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Cost Effectiveness and Resource Allocation

RESEARCH

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# Pharmacoeconomic evaluation of treatments for Poly Cystic Ovarian Syndrome (PCOS)

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## Abstract

**Background** Treatment cost and high prevalence of Poly Cystic Ovarian Syndrome (PCOS) is a very challenging issue globally. Due to this reason; current study was conducted to determine pharmaco-economy of conventional and non-conventional treatments for the management of PCOS.

**Methods** Prospective Cross-Sectional study was conducted in the metropolitan city of Karachi from January – December 2019. Primary data of 200 PCOS patients were collected from different hospitals and clinics. An instrument was used to collect data pertaining to the direct and indirect cost associated with the disease management. Collected data was analyzed by the tools for cost analysis and software called Statistical Package of Social Sciences (SPSS) – 22.

**Results** In Cost Minimization Analysis (CMA); Allopathic treatment [Mean cost/month: PKR:4479.32 ± 350.95 (USD:27.46 ± 2.15)], Herbal treatment [Mean cost/month: PKR:1527.78 ± 78.15 (USD:9.37 ± 0.48)], Combination treatment [Mean cost/month: PKR:2803.09 ± 654.22 (USD:17.18 ± 4.01)], and Homoeopathic treatment [Mean cost/month: PKR:976.95 ± 46.19 (USD:5.99 ± 0.28)]. Incremental cost/month for Allopathic treatment is 358%, Herbal treatment is 56%, Combination treatment is 187%. In Cost Effectiveness Analysis (CEA); Allopathic treatment (Incremental cost-effectiveness ratio/month: 1334.24), Herbal treatment (Incremental cost-effectiveness ratio/month: 936.41), Combination treatment (Incremental cost-effectiveness ratio/month: 1017.09). Due to lowest cost of Homeopathic treatment, cost of Homeopathic treatment was considered as a threshold value. In-direct cost/month of Allopathic treatment is PKR:593.33 ± 24.00 (USD:3.64 ± 0.15), Herbal treatment is PKR:307.84 ± 26.69 (USD:1.89 ± 0.16), Combination treatment is PKR:409.09 ± 45.63 (USD:2.51 ± 0.28) and Homoeopathic treatment is PKR:300.00 ± 26.39 (USD:1.84 ± 0.16).

**Conclusion** The most cost-effective is treatment is Homeopathic; Herbal treatment is second most cost-effective option for the treatment of PCOS. Lowest direct and indirect costs and short treatment duration collaboratively lessen the %incremental cost per year and incremental cost effectiveness ratio per year.

**Keywords** Poly Cystic Ovarian Syndrome, Cost minimization analysis, Cost effectiveness analysis, Direct cost, Indirect cost, Incremental cost effectiveness ratio

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## Background

The Polycystic Ovarian Syndrome (PCOS) is one of the common female disorders; complications pertaining to PCOS are reproductive, metabolic, or psychological disorders. Prevalence rate of PCOS in different age group of women have been quantitatively measured in the range of 2.2–22.5% globally [1]. Due to high prevalence of PCOS, it is expected that the cost of treatment would be very high. According to one of the literature; the healthcare cost of treatment of PCOS in U.K (United Kingdom) is approximately 237 million GBP (British Pounds) in 2014, which is expected to rise in upcoming years [2]. Average cost per year per patient is in a range of 723–950 GBP for the duration of around 25 years follow up [2]. Highest cost burden is due to management of type-II diabetes in PCOS patients [3].

Oral contraceptives, metformin and ovulation induction drugs have been commonly prescribed as a pharmacological agents for the management of PCOS [4]. Complementary and alternative medicine (CAM) system of treatments have gained substantial recognition by advanced research studies [5]. Herbal medicines and Homeopathic medicines are listed as the top of the CAM therapies [6]. PCOS is believed to be a complex disorder that significantly compromises the quality of life and thereby increasing the healthcare burden [7]. According to another estimate, the economic burden of PCOS is about 8 billion USD annually in 2020 [8]. Healthcare decision-makers should develop policies and prioritize possible interventions for the management of PCOS [9].

Utilization of CAM has substantially increased from 25 to 50% [10]. In Pakistan, approximately half of the population prefers to use CAM for treating different ailments. Homeopathy, Herbal and combination therapies are the most preferred modes of alternative treatments [11]. Specifically, women use CAM commonly for many gynecological problems [12]. However, sound data is not available regarding cost-effectiveness and duration of treatment of CAM. Some published evidences of pharmaco-economics exists for the Allopathic medicines; yet there is a lack of such research studies on Alternative medicines [13] especially for PCOS. By considering all these scenarios, current study was conducted to compare Pharmaco-economics of PCOS with conventional and unconventional treatment options.

## Methods

### Study design and duration

Observational, cross-sectional study was conducted in the metropolitan city Karachi, Pakistan from January 2019 to December 2019.

### Place of study

Outpatient clinics at multiple centers, hospitals, private Homeopathic Clinic and Matabs of Herbal medicine practitioners (Hakeems).

### Sample size

Precision analysis technique was used to calculate the number of participants in the study [14]. Minimum sample size of study was 198 patients. Two hundred ($N=200$) patients with PCOS were recruited and interviewed.

### Primary data collection

A specially designed, validated and structured instrument entitled "Comparative Effectiveness of Treatments for PCOS" (CET-PCOS) was used to collect the data [5]. Inform consent was taken from each patient before collection of data.

### Inclusion criteria

Women that have been diagnosed with PCOS, in the age group of 18–45 years. Participants must meet the Rotterdam diagnostic criteria of PCOS [15], which defines PCOS by the presence of any two or all the three clinical features i.e. oligo/amenorrhea, hyperandrogenism and polycystic ovaries on ultrasound.

### Exclusion Criteria

Females were excluded if not met Rotterdam diagnostic criteria, suspects of PCOS, pregnant and breastfeeding PCOS patients, patients on weight-loss medications.

### Ethical approval

The Institutional Bio-Ethical Committee (IBC) of University of Karachi approved the study design and methods (Reference Number: IBC-KU 50). Study is also approved by Advanced Studies & Research Board, University of Karachi (Reference Number: ASRB/No./04164/Pharm.). Prior to initiating the survey, a written informed consent was obtained from each patient after explaining the research and its objectives. All researchers ensured the maintenance of patient data confidentiality in compliance with the Declaration of Helsinki [16].

### Comparative effectiveness of treatments for PCOS instrument

A 40-items instrument entitled "Comparative Effectiveness of Treatments for PCOS" (CET-PCOS) was developed in which conventional and alternative therapies were compared in terms of patient's satisfaction and the total cost of therapy. A detailed section of questionnaire was based on patient's chosen system of treatment, number and cost of physician's visits, duration of treatment, cost of medicines and outcome measures of these respective treatments.

**Table 1** Cost minimization analysis (CMA)

| Tx Type | Mean Cost/month (PKR) | % Incremental Cost/month |
|---|---|---|
| Allopathic Tx | 4479.32 | 358% |
| Homeopathic Tx | 976.95 | 0% |
| Herbal Tx | 1527.78 | 56% |
| Combination Tx | 2803.09 | 187% |

**Table 2** Cost effectiveness analysis (CEA)

| Tx Type | Mean Duration of Tx (Years) | Mean Cost/month (PKR) | Cost Differences/month (PKR) | ICER*/month |
|---|---|---|---|---|
| Allopathic Tx | 2.63 | 4479.32 | 3502.37 | 1334.24 |
| Homeopathic Tx | 0.72 | 976.95 | 0.00 | 0.00 |
| Herbal Tx | 0.59 | 1527.78 | 550.83 | 936.41 |
| Combination Tx | 1.80 | 2803.09 | 1826.14 | 1017.09 |

**Table 3** Descriptive statistics homeopathic Tx**

| Costs | *N* | PKR* Mean Cost | PKR* Std. Error |
|---|---|---|---|
| Cost of Medicine/Month | 42 | 274.57 | ±37.62 |
| Cost of Medicine/Year | | 4889.14 | ±407.77 |
| Cost of Physician Consultation/Month | | 595.23 | ±39.88 |
| Direct Cost of Total Tx**/Month | | 976.95 | ±46.19 |
| Direct Cost of Total Tx**/Year | | 19803.42 | ±1420.56 |
| In-Direct Cost/Physician Visit | | 300.00 | ±26.39 |

*PKR=Pakistani Rupees, **Tx=Treatment

**Table 4** Descriptive statistics herbal Tx**

| Costs | *N* | PKR* Mean Cost | PKR* Std. Error |
|---|---|---|---|
| Cost of Medicine/Month | 51 | 808.17 | ±62.59 |
| Cost of Medicine/Year | | 9698.11 | ±751.14 |
| Cost of Physician Consultation/Month | | 596.07 | ±41.15 |
| Direct Cost of Total Tx**/Month | | 1527.78 | ±78.15 |
| Direct Cost of Total Tx**/Year | | 18333.41 | ±937.84 |
| In-Direct Cost/Physician Visit | | 307.84 | ±26.69 |

*PKR=Pakistani Rupees, **Tx=Treatment

**Table 5** Descriptive statistics Combination Tx**

| Costs | *N* | PKR* Mean Cost | PKR* Std. Error |
|---|---|---|---|
| Cost of Medicine/Month | 11 | 1866.72 | ±651.59 |
| Cost of Medicine/Year | | 22400.72 | ±7819.13 |
| Cost of Physician Consultation/Month | | 690.90 | ±99.50 |
| Direct Cost of Total Tx**/Month | | 2803.09 | ±654.22 |
| Direct Cost of Total Tx**/Year | | 33637.09 | ±7850.73 |
| In-Direct Cost/Physician Visit | | 409.09 | ±45.63 |

*PKR=Pakistani Rupees, **Tx=Treatment

**Table 6** Descriptive statistics allopathic Tx**

| Costs | *N* | PKR* Mean Cost | PKR* Std. Error |
|---|---|---|---|
| Cost of Medicine/Month | 96 | 1802.96 | ±346.08 |
| Cost of Medicine/Year | | 21635.62 | ±4153.02 |
| Cost of Physician Consultation/Month | | 803.03 | ±33.11 |
| Direct Cost of Total Tx**/Month | | 4479.32 | ±350.95 |
| Direct Cost of Total Tx**/Year | | 53751.87 | ±4211.42 |
| In-Direct Cost/Physician Visit | | 593.33 | ±24.00 |

*PKR=Pakistani Rupees, **Tx=Treatment

### Data analysis

To calculate the ultimate economic outcomes of all therapies in terms of direct and indirect cost and healthcare effects, the cost minimization analysis (CMA) and cost effectiveness analysis (CEA) were performed. CMA is a method of economic evaluation that chooses the least expensive alternative while the CEA is an important tool that compares interventions along with two separate dimensions; costs and effectiveness [17]. Statistical Package for Social Sciences (SPSS version 22) was employed for data processing and statistical analysis of the mean and standard error of direct cost (cost of medicine + physician consultation fee) and the mean and standard error of indirect cost of treatment (travelling fee). Two way sensitivity analyses was done by keeping 5% discount rate to enhance the strength of cost effectiveness analyses.

## Results

Cost minimization analysis (CMA) computed the mean cost and % incremental cost per month (Table-1). Cost effectiveness analysis (CEA) calculated the mean cost and incremental cost effectiveness ratio (ICER) per month and revealed that most economic treatment is Homeopathic, which is then followed by the Herbal, Combination, and Allopathic (Table-2).

Mean direct cost of Homeopathic (Table-3) and Herbal treatments (Table-4) were found less than 20,000 PKR (122.61 USD) [18] annually compared to Combination (Table-5) and Allopathic treatments (Table-6). Mean indirect cost per physician per visit of Homeopathic, Herbal and Combination treatments were found less than 500 PKR (3.07 USD) except Allopathic treatment [18]. Annual expenses on medicines were found highest in Combination and Allopathic treatments i.e. 22400.72 PKR (137.33 USD) [18] and 21635.62 PKR (132.64 USD) [18] respectively.

The most frequently prescribed medications in Allopathic medicine are metformin (56%), metformin + spironolactone (21%), metformin + orlistat (5%), atenolol + metformin (4%) and metformin + letrozole (2%) and letrozole + spironolactone (2%). In Homeopathic medicine the order of frequency were bioplasgen 15 (12%), sepia + thuja (10%), pulsatilla + thuja (10%), sepia (7%), pulsatilla (7%), calcarea carb + pulsatilla (7%), calcarea carb + thuja (7%), pulsatilla + sepia (5%), natrum

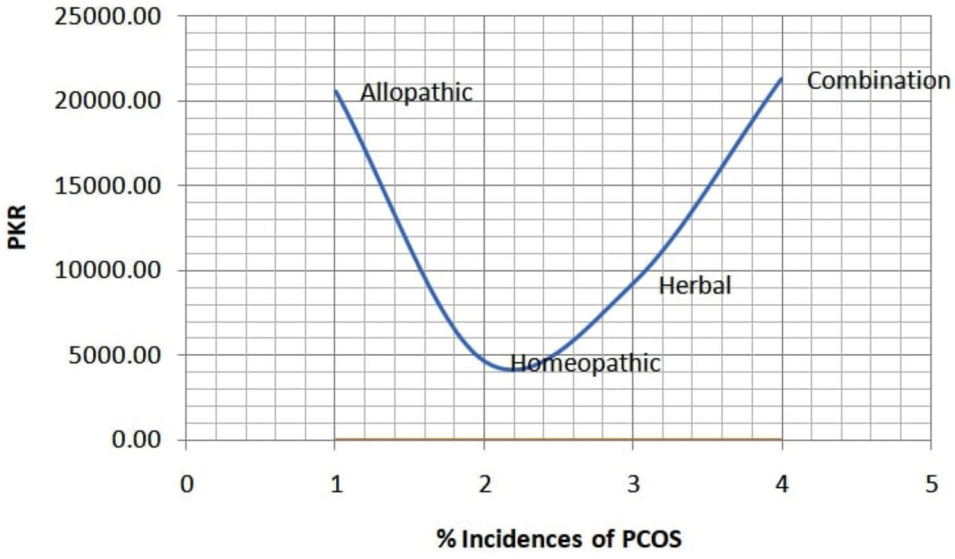


**Fig. 1** 2-Way sensitivity analysis of the parameters

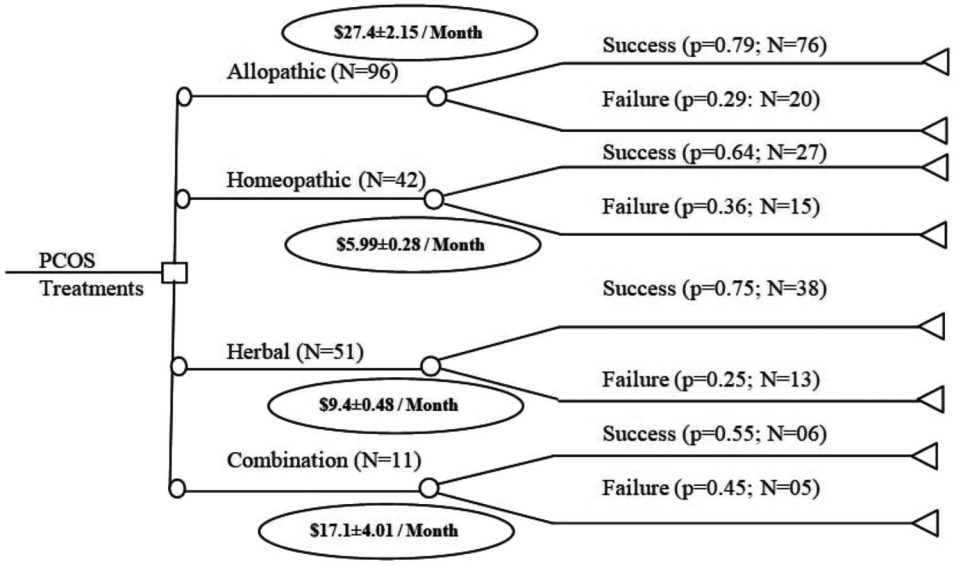


**Fig. 2** Decision tree with per month cost

mur+pulsatilla (5%), graphite+thuja (5%). Similarly in Herbal medicine the order of frequency was masturin (14%), masturin+suparipak (10%), vitex (10%, Khatooni (6%), khatoni+majun muhazzil (6%), majun dabeed-ul-ward+masturin (6%), masturin+majun muhazzil (6%), khatoni_suparipak (4%) and majun muqul+masturin+sharbat folad (4%). Some patients were prescribed combination of medicines from herbal, homeopathic and herbal systems. More than half (55%) patients were prescribed combination medicine of Allopathic+Herbal; while 27% Allopathic+Homeopathic and 18% Herbal+Homeopathic.

Sensitivity analysis (Figure-1) of ICER in cost-effectiveness and decision tree are further validate the findings (Figure-2).

## Discussion

It is a bleak reality that many patients belong to low socioeconomic class or patients living in poverty seek additional complementary medicine for treatments of their diseases [19, 20]. The cost effectiveness of alternative treatment and its reimbursement by health insurance companies are part of ongoing debates. Pakistan is a country, where the poverty rate is very high due to the high inflation rate i.e. 10.58% (5.5% increase from 2018) [21] and lower GDP (Gross Domestic Product) per

capita (1,285 USD) [22]. Decline of Pakistani currency was noted by 13.33% since 2018 [18]. Moreover, PCOS has history of augmentation of economic burden of disease since past years [8]. For evaluation of cost for treatment, there are many tools used in Pharmacoeconomics such as; cost minimization analysis, cost benefit analysis, cost effectiveness analysis, cost utility analysis, and budget impact analysis [17].

Cost-minimization analysis (CMA) is a method of economic evaluation that chooses the least expensive alternative while the cost-effectiveness analysis (CEA) is an important tool that compares interventions along with two separate dimensions; costs and effectiveness [17]. In cost minimization analysis, the expenditure on PCOS treatment calculated in terms of incremental cost per month. The incremental cost per month of Allopathic, Herbal and combination treatment were found 358%, 56% and 187% respectively; higher than Homeopathic treatment. In the cost effectiveness analysis, the Homeopathic ICER (Incremental Cost-Effectiveness Ratio) per month value is considered as a standard or threshold value and compared with the ICER values of other treatments to determine whether these interventions are cost-effective [23]. The substantially higher values of ICER per month of Allopathic, Herbal and combination treatments are PKR: 1334.24 (USD: 8.18), PKR: 936.41 (USD: 5.74) and PKR: 1017.09 (USD: 6.24) respectively [18]; which demonstrates, they are less cost effective than the Homeopathic treatment. Contrary to findings of current study, mixed type of literature is available about economy of Homoeopathic system. Some economic evaluations have shown homeopathy is a more expensive treatment system [24]; yet there are also many studies supporting the evidences that Homeopathy offers a cost-saving alternative treatment [25]. The 2-way sensitivity analysis revealed in current study that Homeopathy is most cost-effective compare to Allopathic and other systems of treatment after adjusting the 5% discount rate. The decision tree was further validated this finding. In a retrospective observational study conducted on patients suffering from chronic respiratory disease, the costs for Homeopathic therapy were found significantly (42.4%) lower than the conventional pharmacological therapy [26]. Another study revealed, the treatment with the Homeopathic was found overall 35% less cost than Allopathic treatment [27]. Herbal treatment with values of 56% incremental cost and ICER PKR: 936.41 (USD: 5.74) per month does not justify cost-effectiveness among compared treatments; however, still it is 1.42 times cheaper than the conventional mode of treatments. Nevertheless; Ahmed et al. performed few extensive pharmacoeconomic studies and compared the Herbal and conventional mode of treatments for common ailments like common cold, depression and trauma; his conclusion is that the herbal treatment is a cost-effective therapy [9, 28]. Regarding frequency of prescription of patients, 27% taken combination of Allopathic and Homeopathic treatments, 55% combination of Allopathic and Herbal treatments, 18% combination of Herbal and Homeopathic treatments. The combination treatment's larger value of incremental cost and ICER were making it more expensive treatment than Homeopathic and Herbal therapies but less costly than Allopathic treatment. (Table-1-2)

The mean direct cost of any therapy has eminent effect on the total treatment cost [29]. Due to this reason current study found that per year mean direct cost of Allopathic treatment is PKR:53751.87±4211.42 (USD:329.52±25.82); which was higher than Homeopathic, Herbal and combination therapies i.e. PKR:19803.42±1420.56 (USD:121.40±8.71), PKR:18333.41±937.84 (USD:112.39±5.75), PKR:33637.09±7850.73 (USD:206.21±48.12) respectively [18]. As a major constituent of direct cost, the cost of medicine takes an oversized proportion of the NHS (National Health Services) budget [30]. It's a general perception that the medicines alone accounts for at least 10% of expenses [9]. The study found that the annual cost burden for combination medications is highest i.e. PKR:22400.72±7819.13 (USD: 137.33±47.93), while such burden is lowest with Homeopathic treatment i.e. PKR: 4889.14±407.77 (USD:29.97±2.50). Mean cost of Allopathic medicines per month i.e. PKR:1802.96±346.08 (USD:11.05±2.12) seems to be greatly influenced by most commonly prescribed drug metformin. Main drugs which cost in Allopathic therapy includes; metformin, combined oral contraceptive pills (COCPs), spironolactone, clomiphene citrate, antiandrogens, aromatase inhibitors and local treatments for hirsutism and acne [31]. Metformin has been used by 56% of Allopathic enrolled patients. Spironolactone is not a cheap medicine but prescribed commonly for hirsutism [32]. Despite such findings that more than half of the Allopathic enrolled patients are on Metformin which is a low-priced and easily affordable medicine; ICER per month/year of Allopathic treatment is noticeably highest than the other treatments. However, in the field of economical evaluation of any treatment there are possibilities that medicine can be costlier but provide more utility to a patient with a certain disease [9]. In Homeopathic; 12% of PCOS patients used Bioplasgen-15, 7% used Pulsatilla pratensis, 7% used Sepia officinalis, 2% used Natrum muriaticum and 2% used Thuja occidentalis alone. 70% patients used the combination of two or more of the Homeopathic medicines. Dewan et al., also mentioned frequent use of above-mentioned Homeopathic medicines [31]. Mean cost of Homeopathic medicines per month is PKR:274.57±37.62 (USD:1.68±0.23), which is fairly lower than the mean cost of Herbal medicines as well as

Allopathic or conventional medicines. Rossi et al. and Colas et al. stated that the Homeopathic prescriptions are two times less costly than the conventional medicines [30].

In Herbal system of medicine; several herbs can be used individually or in combination to relieve risk factors associated with PCOS. Few herbs when given in a combination produced a synergistic effect. The pharmacological action is seen more in combination than as single entity [33]. In this survey; Herbal products or combination of herbs are Femirin syrup, Herbal tea, Khatooni syrup, Majoon Dabeed-ul-Ward, Majun muhazzil, Majun muqil, Marhaba anti acne herbal cream, Masturin, Mensofar, Safi syrup, Sharbat folad, Suparipak. Only three of the Herbal products have single herb ingredient such as Ovuline capsules, Macca root capsules and Vitex capsules. 64% of patients received treatment with combination of herbal products. The potential benefits of Herbal medicines lie in their efficacy and relatively low costs [34]. Mean cost of Herbal medicine per month was found PKR:808.17±62.59 (USD:4.95±0.38); which is lower than Allopathic treatment but higher than Homeopathic treatment. In combination therapy; the cost of medicines were found higher i.e. PKR:1866.72±651.59 (USD:11.44±3.99) than all other therapies including Allopathic but interestingly the ICER per month/year is lower than Allopathic treatment; which is a usual finding of another pharmaco-economic study [9]. Another constituent of mean direct cost is the physician consultation. The mean cost of physician consultation per month were found highest in the Allopathic treatment [PKR:803.03±33.11 (USD:4.92±0.20)] and in the Combination treatment [PKR:690.90±99.50 (USD:4.24±0.61). According to another literature the consultation fee of alternative treatment was found higher than general treatment i.e. EUR:22.68 v/s 27.08 respectively ($p<0.0001$) [27]. Indirect costs are those that are not directly influencing the total therapy cost and are hard to be tracked [29]. The indirect cost in current study comprised of travelling cost. It was found that the mean traveling cost of Allopathic treatment was highest [PKR:593.33±24.00 (USD:3.64±0.15)] compared to all other treatments. (Table-3-6) The duration of treatment also influence the total cost of treatment and can be used as measure of performance indicator. The mean duration of treatment of conventional and unconventional therapies are found at great difference in this study [35]. In the Herbal therapy, the mean duration of treatment is shortest i.e. 0.59 years while longest duration is pertaining to Allopathic treatment i.e. 2.63 years (Table-2).

## Conclusion

Lowest direct and indirect costs and short treatment duration collaboratively lessen the %incremental cost per year and incremental cost effectiveness ratio per year. The most cost-effective treatment is Homeopathic; Herbal treatment is second most cost-effective option for the treatment of PCOS. Regardless of type of disease, any intervention that claims to improve health outcomes often causes a considerable cost to the healthcare system and to the patients [17]. In many countries, such economic evidences are increasingly used to regulate important healthcare decision making [36]. The main limitation of current study is the difference of number of participants in each treatment arm; however, study may provide a base for future studies on the topics of pharmaco-economics.

### Abbreviations

| | |
|---|---|
| PCOS | Polycystic Ovarian Syndrome |
| SPSS | Statistical Package Of Social Sciences |
| CMA | Cost Minimization Analysis |
| PKR | Pak Rupess |
| USD | United Stated Dollar |
| CEA | Cost Effectiveness Analysis |
| GBP | Great Britis Pound |
| CAM | Complementary And Alternative Medicine |
| CET-PCOS | Comparative Effectiveness Of Treatment For Polycystic Ovarian Syndrome |
| IBC | Institutional Bioethics Committee |
| ASRB | Advanced Studies And Research Board |
| Tx | Treatment |
| GDP | Gross Domestic Product |
| ICER | Incremental Cost Effectiveness Ratio |
| NHS | National Health Services |
| COCPs | Combined Oral Contraceptive Pills |
| EUR | Euro |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12962-024-00569-6.

Supplementary Material 1

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Not applicable.

### Author contributions

All authors have read and approved the manuscript. Conceptualization and data curation: DM. Formal analysis and methodology: SAK. Validation and visualization: SMA. Writing – original draft: FM. Writing – review and editing: IA.

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### Data availability

Data are available on reasonable request through corresponding author of manuscript.

## Declarations

### Ethical approval and consent to participate

The Institutional Bio-Ethical Committee (IBC) of University of Karachi approved the study design and methods (Reference Number: IBC-KU 50). Study is also approved by Advanced Studies & Research Board, University of Karachi (Reference Number: ASRB/No./04164/Pharm.). Prior to initiating the survey, a written informed consent was obtained from each patient after explaining the research and its objectives. All researchers ensured the maintenance of patient data confidentiality in compliance with the Declaration of Helsinki [16].

### Consent to publish

Not applicable.

### Competing interests

The authors declare no competing interests.

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