COMPARATIVE STUDY BETWEEN ALLOPATHIC AND HERBAL THERAPIES OF COMMON COLD, DEPRESSION AND TRAUMA IN THE CITY OF KARACHI: A COST UTILITY AND RELATIONSHIP ANALYSIS

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ABSTRACT: A comparative cross-sectional study, utilized 1,068 patients (stratified random samples; n=178 per therapy) from 0 to 75+ years of age, belonging to 178 union councils of Karachi, assessing preference among allopathic and herbal therapies in terms of provided utility in common cold, depression and trauma via surveys, assuming no significant relationship between age group, sex and cost of illness with disability-adjusted-life-years. Utilized known costs of illness and prevalence for diseases, calculated the disability-adjusted-life-years and the utility. The differences (allopathic less herbal therapy) in disability-adjusted-life-years; and utility-to-cost-ratio of therapies were: 1,025.18 yrs.; 6.66, 145,869.42 yrs; -1.55 and 82.91 yrs; 24.45 for common cold, depression and trauma, respectively. There were statistically insignificant relationships of age group, sex and cost of illness with disability-adjusted-life-years ($P > 0.05$). Comparatively, the herbal therapies proved less costly, with fewer disability-adjusted-life-years and hence with more utility.

INTRODUCTION

Due to promising potential of herbal medicines and supplements, their uses have been increased for the last thirty years (WHO, 2004; Ekor, 2014). About four billion people are using these medicines worldwide (Mukherjee, 2002). In the developed countries, the use is linked to a belief that it will help in improved living (Alters *et al.*, 2012).

Although, there are numerous diseases that fill the top lists of healthcare expenses in the society, yet it is said that medicines alone account for at least 10 percent of expenses globally (Wertheimer, 2014). Due to such expenditures and regardless of the type of disease, there must be a fair comparison of allopathic and herbal medicine to switch onto the preferred therapy. Because a medicine can be costlier but comparatively it can provide more utility to a patient with a certain disease. This is where pharmacoeconomics play its role (Wertheimer, 2014). For such evaluations, there are many tools used in pharmacoeconomics. But for the detailed comparison of cost and utility gained, cost utility analysis (CUA) can be employed (Brazier *et al.*, 2016).

Cost utility analysis (CUA) is a type of cost effectiveness analysis (CEA) where therapeutical efficacy is based on the subsequent well-being conditions (Brazier *et al.*, 2016). Like CEA, the CUA also computes therapeutical significances in context of amount and value of life. The outcomes of the CUA are expressed as a therapeutic charge for every quality-adjusted-life-year (QALY) added. It is also expressed as fluctuations in quality-of-life (QOL) for a specified therapeutic charge. Therefore, the CUA is the ratio between the differences in charges of therapeutics and the utility. The utility can be expressed in terms of either the potential-years-of-life-lost (PYLLs), healthy-years-of-life-lost (HYLLs), quality-adjusted-life-years (QALYs) or the disability-adjusted-life-years (DALYs) (Drummond *et al.*, 2015). Mostly, QALYs and DALYs are used in CUA (Sassi, 2006), keeping in mind the difference that the method of modification of the years of life passed with health is known as "quality adjustment" (expressed as QALYs), while the course of modification of the lost years of life passed with health is named "disability adjustment" (expressed as DALYs) (Tulchinsky *et al.*, 2000; Arnesen *et al.*, 2009). However, the preferred use of DALYs is permitted by the World-Health-Organization (WHO) for ordering therapeutic activities in the public well-being. This recommendation is based on its efficiency to express the lessen load of illness (Gaunt *et al.*, 2011).

The common cold, depression and trauma (minor cut) were the type of conditions in the City of Karachi that were chosen for the comparative investigation. This was a part of series of studies conducted by the same team (Syed *et al.*, 2017) for detailed epidemiological and pharmacoeconomical evaluations. It was hypothesized that herbal therapy was more beneficial in terms of efficacy and less cost than the

allopathic therapy. And the age group, sex and cost of illness have no significant relationship with DALYs.

Therefore, the core objectives of the study were to evaluate the preferences among the therapies and statistically evaluating the relationship of DALYs with age group, sex and cost of illness.

MATERIALS AND METHODS

The study was initiated after approval of the project from *Ethical Review Committee,* Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, for the collection of data of patients of common cold, depression and trauma.

Selection of medicines for diseases: Oral infusion of powdered '*G. glabra* L.' (1 cup: 300mg, daily) was engaged as a sample while the allopathic medicine TRIAMINIC DM® Syrup (*Dextromethorphan:10mg/5ml with Pseudoephedrine (HCl):30mg/5ml*) was selected as a control in the study for the common cold. Oral infusion of powdered '*H. perforatum* L.' (1 cup: 200mg, daily) was engaged as a sample while the allopathic medicine FLOXAC® 20mg Tablets (*Fluoxetine [HCL] 20mg*) was used as a control in the study for depression. Topical application of tincture of '*C. officinalis* L.' (2 − 5 drops every 12 − 24 hours) depending on the area and severity of trauma) was engaged as a sample while the allopathic

medicine PYODINE® Solution (*Povidone-Iodine 10%w/v*) was selected as a control in the study for trauma.

Setting and sample size: A total of 1,068 patients, 356 patients for each disease (sample size N=178, each for allopathic and herbal based therapies) were selected as stratified random samples. For common cold and trauma, the samples were taken from the populace of 20,819,302 from each of the 178 union councils (UCs) which were divided for age wise data collection in accordance with proportions of each age groups. Out of 16 different age groups (Table 1) as defined by Pakistan Bureau of Statistics (Anonymous, 2006). For depression, the samples were taken from the populace of 7,755,189 from each of the 178 UCs which were divided for age wise data collection in accordance with proportions of each age groups out of 11 different age groups (Anonymous, 2006) (Table 1). Following formula was used for age group based sample size:

Age group based sample size

$$= \frac{Percentage\ of\ age\ group\ in\ population}{100} X\ Sample\ size$$

The calculation for the number of patients in depression was done by dividing the percentages of age groups by populace 37.25 instead of 100, e.g.

Age grouped sample size $= \frac{7.37}{37.25}$ x 178.

Table-1: Percentage-wise division of sample size of 178 patients among age groups in common cold, depression and trauma.

Group No.	In Cases of Common Cold and Trauma			In Cases of Depression		
	Age Groups (in yrs.)	Percentage of Total Population	Age Group Wise Sample Size (No. of Patients)	Age Groups (in yrs.)	Percentage of Total Population	Age Group Wise Sample Size (No. of Patients)
1	0 – 4 yrs.	14.80%	26	25 – 29 yrs.	7.37%	35
2	5 – 9 yrs.	15.65%	28	30 – 34 yrs.	6.22%	30
3	10 – 14 yrs.	12.95%	23	35 – 39 yrs.	4.77%	23
4	15 – 19 yrs.	10.37%	18	40 – 44 yrs.	4.45%	21
5	20 – 24 yrs.	8.97%	16	45 – 49 yrs.	3.53%	17
6	25 – 29 yrs.	7.37%	13	50 – 54 yrs.	3.21%	15
7	30 – 34 yrs.	6.22%	11	55 – 59 yrs.	2.15%	10
8	35 – 39 yrs.	4.77%	9	60 – 64 yrs.	2.04%	10
9	40 – 44 yrs.	4.45%	8	65 – 69 yrs.	1.20%	6
10	45 – 49 yrs.	3.53%	6	70 – 74 yrs.	1.09%	5
11	50 – 54 yrs.	3.21%	6	75 yrs. & up	1.21%	6
12	55 – 59 yrs.	2.15%	4			
13	60 – 64 yrs.	2.04%	4			
14	65 – 69 yrs.	1.20%	2			
15	70 – 74 yrs.	1.09%	2			
16	75 yrs. & up	1.21%	2			

yrs. = years, 16 age groups (0-75 yrs & up) for epidemiological and pharmacoeconomical evaluations of allopathic & herbal therapies of common cold and trauma while 11 age groups (25-75 yrs & up) for depression

The survey instrument and data collection: Layered style interviews, questionnaires and opinion surveys (De Rada, 2016) were used to get maximum input in the study and were comprised of a blend of open and closed-ended questions. Questionnaires and opinion surveys were available to the respondents both in the form of paper-based or an online survey with Limesurvey™ and surveymonkey.com. Opinion surveys were mostly utilized for gathering epidemiological data from union councils.

Data evaluations and statistical analysis: The literature search and bibliography were managed and carried out in Endnote®, data gathered were managed via office software, *i.e.* Microsoft® Excel 2016 while statistical analyses along with graph generation with the help of IBM® SPSS version 23 and Microsoft® Excel 2016, respectively.

Calculations of DALYs and UCRs: Although, there are different methodologies for carrying out CUA like comparing costs with PYLLs, HYLLs, QALYs or DALYs, etc. but present study chosen and utilized DALYs for conducting CUA.

In determining CUA, a general formula for cost utility analysis, *i.e.* Cost Utility Ratio=Cost/Utility (Remington, 2005) was molded into utility defined as DALYs of allopathic ($DALY_A$) and herbal ($DALY_H$) therapies. In this study, the DALYs of a therapy was the sum of the number of years of lifetime misplaced due to early demise (YLLs) and years misplaced owing to incapability (YLDs). Therefore, the formula for calculation of DALYs (Burazeri *et al.*, 2013) utilized in the study was:

$$DALY = YLL + YLD$$

The calculation of YLLs was carried out with a discount rate as:

$$YLL = \frac{N}{r}(1 - e^{-r*L_{DT}})$$

Where,

N = number of deaths
r = discount rate (constant rate of 0.03 in clinical calculations)
e = natural logarithm (constant value of approx. 2.71828)
L_{DT} = standard life expectancy at age of death in years

YLLs were supposed to be zero (0) because of the absence of fatality in either of the therapies, i.e. L_{DT} is zero (0). YLLs for allopathic therapies were recorded as YLL_A while for herbal therapies as YLL_H.

For representation of methodology here, the YLDs for common colds or traumas were calculated with discount rate and prevalence along with its disability weight of 0.007 (value of 0.294 in case of depression) as:

$$YLD = \frac{P * DW(1 - e^{-r*L_{DB}})}{r}$$

Where,

P = Prevalence of common cold

DW = disability weight i.e. 0.007 for common cold and trauma while 0.294 for depression (Haagsma *et al.*, 2015)
L_{DB} = average duration of the case until remission or death (years)
'L_{DB}' was treated as duration in years with medicines (per year) was calculated by:

$$L_{DB} = \frac{L_{PO}}{365} * f$$

Where,

L_{PO} = duration of the condition in days with medicines (per onset)
f = approx. yearly frequency of condition (approx. 3 colds, 1 depression and 4 traumas per year)
For allopathic therapies, YLDs were recorded as YLD_A, L_{PO} as L_{POA}, and L_{DB} as L_{DBA} while for herbal therapies as YLD_H, L_{POH}, and L_{DBH} respectively.

Therefore, for representation of methodology here, the calculation for DALYs both for allopathic and herbal therapies of common colds and traumas were:

$$DALY = [\{\frac{N}{r}(1 - e^{-r*L_{DT}})\} + \{\frac{P * DW(1 - e^{-r*L_{DB}})}{r}\}]$$

DALYs for allopathic therapies were recorded as $DALY_A$ while for herbal therapies were $DALY_H$. The formula used for calculation of differences between DALYs of allopathic and herbal therapies was:

$$Diff. in DALY = DALY_A - DALY_H$$

The formula utilized for UCRs, was a product of the division of utility in terms of DALYs with costs of illness (COIs) of individual therapies, either allopathic or herbal as:

$$UCR = \{(\frac{DALY}{COI}) * (\frac{1}{COI})\}$$

For the difference in UCRs:

$$Diff. in UCR = UCR_A - UCR_H$$

Where,

UCR_A = utility-to-cost-ratio for allopathic therapy
UCR_H = utility-to-cost-ratio for herbal therapy
The results of CUA, both in terms of DALYs and UCRs of individual patients of common cold, depression and trauma for both allopathic and herbal therapies in 178 union councils in the City of Karachi.

Statistical analysis and data representation: Along with the representation of data of 1,068 patients of 178 union councils, the one-way ANOVA for evaluating the relationship between age group, sex and the cost of illness with the DALYs of therapies and the linear regression analysis (Barber *et al.*, 2004) featuring *bivariate correlation* with *Pearson correlation coefficient* (p-corr.) were carried out between COIs and DALYs of all therapies of three diseases. Both the linear regression analysis featuring *bivariate correlation* with *Pearson correlation coefficient* (p-corr.) and one-way ANOVA were carried out using IBM® SPSS version 23.

RESULTS AND DISCUSSION

By measuring and comparing the economic burden of diseases to society, healthcare decision-makers could benefit in setting up and prioritizing health care policies and interventions that they were supposed to implement (Jo *et al.*, 2014). Therefore, for the calculation of UCRs, the values of COIs of allopathic and herbal therapies (Table 3) were: Rs.5.56/- billion (US$ 53.46/- million) and Rs.4.05/- billion (US$ 38.94/- million) for common cold, Rs.218.07/- billion (US$ 2 billion and 96.83/- million) (Syed *et al.*, 2017) and Rs.171.25/- billion (US$ 1 billion and 646.63/- million) for depression and finally Rs.1.84/- billion (US$ 17.69/- million) and Rs.1.7/- billion (US$ 16.35/- million) for trauma.

Table-2: Disability-adjusted-life-years of allopathic and herbal therapies in reducing symptoms and duration of common cold, depression and trauma in the City of Karachi

Diseases	Allopathic Therapy				Herbal Therapy			
	Duration (L_{DBA}) in yrs.	YLL_A in yrs.	YLD_A in yrs.	$DALY_A$ in yrs.	Duration (L_{DBH}) in yrs.	YLL_H in yrs.	YLD_H in yrs.	$DALY_H$ in yrs.
Common Cold	0.1	0	1,951.28	1,951.28	0.07	0	926.10	926.10
Depression	0.76	0	499,020.37	499,020.37	0.64	0	353,150.95	353,150.95
Trauma	0.01	0	83.77	83.77	0.01	0	0.86	0.86

yrs. = years, L_{DBA} = average duration in allopathic therapy, L_{DBH} = average duration in herbal therapy, YLL_A = years of lifetime misplaced in allopathic therapy, YLL_H = years of lifetime misplaced in herbal therapy, YLD_A = years misplaced owing to incapability in allopathic therapy, YLD_H = years misplaced owing to incapability in herbal therapy, DALY = disability-adjusted-life-year, $DALY_A$ = disability-adjusted-life-years in allopathic therapy, $DALY_H$ = disability-adjusted-life-years in herbal therapy

Table 3: Utility-to-cost-ratios of allopathic and herbal therapies of common cold, depression and trauma in City of Karachi.

Diseases	Costs of Illness (COIs)		Utility-to-Cost-Ratios (UCRs)	
	COI_A Rs. in Billion	COI_H Rs. in Billion	UCR_A	UCR_H
Common Cold	5.56	4.05	63.12	56.46
Depression	218.07	171.25	10.49	12.04
Trauma	1.84	1.70	24.74	0.30

Rs. = Pakistani rupees, COI_A = cost of illness in allopathic therapy, COI_H = cost of illness in herbal therapy, UCR_A = utility-to-cost-ratio for allopathic therapy, UCR_H = utility-to-cost-ratio for herbal therapy, Allopathic therapy = TRIAMINIC DM®, FLOXAC® and PYODINE® in common cold, depression and trauma respectively, Herbal therapy = G. glabra, H. perforatum and C. officinalis in common cold, depression and trauma respectively.

DALYs and UCRs for therapies in Common Cold: In the allopathic therapy of common cold (Table 2, Graph 4-a) using TRIAMINIC DM®, the DALYs were found to be 1,951.28 years (yrs.) while the UCR (Table 3) was at 63.12. In herbal therapy (Table 2) using *G. glabra*, the DALYs were found to be 926.10 yrs. while the UCR (Table 3) was at 56.46. The differences in, the DALYs (TRIAMINIC DM® less *G. glabra* therapies) were found to be 1,025.18 yrs., while the UCRs (Table 3) were at 6.66, specifically indicating the preference and superiority of *G. glabra* over TRIAMINIC DM® therapy in case of common cold.

DALYs and UCRs for therapies in depression: In the allopathic therapy of depression (Table 2, Graph 4-b) using FLOXAC®, the DALYs were found to be 499,020.37 yrs. while the UCR (Table 3) was at 10.49. In

herbal therapy, (Table 2) using *H. perforatum*, the DALYs were found to be 353,150.95 yrs. while the UCR (Table 3) was at 12.04. The differences in, the DALYs (FLOXAC® less *H. perforatum* therapies) were found to be 145,869.42 yrs., while the UCRs (Table 3) were at -1.55, partially representing the preference and superiority of *H. perforatum* over FLOXAC® therapy in case of depression as negative difference in case of UCRs represents superiority of FLOXAC® and therefore need to be investigated further.

DALYs and UCRs for therapies in trauma: In the allopathic therapy of trauma (Table 2, Graph 4-c) using PYODINE®, the DALYs were found to be 83.77 yrs. while the UCR (Table 3) was at 24.74. In herbal therapy (Table 2) using *C. officinalis*, the DALYs were found to be 0.86 yrs. while the UCR (Table 3) was at 0.30. The

differences in, the DALYs (PYODINE® less *C. officinalis* therapies) were found to be 82.91 yrs., while the UCRs (Table 3) were at 24.45, representing the preference and superiority of *C. officinalis* over PYODINE® therapy in case of trauma.

The comparison of the percentage of differences between DALYs of allopathic and herbal therapies of all three diseases revealed that *C. officinalis* outclassed PYODINE® from a maximum percentage difference of 98.97% (Graph 5).

After a detailed analysis of DALYs, UCRs; their differences in allopathic and herbal therapies of common cold, depression and trauma, our alternate hypothesis proved right in cases of common cold, depression and trauma where herbal therapy proved to be a better choice, both in terms of lesser COIs and lower DALYs.

Even the linear regression analysis (Barber *et al.*, 2004) featuring *bivariate correlation* with *Pearson correlation coefficient* (p-corr.) revealed no significant relationships (Table 4) of COIs and DALYs for allopathic and herbal therapies of common cold (p-corr. = -0.236 with p-value = 0.002; p-corr. = -0.016 with p-value = 0.83), depression (p-corr. = -0.007 with p-value = 0.93; p-corr. = 0.019 with p-value = 0.80) and trauma (p-corr. = 0.006 with p-value = 0.94; p-corr. = 0.061 with p-value = 0.42). Therefore, the p-values were highly insignificant in comparison with significance level of 0.05 (except in case of allopathic therapy of common cold with TRIAMINIC DM, where p-corr. was -0.236 with p-value of 0.002, *i.e.* significant), however oneway ANOVA confirmed the insignificance of relationships of not only COI (Table 4) but also the age groups and the sex of patients with the DALYs avoided by either of the therapies and hence such insignificance were constantly independent of the types of therapy.

(a)

COI by TRIAMINIC DM® (in Rs.)

(b)

COI by *G. glabra* (in Rs.)
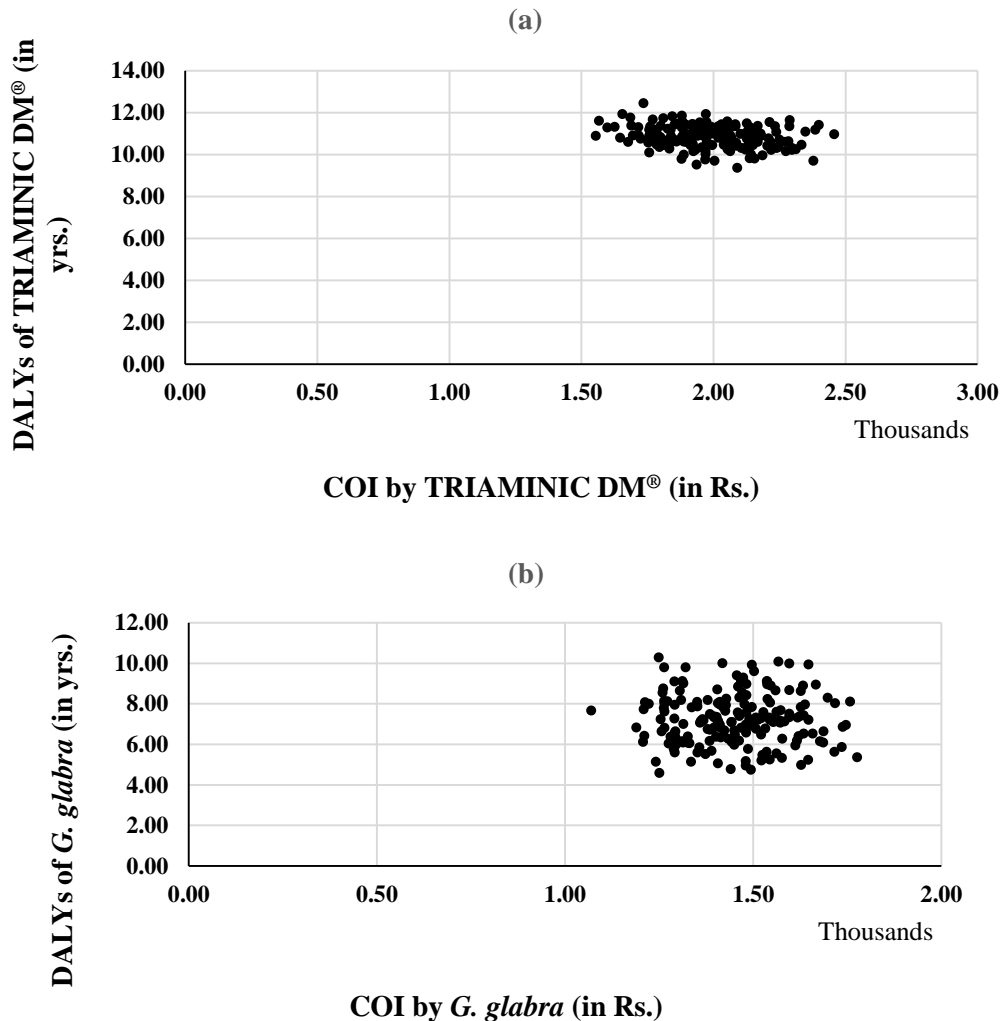
Graph-1: COIs and DALYs related to (a) TRIAMINIC DM® and (b) *G. glabra* based therapies of the common cold in 178 union councils of City of Karachi
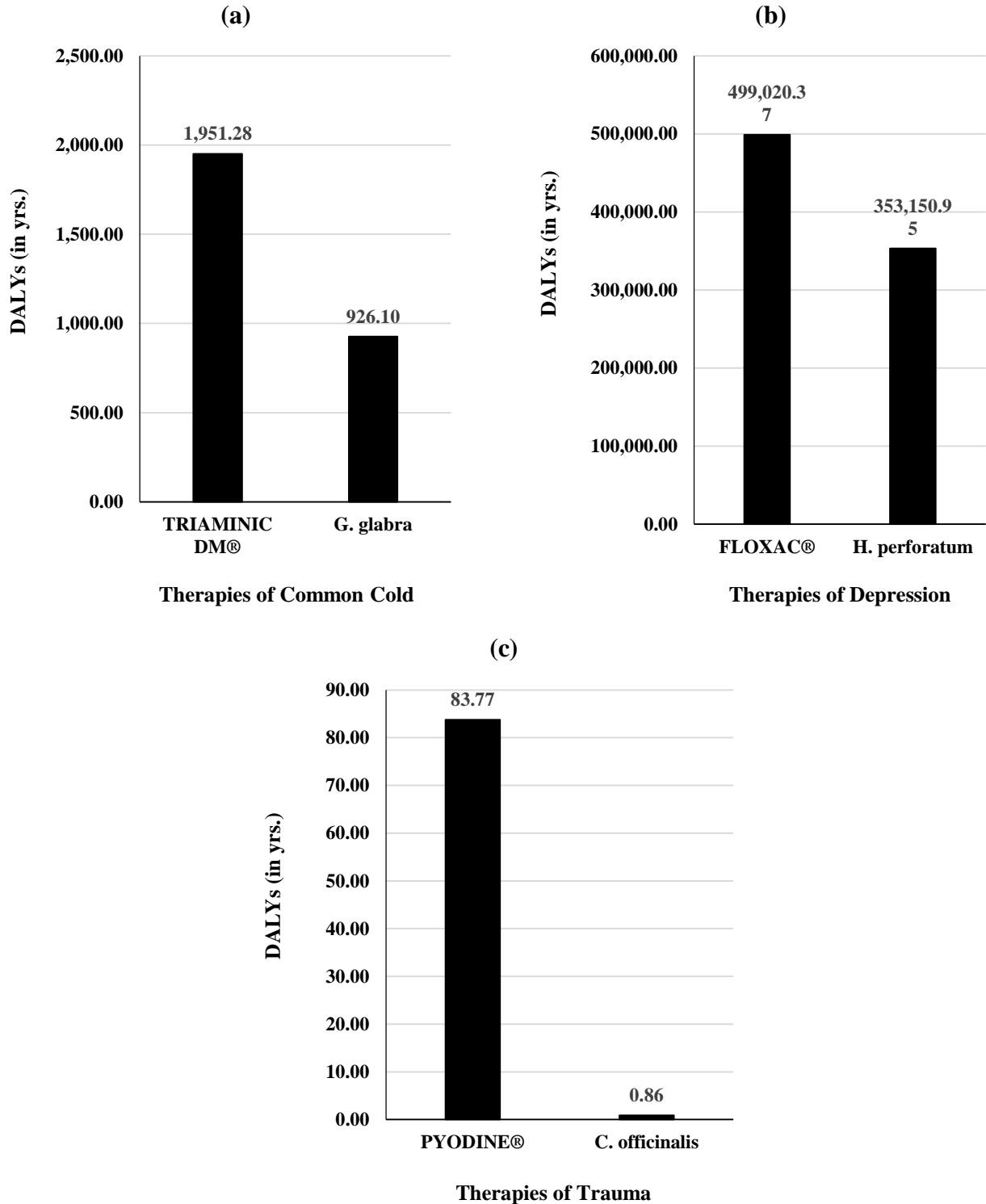
COI = costs of illness, DALYs = disability-adjusted-life-years, Rs. = Pakistani Rupees

(a)

(b)
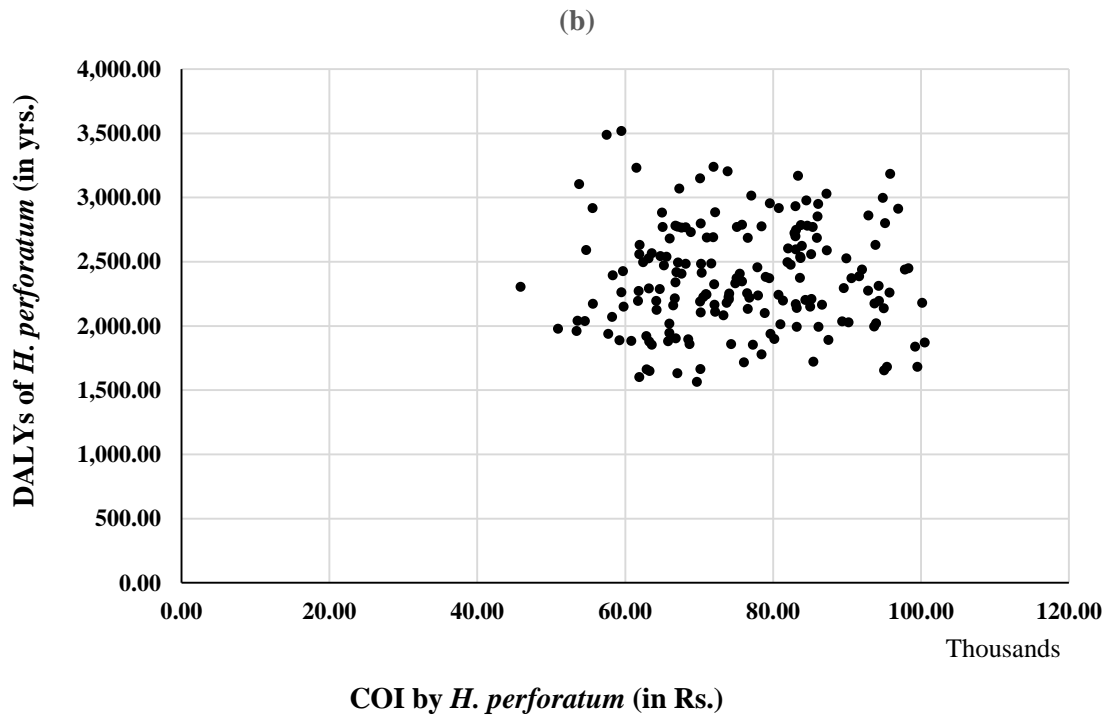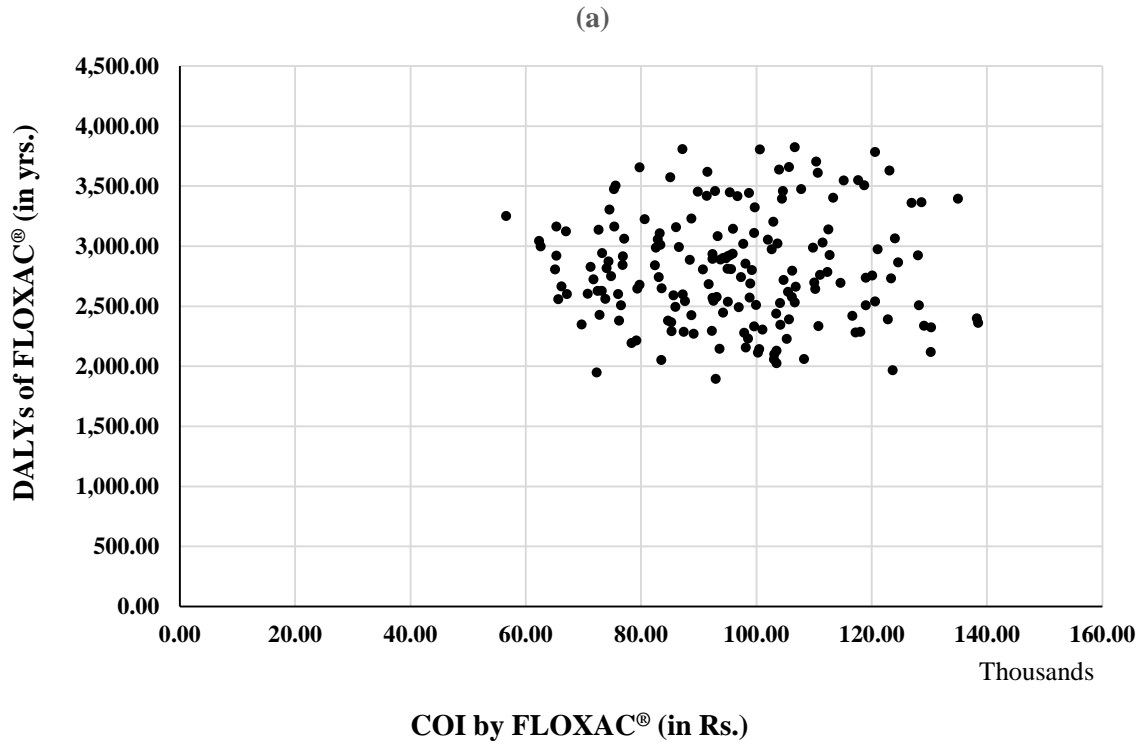
Graph 2: COIs and DALYs related to (a) FLOXAC® and (b) *H. perforatum* based therapies of the depression in 178 union councils of City of Karachi

(a)

(b)
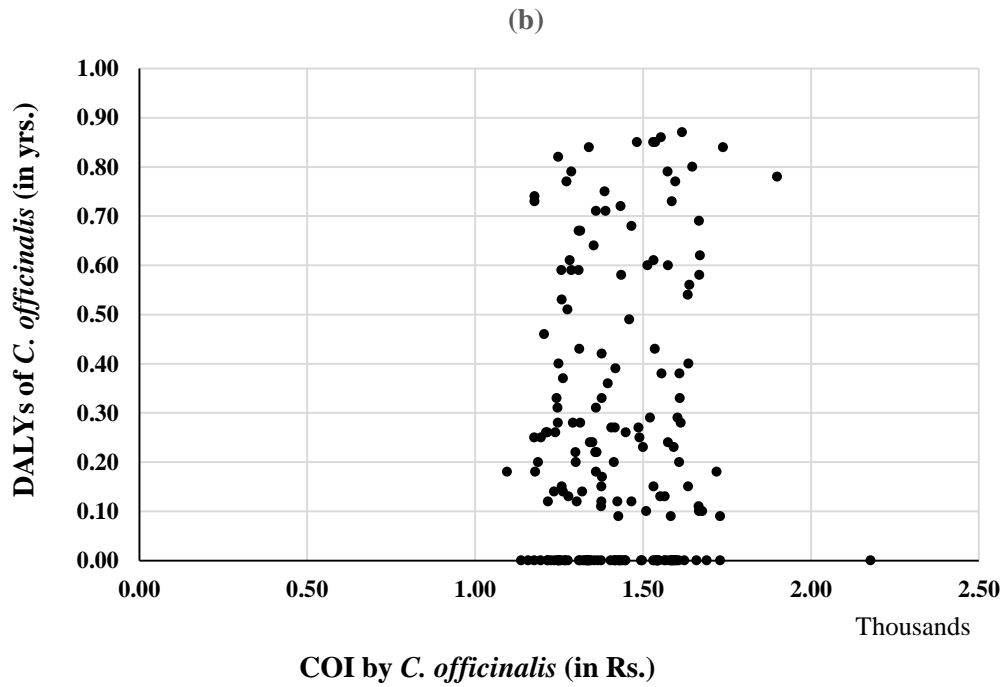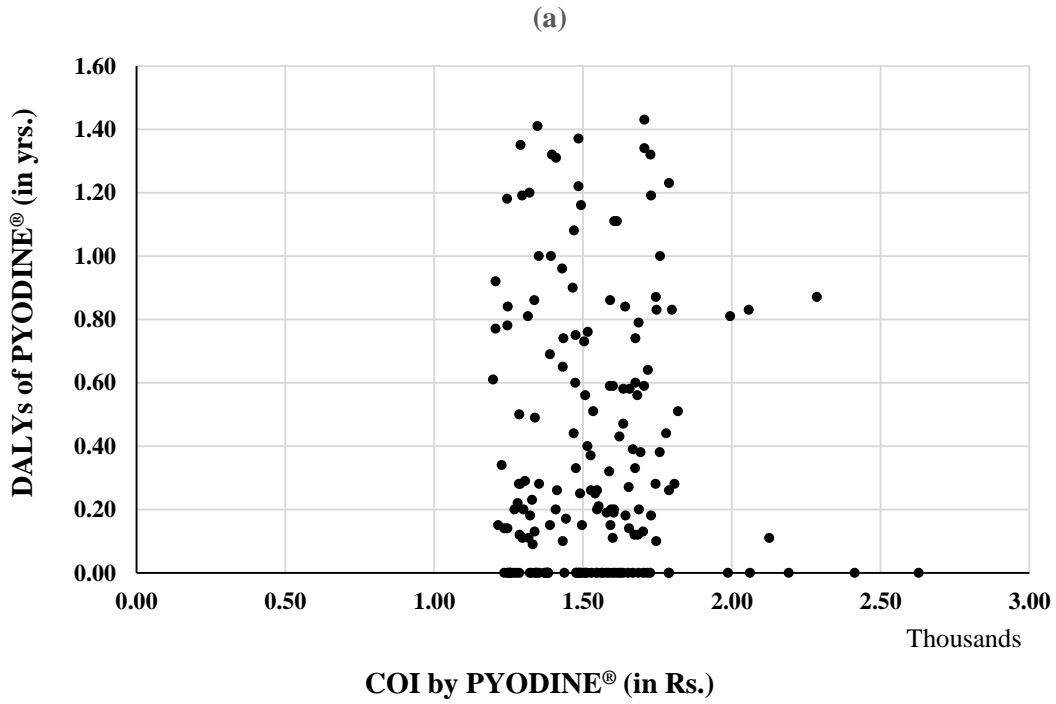
Graph-3: COIs and DALYs related to (a) PYODINE® and (b) *C. officinalis* based therapies of the trauma in 178 union councils of City of Karachi

(a)

(b)

(c)

Graph-4: DALYs of allopathic and herbal therapies of (a) Common cold, (b) Depression and (c) Trauma in City of Karachi

DALYs = disability-adjusted-life-years, Allopathic therapy = TRIAMINIC DM®, FLOXAC® and PYODINE® in common cold, depression and trauma respectively, Herbal therapy = G. glabra, H. perforatum and C. officinalis in common cold, depression and trauma respectively.
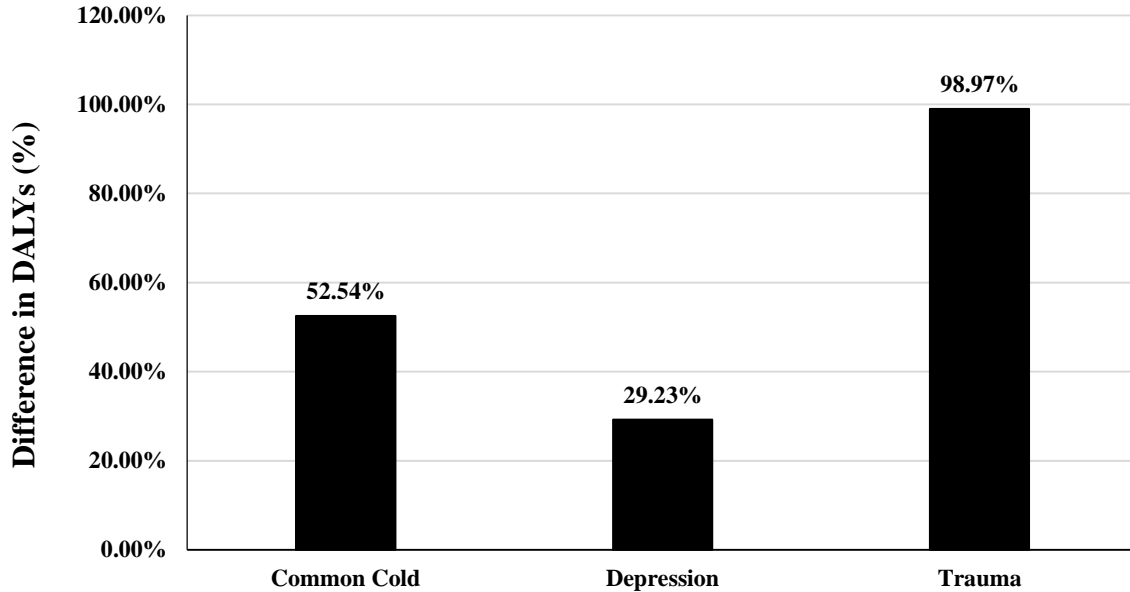
Graph-5: Differences in DALYs of allopathic and herbal therapies of common cold, depression and trauma in City of Karachi

Table-4: Level of significance in statistical analysis for identifying a significant relationship between disability adjusted life years and the age group, sex and cost of illness in common cold, depression and trauma in the City of Karachi.

Therapy	Independent Vs Dependent Variable	Statistical Evaluations		Oneway ANOVA (Sig.)
		Linear Regression		
		Pearson correlation coefficient (p-corr.)	*P-Value*	
Allopathic Therapy for Common Cold (*Triaminic DM*)	Age Group Vs DALYs	-	-	0.929
	Sex Vs DALYs	-	-	0.302
	COI Vs DALYs	-0.236	0.002	0.311
Herbal Therapy for Common Cold (*Glycyrrhiza glabra*)	Age Group Vs DALYs	-	-	0.749
	Sex Vs DALYs	-	-	0.162
	COI Vs DALYs	-0.016	0.832	0.131
Allopathic Therapy for Depression (*Floxac*)	Age Group Vs DALYs	-	-	0.137
	Sex Vs DALYs	-	-	0.717
	COI Vs DALYs	-0.007	0.929	-
Herbal Therapy for Depression (*Hypericum perforatum*)	Age Group Vs DALYs	-	-	0.408
	Sex Vs DALYs	-	-	0.922
	COI Vs DALYs	0.019	0.801	-
Allopathic Therapy for Trauma (*Pyodine*)	Age Group Vs DALYs	-	-	0.003
	Sex Vs DALYs	-	-	0.700
	COI Vs DALYs	0.006	0.937	0.517
Herbal Therapy for Trauma (*Calendula officinalis*)	Age Group Vs DALYs	-	-	0.296
	Sex Vs DALYs	-	-	0.621
	COI Vs DALYs	0.061	0.420	0.543

Lower the DALYs, higher were the probability of suitability of therapy as a choice (Murray *et al.*, 2012). Therefore, if the difference (allopathic less herbal therapy) turned out to be positive, herbal therapy was supposed to be a therapy of choice, i.e. having lesser DALYs. Since, UCRs were derived from DALYs, likewise, if the difference in UCRs was determined as positive, allopathic therapy was supposed to be the less preferred choice of therapy than herbal therapy; similarly, vice versa in case of negative difference.

Conclusion: The study was concluded that the herbal therapies are less expensive, providing more utility thus lowering disability adjusted life years in cases of common cold, depression and trauma in the City of Karachi. Furthermore, it was also concluded that age group and sex of patients as well as the costs of illness in cases of herbal and allopathic therapies have no significant relationship with disability adjusted life years avoided by the therapies.

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