

# Preference of Herbal Therapies: Cost of Illness and Cost Benefit Analysis for Major Diseases in the City of Karachi, Pakistan

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Ahmad *et al.*: Preference of Herbal Therapies: Cost of Illness/Cost Benefit Analysis

The aim of the present study was to assess and compare the allopathic and herbal therapies by carrying out cost of illness and cost benefit analysis after propagation of basic epidemiological and pharmacoeconomic data. The data was recorded from the patient for 3 major diseases, common cold, depression and trauma in all 178 union councils of the city of Karachi, Pakistan, rationalizing the benefits and hence proving the preference of herbal over allopathic therapy. The stratified random sampling (n=178) was used, selecting individual sets of 178 patients for each kind of therapy, utilizing data of epidemiology. The direct and indirect costs were calculated for therapies for selected diseases in patients. However, benefits were analysed by developing uniform method of analysis of costs and benefits, comparing and propagating individual data of union councils on the city level. The differences in costs of illnesses between allopathic and herbal therapies were found to be: Rs.1.51/- billion (USD 14.52/- million), 46.82/- billion (USD 450.19/- million) for depression and Rs.0.14/- billion (Rs.140/- million or USD 1.35/- million) in trauma, respectively. The herbal therapies were proved more effective than allopathic therapies, i.e. 29.85, 11.79 and 4.77 % in cases of common cold, depression and trauma.

**Key words:** Cost of illness analysis, cost benefit analysis, common cold, depression, trauma

Cost of illness (COI) or charges for illness analysis determines the cost incurred by the diseases or condition in the society in a point of time. Such costs can be classified as direct and indirect costs. The direct costs of illness are those directly and indirectly connected with the therapy; whereas, the indirect costs of illness are those that are not connected with the therapy but are related to the result of onset therapy for the disease. These are hard to be tracked and evaluated absenteeism from the job or voluntary support from a household associate or even in the form of losses due to the pain of illness<sup>[1]</sup>.

On the other hand, cost benefit analysis (CBA) is an important pharmacoeconomic evaluation that determines benefits of the incurred costs of therapy. It is a basic instrument that can be used to advance the policymaking in the budgeting of healthcare plans. The methodology employed for calculating the benefit associated with the cost (in relation to the cost incurred for the therapy) can be tricky and difficult<sup>[2-12]</sup>.

Present study is a part of detailed pharmacoeconomic evaluation for allopathic and herbal therapies practiced in the city of Karachi for three major diseases, such as common cold, depression and trauma (minor cut), involving patients belonging to 178 union councils. It utilizes simple methodologies for COI and cost-benefit determinations, and the comparisons to see if herbal therapies are better than the allopathic therapies in respect to low cost and benefit/effectiveness.

## MATERIAL AND METHODS

### Approval of study by ethical review committee:

The study was started after an approval of the research project from Ethical Review Committee, Faculty of

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Pharmacy and Pharmaceutical Sciences, University of Karachi (project approval protocol, dated: September 18, 2012, ref. no. 0671/Pharm./10(28), for data collection of depressed patients. This data collection was confined to the physiological, medical or clinical information, and was constrained for collection of any human biological materials. The methodology of the study was developed according to the good research practices of pharmacoeconomics as provided by the International Society of Pharmacoeconomics and Outcome Research (ISPOR)<sup>[13]</sup>. The methods were validated<sup>[13]</sup> and replicated for the other two studies of the same series of research, i.e. for common cold and trauma in the 178 union councils of the city of Karachi.

### Selection of medicines for diseases:

Acquiring all the herbs and allopathic medicines from the local market, the herb *Glycyrrhiza glabra* was utilized as a sample while the allopathic medicines, dextromethorphan (10 mg/5 ml), pseudoephedrine HCl 30 mg/5 ml (Triaminic-DM<sup>®</sup> syrup) was selected as a control in the study for common cold. *G. glabra* was used as an oral infusion in 1 cup; 300 mg of *G. glabra* once a day. The herb, *Hypericum perforatum* was utilized as a sample while the allopathic medicine fluoxetine HCl 20 mg tablet (Floxac<sup>®</sup>) was selected as a control in the study for depression. *H. perforatum* was used as an oral infusion in 1 cup; 200 mg of *H. perforatum* once a day.

The herb, *Calendula officinalis* was utilized as a sample while the allopathic medicine povidone-iodine 10 % w/v (Pyodine<sup>®</sup> solution) was selected as a control in the study for trauma (minor cut). The tincture of *C. officinalis* was used as a medicine, 2-5 drops of tincture every 12-24 h depending on the area and severity of trauma.

### Setting and sample size:

The required sample size needed for this study was calculated by using the following Eqn.<sup>[14]</sup>,  $n = z^2p(1-p)/d^2$ , where,  $n$  = sample size,  $z$  = standard normal distribution (i.e. 1.96),  $p$  = estimated mean of incidence proportion observed for the depression in the city of Karachi (i.e. 0.05), and  $d$  = standard error (0.05). Therefore,  $n = ((1.96)^2 \times (0.05) \times (1-0.05)) / (0.05)^2 = 73$ . Instead of taking least sample size of 73 patients, a relatively large sample size was taken into consideration, i.e. taking one patient from each strata or union councils ( $n=178$ ) patients each for allopathic and herbal therapies in common cold, depression and trauma. The patients and their data were segregated by their age groups in a population as defined by the Pakistan Bureau of Statistics<sup>[15]</sup>. There were 16 age groups (Table 1, from 0-75+ y with difference of 5 y in between) primarily used in cases of common cold and trauma. However, 11 age groups (Table 1, from 25-75+ y with difference of 5 y in between) were used for the cases of depression. Therefore, for each therapy, the

**TABLE 1: DIVISION OF COMMON COLD, TRAUMA AND DEPRESSION PATIENTS INTO AGE GROUPS**

S. No.	Common cold and trauma			Depression		
	Age groups (y)	Percent of total population	Age group wise actual number of patients	Age groups (y)	Percent of total population	Age group wise actual number of patients
1	0-4 y	14.80	26	25-29 y	7.37	35
2	5-9 y	15.65	28	30-34 y	6.22	30
3	10-14 y	12.95	23	35-39 y	4.77	23
4	15-19 y	10.37	18	40-44 y	4.45	21
5	20-24 y	8.97	16	45-49 y	3.53	17
6	25-29 y	7.37	13	50-54 y	3.21	15
7	30-34 y	6.22	11	55-59 y	2.15	10
8	35-39 y	4.77	9	60-64 y	2.04	10
9	40-44 y	4.45	8	65-69 y	1.20	6
10	45-49 y	3.53	6	70-74 y	1.09	5
11	50-54 y	3.21	6	75 y and up	1.21	6
12	55-59 y	2.15	4			
13	60-64 y	2.04	4			
14	65-69 y	1.20	2			
15	70-74 y	1.09	2			
16	75 y and up	1.21	2			

Total sample size of 178 patients divided into 16 age groups (0-75 y and up) for epidemiological and pharmacoeconomic evaluations of common cold and trauma while 11 age groups (25-75 y and up) for depression

sets of 178 patients were selected as stratified random samples from population of 20 819 302<sup>[15]</sup> in cases of common cold as well as trauma and from a population of 7 755 189<sup>[15]</sup> in cases of depression, combining total of 1068 patients. The process of data collection was completed in accordance with the proportions of, each group out of total age groups selected for cases of common cold, depression and trauma. Following formula was used for the sample size based on age groups, age group based sample size = (percentage of age group in population/100)×sample size.

#### **Clarity of variables in the study:**

The societal perspective was followed for the present study for both the allopathic and herbal therapies for common cold, depression and trauma. The data of the 1068 patients sampled for the allopathic and herbal therapies were collected for 1 y (from March 2015 to February 2016). A simple decision tree model was used as a guide within the specified time horizon. Standard deviation (SD) and standard error of mean (SEM) were used as the two main parameters of statistical uncertainty for the study.

#### **Survey instrument and data collection:**

To obtain the maximum data input from 1068 patients selected in the research study, a bilingual layered style interviews, questionnaires and opinion surveys<sup>[16,17]</sup> were devised, which consists of a blend of open and close-ended questions. The interviews were rarely used in situations where respondents were unable to feedback to the questionnaires due to diversified reasons. The questionnaires and opinion surveys were available to the respondents in the form of choices between paper-based as well as an online (survey with Limesurvey™ and surveymonkey.com). Surveys are the only convenient mode of data collection to gather information. They are found relatively cheap and respondent-friendly than the interviews as surveys can be completed and submitted with patient's own ease and will.

#### **Utilization of database for data collection and preliminary calculations:**

Since there was no database available for the herbal and allopathic therapies chosen in relevance with the scope of the study, therefore, fresh data were collected from 1068 patients from 178 union councils in the city of Karachi. The information gathered from either interviews, questionnaires or opinion surveys were distributed into two categories. The first category of data

deals with epidemiological data including incidences as well as old cases to calculate the prevalence of chosen conditions. The second category of data deals with the addresses of patients including their towns and union councils, their genders and age, for each visit the fees of physicians/herbal practitioners as well as the cost of medicines and transport, loss of income and the loss due to pain experienced. All the data was used to calculate COI and CBA by evaluating the direct and indirect costs as well as the benefit gained from the chosen therapies. As far as the data related to incidence and prevalence, all the major clinics and hospitals as well as herbal clinics in 178 union councils of city of Karachi were surveyed for number of new and old cases of common cold, depression and trauma.

#### **Data analysis:**

The data were gathered gradually and calculated into meaningful and required pharmacoeconomic evaluations (COI and CBA) with Microsoft Excel 2016. The detailed statistical analysis was performed along with graph generation with the help of IBM® SPSS version 23. For the COI and the CBA the process in different stages were divided for better understanding of collected data and ease of calculations.

The COI analysis for individual patients of common cold, depression and trauma was conducted by calculating the direct COI by summing up fees of physician/herbal practitioner as well as the cost related to medicines and transport. The indirect COI was arrived at by adding up the loss of income and loss due to pain. The COI was arrived at by adding the calculated direct and indirect costs. To determine the prevalence of common cold, depression and trauma in 178 union councils of the city of Karachi, the new incidences and old cases found during survey were added up. The duration of the conditions was noted down while recording data from individual patients to calculate mean duration of each condition. To determine the COI on a city level as a product of mean COI, the prevalence, mean duration and frequency of condition.

While, the CBA was carried out in multiple steps including determination of direct and indirect benefits/savings. For determining the direct benefits/savings, first step was to evaluate average effectiveness of therapies in terms of reducing severity of first and second symptoms selected to study common cold, depression and trauma. For common cold as well as the duration of condition, first and second symptoms were sneezing and cough. For depression, these were feeling

bad about oneself and thoughts of hurting oneself, while for trauma, these were the pain and inflammation.

The second step was to determine the physician/herbal practitioner fee savings by utilizing the data gathered for physician/herbal practitioner fee and the average effectiveness of therapies in terms of reducing severity of first and second symptoms of common cold, depression and trauma. The third step was to evaluate transport cost savings by utilizing data collected for transport cost and the average effectiveness of therapies. The fourth step was to combine results of physician/herbal practitioner fee savings and transport cost savings to determine direct benefits/savings.

For indirect benefits/savings, first step was to evaluate income savings from therapies by utilizing the data gathered for loss of income and the average effectiveness of therapies. The second step was to determine the productivity savings by utilizing the results of physician/herbal practitioner fee savings, transport cost savings and income savings. The third step was to evaluate pain savings by utilizing results of productivity savings. The fourth step was to combine results of income savings, productivity savings and the pain savings to determine indirect benefits/savings. The sum of direct and indirect benefits/savings determined the CBA.

#### **Annual frequency of condition:**

The annual frequency of a condition was simply calculated by how many times a condition occurred in a calendar year, while the frequency of chronic conditions like depression was treated as a single onset, i.e. 1.

#### **Prevalence:**

Prevalence was calculated by summing up new cases for reported depression and the old cases existed in Karachi<sup>[18]</sup>. The data for the total population were calculated from the Pakistan Bureau of Statistics<sup>[15]</sup>. While incidences and data of old cases were gathered from clinics and hospitals existed in all 178 union councils of Karachi. Prevalence was calculated using the formula<sup>[19]</sup>  $\text{Prevalence} = (\text{new incidences} + \text{old cases})$ , where, new incidences are the number of new cases reported within time of study, and old cases refer to number of old cases reported within the time of study.

#### **Duration per onset of condition:**

The duration per onset of the condition is simply

calculated using,  $\text{duration} = \text{time of end of condition} - \text{time of start of condition}$ .

#### **Average effectiveness:**

Average effectiveness was calculated by taking the average of percent reduction in 1<sup>st</sup> and 2<sup>nd</sup> symptoms as well as the duration of the condition for each therapy involved in common cold, depression and trauma.  $\text{Average percent effectiveness} = [(\text{average percent effectiveness for 1}^{\text{st}} \text{ symptom} + \text{average percent effectiveness for 2}^{\text{nd}} \text{ symptom} + \text{average percent effectiveness in reducing duration of condition})/3]$ .

#### **Cost of illness analysis:**

The COI was calculated by summing up direct and indirect costs<sup>[18]</sup>,  $\text{COI} = (\text{direct costs} + \text{indirect costs}) \times \text{annual frequency of condition}$ , where, direct costs = (fee of practitioner + costs of medicine + transport costs) and indirect costs = (loss of income + loss due to pain), and loss due to pain = (loss of income  $\times$  1.1). This 110 % value of loss due to pain was an approximate measure from grieving of income loss mixed with pain as extracted from the data submitted by respondents and was therefore fixed throughout the study to reduce variations.

#### **Cost benefit analysis:**

The methodology for CBA was developed and was comprised of calculating the cost benefit as well as calculating benefit to cost ratio. The cost benefit was calculated using the formula,  $\text{cost benefit} = (\text{direct benefits} + \text{indirect benefits})$ , where, direct benefits = (physician or herbal practitioner fee savings + transport cost savings) in which physician or herbal practitioner fee savings = physician or herbal practitioner fee  $\times$  (1 - average percent effectiveness), transport cost savings = transport cost  $\times$  (1 - average percent effectiveness); the indirect benefits = (income savings + productivity savings + pain savings) in which income savings = loss of income  $\times$  (1 - average percent effectiveness), productivity savings = 0.25  $\times$  (physician or herbal practitioner fee savings + transport cost savings + income savings)/3, and pain savings = (0.25  $\times$  productivity savings).

## **RESULTS AND DISCUSSION**

The annual frequency of common cold, depression and trauma in selected population of Karachi was on average at 3 colds per annum, single onset of depressive event a year and 4 incidents of trauma per annum. The

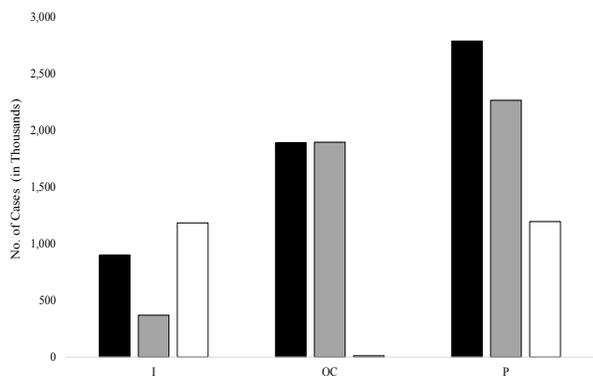
prevalence of common cold (fig. 1) in selected population of Karachi was found to be at 2 791 719 (approx. 2.79 million) people while depression at 2 268 127 (approx. 2.27 million) people and trauma at 1 196 860 (approx. 1.20 million) people.

The mean duration of common cold in selected population of Karachi was estimated at  $10.04 \pm 0.70$  d per onset with therapies. For depression it was  $254.74 \pm 15.50$  d per onset and for trauma it was estimated at  $0.81 \pm 0.54$  d per onset with therapies.

In case of common cold, the average effectiveness in triaminic DM-based therapy was estimated at 27.13 % while that of *G. glabra*-based therapy was calculated at 56.98 %. In depression, the average effectiveness in fluoxetine-based therapy was estimated at 24.31 % while that of *H. perforatum*-based therapy was calculated at 36.10 %. In trauma, the average effectiveness in pyodine-based therapy was estimated at 85.53 % while that of *C. officinalis*-based therapy was calculated at 90.30 %.

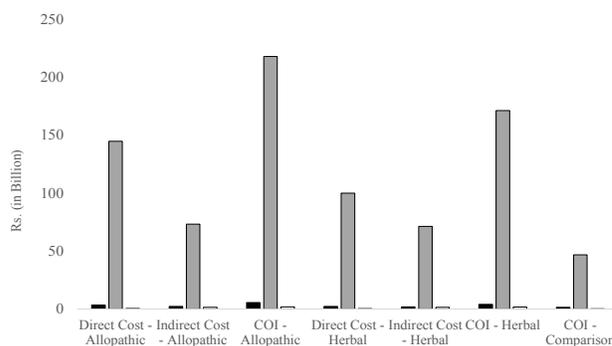
The annual COI (fig. 2) in triaminic DM-based allopathic therapy was estimated at Rs.1 993.89  $\pm$  181.63/- (USD 19.17  $\pm$  1.75 at Rs.104/- per USD) per patient and Rs.5.56 billion (USD 53.46 million) for the prevalent population. For *G. glabra*-based therapy, it was Rs.1453.02  $\pm$  139.90/- (USD 13.97  $\pm$  1.35) per patient and Rs.4.05/- billion (USD 38.94 million) for the prevalent population. There was a clear difference of Rs.1.51/- billion (USD 14.52 million) between the 2 therapies if projected over the patients of common cold in the city of Karachi.

The annual COI (fig. 2) in fluoxetine-based allopathic therapy was estimated at Rs.138 503  $\pm$  17 659.92/- (USD



**Fig. 1: Basic Epidemiology of common cold, depression and trauma in Karachi**

**Basic Epidemiology of common cold, depression and trauma in the population of the city of Karachi, I = incidence, OC = old cases, P = prevalence, (■) common cold (■) depression, (□) trauma**



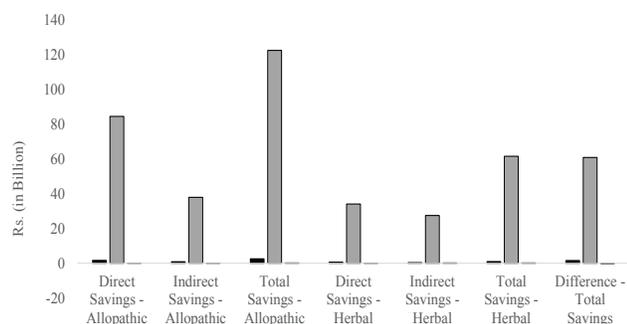
**Fig. 2: Comparative costs incurred for allopathic and herbal therapies of common cold, depression and trauma in Karachi Comparison of costs incurred for allopathic and herbal therapies of common cold, depression and trauma among the population of city of Karachi, COI = cost of illness, Rs. = Pakistani Rupees, (■) common cold, (■) depression, (□) trauma**

1331.76  $\pm$  169.81) per patient and Rs.218.07/- billion (USD 2 billion and 96.83 million) for the prevalent population. For *H. perforatum*-based therapy, it was Rs.75 501.19  $\pm$  12 204.15/- (USD 725.97  $\pm$  117.35) per patient and Rs.171.25/- billion (USD 1 billion and 646.63 million) for the prevalent population. There was a clear difference of Rs.46.82/- billion (USD 450.19 million) between the two therapies if projected over the patients of depression in the city of Karachi.

The annual COI in (fig. 2) pyodine-based allopathic therapy was estimated at Rs.1534.35  $\pm$  229.71/- (USD 14.75  $\pm$  2.21) per patient and Rs.1.84/- billion (USD 17.69 million) for the prevalent population. For *C. officinalis*-based therapy, it was at Rs.1427.39  $\pm$  167.57/- (USD 13.72  $\pm$  1.61) and Rs.1.7/- billion (USD 16.35 million) for the prevalent population. There was a clear difference of Rs.0.14/- billion (Rs.140/- million or USD 1.35/- million) between the 2 therapies if projected over the patients of trauma in the city of Karachi.

The annual cost benefits (fig. 3) in triaminic DM-based allopathic therapy was estimated at Rs.934.49  $\pm$  82.58/- (USD 8.99  $\pm$  0.79) per patient and Rs.2.61/- billion (USD 25.10 million) or 47.12 % of total costs for the prevalent population. For *G. glabra*-based therapy, it was Rs.362.68  $\pm$  37.39/- (USD 3.49  $\pm$  0.36) per patient and Rs.1.02/- billion (USD 9.81 million) or 25.19 % of total costs for the prevalent population. There was a clear difference of Rs.1.60/- billion (USD 15.38 million) or 21.94 % of difference in total costs of both therapies.

The annual cost benefits (fig. 3) in fluoxetine based allopathic therapy was estimated at Rs.53 961.63  $\pm$  13 634.18/- (USD 518.86  $\pm$  131.10) per patient and



**Fig. 3: Comparative savings of allopathic or herbal therapies for common cold, depression and trauma in Karachi**  
**Comparison of savings of allopathic or herbal therapies used for common cold, depression and trauma among the population of city of Karachi, Rs. = Pakistani Rupees, (■) common cold, (■) depression, (□) trauma**

Rs.122.39/- billion (USD 1 billion and 176.83 million) or 56.12 % of total costs for the prevalent population. For *H. perforatum*-based therapy, it was Rs.27 126.50±5868.98/- (USD 260.83±56.43) per patient and Rs.61.52/- billion (USD 591.54 million) or 35.92 % of total costs for the prevalent population. There was a clear difference of Rs.60.87/- billion (USD 585.29 million) or 20.20 % of difference in total costs between the two therapies if projected over the patients of depression in the city of Karachi.

The annual cost benefits (fig. 3) in pyodine-based allopathic therapy was estimated at Rs.162.17±162.25/- (USD 1.56±1.56) per patient and Rs.0.19/- billion (Rs.190/- million or USD 1.83 million) or 10.33 % of total costs for the prevalent population. For *C. officinalis*-based therapy, it was at Rs.99.81±99.97/- (USD 0.96±0.96) and Rs.0.24/- billion (Rs.240/- million or USD 2.31 million) or 14.12 % of total costs for the prevalent population. There was a clear difference of Rs.-0.05/- billion (Rs.-50/- million or USD -0.48 million) or -3.79 % of difference in total costs between the two therapies if projected over the patients of trauma in the city of Karachi.

Although, after the detailed analysis of costs and benefits of allopathic and herbal therapies of common cold, depression and trauma, at first it seems like if allopathic therapy provided more benefits than herbal therapy (fig. 3), but it is because the methodology involved for cost benefits that used components from costs and thus calculating more benefits against higher cost. However, the herbal therapies that cost less in first place, have provided more average effectiveness and hence proved more beneficial in a developing country like Pakistan, where the budget of healthcare is already

all time low<sup>[19]</sup>. From this research work, it could be concluded that the use of herbal therapies for treatment and management of common cold, depression and trauma is preferable than the allopathic therapies.

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### Conflict of interest:

There are no conflicts of interest.

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Nil.

### REFERENCES

1. Marcellusi A, Viti R, Mecozzi A, Mennini FS. The direct and indirect cost of diabetes in Italy: a prevalence probabilistic approach. *Eur J Health Econ* 2016;17(2):139-47.
2. Boardman AE, Greenberg DH, Vining AR, Weimer DL. Cost-benefit analysis: concepts and practice. Cambridge, UK: Cambridge University Press; 2017.
3. Muennig P, Bounthavong M. Cost-effectiveness analysis in health: a practical approach. San Francisco, CA, USA: Jossey-Bass Inc.; 2016. p. 46-47.
4. Nas TF. Cost-benefit analysis: Theory and application. Lanham, MD, USA: Lexington Books; 2016. p. 8.
5. Mishan EJ. Elements of Cost-Benefit Analysis (Routledge Revivals). Abingdon, UK: Routledge; 2015.
6. De Gruyter E, Ford G, Stavreski B. Economic and social impact of increasing uptake of cardiac rehabilitation services—a cost benefit analysis. *Heart Lung Circ* 2016;25(2):175-83.
7. Frederix I, Vandijck D, Hens N, De Sutter J, Dendale P. Economic and social impact of increased cardiac rehabilitation uptake and cardiac telerehabilitation in Belgium - a cost-benefit analysis. *Acta Cardiol* 2018;73(3):222-9.
8. Werner EF, Hauspurg AK, Rouse DJ. A Cost-Benefit Analysis of Low-Dose Aspirin Prophylaxis for the Prevention of Preeclampsia in the United States. *Obstet Gynaecol* 2015;126(6):1242-50.
9. Carande-Kulis V, Stevens JA, Florence CS, Beattie BL, Arias I. A cost-benefit analysis of three older adult fall prevention interventions. *J Safety Res* 2015;52:65-70.
10. Malet-Larrea A, Goyenechea E, Gastelurrutia MA, Calvo B, García-Cárdenas V, Cabases JM, et al. Cost analysis and cost-benefit analysis of a medication review with follow-up service in aged polypharmacy patients. *Eur J Health Econ* 2017;18(9):1069-78.
11. Russell LB. The science of making better decisions about health: cost-effectiveness and cost-benefit analysis [dissertation]. New Brunswick, Newark and Camden, NJ, USA: Rutgers University, The State University of New Jersey; 2014.
12. Sanghera S, Frew E, Gupta JK, Kai J, Roberts TE. Exploring the use of cost-benefit analysis to compare pharmaceutical treatments for menorrhagia. *Pharmacoeconomics* 2015;33(9):957-65.

13. Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB, *et al.* Model transparency and validation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. *Med Decis Making* 2012;32(5):733-43.
  14. Pakpour AH, Hidarnia A, Hajizadeh E, Kumar S, Harrison AP. The status of dental caries and related factors in a sample of Iranian adolescents. *Med Oral Patol Oral Cir Bucal* 2011;16(6):e822-7.
  15. Pakistan Statistical Year Book 2012. Available from: <http://www.pbs.gov.pk/content/pakistan-statistical-year-book-2012>.
  16. Groves RM, Fowler FJ, Couper MP, Lepkowski JM, Singer E, Tourangeau R. *Survey methodology*. 2nd ed. Hoboken, NJ, USA: Wiley; 2011.
  17. Dillman DA, Smyth JD, Christian LM. *Internet, phone, mail, and mixed-mode surveys: the tailored design method*. Hoboken, NJ, USA: Wiley; 2014.
  18. Sullivan SD, Mauskopf JA, Augustovski F, Caro JJ, Lee KM, Minchin M, *et al.* Budget impact analysis—principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health* 2014;17(1):5-14.
  19. Ahmed J, Shaikh BT. An all-time low budget for healthcare in Pakistan. *J Coll Physicians Surg Pak* 2008;18(6):388.
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