Health-related quality of life measurement in women with polycystic ovary syndrome: a systematic review

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The symptoms typically associated with polycystic ovary syndrome (PCOS) such as acne, hirsutism, irregular menses, amenorrhoea, obesity and subfertility are a major source of psychological morbidity and can negatively affect quality of life (QoL). We systematically searched the literature to identify the impact of symptoms and treatments for PCOS on health-related QoL (HRQoL) and to report on the types and psychometric properties of the instruments used. Papers were retrieved by systematically searching four electronic databases and hand searching relevant reference lists and bibliographies. Nineteen papers used a standardized questionnaire to measure health status; of these 12 (63.2%) used generic tools and 8 (42%) used the disease-specific PCOS questionnaire. Although a meta-analysis was not possible, it appears that weight concerns have a particular negative impact upon HRQoL, although the role of body mass index in affecting HRQoL scores is inconclusive from the available evidence. Acne is the area least reported upon in terms of its impact upon HRQoL. With the exception of three studies, most of the research has focused upon adult women with PCOS. Despite the benefits of HRQoL measures in research, few are being used to evaluate the outcomes of treatment for PCOS upon the subjective health status of women with the condition.

Keywords: health-related quality of life; polycystic ovary syndrome

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder, affecting women of reproductive age (Hart et al., 2004), with an estimated prevalence, depending upon the definitions used for diagnosis, of between 4% and 25% (Balen and Michelmore, 2002; Homburg, 2002). It is characterized by irregular menses, anovulation, clinical and/or biochemical signs of hyperandrogenism (including hirsutism, acne and alopecia), ovarian micro-poly-cystic appearance and metabolic abnormalities, such as hyperinsulinaemia and obesity (Fratantonio et al., 2005). As there is currently no cure, the management of PCOS is directed towards improving the patients’ health-related quality of life (HRQoL) by means of symptomatic alleviation and prevention of long-term complications (including development of the metabolic syndrome and associated sequelae, i.e. cardiovascular disease and type II diabetes mellitus).

HRQoL is defined as a multidimensional concept that encompasses physical, emotional and social aspects associated with a specific disease or its treatment (Colwell et al., 1998). HRQoL measurement therefore provides important information on the benefits of medical therapies or interventions from the patient’s perspective (Jones et al., 2002). This is particularly important given that subjective clinical data do not correlate with HRQoL (Coulter, 1994). HRQoL measurement also has an important role in measuring the impact of chronic disease (Guyatt et al., 1993) and in evaluative research as a measure of outcome, particularly in clinical trials where health status tools can assist in clinical decision-making regarding treatment choice and policy decisions.

Prior research has suggested that PCOS and its associated symptom profile have a negative effect on HRQoL. For example, acne and hirsutism have been identified as major causes of social and emotional stress and psychological morbidity (Barth et al., 1993; Sonino et al., 1993; Mallon et al., 1999). Irregular menses and infertility issues have been suggested to cause tensions within the family, altered self-perception, impaired sexual functioning and problems in the workplace (Downey et al., 1989; Paulson et al., 1988).

Jones et al. (2002) performed a systematic review focusing on the HRQoL of women with common benign gynaecological conditions and concluded that limited research had been performed to assess the impact that the symptoms and associated treatments for PCOS have upon the HRQoL of women with the condition. Only one paper was identified; a methodological paper concerned with
establish the effects of PCOS and its associated treatment HRQoL, (ii) to identify the HRQoL instruments used and (iii) to establish the effects of PCOS and its associated treatment regimes on a woman’s health status.

Materials and Methods

The electronic databases searched included Medline (1966 to April 2007), Embase (1980 to April 2007), PsychINFO (1887 to April 2007) and CINAHL (cumulative index to nursing and allied health literature) (1982 to April 2007). The search terms relating to HRQoL included ‘quality of life’, ‘health-related quality of life’, ‘health status measurement’, ‘functional status’ and ‘subjective health status’. These terms were each combined with a further search term relating specifically to PCOS. These consisted of ‘polycystic ovary syndrome’, ‘polycystic ovarian syndrome’ and ‘polycystic ovaries’.

Bibliographies and reference lists of those papers that were considered relevant were also manually searched for additional citations. The following inclusion criteria were used to identify relevant sources: (i) the full text was available in the English language, (ii) the tool/questionnaire used to assess HRQoL measured more than one dimension (i.e. articles that measured one area of well-being, e.g. sexual health, were excluded). HRQoL is a multidimensional term incorporating physical, social and psychological aspects, and hence studies appraising a single dimension are not considered complete QoL measures (Montazeri et al., 1996). Studies were also excluded if an ad hoc questionnaires/instrument had been used only, for example, a visual analogue scale (VAS). The VAS and other ad hoc instruments incorporated are not standardized instruments. This is because reliability and validity of their psychometric properties have not been established, and hence, HRQoL is not measured systematically. Consequently, for this reason, the results obtained and reported through the use of these ad hoc tools have not been included in this review. In view of the multiple outcome measures that were used, the results were considered unsuitable for formal meta-analysis, in keeping with other reviews of HRQoL literature (Fallowfield, 1993; Jones et al., 2002, 2006; Montazeri et al., 1996).

Results

Literature search

A total of 159 publications were identified by the literature search (Table 1). However, 103 (64.8%) of these publications were repetitions, appearing in more than one of the databases, were not available in English or alternatively were not relevant or specific to the study topic.

From the remaining 56 articles that appeared meaningful, a further 37 papers were discarded for the following reasons: (i) the articles referred to PCOS and/or HRQoL (or equivalents of these terms) in the abstract only; (ii) the articles were focusing on clinical aspects of PCOS, mentioning the term QoL (or equivalent) briefly within the text; (iii) the publication was unable to be obtained. In addition, three PCOS literature reviews were also identified: a systematic review of HRQoL for common benign gynaecological diseases (Jones et al., 2002), a literature review of PCOS and HRQoL (Coffey and Manson, 2003) and a review considering the relationship between PCOS and its impact upon mental health (Himelein and Thatcher, 2006). Two qualitative papers were also identified which had focused upon the impact of PCOS and HRQoL (Kitzinger and Willmott, 2002; Snyder, 2006). Whereas one of the main aims of quantitative methods is to explain causal relationships, qualitative research searches for reasons, motives or explanations (Porter, 1996); thus aiming to describe and interpret the meanings and experiences of people as accurately as possible. Consequently, the two qualitative studies used in-depth semi-structured interviews to gain an understanding of the impact of PCOS upon women’s daily lives and well being, rather than using self-report questionnaires which is a methodology commonly used in quantitative research.

Table 1 displays and summarizes the remaining 19 articles that used a standardized questionnaire to measure HRQoL and lists the primary objectives of each study. These include: (i) methodological studies (n = 4). These include articles related to the development and evaluation of psychometric properties of a disease-specific tool for measuring HRQoL in PCOS. (ii) Quantitative studies to elicit the impact of symptoms on HRQoL (n = 3). (iii) Quantitative studies comparing HRQoL of PCOS women (a) with the normative population (n = 4), (b) with other gynaecological populations (n = 3) and (c) of different cultures/ethnicities (n = 2). (iv) Treatment-related studies, involving the measurement of the impact of different interventions upon HRQoL (n = 3).

The majority of the research regarding HRQoL in PCOS has been conducted in the UK (n = 4), USA (n = 5) and Germany (n = 4). Most studies have also employed a cross-sectional design, however, two randomized controlled trials (RCTs) were identified (van Wely et al., 2004; Clayton et al., 2005). With the exception of three cross-sectional comparative studies completed in the USA (Trent et al., 2002, 2003, 2005), which had specifically focused on the HRQoL of adolescents with PCOS, the main focus of the research has been on the HRQoL of adult women with PCOS.

Instruments used

A wide variety of (or components of) instruments were used (Table 3). Generic, multidimensional, standardized HRQoL
# Table 2: Studies that measured the QoL of women with POS using a standardized questionnaire

<table>
<thead>
<tr>
<th>Objective</th>
<th>Reference</th>
<th>Study aim</th>
<th>Study sample</th>
<th>Mean age/age range of participants</th>
<th>Mean BMI kg/m²</th>
<th>Country in which research was conducted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Cronin et al. (1998)a</td>
<td>To develop a disease specific questionnaire (PCOSQ) for measuring HRQoL in women with PCOS</td>
<td>100</td>
<td>18–45 years</td>
<td>Not stated</td>
<td>USA</td>
</tr>
<tr>
<td></td>
<td>Wong et al. (2001)a,b</td>
<td>To examine the relative impact of number and severity of patient problems on HRQoL</td>
<td>100 IBS 100 PCOS</td>
<td>30.5 years; SD: 6.7 years</td>
<td>Not stated</td>
<td>Canada</td>
</tr>
<tr>
<td></td>
<td>Guyatt et al. (2004)c</td>
<td>To examine the psychometric properties of the PCOSQ</td>
<td>393 at baseline</td>
<td>Placebo: 30.1; SD: 6.0 (n = 73)</td>
<td>Placebo: 37.9; SD: 8.3 (n = 73)</td>
<td>Canada</td>
</tr>
<tr>
<td></td>
<td>Jones et al. (2004)a</td>
<td>To evaluate the psychometric properties of the PCOSQ</td>
<td>92</td>
<td>29.4 years; SD: 5.7 years</td>
<td>BMI &gt; 28: 52.2%</td>
<td>UK</td>
</tr>
<tr>
<td></td>
<td>McCook et al. (2005)</td>
<td>To evaluate the influence of obesity, fertility status and androgenism scores on HRQoL in women with PCOS</td>
<td>128</td>
<td>30.4 years; SD: 5.5 years</td>
<td>BMI &lt; 18.5–24.9: 8.6%</td>
<td>USA</td>
</tr>
<tr>
<td></td>
<td>Elsenbruch et al. (2006)b</td>
<td>To analyse the incidence of mental distress in women with untreated PCOS, to characterize PCOS patients at risk for psychiatric disease with regard to socio-demographic and clinical characteristics, and to assess the impact of emotional distress on QoL</td>
<td>143</td>
<td>Global severity index ≥ 63 (n = 22): 31.3; SD: 1.3 years Global severity Index ≤ 63 (n = 121): 28.6; SD: 0.5 years</td>
<td>GSI &gt; 63: 35.0 GSI ≤ 63: 30.1</td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>Lipton et al. (2006)a,b</td>
<td>To report on the psychological and behavioural burden of facial hair in women with suspected PCOS</td>
<td>88</td>
<td>33 years; SD: 7.4 years</td>
<td>Not stated</td>
<td>UK</td>
</tr>
<tr>
<td></td>
<td>Elsenbruch et al. (2003)b</td>
<td>To examine QoL, psychosocial well-being and sexual satisfaction in women with PCOS</td>
<td>50 control 50 PCOS</td>
<td>PCOS: 28.4; SD: 5.0 years Control: 29.9; SD: 5.7 years</td>
<td>PCOS: 30.1 Control: 24.4</td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>Hahn et al. (2005)b</td>
<td>To examine the extent of different PCOS symptoms on QoL, psychosocial well-being and sexual satisfaction</td>
<td>50 control 120 PCOS</td>
<td>PCOS: 29; SD: 5.4 years Control: 30; SD: 5.7 years</td>
<td>PCOS: 31 Controls: 24</td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>Coffey et al. (2006)</td>
<td>To examine whether women with PCOS have poorer HRQoL than women in the general population and than patients with other medical conditions</td>
<td>96 control 22 PCOS</td>
<td>PCOS: 27.5 years Control: 28.8 years</td>
<td>PCOS: 33.3 Control: 23.4</td>
<td>UK</td>
</tr>
<tr>
<td></td>
<td>Ching et al. (2007)</td>
<td>To examine whether women with PCOS have poorer HRQoL than women in the general population and to compare this with the quality of patient information</td>
<td>203 PCOS 173 control</td>
<td>PCOS: range 15–65 years Control: range 18–44 years</td>
<td>PCOS: 33.6 Control: 33.7</td>
<td>Australia</td>
</tr>
</tbody>
</table>

Continued
instruments (which can be used to measure the health status of any medical condition) were most commonly used, with 12 (63.2%) studies incorporating these in their methodology. The most frequently used generic questionnaire was the Short Form-36 (SF-36) (n = 9). It is a reliable and widely validated generic instrument used in the assessment of HRQoL in a variety of medical conditions. Only one PCOS disease-specific instrument is currently available to measure HRQoL, the PCOSQ (Cronin et al., 1998). Only eight (42%) studies incorporated the PCOSQ into their methodologies. Of these, three were methodological studies (development and validation of the PCOSQ), two were cross-sectional studies comparing HRQoL in PCOS between cultures and ethnicities and three were cross-sectional studies focusing on the impact of symptoms of PCOS upon HRQoL.

**Overall impact of PCOS**

All of the studies have concluded that PCOS has a negative impact upon HRQoL. When compared with healthy controls (i.e. without gynaecological disorders) or normative data, it appears that women with PCOS have a worse HRQoL than their peers, with all four studies showing a worse HRQoL for the women with PCOS compared with these control groups. Ching et al. (2007) found that SF-36 scores were significantly lower in women with PCOS compared with healthy controls.

### Table 2: Continued

<table>
<thead>
<tr>
<th>Objective</th>
<th>Reference</th>
<th>Study aim</th>
<th>Study sample</th>
<th>Mean age/age range of participants</th>
<th>Mean BMI kg/m²</th>
<th>Country in which research was conducted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative: comparisons with gynaecological population</td>
<td>Trent et al. (2002)ᵇ</td>
<td>To examine HRQoL in adolescents with PCOS compared with healthy adolescents, and to determine whether clinically observed or self-perceived severity of illness affects their HRQoL</td>
<td>186 control 97 PCOS</td>
<td>PCOS: 16.9 years Control: 17.0 years</td>
<td>PCOS: 31.7 Control: 23.5</td>
<td>USA</td>
</tr>
<tr>
<td></td>
<td>Trent et al. (2003)ᵃᵇ</td>
<td>To examine the fertility concerns and sexual behaviour of adolescent girls with PCOS as compared with healthy counterparts and the effect of these concerns on HRQoL.</td>
<td>186 control 97 PCOS</td>
<td>PCOS: 16.9 years Control: 17.0 years</td>
<td>PCOS: 31.7 Control: 23.5</td>
<td>USA</td>
</tr>
<tr>
<td></td>
<td>Trent et al. (2005)ᵇ</td>
<td>To evaluate the effect of BMI on QoL disturbances in adolescent girls with PCOS</td>
<td>186 control 97 PCOS</td>
<td>PCOS: 16.9 years Control: 17 years</td>
<td>PCOS: 31.7 Controls: 23.5</td>
<td>USA</td>
</tr>
<tr>
<td>Quantitative: comparisons between cultures/ ethnicity’s</td>
<td>Hashimoto et al. (2003)ᵃ</td>
<td>To assess differences in symptomatology and symptom perception in women with PCOS according to cultural background and weight status</td>
<td>31 Austrian PCOS 102 Brazilian PCOS</td>
<td>Austrian: 23.8 years; SD: 4.7 years Brazilian: 25.5 years; SD: 3.9 yrs</td>
<td>Austrian: 23.73 Brazilian: 27.49</td>
<td>Brazil</td>
</tr>
<tr>
<td></td>
<td>Schmid et al. (2004)</td>
<td>To examine the symptomatology of PCOS and the HRQoL among infertility patients suffering from PCOS with different socio-cultural and ethnic background</td>
<td>14 Muslim PCOS 35 Austrian PCOS</td>
<td>28.27 years; SD: 5.35 years</td>
<td>Muslim: 26.9 Austrian: 26.5</td>
<td>Austria</td>
</tr>
<tr>
<td>Quantitative: the impact of treatment on HRQoL</td>
<td>van Wely et al. (2004)</td>
<td>RCT evaluating the impact of laparoscopic electrocautery of the ovaries versus recombinant FSH in clomiphene citrate-resistant PCOS on QoL.</td>
<td>168 Electrocautery: 28.5 years rFSH: 28.7 years</td>
<td>EC: 27.9 rFSH: 27.3</td>
<td>Netherlands</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clayton et al. (2005)ᵃᵇ</td>
<td>RCT to evaluate the impact of laser treatment on facial hirsutism and psychological morbidity</td>
<td>88 Intervention: 33.5; SD: 8.0 years</td>
<td>Not stated</td>
<td>UK</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hahn et al. (2006)ᵃᵇ</td>
<td>A prospective, observational study to analyse the effects of metformin treatment on HRQoL, emotional well-being and sexuality in PCOS</td>
<td>64 BMI &lt; 25: 26.5%</td>
<td>BMI 25–29.9: 25% BMI 30+: 48.5%</td>
<td>Germany</td>
<td></td>
</tr>
</tbody>
</table>

SD, standard deviation; IBS, irritable bowel syndrome.

ᵃIncorporates an element of qualitative methodology.

ᵇIncorporates an ad hoc questionnaire.

ᶜMean BMIs based on original randomized double-blind placebo controlled study data as reported in Azziz et al. (2001).
lower for their Australian PCOS sample of women \((n = 203)\) compared with 173 age and sex matched Australian SF-36 normative data \((P < 0.01)\). Similarly, Hahn et al. (2005) and Else
bruch et al. (2003) compared 50 age-matched healthy controls (recruited from a health screening program for University employees) with 120 and 50 women with PCOS, respectively. They both found a reduced HRQoL compared in the women with PCOS compared to the controls; significantly in the areas of physical role function, bodily pain, vitality, social function, emotional role function and mental health as measured on the SF-36.

Coffey et al. (2006) carried out the only study in the UK to compare the HRQoL of PCOS women with normative UK data. However, the main aim of this was to compare the SF-36 scores of people with asthma, epilepsy, diabetes, back pain, arthritis and coronary heart disease, collected as part of the Oxford Health and Lifestyle Survey with the PCOS women’s scores \((n = 22)\). Although the PCOS sample was small, the physical sum score for the PCOS group was comparable with those of the asthma, epilepsy, diabetes and back pain groups, and was higher (indicating better HRQoL) than those of the arthritis and coronary heart disease groups. However, the psychological sum

<table>
<thead>
<tr>
<th>Study</th>
<th>Instrument</th>
<th>Feature</th>
<th>Items</th>
<th>Dimensions</th>
<th>Areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong et al. (2001)</td>
<td>SF-36</td>
<td>Generic</td>
<td>36</td>
<td>9</td>
<td>Physical functioning, emotional role limitations, physical role limitations, energy/vitality, health perceptions, change in health, mental health, social functioning and bodily pain</td>
</tr>
<tr>
<td>Hahn et al. (2006)</td>
<td>WHOQOL-BREF</td>
<td>Generic</td>
<td>26</td>
<td>6</td>
<td>QoL, general health, physical health, psychological health, social relationships, environment</td>
</tr>
<tr>
<td>Clayton et al. (2005)</td>
<td>Rosenberg self-esteem</td>
<td>Generic</td>
<td>10</td>
<td></td>
<td>Global and unidimensional self-esteem</td>
</tr>
<tr>
<td>Trent et al. (2002)</td>
<td>CHQ-CF87</td>
<td>Generic</td>
<td>87</td>
<td>12</td>
<td>Change in health in the last year, role/social emotional, role/social behavioural, bodily pain, behaviour, mental health, self-esteem, general health perceptions, family activities, family cohesion, physical functioning, role/social physical</td>
</tr>
<tr>
<td>Wong et al. (2001)</td>
<td>Sickness impact profile (SIP)</td>
<td>Generic</td>
<td>136</td>
<td>12</td>
<td>Sleep and rest, eating, work, home management, recreation and pastimes, ambulation, mobility, body care and movement, social interaction, alertness behaviour, emotional behaviour, communication</td>
</tr>
<tr>
<td>Clayton et al. (2005)</td>
<td>General health questionnaire (GHQ)</td>
<td>Generic</td>
<td></td>
<td></td>
<td>Vision, hearing, speech, ambulation, dexterity, emotion, cognition, pain</td>
</tr>
<tr>
<td>Wong et al. (2001)</td>
<td>Health utilities index (HUI)</td>
<td>Generic</td>
<td>41</td>
<td>8</td>
<td>Health, work and profession, finances, leisure activities, marriage and relationships, relationship to children, self, sexuality, friends and relatives, living conditions</td>
</tr>
<tr>
<td>Elsebruch et al. (2003)</td>
<td>Fragebogen zur Lebenszufriedenheit (FLZ)</td>
<td>Generic</td>
<td>70</td>
<td>10</td>
<td>Depression, anxiety, severity</td>
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<tr>
<td>Clayton et al. (2005)</td>
<td>HADS</td>
<td>Condition specific</td>
<td>14</td>
<td>3</td>
<td>Depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, sleep disturbance</td>
</tr>
<tr>
<td>Lipton et al. (2006)</td>
<td>The CES-D</td>
<td>Condition specific</td>
<td>20</td>
<td>6</td>
<td>Somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, aggression, phobia, paranoid ideation, psychoticism</td>
</tr>
<tr>
<td>van Wely et al. (2004)</td>
<td>Symptom checklist 90 (SCL-90-R)</td>
<td>Condition specific</td>
<td>90</td>
<td>9</td>
<td>Psychological distress, physical symptoms, activity level, overall QoL</td>
</tr>
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<td>Elsebruch et al. (2003)</td>
<td>RSCIL</td>
<td>Cancer specific</td>
<td>38</td>
<td>4</td>
<td>Emotions, body hair, weight, menstrual problems, infertility</td>
</tr>
<tr>
<td>Hahn et al. (2005)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
<td>5</td>
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<td>Elsebruch et al. (2006)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
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<td>Ching et al. (2007)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
<td>5</td>
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<tr>
<td>Clayton et al. (1998)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
<td>5</td>
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<td>Hashimoto et al. (2003)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
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<tr>
<td>Guyatt et al. (2004)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
<td>5</td>
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</tr>
<tr>
<td>Jones et al. (2004)</td>
<td>PCOSQ</td>
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<td>26</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Ching et al. (2007)</td>
<td>PCOSQ</td>
<td>Disease specific</td>
<td>26</td>
<td>5</td>
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</tbody>
</table>
score indicated poorer psychological-related HRQoL in women with PCOS (20% lower), than woman with any of the other conditions analysed.

Comparisons with controls (other gynaecological population)

Studies, which have compared the HRQoL of women with PCOS with other gynaecological populations, have reported worse HRQoL scores for those women with PCOS. For example, Coffey et al. (2006) also compared their sample of PCOS women with a control group of 96 women attending the family planning clinic. They found significantly worse HRQoL scores on all domains of the PCOSQ and with the exception of physical and social functioning on all other six domains of the SF-36. Similarly, Trent et al. (2002) carried out a cross-sectional study to examine HRQoL in 97 American adolescents with PCOS, compared with 186 healthy adolescents (presenting for routine or sports physicals, or treatment of minor medical problems in primary care adolescents presenting for routine gynaecologic care and contraceptive advice were also recruited). The results of the CHQ-CF87 indicated that HRQoL in the domains of general health perception, behaviour, physical function and family activities were significantly lower in PCOS patients than the healthy adolescents (P < 0.05). However, significantly higher scores in the domain of ‘change in health’ in the last year were found for adolescents with PCOS compared with their healthy counterparts. Later analyses focusing specifically on fertility concerns and sexual behaviour (Trent et al., 2003) and weight issues (Trent et al., 2005) also found significant differences between these groups and are discussed later.

Impact of symptoms on HRQoL

Overall, the symptoms typically associated with PCOS; amenorrhoea, oligomenorrhoea, hirsutism, obesity, subfertility, anovulation and acne have all been shown to lead to a significant reduction in QoL. However, it is weight gain which appears to exert greatest negative influence upon HRQoL in PCOS. Five cross-sectional studies that used the PCOSQ all found the weight domain to be the area most negatively affected. On a scale where 1 represents poorest functioning and 7 optimal functioning, mean PCOSQ weight scores were 2.1 (Coffey et al., 2006); 2.85 (Guyatt et al., 2004); 2.33 (McCook et al., 2005); 2.86 (Ching et al., 2007) and 2.94 (Jones et al., 2004). For example, McCook et al. (2005) completed a cross-sectional, correlational study observing the influence of obesity, fertility status and androgenism scores on HRQoL in 128 adult women with PCOS in the USA (mean age: 30.4 ± 5.5 years). Body Mass Index (BMI), Waist-Hip Ratio (WHR) Ferriman-Gallwey (F/G) scores, fertility status and biochemical evaluation of hyperandrogenism were obtained from each participant. Although the demographically homogeneous nature of the participants may not be representative of the PCOS population (the study sample mainly consisted of Caucasian (96.9%) and married (78.1%) women, recruited from a private reproductive medicine practice) it was found that for the five domains of the PCOSQ, the most significant was weight, followed by menstrual problems, infertility, emotions and body hair.

However, one cross-sectional study which compared the HRQoL between an Austrian (n = 31) and Brazilian (n = 102) sample of women found the weight domain to be the worst area of HRQoL affected by PCOS but only for the Austrian women (Hashimoto et al., 2003). A second study which used the PCOSQ to also compare the HRQoL of 35 Austrian women with 14 Muslim women (the Muslim participants were reported to originate predominantly from Turkey, and the near East; however, further detailed classification of birthplace/nationality was not provided) also found the weight domain to be poor for the Austrian women but this was ranked second, with infertility causing the most concern for these women (Schmid et al., 2004).

The role of BMI

With weight issues appearing to be a primary source for poor QoL, scores, are worse weight domain scores as measured on the PCOSQ evident in those women with a higher BMI? The results suggest that the role that BMI plays in the QoL of women with PCOS appears to be complex. Some studies have shown that reductions in HRQoL are associated with an elevated BMI. McCook et al. (2005) found that BMI was significantly and negatively correlated with the weight domain of the PCOSQ (P = 0.001), and a simple linear regression established that the weight scale scores were predicted by BMI. Thus, the higher the BMI, the lower the score for the weight domain on the PCOSQ. Similarly Hahn et al. (2005) found a significant correlation (P < 0.05) between elevated BMI (>25 to <30 kg/m²) and worse SF-36 physical summary scores compared with PCOS women with a normal BMI (<25 kg/m²) who reported higher physical sum scale scores, thus indicating better QoL. Elsenbruch et al. (2006) also determined that BMI was a predictor of physical sum scores on the SF-36. Trent et al. (2005) also concluded that elevated BMI contributed significantly to the differences in QoL observed between PCOS adolescents and age-matched controls, particularly on the domains of general health perceptions, physical functioning and family activities as measured on the child-health questionnaire (CHQ-CF87).

In this study, 54% of participants with PCOS were overweight, and 22% at risk of being overweight, compared with 14% and 17% in the control group, respectively. The mean BMI for adolescent girls with PCOS was 8.2 points (significantly) higher than that of their healthy counterparts (31.7 kg/m² and 23.5 kg/m², respectively). When BMI was added as a continuous variable to the multivariate linear regression models, the regression coefficients associated with PCOS status were reduced on average by 3 points and became non-significant, thus indicating that the differences in QoL were largely explained by the higher BMI in the PCOS group (although this being a cross-sectional study, causality cannot be assumed for observed relationships).

However, the results from other studies do not suggest a relationship between BMI status and HRQoL in PCOS women. For example, even when significant differences in BMI exist between two ethnicities (the Austrian women were significantly leaner than the Brazilian women), HRQoL weight scores (as measured on the PCOSQ) have been found to be similar (Hashimoto et al., 2003). However, despite the similar weight scores, the weight domain was still the worst area of HRQoL affected by PCOS Austrian women. Similarly, other
studies, which have controlled for BMI in their analysis of PCOSQ weight scores, have found that PCOS women who have a ‘normal weight’ still report problems with their weight (Coffey et al., 2006).

The complex relationship between BMI measurement and self-reported QoL weight scores is also evident in relation to other domains of HRQoL. For example, McCook et al. (2005) found that although BMI was a predictor of weight domain scores, no such relationship existed between BMI and the other domain scores on the PCOSQ. However, Hashimoto et al. (2003) reported a significant association between weight status and body hair scores on the PCOSQ in Brazilian participants. Finally, controlling for an elevated BMI has been found to have no impact upon psychosocial well-being and sexual satisfaction; thus leading the authors to conclude that obesity is not the only determinant of a poor HRQoL (Elsenbruch et al., 2003).

Infertility and sexual concerns

As mentioned earlier infertility has been reported as the worse domain of HRQoL in some studies. McCook et al. (2005) found that reproductive history and more specifically the delivery of a viable infant were shown to predict scores on the infertility domain of the PCOSQ (P = 0.001). Women with PCOS who had been pregnant, but had experienced spontaneous abortion(s) (no viable infants), reported the lowest scores on the infertility domain, exceeding those of women who had been unsuccessful in establishing pregnancy. Both of these groups exhibited poorer functioning in this domain than the groups of fertile women who had given birth to at least one viable infant (P = 0.001).

Elsenbruch et al. (2003) found that in their comparison of 50 PCOS women with 50 age-matched healthy controls the PCOS sample had a significantly higher unfulfilled wish to conceive than the control sample (P < 0.001). However, this may be because 30% of the PCOS participants in the study were referred from their Gynaecologist due to ‘infertility’ problems, thus introducing the possibility of selection bias. This finding was supported in a study by Hahn et al. (2005) who found that the number of control patients with one or more children was significantly higher than in the PCOS group, and the number of PCOS patients wishing to conceive was significantly higher than that of the control group.

One of the most comprehensive analyses of fertility and sexual concerns was carried out by Trent et al. (2003). The authors used the same cohorts of PCOS and control participants to investigate the fertility concerns and sexual behaviour of adolescent girls with PCOS as an earlier study mentioned above. The study found that control subjects (mean age = 17.0 years) were 2.8 times more likely to have had sexual intercourse than PCOS subjects (mean age = 16.9 years). The mean ages of initiation of sexual activity for girls who had engaged in sexual intercourse were not significantly different.

Adolescents with PCOS were also 3.4 times more likely than their healthy counterparts to be concerned about their ability to conceive in the future. Among the PCOS patients, clinical and perceived severity of illness and worry about ability to have children in the future was not associated with the odds of having engaged in sexual intercourse. Concern about ability to have children in the future was found to be associated with lower QoL as indicated by the results of the CHQ-CF87. Participants with PCOS who were worried about their ability to have children in the future scored significantly lower on 10 of the 12 subscales of the CHQ-CF87, including all domains with the exception of physical functioning and change in health in the last year.

Hirsutism

The negative impact of hirsutism upon both PCOS and non-PCOS women’s daily lives and well-being has been well-reported and qualitative studies in particular have highlighted the negative impact of excessive hair growth on self-image and esteem (Kitzinger and Wilmott, 2002; Snyder, 2006).

A recent quantitative cross-sectional study, UK study, assessed the psychological and behavioural burden of unwanted facial hair in 88 women (mean age = 33.0 years) with suspected PCOS (Lipton et al., 2006). This study was conducted in conjunction with the treatment-related study completed by Clayton et al. (2005). The hospital anxiety and depression scale (HADS), Rosenberg self-esteem scales and WHQoL-BREF were applied to participants at baseline (prior to commencement of laser therapy) to measure psychological well-being and HRQoL. It should be noted that the women recruited for this study were only suspected of having PCOS, with no evidence from biochemical, metabolic or clinical tests to confirm this diagnosis, and ethnic minorities were under-represented in this study (20%) because the Alexandrite laser treatment is not suitable for dark skin types. The results of the HADS questionnaire revealed that ~30.2% of women demonstrated clinical levels of depression and 74.4% clinical levels of anxiety. About 29.1% of women demonstrated clinical levels of morbidity for both these, and 24.4% for neither. Levels of anxiety and depression were observed as being strongly correlated. However, moderate to high levels of self-esteem were established within the patient group according to the results of the Rosenberg self-esteem scale, although women reporting low self-esteem achieved higher scores (indicating increased morbidity) on the scales of depression and anxiety as measured on the HADS.

HRQoL as assessed by the WHQoL-BREF indicated moderate to good scores overall, with more than half the sample achieving above the midpoint for each domain. All domains of HRQoL correlated significantly and negatively (P < 0.001) with depression and anxiety scores, suggesting that those with high levels of depression and anxiety report a poorer HRQoL. In addition, all domains of the WHQoL-BREF were found to correlate significantly (P < 0.001) with scores on the Rosenberg self-esteem scale, especially with regard to the psychological health domain. Self-reported duration of time affected by facial hair was found to be correlated with anxiety and depression scores (P < 0.01), and ‘being overwhelmed’ with efforts to control facial hair was associated with low self-esteem (P < 0.01).

Similar to the studies which have assessed the role of BMI with weight PCOSQ scores, studies which have measured the relationship between clinical measures of hair growth, i.e. F/G scores and HRQoL have found inconsistent results. For example, although McCook et al. (2005) found body hair to be the least affected domain on the PCOSQ, F/G scores were negatively correlated with body hair scores on the PCOSQ (P = 0.001), i.e. a higher F/G score was associated with a poorer HRQoL as expected.
In addition, F/G scores were found to be negatively correlated with the scores in the emotion domain \( (P = 0.001) \). Similarly, Hahn _et al._ (2005) found F/G scores to be significantly correlated with bodily pain, general health perceptions and the sum physical component SF-36 domains \( (P < 0.05) \).

However, Guyatt _et al._ (2004) found that the hair domain of the PCOSQ did not detect the positive impact of treatment despite hirsutism scores (this was a combination of four objective measures of facial hair growth but included F/G scores) improving after treatment with Troglitazone therapy. However, as the authors point out there was only a modest improvement in the hirsutism score and this may have not been enough to alter patient’s perception of their body hair. Similarly, in a sample of PCOS adolescents who had a clinical severity score of moderate to severe based upon a F score of 8, a global acne (GA) rating of >0 and a BMI \( > 30 \) kg/m\(^2\), this group only rated their HRQoL as mild (Trent _et al._, 2002).

**The impact of treatment on HRQoL**

Despite the array of treatments available to symptomatic women with PCOS, it was surprising to find that only three studies were concerned with the impact of treatment on the HRQoL. All three compared different therapies which included metformin (Hahn _et al._, 2006), infertility treatment (van Wely _et al._, 2004) and hirsutism (Clayton _et al._, 2005). In 2004, van Wely carried out a multicentre, RCT in the Netherlands in which 168 women with PCOS were randomized to receive either laparoscopic electrocautery of the ovaries \( (n = 83) \) or recombinant Follicle stimulating hormone (rFSH) \( (n = 85) \). HRQoL was assessed by means of the SF-36, the Rotterdam Symptom Checklist (RSCL) and the Centre for Epidemiological Studies Depression Scale (CES-D) and were administered to patients prior to randomization and 2, 12 and 24 weeks thereafter.

The results of the SF-36 indicated that baseline values were comparable with values from the reference population, thus reflecting the relatively healthy status of the participants. Intention to treat (ITT) analysis comparing the electrocautery and rFSH strategies revealed no statistically significant treatment effects on any of the SF-36 domains. Two weeks after diagnostic laparoscopy, women on both treatment arms reported significantly more limitations in physical functioning, social functioning, role physical, vitality and bodily pain; however, these limitations had disappeared at weeks 12 and 24. The occurrence of an ongoing pregnancy resulted in significantly more role limitations due to physical problems, however, fewer role limitations due to emotional problems and improved mental health. When the analysis was limited to females without ongoing pregnancy, analyses revealed no significant differences in either treatment or time effect.

A second RCT was carried out by Clayton _et al._ (2005) in the UK to evaluate the impact of laser treatment on the severity of facial hirsutism and on psychological morbidity in women with PCOS. Eighty-eight subjects were recruited and randomized to receive either five high-fluence treatments (intervention group \( n = 51) \) or five low-fluence treatments (control group \( n = 37) \) performed over a 6-month period. HRQoL was measured using the WHOQoL-BREF, and self-esteem (measured with the Rosenberg self-esteem scale).

Although the study participants were generally white, well educated, of high social class and employed, and thus may not be representative of the overall PCOS population, laser treatment had a positive impact upon HRQoL. Significantly greater change scores were found in the intervention group compared with the control group over the 6-month study period for self-reported severity of hirsutism, self-reported time spent on hair removal and mean HADs depression and anxiety score. The WHOQoL mean scores in the psychological domain increased from 49.6 at baseline to 61.2 at 6 months for the intervention group and 50.1 to 51.5 for the control group. This difference between the groups was statistically significant on ANCOVA testing \( (P < 0.05) \). There were no significant differences between the groups with regard to the change in self-esteem scores, or the QoL scores for the environmental, social and physical domains.

Finally, Hahn _et al._ (2006) completed a prospective observational study in Germany with 64 women with PCOS (mean age = 29.31 years) to analyse the effects of metformin treatment on HRQoL, emotional well-being and sexuality. All participants received monotherapy with metformin, with dosages titrated in accordance with weight status. At baseline, and again at 1 month and 6 months after commencement of treatment, clinical, metabolic and endocrine parameters were assessed, and women were asked to complete the SF-36 and SCL-90-R questionnaires, to evaluate HRQoL and psychological distress, respectively.

Prior to commencement of treatment, PCOS patients demonstrated significant reductions in QoL compared with the normative population, particularly with regard to psychological domains of the SF-36 (reflected in significantly lower psychological sum scores on the SF-36). Lower scores were also recognized in some physical aspects of HRQoL, although the physical sum score was not significantly lower for PCOS women compared with healthy counterparts. In response to treatment, significant time effects, indicative of improvements, were found in the domains of role physical, general health perceptions, energy and vitality, social functioning and psychological sum scores. Overall, treatment effects were observed to be clearly larger for psychological aspects of QoL than physical. Despite a number of significant improvements after 6 months, QoL remained significantly reduced in PCOS patients compared with the German normative population.

**Discussion**

The studies identified in this review have shown that PCOS is a major cause of psychological morbidity and a vast contributor to an overall diminished HRQoL. This has been supported by the qualitative research which has been carried out in this area (Kitzinger and Willmott, 2002; Snyder, 2006). One of the most encouraging findings of this review is that despite the relatively small number of studies that have been conducted specifically to measure HRQoL in PCOS \( (n = 19) \), this number has risen dramatically since the first systematic review (Jones _et al._, 2002) revealed only one published paper in this area (Cronin _et al._, 1998).

The majority of studies in which the PCOSQ was applied observed that the most adversely affected domain was weight. The infertility domain of the PCOSQ was also identified as being one of the areas of poorest functioning for women with
PCOS. In contrast, the domains of body hair, and emotions were frequently identified as the areas least affected by PCOS. The symptom that was least reported upon was acne. However, given that this is not included as a domain on the PCOSQ or the generic instruments, it is perhaps not surprising. Hahn et al. (2005) did compare mean scores of PCOS patients with and without acne and revealed no significant differences between these groups on any of the SF-36 scales. Similarly, Hahn et al. (2006) found significant improvements in acne scores in 12 of the 22 affected women ($P < 0.05$) following treatment with metformin. However, more studies are needed to specially look at the relationship between acne and HRQoL in PCOS patients.

The finding that weight issues have the most negative impact upon HRQoL is perhaps not surprising. It is well known that overweight people find it very difficult to lose weight and with the exception of surgery, interventions to lose weight are often unsuccessful and associated with high rates of weight regain (Hoeger, 2006). There is debate as to whether overweight women with PCOS have a different metabolic rate or control of satiety as compared with overweight women with normal ovaries (Norman et al., 2004). Also there is no clear evidence of benefit for different approaches to diet and weight loss for women with PCOS compared with normal women. Nonetheless, it is perhaps not surprising that many PCOS women typically report frustration with inability to lose weight, low self-esteem and consequently a poor body image (Cronin et al., 1998).

When achieved though, a reduction in weight appears to significantly improve HRQoL (Kolotkin et al., 2001). In specific relation to PCOS, treatment with metformin in a sample of PCOS women lead to an improvement in SF-36 HRQoL scores and these were significantly correlated with a reduction in weight (Hahn et al., 2006). Therefore, efforts to identify appropriate long-term weight loss programmes/treatments would also be beneficial to women; particularly those women with PCOS. However, the best ways of achieving this are unclear; particularly when obesity in women has been found to impair access to healthcare (Drury and Louis, 2002) and long-term weight loss interventions are seldom successful.

In relation to weight, a poor body image in PCOS women may be compounded by cultural influences as it has been shown that android fat pattern, commonly associated with PCOS, is considered unattractive in many cultures (Brown, 1991; Deurenberg et al., 2002). However, other explanations particularly as found in Western cultures regarding women, e.g. societal expectations of thinness, may also be responsible. This is particularly evident in relation to adolescent PCOS girls. Dramusic et al. (1997) found that 87.5% of 50 adolescents with PCOS in Singapore reported being ‘unhappy about their body weight’. High ‘drive for thinness’ and ‘body dissatisfaction’ scores were also observed in PCOS adolescents compared with their normative counterparts. Although two studies which have investigated the relationship between a clinical eating disorder (i.e. bulimia nervosa) and polycystic ovaries in a UK sample have reached different conclusions, the psychological consequences of weight concerns for young PCOS women are evident and suggest that more psychological support is needed in this area (Michelmore et al., 2001; Morgan et al., 2002).

There is conflict in the present literature as to the extent to which BMI affects HRQoL in PCOS. These results are not specific to studies in gynaecology. Indeed, research investigating the role of weight on HRQoL in other conditions, e.g. bariatric surgery, has found that an elevated BMI is not associated with a worse HRQoL (Sendi et al., 2005). In the aforementioned survey, one explanation may have been because only patients with class II and class III obesity were studied (i.e. $> 35$ kg/m$^2$) and therefore it may be that once above the threshold of severe obesity, the impact of BMI is reduced.

As some PCOS studies found no relationship between BMI and HRQoL, as also suggested by Coffey et al. (2006), these findings indicate that all women with PCOS, regardless of their BMI measurement, have weight concerns and therefore relying on this clinical measurement alone as an indicator of poor QoL would overlook the difficulties experienced by PCOS women who have a normal weight as defined by BMI. One potential explanation for this may be that PCOS women with a normal BMI struggle to maintain their weight at this level although further research is needed to explore this issue further.

There may be a number of other possible explanations for the inconsistencies found regarding the role of BMI. First, with the exception of a few studies and research on PCOS adolescents where it has been appropriate to use the cited percentiles based on Centers for Disease Control and Prevention population data to determine overweight and obesity (Trent et al., 2005) most have used BMI cut offs to define obesity which do not correspond to the WHO guidelines. For example, Jones et al. (2004) also used a BMI > 28 in their research. Elsenbruch et al. (2003, 2006) and Hahn et al. (2005) reported a BMI $\geq 25$ kg/m$^2$ to be associated with clinical obesity.

Although use of these non-standardized criteria has been justified, e.g. the aim has been to catch the high end of overweight individuals including those who are obese, this heterogeneity in BMI definition may affect the comparative value of the results and conclusions reported, and thus comparisons should be viewed with caution. Recent publications related to PCOS have also stressed the need to look beyond BMI and also measure waist circumference which is more directly proportional to total body fat and the amount of metabolically active visceral fat and therefore a more accurate measure of metabolic risk (Haslam et al., 2006). In future studies of obesity in gynaecology, the relationship between this parameter and HRQoL outcomes may give a more accurate picture of the role of weight upon a woman’s health status and help unravel some of the conflicting results that currently exist regarding BMI in this area.

Secondly, the lack of correlation between other clinical scores and HRQoL has been found for other areas of PCOS, e.g. F/G score. There is now considerable evidence that the assessments patients themselves make about their health status differ from the reports that healthcare professionals make about them (Fitzpatrick et al., 1994), both in a non-gynaecological sample (Present, 1991; Woodend et al., 1997; Slevin et al., 1988) and a gynaecology sample of women (Coulter et al., 1994). In this review, it was found that Trent et al. (2002) found no significant differences with regard to HRQoL between PCOS adolescents who had been allocated to mild, moderate and severe categories (participants were allocated based on clinical severity; the most severe being a F/G score $> 8$, a GA score rating of $> 0$ and a BMI $> 30$ kg/m$^2$). Instead, self-perceived severity of illness was found to correlate more directly with HRQoL, than clinical
assessments in PCOS, thus further supporting the importance of measuring HRQoL from the patient’s perspective.

**Methodological issues**

Only seven studies used the disease specific questionnaire, the PCOSQ to measure HRQoL in PCOS; indeed the PCOSQ has yet to be applied to an adolescent population of PCOS patients. The remaining studies used one or more generic instruments to perform assessments of HRQoL. Generic instruments are designed to gauge HRQoL over a broad spectrum of diseases, and thus may not be sensitive enough to measure HRQoL in specific illnesses (Jenkinson, 1997). For example, the domains of weight and infertility, observed as being significantly affected on the PCOSQ would not be identified using only a generic questionnaire (i.e. the SF-36), as there are no items pertaining to these dimensions. Questionnaires in which the items are patient generated, hence designed specifically for patients with a particular disease, should theoretically be more sensitive to changes in health status, subject to establishment of validity, reliability and responsiveness.

It has been suggested that, ideally, both a generic and disease-specific instrument should be applied in measuring HRQoL, thus enabling comparisons to be made at a generic level and specifically to the disease of interest (Patrick and Bergner, 1990; Jones et al., 2002). Although 10 studies used more than one tool to measure HRQoL, only three incorporated both a generic and a disease-specific instrument into their methodologies, as per this recommendation (Jones et al., 2004; Coffey et al., 2006; Ching et al., 2007). Because only one disease-specific questionnaire is currently available to measure the HRQoL of women with PCOS, HRQOL instruments that have been validated for specific complaints in PCOS but which are not specific for PCOS such as obesity, hirsutism, acne and infertility QoL questionnaires could also be used. There are numerous validated questionnaires available particularly for the conditions of obesity, acne and infertility. A detailed appraisal of these instruments is outside the scope of this review but to aid potential researchers designing future studies in these areas we refer to other sources of useful information (Bowling, 2001; Kolotkin et al., 2001; Dreno, 2006; www.qolid.org).

A number of study limitations have been identified and discussed within the text. The most frequently encountered limitation was small sample size (Hashimoto et al., 2003; Schmid et al., 2004; Coffey et al., 2006). This was especially evident in the study by Schmid et al. (2004), in which only 14 Muslim and 35 Austrian PCOS participants were recruited, hence introducing uncertainty regarding the strength and reliability of the conclusions derived.

**Conclusions**

The results of this systematic review indicate that overall PCOS has a significant negative impact on a woman’s HRQoL. Considering the array of treatments available to offer symptomatic relief to women with PCOS, more studies observing the affect of treatment on HRQoL would be beneficial in order to provide guidance in clinical decision-making to prescribing physicians. In addition, further studies are required to explore the impact of PCOS upon HRQoL in different cultures and ethnicities. Again, understanding these effects may aid in clinical decision-making regarding the management and treatment of individual patients. More qualitative studies to explore the subjective meanings, opinions and experiences of patients with PCOS are required. To date, only two qualitative studies focusing on HRQoL in adult women with PCOS have been published. Complimentary studies and qualitative studies exploring HRQoL in adolescents with PCOS provide beneficial contributions to the existing literature.

In addition to qualitative studies, more quantitative studies are required to explore the HRQoL of adolescents with PCOS as this has been identified as an area in which limited research currently exists. The PCOSQ, the disease-specific HRQoL, instrument for PCOS, has yet to be applied to an adolescent population and would provide a more specific insight into the domains of HRQoL affected in this patient group. In addition, this would provide a basis for comparative studies to elicit the differences in HRQoL between adults and adolescents with PCOS. A greater comprehension of HRQoL in PCOS adolescents may aid in clinical decision-making regarding the management, treatment and supportive interventions implemented. Early and effective management of PCOS may result in the improvement of HRQoL in adolescence and the transition to adulthood.

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