

A targeted literature review of the economic burden associated with polycystic ovary syndrome

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Objectives

- Polycystic ovary syndrome (PCOS) is the most common health problem caused by an imbalance of reproductive hormones. PCOS can cause missed or irregular menstrual periods, which can lead to development of cysts (small fluid-filled sacs) in the ovaries, and infertility.^{1,2} It is complex, with reproductive, metabolic and psychological features
- Prevalence is between 8% and 13%, depending on the population studied and definitions used.³ Around ~75% of women with PCOS are infertile due to anovulation, making PCOS by far the most common cause of anovulatory infertility⁴
- The total cost of evaluating and providing care to reproductive-aged women with PCOS in the US was \$4.36 billion in 2004.⁵ The current estimated annual costs of diagnosing and treating infertility secondary to PCOS in the UK range from £16 million to £22 million⁶
- A targeted literature review was conducted to collate evidence from published studies evaluating the economic burden of PCOS

Methods

- A literature search was conducted on 09 May 2019 in Embase® and MEDLINE® to identify economic evidence published from 2009 to 2019
- The search terms used were a combination of MeSH and free-text terms for 'polycystic ovary' combined with a 'cost and resource use' study design filter based on that of the Scottish Intercollegiate Guidelines Network⁷
- The searches were limited to studies published in the English language in the last 10 years (2009–2019); however, no country restrictions were applied. The retrieved titles and abstracts were manually screened against pre-defined eligibility criteria (Table 1). The same eligibility criteria were applied to the full publications of the included studies, and studies reporting cost and resource use data were finally included and extracted. Conference proceedings of the International Society for Pharmacoeconomics and Outcomes Research were also searched for last 2 years (2017–2019)
- One reviewer assessed study eligibility, and another independent reviewer performed a random cross check of 20% of the screened hits. One reviewer extracted data using a standard data extraction form, with a quality check by a second reviewer

Table 1: Inclusion and exclusion criteria

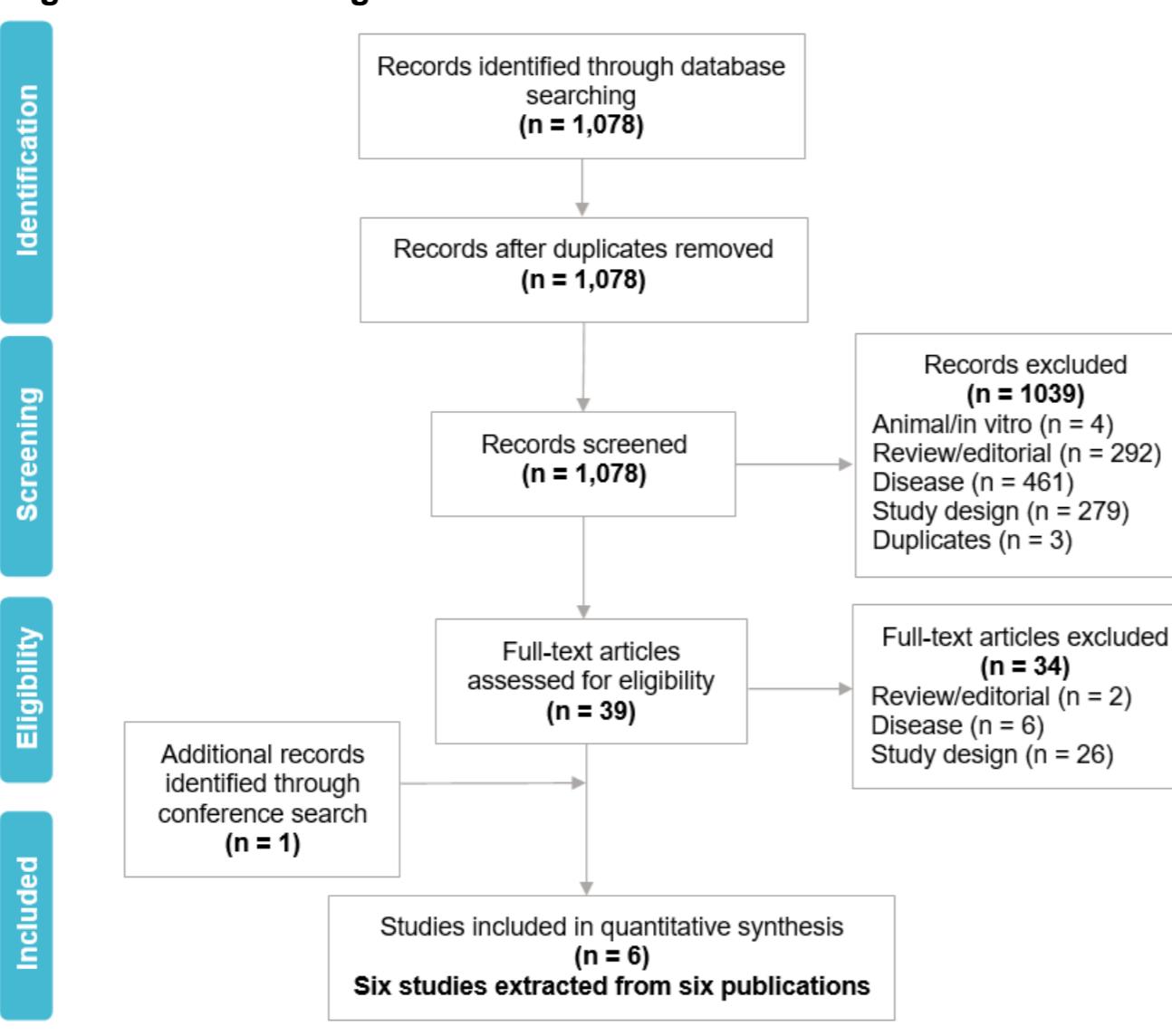
Category	Inclusion criteria	Exclusion criteria
Population	Women with polycystic ovary syndrome	Diseases other than polycystic ovary syndrome
Intervention/comparator	No restrictions	Not applicable
Outcomes	Cost and resource use evidence	Clinical evidence
Study design	Studies reporting costs and resource use: <ul style="list-style-type: none"> • Cost of illness studies • Cost-benefit analyses • Cost-minimization analyses • Budget-impact models • Cost-consequence studies • Cost of illness studies • Economic evaluations reporting costs or resource use 	<ul style="list-style-type: none"> • Reviews, letters and comment articles • Studies reporting clinical data only • Studies reporting only cost-effectiveness arguments and no data pertaining to cost or resource use • Systematic reviews • Health technology assessments
Time	From 2009 onwards	Prior to 2009
Language	English	Non-English
Country	No restrictions	Not applicable
Publication type	No restrictions	Not applicable

Results

Study identification

Electronic database searches identified 1,078 publications; after screening, six unique studies were finally included. Full details of the process are shown in Figure 1.

Figure 1: PRISMA diagram



Overview of the studies

Of the six included studies, three were economic evaluations (one was an economic modelling study⁸, and two were economic evaluations alongside a trial^{9,10}), two were cohort studies (one was a population-based retrospective cohort study¹¹, and another was a cross-sectional analysis of a longitudinal cohort study¹²), and one was a cost of illness study.¹³

Two of the economic evaluation studies were conducted with a healthcare perspective.^{8, 9} Perspective was not reported in the remaining four studies.^{10–13}

Three studies reported cost data only^{8,10,13}, two studies reported resource use data only^{11,12}, and one study reported both cost and resource use data.⁹

Costs

Four studies reported cost data.^{8–10,13}

A cost of illness study conducted from a Hungarian healthcare perspective reported an annual health insurance cost of PCOS of HUF 78.9 million (€281,160) in 2009 (Figure 2) with an annual per capita health insurance expenditure of HUF 7,679 (€27) per patient per year.¹³

A Bayesian modelling study was conducted from a UK healthcare perspective by Ding et al., to assess the economic burden associated with PCOS in the UK.⁸ The study reported the incidence and prevalence of Type 2 diabetes in women with PCOS as 3–33 per 1000 person years and 26.5%, respectively, with the estimated healthcare cost of PCOS being ~£237 million (95% confidence interval [CI]: £237–£238 million) in 2014. This increased to a present value of disease burden of over £7 billion (95% CI: £6.8–7.3 billion) after applying discounting. The mean costs per patient per year were reported to be within the range of £723–£950 million during a 25-year period (£723 million in 2014, increasing to a projected discounted value of £950 billion in 2023).⁸

A study recruiting clomiphene citrate resistant PCOS patients was performed between February 1998 and October 2001 in 25 Dutch hospitals. A follow-up study was conducted 8–12 years later among 168 of these women. The follow-up study assessed the costs of laparoscopic electrocautery of the ovaries and compared it with a strategy starting with ovulation induction using recombinant follicle-stimulating hormone (rFSH). The mean (95% CI) total costs for the first live birth, including delivery, as expressed per woman until the first live birth or during the follow-up period after randomization, were €9,560 (€8212–€10,907) for the electrocautery strategy and €11,708 (€9,845–€13,561) for the rFSH strategy, resulting in a difference of €2,148 (€153–€4,450), which was not statistically significant.⁹ The mean direct cost per women for the first and all live births per woman is shown in Table 2.

Table 2: Mean costs associated with the first and all live births per woman with CC resistant PCOS

Cost category	Electrocautery strategy (n = 83)		rFSH strategy (n = 85)	
	First live birth per woman, €	All live births per woman, €	First live birth per woman, €	All live births per woman, €
Operative procedure	1,151	1,151	676	676
Medication (CC–rFSH–hCG)	1,353	1,729	3,413	3,918
Additional treatment costs (IUI–IVF–ICSI)	856	1,357	1,046	1,480
Additional electrocautery	15	-	45	-
Monitoring	3,244	3,988	3,188	3,944
Pregnancy and delivery	2,941	5,820 (95% CI: 4,841–6,800)	3,339	5,628 (95% CI: 4,496–6,760)
Total treatment costs	6,619	8,226 (95% CI: 6,851–9,601)	8,369	10,017 (95% CI: 7,749–12,285)
Total direct medical costs	9,560 (95% CI: 8,212–10,907)	14,047 (95% CI: 12,318–15,775)	11,708 (95% CI: 9,845–13,561)	15,645 (95% CI: 13,244–18,045)

Key: CC, clomiphene citrate; CI, confidence interval; hCG, human chorionic gonadotropin; ICSI; intracytoplasmic sperm injection; IUI; intrauterine insemination; IVF, in vitro fertilization; PCOS, polycystic ovary syndrome; rFSH, recombinant follicle-stimulating hormone.

Source: Nahuis et al. 2012.⁹

An economic evaluation was conducted alongside a trial in 218 women with clomiphene citrate resistant PCOS. Women were randomly allocated treatment with clomiphene citrate in combination with highly purified, urinary follicle-stimulating hormone (HP uFSH) or HP uFSH alone. A low treatment mean (standard deviation) cost per cycle for clomiphene citrate in combination with HP uFSH was less than that of HP uFSH alone (Egyptian pound [£E] 305.4 [130.4] versus £E688.8 [370.8], respectively).¹⁰ Further, it was reported that an exogenous low dose HP uFSH step-up protocol with co-administration of clomiphene was more cost effective than a low dose step-up HP uFSH protocol in clomiphene-resistant PCOS women (cost-effectiveness ratio: 523 versus 5,236; the difference between the two protocols was 4713).¹⁰

Resource use

Three studies reported resource use data.^{9,11,12}

A study conducted by Nahuis et al. reported the average resource use for all live births in clomiphene citrate resistant PCOS women, shown in Table 3.⁹

Table 3: Average resource use per woman until conception for all live births

Treatment	Electrocautery strategy (n = 83)	rFSH strategy (n = 85)	Price/unit (€)
Clomiphene citrate (50 mg tablet) ^a	25 (28)	7 (15) [*]	0.50
rFSH (75 IU) ^a	51 (91)	116 (105) [*]	33.49
hCG (5,000 IU) ^a	4 (5)	7 (6) [*]	4.64
IUI ^a	0.9 (2.1)	0.6 (1.5)	465
IVF ^a	0.3 (0.9)	0.4 (0.8)	2619
ICSI ^a	0	0	2835
Cryopreserved embryos ^a	0.03 (0.2)	0.08 (0.5)	426
Ultrasound visit ^a	25 (19)	24 (21)	163
Diagnostic laparoscopy	-	1	676

Key: hCG, human chorionic gonadotropin; ICSI, intracytoplasmic sperm injection; IUI, intrauterine insemination; IVF, in vitro fertilization; rFSH, recombinant follicle-stimulating hormone; SD, standard deviation.

Notes: ^a Values are mean (SD); * significant difference (p < 0.05) between treatments.

Source: Nahuis et al. 2012.⁹

The Australian Longitudinal Study on Women's Health, conducted by Joham et al., reported significantly higher use of fertility hormone therapy in women with PCOS than in women without PCOS (63% versus 27%, respectively; p < 0.001). Of the women reporting infertility who sought help or treatment, significantly more women with PCOS reported use of fertility treatment, including ovulation induction or in vitro fertilization (IVF), compared to women without PCOS (65% versus 42%, respectively; p < 0.001). In women with PCOS comorbid with infertility, 86.6% women sought help/treatment. In these women, 62% sought fertility hormones and 23% sought IVF.¹²

A population-based retrospective cohort study conducted by Hart et al. in Western Australia reported higher hospitalization rates for treating gynaecological conditions associated with PCOS than for treating those not associated with PCOS.¹² Women with PCOS had higher rates of hospitalization for non-obstetric indications unrelated to injury than women with no PCOS diagnosis (controls), with medians of five admissions overall among women with PCOS (interquartile range [IQR]: 2–8; range: 0–45) and two admissions in controls (IQR: 0–3; range: 0–22) (p < 0.001).¹¹ The study reported that 77.7% of women with PCOS had one hospital admission, 12.8% had two admissions and 9.5% had at least three.¹¹

Conclusions

PCOS is associated with a high economic burden globally. The major contributing factors are infertility, use of fertility hormone treatment and hospitalization. In women with clomiphene citrate resistant PCOS, laparoscopic electrocautery of the ovaries results in significantly lower costs per live birth than ovulation induction with gonadotrophins for an at least equal effectiveness. Women with PCOS had higher rates of hospitalization for non-obstetric indications unrelated to injury than women without PCOS.

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