [6]. Research in Primary Health care show that the drug spending is only 5% of the total capitation[7].

Based on the investigation research done by the Corruption Eradication Commission, there were weaknesses in the capitation fund management at the Primary Health Care namely regulation, financing, management, resources and supervision. At the regulatory level, there are still problems with the capitation fund distribution for services and operational cost, in this case the distribution of drug cost proportion in the capitation system has not been regulated in the applicable regulations [8]so that it will have an impact on services to health insurance participants. The issue of health service quality provided by primary health facility is very sensitive because it is related to the outcome of therapy and patient's health quality as the participant of National Health Insurance that it will influence patient's perception towards the national Health Insurance program[9].

Pharmaceutical services in health care facilities generally have not met the standard. Based on the data cited in the Ministry of Health Strategic plan for 2015-2018, in 2013 there were Primary Health Care, namely only 35,15% and IFRS, namely 41% which had standardized pharmaceutical services[10]. As shown in the evidence that the use of consensus guidelines improve the health quality services which is provided by giving recommendation on evidence-based best practice care[11].The irrational use of drug in first level health facility was still quite high, it is reaching 39.9%. So that the negative impact on the patients is higher than its benefits. It is necessary to conduct research related to the drug need in capitation system to reduce the clinical outcome impact as irrational treatment. Detailed prescription costing is important in measuring the additional cost caused by a recent diagnosed condition compared to the total cost of service care measurement. Individual primary care cost estimation models can be used to manage capitation payment to providers in primary care and to test for horizontal equity and primary care management requiring improved quality through evidence-based decision making.

Material and methods:

Research design:

Cross-sectional research with a quantitative method of data collection was done between January- marc 2019 . The study was approved by the Gadjah Mada Health Sciences Ethical Committee with the number of approval KE/10The Delphi method modification was applied to obtain the normative drug cost consensus. This method was widely used and accepted as a data collecting method from the experts in each of their field of expertise.[12]. There are two groups in this modified method. (1) working group consist of researcher who organized the instrument based on literature review (2) consensus group member of the expert panel who is considered capable of providing input on the cost of normative drug in primary care. During the discussion, the panel members were chaired by a leader. This group was set and adjusted in order to suit with the previous study using modified Delphi method[13]. In summary, in this case, the main process is the method which include the initial instrument development based on a working group on the literature review, expert panel selection and consensus assessment uses modified Delphi method.

Initial Instrument

The group based on literature review designed the initial questionnaire[14], [12]. This study used the modified Delphi method, and it was modified to an initial indicator instrument which developed based on the existing literature review. Initial instrumentused in this study was a questionnaire containing a list of twenty largest disease in primary care based on the data in Yogyakarta Special Region Province. Standard group and types of drug based on the national formulary, maximum daily dose, drug unit group, duration of drug use and drug unit price[15], [16], [17], [18].

Expert Panel Member Selection

The modified Delphi method highly depend on expert dynamic. The expert panel research in this study consider the following two major factors: (i) the panel members must demonstrate knowledge or expertise in medicine in the primary care. For this reason, it involves doctors who practice in primary care with a minimum three years of work period.

Representative of practicing doctors from each type of health facility are selected to represent an expert panel, in this case, doctors practicing at Primary Health

Care, *Pratama* clinics and Independent General Practitioner. Furthermore, geographic reasoning are considered by involving doctors practicing in the city because it allows the type and availability of drugs in primary care so they are familiar with the variety of drugs.

Delphi Rounds

Theoretically, The Delphi method allows continually repetition up to reaching the consensus among the Expert Panel. However, several studies started that in most cases two rounds are sufficient to collect information and to reach a consensus[19], the Delphi method is modified twice rounds. In each round, expert panel responses were revised by the working group based on the feedback taken from the group consensus. All participants are anonymous.

In the first round, the expert panel gave an assessment of each statement using a Likert scale and it was recommended to change it by deleting, adding, or changing the existing statements. Afterwards, they continue with a discussion session. The researcher altered the normative drug cost based on the result from round one (including changes according to experts' suggestion and result from the discussion). In the authenticDelphi method, the experts would not meet or interact directly, which imply that the information was only gain by exchanging it between individuals (which could be many and geographically dispersing) in a repetitive process. It is done in the belief that there will be advantages from exchanging information. Additionally, these exchanges are tightly controlled to limit the potential for disadvantages of interaction process [20]. However, there is a critic on traditional Delphi method. Since it does not facilitate the expert panel member meeting even though the interaction between experts is important in a complex decision-making process which require clarification of the language used and recommendation to be made.[21]. Hence, this study used modified Delphi method which allows the expert panel member meeting in a discussion session. In order to reduce the bias due to the interaction between experts, the discussion is directed more at equating the expert panel members' perception than changing the expert panel's judgment.

At the second round, it was provided re-assessment of each standard therapy to the expert panel member which aimed to determine the revised normative cost of round 1and the recommended changes by removing, adding or changing diction in the second round. The expert panel can change the diction and the assessment in the second round and after that the discussion session is conducted. The researcher altered the duration of drug use, dose and amount of drug as suggested.

Data Analysis

Likert scale starting from 1 (strongly disagree) to 4 (Strongly agree) was used to access the agreement of expert panel members on normative drug cost in primary care that were made previously based on the standard therapy for doctors in primary care. Consensus measurement is Delphi data analysis and interpretation[22]. However, there is no consensus on the agreement level, that is the best approach in the modified Delphi method[23], So in this study, two indicators were selected for consensus assessment: mean and interquartile range (IQR). This study adopt the approach of several previous studies from where consensus were obtained if the indicator had a minimum mean of 70% or the value is more than 3 with a maximum value of 4,[23], [24]and where an IQR of 0-1means high level of consensus, 1,01-1,99 means moderate consensus and more than 2 means no consensus[25]. For second roing, the consensus in indicator has been reaching a mean value of $f > 3$ and IQR score is in the category of moderate or high level consensus.

Ethical of Study: The study was approved by the Gadjah Mada Health Sciences Ethical Committee with approval number KE/1001/EC/2017.

Result

The result of the study in calculating normative drug cost with the Delphi test was shown in

Table 1 Expert Panel Distribution of Delphi Test

Category	Numbers of Doctors	Agreed to participate	Round 1	Round 2
General Practitioner in primary care at Yogyakarta Province	11	11	11	11

Table 2. The Characteristic of Expert Panel

Category	Information	N(%) 11 (100)
Type of Primary care	Primary Health Care *Pratama* Clinic Independent Medical Practice	9(81) 1(9) 1(9)
Gender	Male Female	2(18) 9(82)

Category	Information	N(%) 11 (100)
Age	20–30 Years 31–40 Years 41–50 Years	1(9) 6(55) 4(36)
Working Area	Yogyakarta	11(100)
Years of Service	3-5 Years > 6 Years	1(9) 10(91)

Table 3. Types of Drug Omitted for Second Round

Type of Drug	Mean	SD	IR	Reason
Amoxicillin for influenza	2	0.786	3	No need antibiotic
Amoxicillin for Acute Respiratory Infection	2	0.924	3	Antibiotic is not needed for Acute Respiratory Infection- The drug is give 3-5 day
Codeine for Cough	2	0.539	2	Codeine is not available in Primary Health Care, Codeine is a medicine with a specific indication, for persistent cough Usually given GG & ambroccol/acetyl cysteine

Tabel 4. The Result of Delphi Consensus

No.	Disease Code (ICD 10)	Disease Diagnosis	Round 1		Round 2	
			Average	IR	Average	IR
1	J00	Influenza	2.4	2.3	3.0	1,6
2	J06	Acute Respiratory Infection	2.3	2.3	2.8	1,3
3	K30	Ulcer	2.7	1.6	3.0	1,3
4	R50	Fever	2.9	2.0	3.0	1,3
5	M79	Arthritis	2.9	0.6	3.0	1,3
6	I10	Hipertension	3.0	1.6	3.0	1,3
7	K29	Colitis	2.8	1.3	3.0	1,3
8	J02	Sore Throat	2.6	2	2.8	2.0
9	L23	Skin allergy	3.0	0.6	3.0	1,3
10	R51	Headache with vomiting	2.3	1.3	2.7	1,3
11	K04	Tooth and hard tissue disease	2.9	1.3	3.1	1,6
12	R05	Cough	2.4	1.6	3.0	2.0
13	N39	Urinary Tract Infection	2.9	0.6	3.0	1,3
14	E11	Diabetes Mellitus Type 2	2.8	1.0	3.0	1,6
15	H81	Vertigo	2.8	1.3	3.2	1,3
16	A09	Diarrhea with infection	2.7	1.6	2.7	2.0
17	E78	Hypercolesterol	2.8	1.0	3.0	1,6
18	H10	Eye lining inflammation	2.7	1.6	2.9	2.0
19	B35	Fungal Skin infection	2.9	1.3	3.1	2.0
20	L50	Hives	2.8	1.3	3.2	1,5

Discussion

The result table 1. There are 11 (100%) Expert Panel agreed to participate in the first and second round. The characteristics of expert panel in table 2 showed that practicing in Primary Health Care is 81%, female (82%), with the average age of expert panel between 31-40 years namely 82%, work in Yogyakarta Special Region Province with >6 years of work, namely 91%.

The consensus assessment based on the average score indicates the number of statements approved by the expert panel increase in each round. Consensus assessment based on the average mean and IQR (interquartile Range). The potential of low respond is a crucial problem that must be overcome using the Delphi method, considering that this method needs a lengthy of time to complete in several rounds depending on the agreement of the expert panel [26]. However, this study obtained a high response value, namely 11 out of 11 expert (100%) were willing to take the Delphi test with two-round process.

The result of the first round test are shown in table 3 and the detail is in table 4 In influenza and upper respiratory tract treatment, it shows low average value, namely 2, which means it does not agree with IQR value of 2-3 that amoxicillin and codeine are not recommended for influenza and upper respiratory infection. The experts said that it is because antibiotics are not needed in the disease.

Excessive use of antibiotics lead resistance, increases medical cost and increases side effect including the risk of anaphylaxis and severe drug allergy. The codeine type of drug is not recommended for cough. According to expert panel, this is a drug with a specific indication for persistent cough. The alternative cough medicine recommended by the expert panel was given glacerylguaiacolate tablets and amboxol or acetyl cysteine. It is supported by research[27], [28]that placebo is more effective than codeine in suppressing

Tabel 5. The Result of Consensus on Type of Drug and Normative Drug Cost in Chronic Diseases

No.	Disease Code (ICD 10)	Disease Diagnosis	Main Drug Choice	Daily Dose	Drug Group	Duration of Treatment (day)	Drug Unit Cost(IDR)	Drug Cost (IDR)	Standard Value (IDR)
1.	I10	Hypertension	HCT Captopril	25mg 50mg	12.5mg 12.5mg	30 30	155 66	9,300 7,920	17,220
2.	E11	Diabetes Mellitus Type 2	Glimepiride Metformin	2mg 2000mg	1mg 500mg	30 30	315 160	18,900 19,200	38,100
3.	E78	Hypercholesterol	Simvastatin	30mg	10mg	30	217	19,530	19,530

Tabe6: Result of Therapy and Treatment cost of Acute Disease Consensus

No.	Disease Code (ICD 10)	Disease Diagnose	Main Drug Choice	Daily Dose	Unit Drug Group	Duration of Treatment (Day)	Unit Drug Cost (IDR)	Drug Cost	Standard Value (IDR)
a	B	c	d	e	f	g	$H=(d/e)*(fxg)$	$I(Pc1+pc2+..)$	
1.	J00	Influenza	Paracetamol CTM	3000 mg 16mg	500mg 4mg	5 5	53 23	1,590 460	2,050
2.	J06	Acute Respiratory Tract Infection	Paracetamol CTM	3000 mg 16mg	500mg 4mg	5 5	53 23	1,590 460	2,050
3.	K30	Ulcer	Omeprazole	20mg	20 mg	5	139	695	695
4.	R50	Fever	Paracetamol	3000 mg	500mg	5	53	1,590	1,590
5.	M79	Arthritis	Natrium diklofenak	100mg	5mg	5	137	2,740	2,740
6.	K29	Colitis	Lansoprazole Aluminium hidroksida	30mg 400mg	30mg 200mg	5 5	323 58	1,615 580	2,195
7.	J02	Sore Throat	Paracetamol CTM	3000 mg 16mg	500mg 4mg	5 5	53 23	1,590 460	2,050
8.	L23	Skin Allergy	Loratadine	10mg	10mg	5	131	655	655
9.	R51	Headache with Vommiting	AsamAsetilsalisilat (asetosal) Metoklopramid	4000mg 30mg	80mg 5mg	5 5	105 121	26,250 3,630	29,880
10.	K04	Dental Hard Tissue Disease	Amoxcicilin Diklofenak 100 mg	1500mg 100mg	500mg 25mg	5 5	2,940 2,740	2,940 2,740	5,680
11.	R05	Cough	N-AsetilSistein CTM	600mg 16mg	200mg 4mg	5 5	373 23	5,595 460	6,055
12.	N39	Urinary Tract Infection	Paracetamol Kotrimoksazol	3000mg 960mg	500mg 120mg	5 5	53 133	1,590 5,320	6,910
13.	H81	Vertigo	Betahistin	24mg	6mg	5	110	2,200	2,200
14.	A09	Specific Diarrhea	Atapulgit Ciprofloxacin Metronidazole	7200mg 1000mg 500mg	600mg 500mg 250mg	5 5 5	145 360 185	5,220 3,600 1,850	8,820
15.	H10	Eye Lining Inflamation	Eritromisin 500 mg Tetes matakloramfenikol	1000mg 3mg	250mg 3mg	5 5	583 2,007	11,660 6,021	17,681
16.	B35	Fungal Skin Infection	Ketokonazol Mikonazolsalep 2%	400mg 200mg	200mg 200mg	5 5	288 3,414	2,880 17,070	19,950
17.	L50	Hives	Loratadine Metilprednisolon	10mg 8mg	10mg 4mg	5 5	131 143	655 1,430	2,085

coughs which is caused by upper respiratory disorder or chronic obstructive pulmonary disease. Moreover, it potentially create respiratory problem and opoid toxicity.

In the second round (table 4) fifteen types of disease have obtained a mean value of >3 and IQR <2, this indicates the consensus category and this has met at least 70% consensus so that there is no further rounds needed. However, there are five types of disease that did not receive the approval from the expert panel member, namely acute respiratory infection with an average score of 2.8 and the IQR score is 1.3, sore throat with average score 2.8 and the IQR is 2, headache with vomiting with the average score is 2.7 and the IQR is 2, lining eye ball inflammation with the average score is 2.9 and the IQR is 2. Therefore, these five type of diseases were not included in the consensus category. In the acute respiratory infection, sore throat, and headache, the expert paneldid not agree on the duration use, namely five days, because so far it was only given for three days.

Overall, it can be seen that prescription under the normative duration (under prescribing) are more dominant that prescription according to normative ones. This is supported by Sudarsono (2016), that there is a fairly high percentage of drugs under the normative duration with results showing that the duration of treatment is too short, namely 70.08%. According to[29], the use of drug is said rational if it meets the criteria as the disease indication, available at anytime at an affordable price, given the right dose, the right way and time interval, the right duration and the drug given must be effective with safe and guaranteed quality.

Patient could give an essential contribution towards the rational prescribing decision[30], [31]. Patients' belief and expectation influence the goal of the therapy and help in assessing the benefit and disadvantages that can be receive when they are choosing the treatment. Patients play an important role in monitoring the medication, especially on giving information about the side effect after taking the prescribed drug. Patient who were clearly communicate with the doctor on the reason of drug choice, purpose, duration of the treatment and the potential side effect were more likely to have increased the adherence, more trust to the prescriber and greater satisfaction with the health care services[32]. Thus, it is possible, patients should be informed of the medicine they have been prescribed.

Normative Drug Cost in Chronic Disease based on Delphi Test

Non-communicable disease are the globally leading causes of death[33]. The distribution of obesity in the population without diabetes from time to time will remain stable with ☐65% of individuals from the overweight population or obese. In study [34]between 20019 and 20134, the number of diagnosed and non-diagnosed diabetes patient will increase from 23,7 million become 44,1 million. The result of the study is shown in table 6, in the first round, DM type 2 therapy recommend metformin and glibenclamide, However in the second round, it was agreed to use a combination of sulfonylurea class namely glimepiride and binguanid drugs, for example metformin. According to the expert panel, hypoglycemic often happen in glibenclamide. It is supported by the researches[35], [36]that glibenclamide potentially causing side effect of hypoglycemic, 15.79%.

The result of the normative drug cost calculation in table 5 showed that diabetes mellitus wasIDR 38,100 in one treatment. Another study calculated that the estimated cost of diabetes diagnosis in 2017 was $327 billion, which include$237 billion for direct medical cost[37]. Other studies predicted the cost associated with diabetes mellitus in 2009 until 2034 are expected to increase from $113 billion to $336 billion. This because the diabetes population was expected to increase from 8.2 million in 2009 to 14.6 million in 2034[34]. Three articles[38]predicted the changes in the total economic burden of diabetes in 180 countries in the world. They estimated that diabetes global cost will increase from $1.3 trillion in 2015 and in 2030 in between $ 2.1 and $2.5 trillion.

Dyslipidemia is caused by disruption of lipid metabolism due to the interaction of genetic and environmental factors. There is a strong evidence of the relation of LDL cholesterol and cardiovascular events based on clinical studies [39]so that LDL cholesterol is the main target in the management of dyslipidemia[40]. High cholesterol brings significant risk factor for cardiovascular disease (CVD) and especially for coronary heart disease (CHD). One of the leading cause of death in the US is cardiovascular disease. In fact, Many Americans were killed each year, it is more risky than any other cancer. Approximately 17% of all nation health care spending focuses on this disease only[41].

In hypercholesterolemia disease in the first round, it was recommended simvastatin and fenofibrate, however this is not the agreement of the expert panel because the use of simvastatin is not recommended at the same time with fibric acid. This is supported by the research [42]that there is a toxicity risk in the combination of simvastatin and fenofibrate in various doses. In another study, fibrates had much greater effect on reducing plasma lipoprotein concentration compared to statin[43]. Therefore it could consider the use of the combination of statin and fenofibrate. However, patient should be given a clear information about the risk, benefits and possible side effects. The result of normative cost calculation in dyslipidemia based on the Delphi test are IDR 19,530.00. In a study[44] in the UK, the estimated cost of these drugs was around £209. Direct medical costs for cardiovascular disease in the US are estimated to triple from $ 273 billion today to $ 818 billion in 2030. Due to lost productivity, the indirect cost are predicted to increase about 60% over the same period, from $172 billion to $276 billion. Over all, the total of cardiovascular cost will be multiple more for the next 20 years, to be more than one trillion dollars[41].

Economic burden from the certain cardiovascular forms, such as CHD (coronary heart disease) and stroke directly associated with high cholesterol increasing and predicted to increase. In 2010, the amount spent on cholesterol drugs was $18.7 billion. CHD or dangerous narrowing blood vessel in the heart due to plaque accumulation are currently cost $108.9 billion every year and it is predicted to be doubled by 2030, to $218.7 billion. The stoke total cost will nearly three times increasing from $53.9 billion to $140 billion.

Drug Cost of Acute Disease Based on Delphi Test

Rising of health care cost is a main public health problem. Therefore, the study on accurate predicting future cost and understanding factors contributing to the increase of health care spending is important[45]. The calculation of normative drug cost in acute disease was carried out by Delphi testing on eleven Expert Panel representing each type of First level health facility including Primary Health care, *Pratama* Clinic, Independent Practitioners. All expert panel participated in two rounds to determine normative drug cost in acute disease. Literature searching was undertaken to identity clinical guidelines. The search was carried out by identifying doctor's practicing guideline in primary care[18]and other supporting literature such as maximum daily dose obtained from WHO normative[17]and another supporting literature [16]. The evidence from pre-existing guidelines and the additional searching literature was also referred during the consensus statement development to ensure that the highest level of consensus was reached, with 60 statements distributed to all expert panel members on the first round.

The result of Delphi test in acute disease are shown in table 6 that the highest cost was headache with vomiting about IDR 29,880.00 and then it is followed by fungal skin infection about IDR 19,950.00, followed by eye lining inflammation about IDR 17,681.00. The difference of the drug cost in each disease is due to the difference amount and types of drugs in each amount and duration of use. The last two decade, the focus of international health is on communicable and non-communicable disease issue with low priority at the global level [46]. However, the data show that chronic non-communicable disease are increasing in developing countries, compared to chronic infectious disease (e.g tuberculosis and HIV) and non-chronic disease[47].The focus on non-chronic disease is increasing for several reasons: 1) it has great negative economic impact, and it is a significant barrier to human development, 2) the effect of globalization which is likely to have a special impact on non-chronic diseases, including diabetes, hypertension, condition which related to smoking and obesity; and 3) recent advances in mobilizing funds and improving response to infectious disease (particularly HIV?AIDS, tuberculosis and malaria) have been enabled a shift to a broader view of global health[48].

The highest cost calculation in acute disease is headache with vomiting. It is estimated that between 25 until 28 million people in the US suffer from headaches, make it to the most common diseases. The prevalence was 18% among women and 6% for men[49]. Migraine is a chronic congenital disease which is characterized by moderate to severe pain that is often unilateral but it can be bilateral. Headaches are usually accompanied by symptoms like nausea, dizziness, photophobia, sonophobia or osmophobia. Exacerbation of headaches due to bending or other

movements are common, such as neck pain. Fairly common symptoms; up to 25% of headache sufferers experience such symptoms but they are not in every headache. Prodromal and/or postdormal fatigue and mood swings are common[50]. Migraine can start at any age, generally occur in children and adolescents. At least 1% of 6 years old and 4% of 10 years old children suffer from episodic disease. Boys and girls at the age of 12 years suffer migraine in the equal number. During puberty, the known female-male ration of 3:1 is reached, and the ration is maintained for the rest of the life. Many migraine patient manage to relieve their headaches with over the counter (OTC) drugs [51].

In the first round, the type of headache with vomiting was in the anti-inflammation (NSID) and antiemetic groups with the type of salicylic acid drug of 4000mg dose per day and metoclopramide of 300mg per day with the duration of use is ten days. In the first round, the three statements has not been agreed, especially on the duration of drug use, in this case, in the first round, the duration of use was ten days in one therapy. Whereas, in the second round, the duration of the drug use was five days. The expert panel suggested that the need to add other type of NSID, this is in accordance with[52]the need for non-steroidal anti-inflamatory drugs (NSAIDs) and triptans, oral metoclopramide or domoperidone which is useful when the sufferer experienced nausea. For the relapsing mild to severe migraines, oral NSAIDs and triptans are recommended while for the attacking severe pain (e.g menstrual migraine) subcutaneous sumatripan is recommended.

A study calculated the direct and total cost of headaches in adults and in children. This is done relate to the presence or absence of the comorbidities such as depression and anxiety. Adults and children suffering from headache experienced an increase in medical cost between2.4 and 4 times than non-migraine group. Children with migraine and comorbid anxiety/depression have up to 8.4 times annual cost treatment. Another recent study looked at the total health care cost in families with migraine sufferers (data on pharmaceutical and medical claims and short-and long-term absence from work and disability). The total cost of health care for families with migraine sufferers is 70% higher; even more cost are associated with a child suffering from migraines

compared to adults. However, when parent and child are suffering migraines, the total cost are more than $ 2.500 and direct and indirect cost increase[53].

Superficial fungal infection of skin, hair and nails are commonly happen worldwide with the prevalence 20-25%. The common causative agent of these diseases is dermatophytes[54]. Dermatofitosis is defined as an infection of the hair, nail or skin by the dermatofia which include three genera, namely *Trichophyton spp., Microsporum spp*, and*Epidermophyton*. Because dermatophytic infections of the hair mainly require systemic antifungal therapy[55]. Dermatophytiosis treatment consists of oral or tropical antifungal drugs or the combination of both, it depends on the degree and severity, site of infection and cause of the organism[56]Tropical antifungal agents are generally considered as first-line therapy for uncomplicated superficial dermatomycosis due to their high effectiveness and low potency of systemic side effect. These drugs are formulated into some types of preparations, namely creams, lotions, gels or spays to facilitate penetration and their effectiveness depends on the disease[55].

The cost of fungal skin infections is estimated to cost more than $ 7.2 billion in 2017, it is including $ 4.5 billion from 75.055 hospitalizations and $ 2.6 billion from 8.993.230 outpatients visits. Hospitalization for *Candida* infection (n = 26,735, total cost $ 1.4 billion) and *Aspergillus*infection (n = 14.820, total cost $ 1.2 billion)considered as the highest total cost of hospitalization for any disease. More than half of the outpatient visists were for dermatophyte infection (4.981.444 visits, total cost $ 802 million and 3.639.037 visits occurred for non-invasive candidiasis (total cost $ 1.6 billion)[57].

This study has several limitation, the problem arising in using he Delphi method is the potential interest[21]. During the discussion session, several Expert Panel filled out a questionnaire for determining normative drug cost based on normative therapy standards for the treatment of twenty most disease with what has been practicing so far regarding the duration of drug use, and therapy undertaken by the patients. it is supported by the previous research that low drug cost are influenced by the short duration of drug use, only 3-5 days for each patients[9] .

Conclusions and recommendations:

This study highlight the difference between the clinical guidelines and practice, and the need to address the challenges to ensure the treatment management of twenty most diseases in primary care from the patterns of treatment and cost estimates. Despite the limitation of the Delphi method, we obtained a high level of approval. However, one third of the proposed statements did not reached consensus; which remain uncertain regarding the validity of current WHO guidelines and the duration of antibiotic use. Further debate can contribute to better understanding how costs incurred by primary health care facilities that can be best managed in clinical practice and how drug options are selected.

Authors' contributions

Conception and design: S, SAK, AGM

Analysis and interpretation of the data:IHS, S, SAK, AGM

Drafting of the article: IHS

Critical revision of the article for important intellectual

content: IHS, S, SAK,

Final approval of the article: IHS, S, SAK, AGM

Provision of study materials or patients: IHS

Statistical expertise: IHS

Obtaining of funding: S, SAK, AGM

Administrative, technical, or logistic support: IHS, S, SAK,

Collection and assembly of data: IHS, S, SAK

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