The Prevalence of Clinical Characteristics of Polycystic Ovary Syndrome among Indigenous Women: A Systematic Search and Review of the Literature

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Abstract

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among reproductive-aged women; however, to date there has been no synthesis of the burden of PCOS specifically among indigenous women. We aimed to systematically identify and collate studies reporting prevalence and clinical features of PCOS among indigenous women worldwide. We performed a comprehensive search of six databases (Ovid MEDLINE, MEDLINE In Process & Other Non-Indexed Citations, EMBASE, EBM reviews, CINAHL, and SCOPUS) supplemented by gray literature searches and the screening of reference lists. A narrative synthesis was conducted. Fourteen studies met inclusion criteria; however, one was excluded as it assessed only children and adolescents younger than 15 years, with limited clinical relevance. Studies examined indigenous women from Australia, Sri Lanka, New Zealand, and the United States. Prevalence of PCOS was reported in only four studies and ranged from 3.05% for women in Sri Lanka to 26% for women in Australia. All included studies reported on at least one clinical feature of PCOS. Of the studies that reported on a comparison group from the same country, there was evidence of more severe features in indigenous women from New Zealand and the United States. The limited evidence available warrants further investigation of the burden of PCOS in indigenous women to build the knowledge base for effective and culturally relevant management of this condition.

Keywords
- polycystic ovary syndrome
- indigenous
- Aboriginal
- first nation
- prevalence

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Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among reproductive-aged women[1] and is underpinned by insulin resistance (IR) and hyperandrogenism.[2] It is a complex condition and its diverse clinical features contribute to adverse reproductive (hirsutism, irregular menstrual cycles, oligo/anovulation, subfertility, and pregnancy complications), psychological (anxiety, depression, and poor body image), and metabolic (metabolic syndrome [MetS], type 2 diabetes mellitus [T2DM] consequences, and an increased risk factors for cardiovascular disease) outcomes.[3] The phenotype typically varies across the lifespan,[4] between ethnicities,[5] and by body mass index (BMI).[6] The etiology of PCOS remains unclear, though genetics, lifestyle, and environmental factors are implicated.[7]

The prevalence of PCOS varies according to the diagnostic criteria used,[8] but is commonly reported as between 4 and 8% of reproductive-aged women.[9] Prevalence is higher among overweight and obese women and in populations with an excess risk of IR and MetS. For example, PCOS affects up to 13% of Mexican American women with the highest age-specific prevalence of IR/MetS compared with non-Hispanic Caucasians and African Americans.[10] Indian, Pakistani, and Bangladeshi women also have higher rates of IR,[11] developing more risk factors for MetS compared with Caucasians,[12] with 9 to 22% of Indian women reporting PCOS.[13,14] Many genetic variants have been associated with PCOS[15]; however, ethnic-specific variants are yet to be identified,[16] suggesting that the disparity between ethnic groups may be due to environmental and/or social factors.

Worldwide, there are approximately 476 million indigenous peoples, representing approximately 5,000 different cultures, in more than 90 countries.[17] Overall, indigenous people experience poorer health and social outcomes than nonindigenous people.[18] This reflects a complex range of factors including social disadvantage arising from a shared history of colonization and dispossession of land and economic power and poorer access to culturally relevant health care.[19,20] A high prevalence of IR, obesity, and MetS has been noted in some indigenous populations, including in Australia[21] and Canada,[22] with T2DM reaching epidemic proportions in some communities. Although there is evidence of a disproportionate burden of PCOS, obesity, and metabolic disease in some indigenous populations, this has not been systematically examined. Increasing our understanding of PCOS among indigenous women would support effective and culturally appropriate detection and management. The aim of this systematic review is to summarize the evidence for the prevalence and clinical features of PCOS among indigenous women worldwide.

Methods

Protocol and Registration

This review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[23] The methodology was established a priori and registered with the international prospective register of systematic reviews, PROSPERO (CRD42018100109).

Definitions

The authors of this review acknowledge the diversity of indigenous peoples both between and within countries. Therefore, rather than employing a definition of indigenous status, the modern and inclusive understanding of the term "indigenous" developed by the United Nations (UN) was followed. Accordingly, indigenous refers to individuals who (1) self-identify and are recognized and accepted by their community as indigenous; (2) demonstrate historical continuity with pre-colonial and/or pre-settler societies; (3) have strong links to territories and surrounding natural resource; (4) have distinct social, economic, or political systems; (5) maintain distinct languages, cultures, and beliefs; (6) form nondominant groups of society; and (7) resolve to maintain and reproduce their ancestral environments and systems as distinctive peoples and communities. We recognized other terms used to self-identify, including, but not limited to, tribes, first peoples/nations, Aboriginal, and ethnic groups. As outlined by the UN system, these fall within this modern understanding of the term indigenous. However, studies were also included if the authors described them as such without any definition. See ►**Supplementary 1** for a list of included indigenous groups.

Capitalization

In accordance with the AMA manual of style (11th ed.), racial and ethnic terms that are derived from geographic nouns such as Maori and Alaskan Native have been capitalized. The term "indigenous" is capitalized when referring to a specific group, that is, Indigenous Australians, but not when referring generically to the original inhabitants of a specific continent (because here it is not derived from a proper noun).

Literature Search

The electronic databases MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, EBM reviews, CINAHL, and SCOPUS were searched to identify relevant published articles (from the database inception to July 2020). Search terms were developed according to the Participant, Interventions/Exposure, Comparisons, Outcomes (PICO) criteria and modified based on an earlier preliminary search (by E. G.), as outlined in ►**Table 1**. Search terms included "PCOS," "polycystic ovary syndrome," "indigenous people," "Aboriginal," and "first nation." The complete search strategy for each database is provided in ►**Supplementary 2**. Gray literature searching was also undertaken using (1) gray literature databases, (2) targeted Web sites, and (3) Google and Google Scholar custom searches, for any related non–peer review literature, research reports, or articles. Reference lists of included studies were also screened to identify any potentially relevant studies. Additional ongoing reviews were identified from searching PROSPERO (*http://www.crd.york.ac.uk/PROSPERO/*).

Eligibility Criteria and Study Collection

Articles were included if they met the following criteria: (1) the study investigated prevalence of PCOS or reported on at

least one diagnostic feature of PCOS, as per the Rotterdam criteria (hyperandrogenism [clinical or biochemical], polycystic ovary [PCO] on ultrasound, or oligo/-anovulation)[24] and (2) the study included an indigenous population. All age ranges were included. All study designs were included except for review articles unless they reported original data. No language, publication date, or publication status restrictions were imposed.

Study Selection and Data Extraction

Following removal of duplicates, identified records from the literature search were title and abstract screened for suitability. Two independent reviewers (E.G. and J.A. or E.G. and R.B.) then retrieved all screened articles that met the inclusion criteria for detailed full-text assessment to confirm eligibility. The full-texts of studies identified as potentially relevant were reviewed by two independent investigators (E. G. and J.A. or E.G. and R.B.). Any discrepancies between investigators were resolved through discussion, and if consensus could not be reached, a third reviewer (J.B.) made the final decision.

Two independent reviewers (E.G. and J.A. or E.G. and R.B.) extracted data using a standardized data collection form. Where possible, data extracted from the eligible studies included authorship, publication year, country, study design, sampling method, recruitment period, population, sample size, age, BMI, and PCOS diagnostic criteria used. The primary outcome measure was prevalence of PCOS, defined by clinical, laboratory, or self-reported measures. Secondary outcome measures included clinical markers of hyperandrogenism (hirsutism and acne), biochemical markers of hyperandrogenism (androgen levels), PCO on ultrasound, and oligo-/anovulation (menstrual irregularity and/or oligo-/anovulation). Data extraction was conducted independently by at least two reviewers (E.G. and J.A. or E.G. and R.B.), with discrepancies resolved through discussion.

Quality Assessment

For nonrandomized studies, the Newcastle-Ottawa Scale (NOS) protocol was followed.[25]

The NOS assesses three main sources of bias: selection of study groups, the comparability of groups, and the ascertainment of either the exposure or outcome of interest for case–control or cross-sectional and cohort studies, respectively. For each criterion, a score of 0 or 1 was assigned according to whether it was satisfactorily fulfilled. There was a maximum score of 10 for cross-sectional studies and 9 for case–control and cohort studies. Studies were classified as having a high risk of bias if they had a total score of 1 to 3, a medium risk of bias if they had a score of 4 to 6, and a low risk of bias if they had a score of $\geq$7. The risk of bias for the single randomized controlled trial (RCT) was assessed using the Cochrane Collaboration tool.[26] This tool includes the domains of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias, which are assigned as either "low risk of bias," "unclear risk of bias," or "high risk of bias." The study was considered as low, high, or unclear in each domain. The risk of bias assessment criteria for the tools used in this review are outlined in ►**Supplementary 3**.

Data Synthesis

Due to heterogeneity of populations, interventions, and outcomes, it was not appropriate to combine outcomes in a meta-analysis. As such, results of included studies were narratively synthesized and presented in tabular format organized by country, and by indigenous population. Direct comparisons between indigenous populations in different countries are highly problematic due to differing definitions of indigenous people between countries, variation in data collection, and methodological approaches and the lack of standardization of measures.[18] As such, we focused on summarizing data for specific indigenous populations and the difference in prevalence between indigenous and nonindigenous populations within the same country (where available).

Results

Literature Search

A search of electronic databases yielded 561 records, with an additional three identified through other sources. After removing duplicates, 458 remained for screening. Following title and abstract review, 428 records were excluded leaving 30 for detailed, full-text evaluation. Of these, fourteen articles met the inclusion criteria. However, one Canadian study assessed children and adolescents younger than 15 years. International guidelines acknowledge the difficulty of diagnosing regular menstrual cycles less than 2 years postmenarche and polycystic ovary morphology in younger than 20 years.[3] As such, the diagnostic reliability of the study was limited and it was therefore excluded. The PRISMA flow diagram of systematic search and included studies is illustrated in ►**Fig. 1**.

Characteristics of Selected Studies

The study characteristics and PICO framework of the 13 included studies (all English, published between 1981 and 2018) are summarized in ►**Table 1**. Eight studies (61.5%) had a cross-sectional design,[27–34] while the rest employed a case–control,[35,36] cohort study,[37] RCT,[38] or mixed methods design.[39]

Five studies were conducted in Australia,[28–30,37,39] five in the United States,[27,31,32,35,38] two in Sri Lanka,[33,36] and one in New Zealand.[34] Studies involving populations of indigenous women in Australia identified women as either Indigenous Australian,[28–30] Aboriginal,[37] or as Aboriginal and Torres Strait Islander.[39] Studies conducted in the United States identified indigenous women as Native American,[27] American Indian, Alaskan Native,[38] or Pima Indian.[31,32,35] Studies in Sri Lanka identified women as Indigenous South Asian women[33,36] and the study in New Zealand identified women as either Maori or Pacific Islander.[34] None of the studies involving indigenous women in Australia or Sri Lanka included a comparison group of nonindigenous women. Some of the studies involving indigenous women in the

Table 1 Study characteristics of included studies (presented alphabetically by author)

First author (year)	Study design	Country (indigenous population)	Study population selection	Comparison	Sample size (*n*)			Age (y) (mean ± SD)	BMI (kg/m^2) (mean ± SD)	Total quality scores[a] (maximum score)
Afifi (2017)[27]	Cross-sectional	USA (Native American)	Women attending multidisciplinary PCOS clinic	PCOS vs. non-PCOS groups w/ ethnic subgroups: Native American women vs. African American, South Asian, East/Southeast Asian, Caucasian, Ashkenazi Jewish, Middle Eastern, Hispanic, mixed/other	Ethnicity	PCOS	non-PCOS	PCOS: 28.1 ± 6.02 non-PCOS: 32.8 ± 9.63	PCOS: 30.3 ± 8.18 non-PCOS: 28.9 ± 8.37	9 (10)
					Native American	0	4			
					African American	1	16			
					South Asian	2	8			
					East/Southeast Asian	2	37			
					Caucasian	34	123			
					Ashkenazi Jewish	0	17			
					Middle Eastern	1	10			
					Hispanic	2	30			
					mixed/other	4	27			
Boyle (2012)[29]	Cross-sectional	Australia (Aboriginal and/or Torres Strait Islander women [urban])	DRUID study	–	248			Median (IQR): 31 (22.0–38.0)	Median (IQR): 27 (22.5 -32.6)	10 (10)
Boyle (2015)[28]	Cross-sectional	Australia (Aboriginal and/or Torres Strait Islander women)	DRUID study	Aboriginal and/or Torres Strait Islander women with or without PCOS	w/ PCOS: 35 w/out PCOS: 74			w/ PCOS: Median (IQR): 32.0 (21.0–37.0) non-PCOS: Median (IQR): 33 (23.0–39.0)	w/ PCOS: median (IQR): 33.4 (27.7–39.7) non-PCOS: median (IQR): 23.8 (20.8–28.1)	10 (10)
Boyle (2017)[39]	Mixed method (medical record audit, semi-structured interviews and focus group discussion)	Australia (Majority Torres Strait Islander women [75%])	Women attending a pilot PCOS clinic on Thursday Island	–	36			Range: 15–44 Mean: 30	25–29.9: 11.11%[b] 30–34.9: 25%[b] ≥35: 61.11%[b]	9 (10)
Davis (2002)[30]	Cross-sectional	Australia (Aboriginal and/or Torres Strait Islander women)	Women in communities of Kimberley region of Western Australia, and the southwestern region of VIC, at the time of researcher visit	–	38			>18 y	33.28 ± 8.4	6 (10)
Ellis (2018)[37]	Cohort study: retrospective clinical audit	Australia (Aboriginal and/or Torres Strait Islander women)	Women who had attended the Aboriginal primary healthcare center in the last 2 y and had PCOS listed as a clinical diagnosis on the electronic patient information management system	–	63			24.1 ± 5.3	37.6 ± 8.5	7 (9)
Legro (2006)[38]	RCT	USA (American Indian or Alaskan Native women)	Academic medical centers	American Indian or Alaskan Native women vs. Caucasian, African American, Asian women	American Indian or Alaskan Native women: 72 Caucasian: 435 African American: 109 Asian: 17			American Indian or Alaskan Native women: 27.6 ± 4.1 Caucasian: 28.2 ± 3.9 African American: 27.9 ± 4.3 Asian: 30.4 ± 3.0	American Indian or Alaskan Native women: 34.3 ± 8.8 Caucasian: 35.4 ± 8.8 African American: 36.0 ± 8.4 Asian: 34.3 ± 8.0	Low risk[c]

(*Continued*)

Table 1 (*Continued*)

First author (year)	Study design	Country (indigenous population)	Study population selection	Comparison	Sample size (*n*)	Age (y) (mean ± SD)	BMI (kg/m^2) (mean ± SD)	Total quality scores[a] (maximum score)
Purifoy (1981)[31]	Cross-sectional	USA (Pima Indian women)	N/A	Pima Indian women vs. Caucasian women	Pima Indian: 20 Caucasian: 31	Pima Indian, range: 19–44 Caucasian, range: 20–46	Pima Indian, mean: 38.9 Caucasian, mean: 21.7	6 (10)
Roumain (1998)[32]	Cross-sectional	USA (Pima Indian women[4])	Ongoing epidemiological study of diabetes among residents of the Gila River Indian Community of Arizona	Pima women with or without history of menstrual irregularity	695	18–24 y: 24.6%[b]	w/ menstrual irregularity: 33.5 ± 7.7 w/out irregularity: 37.6 ± 9.1	9 (10)
						25–34 y: 42.6%[b]	w/ menstrual irregularity: 35.7 ± 7.2 w/out irregularity: 39.3 ± 10.2	
						35–44: 32.8%[b]	w/ menstrual irregularity: 36.4 ± 7.6 w/out irregularity: 38.9 ± 7.9	
Weiss (1994)[35]	Case–control	USA (Pima Indian women)	National Institutes of Health, Phoenix, AZ; longitudinal study of risk factors for the development of non–insulin-dependent diabetes	Pima Indian women with or without hyperinsulinemia	w/ hyperinsulinemia: 20 non-hyperinsulinemia: 20	w/ hyperinsulinemia, median (IRQ): 24.7 (22.5–29.3) Non-hyperinsulinemia, median (IRQ): 27.2 (23.2–32.0)	w/ hyperinsulinemia, median (IRQ): 28.6 (24.2–37.2) Non-hyperinsulinemia, median (IRQ): 38.1 (34.2–43.0)	8 (9)
Wijeyaratne (2006)[36]	Case–control	Sri Lanka (Indigenous South Asian women)	Consecutive women managed at the University Maternity Unit of De Soya Hospital for women, Colombo	Indigenous South Asian women with or without previous history of GDM	w/ GDM: 274 no GDM: 168	w/ GDM: 33.4 ± 0.6 no GDM: 32.3 ± 0.8	w/ GDM: 24.3 ± 3.4 no GDM: 21.65 ± 3.8	8 (9)
				Sub-analyses: Indigenous South Asian women with previous history GDM with or without PCOS	w/ GDM, w/ PCOS: 86 no GDM, w/out PCOS: 61	w/ GDM, w/ PCOS: N/A no GDM, w/out PCOS: N/A	w/ GDM, w/ PCOS: 25.4 ± 3.3 no GDM, w/out PCOS: 23.2 ± 4.2	
Wijeyaratne (2011)[33]	Cross-sectional	Sri Lanka (Indigenous South Asian women)	Consecutive women enrolled at the Endocrine Clinic of the University of Obstetrics and Gynecology Unit, Colombo, Sri Lanka	Indigenous South Asian women with or without PCOS	w/ PCOS: 469 w/out PCOS: 231	w/ PCOS, median (IQR): 25 (14–34) w/out PCOS, median (IQR): 29 y (20–38)	w/ PCOS, median (IQR): 25.0 (18.33–31.67) w/out PCOS: N/A	9 (10)
Williamson (2001)[34]	Cross-sectional	New Zealand (Maori, Pacific Islander)	Women presenting to gynecological endocrine clinic at the National Women's Hospital with symptoms of PCOS	Maori and Pacific Islander versus European, Indian, Chinese, "Other" Asian, Other	Maori: 16 Pacific Islander: 15 European: 101 Indian: 23 Chinese: 0 "Other" Asian: 4 Other: 6	Range: 16–42	Maori: 32.3 ± 4.3 Pacific Islander: 34.0 ± 6.0 European: 27.5 ± 6.6 Indian: 28.7 ± 7.4 Other[d]: 24.3 ± 4.6	10 (10)

Abbreviations: BMI, body mass index; DRUID, Darwin Region Urban Indigenous Diabetes study; GDM, gestational diabetes mellitus; IQR, interquartile range; PCOS, polycystic ovary syndrome; RCT, randomized controlled trial; SD, standard deviation; USA, United States of America; VIC, Victoria.

Note: Values are mean ± SD, *n*, or as otherwise indicated.

[a]Using adapted Newcastle-Ottawa Scale for cross-sectional studies, Newcastle-Ottawa Scale for case–control and cohort studies, and modified Cochrane Collaboration tool for randomized controlled trials.

[b]Proportion of women.

[c]Judgment classified as unclear, low and high risk for overall bias.[1] Classified as Pima Indian by at least one-half Pima or Tohono O'odham heritage, or a mixture of these two closely related Native American Tribes.

[d]As the numbers of Chinese, "Other" Asian, and other women were low, ethnic groups were combined as other women for statistical analysis.

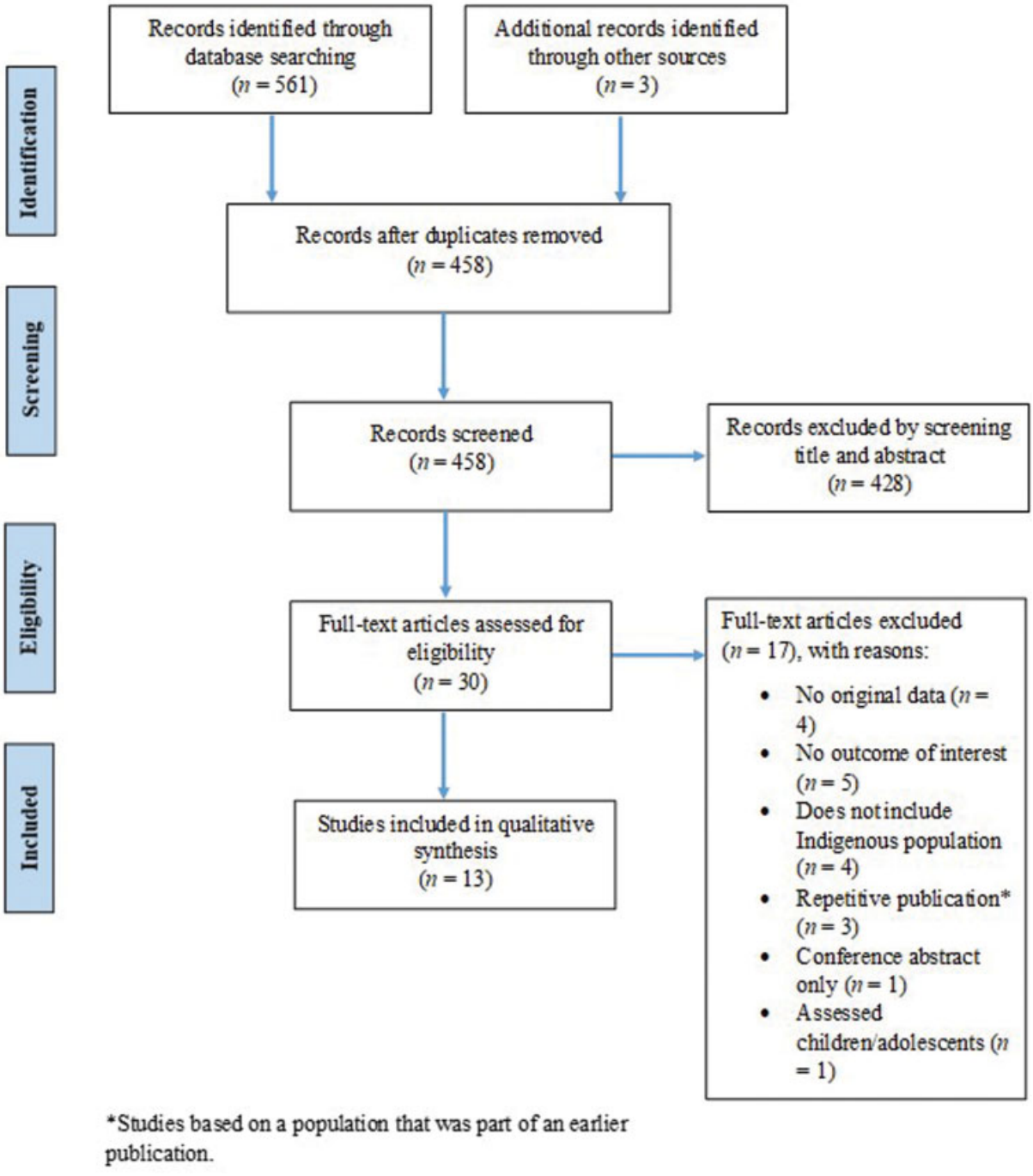

Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

United States included comparison groups of nonindigenous women identified as either a group of Caucasian women[31] or separated into subgroups of Caucasian, African American, or Asian women[38] or into subgroups of Middle Eastern, Ashkenazi Jew, other Caucasian, East/Southeast Asian, South Asian, Hispanic, African American, Native American, and mixed/other.[27] The study in New Zealand included comparison groups of nonindigenous women identified as European, Indian (including Fijian Indian), Chinese, other Asian or others.[34]

Sample selection methods varied widely. Four studies used retrospective clinical audits of patient records,[27,34,36,38] three studies collected clinical data,[32,35,39] and three used data from community studies.[28,29,33] One study recruited via convenience sampling,[37] while another utilized geographically defined purposive sampling.[31] Recruitment was not reported for one study.[30] Sample sizes of indigenous populations ranged from 20 participants[31] in a single community to 700 participants across a capital city.[33] Participants' age varied across reproductive years (i.e., 15–49 years).

Methodological Quality

The risk of bias assessment indicated that 10 studies had a low risk of bias,[27–29,32–39] two studies had a medium risk of

bias,[30,31] and none of the studies were classified as high risk. Cross-sectional studies ranged in scores from 6 to 10 out of a maximum score of 10 (lowest risk) on the NOS (adapted for cross-sectional studies). The cross-sectional studies rated as medium risk of bias were because of concerns about the representativeness of the sample (due to use of clinic populations and volunteers), missing descriptions of response rates, missing descriptions of measurement tools, and the inadequate control of confounding factors.[30,31] Both case–control studies scored an 8 out of a maximum of 9 (lowest risk) on the NOS because of concerns about selection bias brought about by controls being recruited exclusively from hospitals and clinics.[35,36] The cohort study was assigned a score of 8 out of a maximum score of 9 (lowest risk of bias) on the NOS (adapted for cohort studies) due to the exposed cohort being a selected group of users.[37] The randomized control study was judged to be at low risk of bias for all domains, and the overall risk of bias was classified as low. Bias assessments for all studies are presented in ►**Supplementary 4**.

Prevalence of PCOS among Indigenous Populations

Four moderate- to high-quality studies assessed the prevalence of PCOS. These included indigenous populations from Australia,[29,30] New Zealand,[34] and Sri Lanka.[36] Only the study involving indigenous women in New Zealand assessed prevalence against comparison groups of nonindigenous women. ►**Table 2** shows the prevalence of PCOS among indigenous populations.

Australia

Two identified studies investigated PCOS prevalence among Indigenous Australians. In a small ($n = 38$) sample of indigenous women from Western Australia and Victoria, Davis et al[30] reported prevalence according to the National Institute of Health (NIH) criteria at 18%, but possibly as high as 26% (accounting for missing androgen concentration data). A larger sample ($n = 248$) of Indigenous women from the Northern Territory included in Boyle et al[29] reported a prevalence according to the NIH criteria of 15.3%; higher BMI was significantly associated with increased prevalence (BMI $\geq$ 30.0 kg/m^2: 30.5% vs. BMI = 25–29.9 kg/m^2: 8.2% vs. BMI < 25.0 kg/m^2: 7.0%). Neither Davis et al[30] nor Boyle et al[29] reported comparable prevalence data for non-Indigenous Australian women.

New Zealand

The occurrence of PCOS among indigenous women of New Zealand; Maori, and Pacific Islander women was included in a larger cross-sectional study on the impact of ethnicity on PCOS. Williamson et al[34] compared ethnic composition of women ($n = 162$) presenting to a gynecological endocrine clinic with PCOS symptoms to the ethnic composition of the general population in a hospital catchment area. PCOS was confirmed by ultrasound or laparoscopy. Women were identified as Maori, Pacific Islander, European, Indian (including Fijian Indian), Chinese, other Asian, or others. Although the prevalence was not ascertained, the authors reported that the proportion of Maori and Pacific women in the PCOS cohort was broadly representative to the population of the hospital catchment area (Maori: 9.9 vs. 13.5%; Pacific Islander: 9.3 vs. 9.8%). Similarly, the proportion of European women presenting with PCOS was representative (69.2 vs. 57.7%), whereas Indian women were considerably overrepresented in the sample (11.7 vs. 2.1%) and Chinese and Other Asian women were underrepresented (0 vs. 4.5% and 2.4 vs. 4.2%, respectively).

Sri Lanka

Wijeyaratne et al[36] assessed PCOS prevalence among Indigenous Sri Lankan population, in a case–control study exploring associations between gestational diabetes mellitus (GDM) and subsequent PCOS and MetS. Women with previous GDM ($n = 147$) and ethnically matched control women ($n = 67$) were recalled 3 years postpartum and assessed for PCOS characteristics and related metabolic features. Diagnosis of PCOS was based on the modified Rotterdam criteria. PCOS prevalence was 40% for women with a GDM history and 3% for controls ($p \leq 0.01$).

Clinical Characteristics of PCOS among Indigenous Populations

All thirteen studies included an assessment of the clinical characteristics of PCOS. These included indigenous populations from Australia,[28–30,37,39] New Zealand,[34] Sri Lanka,[33,36] and the United States.[27,31,32,35,38] Three of the studies from the United States[27,31,38] and the study from New Zealand[34] included comparison groups of nonindigenous women. ►**Table 2** outlines clinical characteristics of PCOS among indigenous populations.

Australia

Community surveys: Davis et al[30] found 10 of 38 (26%) women surveyed reported symptoms of oligomenorrhea (irregular cycles with cycle length >35 days). Of these women, six had excessive facial hair and one had elevated free androgen index (FAI). Nine women reported regular menses and hirsutism, with assessment of blood biochemistry for four women showing three had a markedly elevated FAI. Boyle et al[29] reported PCOS in 38 of 248 women based on NIH criteria of oligomenorrhea and biochemical evidence of hyperandrogenism. Women with PCOS had significantly higher BMI and systolic and diastolic blood pressure (BP) when compared with women without PCOS. In an additional study, Boyle et al[28] restricted the sample to women with PCOS ($n = 35$) and non-hyperandrogenic women without PCOS ($n = 74$) and explored the impact of PCOS on MetS. They reported women with PCOS had a significantly higher BMI (33.4 vs. 23.8; $p = 0.001$), and MetS was more frequent in women with PCOS than those without (51 vs. 23%; $p = 0.003$, indicated by higher waist circumference, systolic and diastolic BP, fasting insulin, homeostatic model assessment (HOMA) index, and glucose and insulin levels 2 hours after a 75-g glucose tolerance test ($p < 0.001$). However, once adjusted for BMI, PCOS was no longer significantly associated with MetS.

Table 2 Prevalence of PCOS and key outcomes for PCOS clinical features of included studies (presented alphabetically by country and chronologically by year of study)

Indigenous population	First author (year)	PCOS diagnostic criteria	PCOS prevalence	Key outcome data	
				Diagnostic category Outcome measure	Results
Australia					
Aboriginal and/or Torres Strait Islander	Davis (2002)[30]	NIH 1990	$N \geq 10/38$ women (26%). *Note:* Diagnosis of PCOS is limited by lack of biochemistry and restriction of assessment of hirsutism	*Regular menses plus normal hair distribution:* BMI (kg/m^2) *Oligomenorrhea/non-hirsute:* BMI (kg/m^2) *Regular menses/hirsute* BMI (kg/m^2) *Oligomenorrhea/ hirsute:* BMI (kg/m^2)	19/38 (50%) 24.3 ± 5.73 4/38 (10.5%) 27.7 ± 6.6 9/38 (23/7%) 25.8 ± 5.5 6/38 (15.8%) 27.2 ± 6.1
	Boyle (2012)[29]	NIH 1990	15.3% (95% CI, 10.8–19.8%)	PCOS BMI (kg/m^2) TT (nmol/L) *Idiopathic hirsutism:* BMI (kg/m^2) TT (nmol/L) *Hyperandrogenemia and regular cycles:* BMI (kg/m^2) TT (nmol/L) *Non-hyperandrogenic:* BMI (kg/m^2) TT (nmol/L)	38/248 (15.3%) Median (IRQ): 28.1 (25.1–34.2) Median (IRQ): 2.3 (1.9–3.0) 25/248 (10.1%) Median (IRQ): 27.4 (23.0–33.4) Median (IRQ): 1.3 (1.2–1.5) 34/248 (13.7%) Median (IRQ): 28.1 (25.5–34.2) Median (IRQ): 2.4 (1.9–2.6) 79/248 (31.9%) Median (IRQ): 23.7 (20.7–27.6) Median (IRQ): 1.3 (1.1–1.6)
	Boyle (2015)[28]	NIH 1990	Case–control study— PCOS prevalence not assessed	*Women w/ PCOS:* BMI (kg/m^2) TT (nmol/L) *Women w/out PCOS:* BMI (kg/m^2) TT (nmol/L)	$N = 35$ Median (IRQ): 33.4 (27.7–39.7) Median (IRQ): 2.3 (1.9–3.0) $N = 74$ Median (IRQ): 23.8 (20.8–28.1) Median (IRQ): 1.3 (1.1–1.6)
	Boyle (2017)[39]	ESHRE/ASRM (2003)	Program evaluation study— PCOS prevalence not assessed	*Women w/ PCOS:* BMI: 25–29.9 (kg/m^2) BMI: 30–34.9 (kg/m^2) BMI ≥ 35 (kg/m^2)	$N = 36$ 11.11%[a] 25%[a] 61.11%[a]
	Ellis (2018)[37]	NIH	PCOS prevalence not assessed	*PCOS diagnosis:* Oligo-ovulation or anovulation Clinical hyperandrogenism Biochemical hyperandrogenism Polycystic ovary on ultrasound 2/3 Rotterdam diagnostic criteria satisfied NIH diagnostic criteria satisfied	56/61 (92%) 32/37 (87%) 50/56 (89%) 33/45 (73%) 60/63 (95%) 50/59 (85%)
New Zealand					
Maori or Pacific Islander	Williamson (2001)[34]	Symptoms of hirsutism, acne, irregular menses, and/or anovulatory infertility, confirmed either by ultrasound or laparoscopy	Ratio of PCOS patients to reference population Maori: 9.9%:13.5% Pacific Islander: 9.3%:9.8% European: 69.2%:57.7% Indian: 11.7%:2.1% Chinese: 0%:4.5% Other Asian: 2.4%:4.2% Other: 3.7%:8.1%	*PCOS diagnosis* Oligomenorrhea Hirsute Acne Infertility Obesity *Clinical characterizes* Hirsutism (FG score <6) TT (≤2.5 nmol/L) LH (IU/L) SHBG (nmol/L)	*% of women from each ethical group* Maori: 44%; Pacific Islander: 57%; European: 45%; Indian: 58%; Other: 50% Maori: 44%; Pacific Islander: 27%; European: 43%; Indian: 32%; Other: 10% Maori: 0%; Pacific Islander: 0%; European: 18%; Indian: 5%; Other: 10% Maori: 63%; Pacific Islander: 80%; European: 46%; Indian: 68%; Other: 60% Maori: 0%; Pacific Islander: 20%; European: 14%; Indian: 5%; Other: 10% Maori: 10.5 ± 9.8; Pacific Islander: 9.1 ± 7.2; European: 8.3 ± 9.0; Indian: 8.3 ± 8.2; Other:

(*Continued*)

Table 2 (*Continued*)

Indigenous population	First author (year)	PCOS diagnostic criteria	PCOS prevalence	Key outcome data	
				Diagnostic category Outcome measure	Results
					3.1 ± 5.5 Maori: 2.9 ± 1.1; Pacific Islander: 2.2 ± 0.7; European: 2.2 ± 1.0; Indian: 2.1 ± 0.6; Other: 2.1 ± 1.1 Maori: 11.3 ± 5.3; Pacific Islander: 12.4 ± 5.5; European: 10.9 ± 7.2; Indian: 10.3 ± 5.7; Other: 12.0 ± 6.6 Maori: 52.0 ± 23.8; Pacific Islander: 36.9 ± 4.7; European: 55.6 ± 17.6; Indian: 44.3 ± 1.5; Other: 49.7 ± 15.5
Sri Lanka					
Indigenous South Asian	Wijeyaratne (2006)[36]	Rotterdam ESHRE/ASRM	Women w/ GDM: 110/274 (40.0%) Women w/out GDM: 5/168 (3.05%)	*Indigenous women w/ GDM, PCO* Menstrual irregularity Hirsutism, FG > 7 Infertility Acanthosis nigricans TT (nmol/L) SHBG (nmol/L) *Indigenous women w/GDM, non-PCO* Menstrual irregularity Hirsutism (FG > 7) Infertility Acanthosis nigricans TT (nmol/L) SHBG (nmol/L)	*N* = 86 16 (18.6%) 11 (13%) 23 (27%) 47 (55%) 2.21 ± 0.04 1.15 ± 0.02 *N* = 61 4 (6.5%) 4 (5%) 9 (15%) 20 (32%) 1.98 ± 0.07 1.34 ± 0.03
	Wijeyaratne (2011)[33]	Rotterdam	Case–control study— PCOS prevalence not assessed	*Women with PCOS, w/ MetS:* Preexisting diabetes Family history of T2D Oligomenorrhea (since menarche) Presence of acanthosis BMI ≥ 25 (kg/m^2) BMI ≥ 27.5 (kg/m^2) BMI ≥ 30 (kg/m^2) TT ≥ 3.0 (nmol/L) SHBG ≤ 12.8 (nmol/L) *Women with PCOS, w/out MetS:* Preexisting diabetes Family history of T2D Oligomenorrhea (since menarche) Presence of acanthosis BMI ≥ 25 (kg/m^2) BMI ≥ 27.5 (kg/m^2) BMI ≥ 30 (kg/m^2) Testosterone ≥ 3.0 (nmol/L) SHBG ≤ 12.8 (nmol/L)	*N* = 121 10 (8.3%) 72 (61.5%) 58 (52.3%) 97 (80.1%) 90 (75.6%) 58 (48.7%) 33 (27.7%) 45 (37.1%) 12 (14.63%) *N* = 274 4 (1.5%) 156 (58.2%) 117 (47.8%) 158 (57.6%) 104 (38.7%) 50 (18.6%) 33 (27.7%) 91 (33.5%) 9 (5.96%)
USA					
American Indian or Alaskan Native	Legro (2006)[38]	NIH (1990)	Randomized control trial of women with PCOS—PCOS prevalence not assessed	*Generalized obesity:* BMI <30 (kg/m^2) BMI 30–34 (kg/m^2) BMI >35 (kg/m^2) *Hirsutism*: FG < 8:	*% of women from each racial group* American Indian/Alaskan Native: 29.2%; Caucasian: 28.3%; African American: 24.8%; Asian: 64.7% American Indian/Alaskan Native: 31.9%; Caucasian: 19.6%; African American: 22.9%; Asian: 11.8%

Table 2 (*Continued*)

Indigenous population	First author (year)	PCOS diagnostic criteria	PCOS prevalence		Key outcome data	
					Diagnostic category Outcome measure	Results
					FG 8–16: FG > 16:	American Indian/Alaskan Native: 38.9%; Caucasian: 52.1%; African American: 52.3%; Asian: 23.5% American Indian/Alaskan Native: 15.3%; Caucasian: 20.9%; African American: 17.4%; Asian: 23.5% American Indian/Alaskan Native: 38.9%; Caucasian: 39.5%; African American: 49.5%; Asian: 47.1% American Indian/Alaskan Native: 45.8%; Caucasian: 39.5%; African American: 33.0%; Asian: 29.4%
Native American	Afifi (2017)[27]	Rotterdam	PCOS diagnosis (women presenting at PCOS clinic)		BMI (kg/m^2) *Clinical hirsutism* No (mFG total <8) Yes (mFG total ≥ 8)	Native American: 38.8 ± 4.83; Middle Eastern: 35.8 ± 10.4; Ashkenazi Jewish: 29.1 ± 8.1; Caucasian (other): 29 ± 7.69; East/South East Asian: 29.7 ± 8.44; South Asian: 23 ± 3.84; Hispanic: 34.2 ± 8.88; African American A: 31.4 ± 6.6; mixed/other: 32 ± 7.85 Native American: 2 (100%); Middle Eastern: 3 (33.3%); Ashkenazi Jewish: 10 (62.5%); C: 66 (60%); East/South East Asian: 19 (57.6%); South Asian: 0 (0.0%); Hispanic: 8 (26.7%); African American: 4 (26.7%); Mixed/Other: 9 (45%) Native American: 0 (0.0%); Middle Eastern: 6 (66.6%); Ashkenazi Jewish: 6 (37.5%); Caucasian: 44 (40%); East/South East Asian: 14 (42.4%); South Asian: 5 (100.0%); Hispanic: 22 (73.3%); African American: 11 (73.3%); Mixed/Other: 11 (55%)
			Yes (meets diagnostic criteria for PCOS): 276/341	No (does not meet diagnostic criteria for PCOS): 48/341		
Pima Indian	Purifoy (1981)[31]	N/A	PCOS prevalence not assessed		Obese Pima vs. normal-weight Caucasians SHBG Testosterone DHEA	*N/A, qualitative description* *N* = 20 Two-sample *t*-test mean SHBG in Pima vs. Caucasians revealed significantly lower SHBG in the Pima (df = 51, $t = 8.883$, $p < 0.0005$). Mean SHBG for the PIMA was 0.85 vs. 2.36 mg % for Caucasians. The slope (R) for SHBG by age for the PIMA = − 9.684 and for Caucasians = −0.626 The slope (R) for testosterone by age for the PIMA = −1.205 and for Caucasians = −0.254 ng% The slope (R) for DHEA-S by age for the PIMA = −4.603 and for Caucasians = 1.365 ng %
	Weiss (1994)[35]	N/A	PCOS prevalence not assessed		*Hyperinsulinemic women:* Gravidity % irregular menses: Testosterone (nmol/L) Androstenedione (nmol/L) DHEAS (micromole/L) *Non-hyperinsulinemic women:* Gravidity: % irregular menses: TT (nmol/L)	*N* = 20 Median (IRQ): 2 (0–4) 0 (0/19)[a] 1.13 3.36 4.55 *N* = 20 Median (IRQ): 2 (0–4) 50 (9/18)[a] 1.13

(*Continued*)

Table 2 (*Continued*)

Indigenous population	First author (year)	PCOS diagnostic criteria	PCOS prevalence	Key outcome data	
				Diagnostic category Outcome measure	Results
				Androstenedione (nmol/L) DHEAS (*μmol/L*)	3.79 2.85
	Roumain (1998)[32]	N/A	PCOS prevalence not assessed	*Women w/ vs. w/out menstrual irregularity* *18–24 y* Gravidity (*n*) Diabetes (%) Ever pregnant (%) *25–34 y* Gravidity (*n*) Diabetes (%) Ever pregnant (%) *35–44 y* Gravidity (*n*) Diabetes (%) Ever pregnant (%)	*N* = 135 vs. 36 1.2 ± 1.5 vs. 1.2 ± 1.5 5.9 vs. 11.1%[a] 51.1 vs. 55.5% *N* = 235 vs. 61 3.0 ± 2.0 vs. 2.1 ± 2.2 22.1 vs. 34.4%[a] 88.5 vs. 62.3%[a] *N* = 180 vs. 48 3.7 ± 2.4 vs. 3.0 ± 2.5 38.3 vs. 47.9%[a] 92.8 vs. 83.3%[a]

Abbreviations: BMI, body mass index;: DHEAS: dehydroepiandrosterone sulfate; ESHRE/ASRM, European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine; FG, Ferriman–Gallwey Hirsutism Scoring System; LH, luteinizing hormone; IQR, interquartile range; MetS, metabolic syndrome; N, number; NIH, National Institute of Health; PCOS, polycystic ovary syndrome; SD, standard deviation; SHBG, sex hormone–binding globulin; T, total testosterone; T2D, type 2 diabetes.
Note: Values are mean ± SD, *n* (% of women), or as otherwise indicated.
[a]Proportion of women.

Clinical audits: Ellis et al[37] performed a retrospective clinical audit at an Aboriginal primary healthcare center in the Northern Territory, Australia, and reviewed 63 patient files of women aged 15 to 44 years diagnosed with PCOS within the last 2 years. Among the women, the trigger for PCOS diagnosis was menstrual irregularity (52/63; 83%), followed by infertility (24/63; 38%), hirsutism/acne (15/63; 24%), PCO (4/63; 6.4%), and "other" (4/63; 6.4%). Comorbid conditions associated with PCOS were common, with at least one comorbidity present in 60% of women. One-third (33%) of women reported associated complications of PCOS including infertility, 14% anxiety and depression, 13% dyslipidemia, 9.5% impaired glucose tolerance (IGT), 9.5% T2DM, and 1.6% GDM. An evaluation of the standard of evidence-based care undertaken by medical file audit in the Torres Strait, Australia,[39] tested the fidelity of clinic practice in relation to the PCOS "Diagnosis Guideline." They reported the Rotterdam criteria were met among the majority of women (32/36; 89%). Among those 32 women, 22 (22/32; 68.7%) displayed PCO on ultrasound, 29 (29/32; 90.6%) reported irregular menstrual cycles, and 30 (30/32; 93.8%) presented with clinical and/or biochemical evidence of hyperandrogenism. Furthermore, 19 women satisfied two of the criteria and 13 women satisfied all the three criteria. Comorbidities associated with PCOS included infertility in 11 women, moderate to severe psychological distress in one-third (as measured by the Kessler Psychological Distress Scale [K10 scale]), and most women had more than one cardiometabolic risk factor, with the majority overweight or obese (97.2%), centrally obese (91.7%), and a third had abnormal glucose tolerance.

New Zealand

Williamson et al[34] examined the effect of ethnicity on PCOS within Maori, Pacific Islander, European, Indian, and "Other" (Chinese, other Asian, and other) groups. The authors reviewed reasons for referral to a gynecological endocrine clinic and analyzed clinical characteristics and laboratory values to capture phenotypic differences between ethnicities. There was a similar proportion of women with oligomenorrhea in all groups, Maori women presented most for hirsutism, and Pacific Islander women presented most for infertility and obesity. Maori and Pacific Islander women had the highest levels of androgens, triglycerides, low-density lipoprotein (LDL) cholesterol, fasting insulin, systolic and diastolic BP, and lowest high-density lipoprotein (HDL) cholesterol among the groups. The authors concluded that Maori and Pacific Islander women with PCOS were most likely to present with an adverse metabolic profile compared with other ethnicities with PCOS.

Sri Lanka

Two studies that described the clinical characteristics of PCOS among indigenous Sri Lankan women were identified. As previously described, Wijeyaratne et al[36] recruited women with previous GDM and controls, who were not taking hormonal contraception and who were more than 12 months postpartum to determine the association between GDM and subsequent PCOS (defined by the Rotterdam criteria) and MetS. Women in the GDM group were further subdivided into women with polycystic ovaries at ultrasound (PCO group) and women with normal ovaries on ultrasound (non-PCO group), and metabolic and endocrine parameters were compared. A higher proportion of women with PCO and previous GDM also had menstrual irregularity ($p = 0.02$), and hirsutism ($p = 0.009$). Metabolic features of women with PCO and previous GDM included a significantly higher BMI ($p = 0.04$), waist-to-hip ratio (WHR; $p = 0.01$), higher insulin ($p = 0.002$), higher fasting plasma glucose (FPG) test ($p = 0.01$), HOMA index ($p = 0.001$) and triglycerides ($p = 0.009$), acanthosis nigricans ($p = 0.03$) with significantly lower HDL ($p = 0.004$), and sex hormone binding globulin (SHBG; $p = 0.02$) concentrations compared with the women without PCO. A higher proportion also reported infertility ($p = 0.007$).

In a more recent cross-sectional study by Wijeyaratne et al,[33] researchers recruited women diagnosed by the Rotterdam criteria from an endocrine clinic in Colombo ($n = 469$ PCOS patients; $n = 231$ controls) and collected baseline clinical, biochemical, and ultrasound data. Prevalence of MetS was determined among women with PCOS and comparison of PCOS characteristics between women with and without MetS examined. Among women with PCOS, 92.3% reported irregular menses, 79.7% reported hirsutism, 64.6% reported acanthosis nigricans, 62.2% reported infertility (married women only), and 48.0% reported a family history of T2DM (first-degree relative). MetS occurred in 30.6% in women with PCOS compared with 6.3% in controls. Women with PCOS and MetS had significantly higher median BMI and BP, a worse lipid profile, poorer glucose tolerance, and more IR compared with women with PCOS alone. Furthermore, they were more likely to have an obese BMI (defined by the authors as BMI > 25 kg/m^2; odds ratio [OR] = 4.83, 95% confidence interval [CI] = 2.91–7.84), have preexisting diabetes (OR = 6.08, 95% CI = 1.86–19.79), develop acanthosis nigricans (OR = 2.97, 95% CI = 1.78–4.92), and high odds of prehypertension (OR = 15.3, 95% CI: 8.83–26.55).

United States

Five studies have assessed clinical characteristics of PCOS among indigenous women of the United States. Purifoy et al[31] measured levels of serum androgens (androstenedione, testosterone, dehydroepiandrosterone sulfate [DHEAS] and SHBG) in obese (mean BMI: 38.9) Pima Indian women ($n = 20$) aged 19 to 44 years and in normal weight (BMI not specified) Caucasian women ($n = 20$) aged 20 to 46 years. This is the only study included in this review that does not reference PCOS and instead satisfies inclusion criteria by evaluating a clinical characteristic of PCOS, that is, hyperandrogenism. Purifoy et al reported all serum levels, except SHBG, were higher in young Pima Indian women, compared with young Caucasian women. With age, androstenedione and DHEA-S declined significantly and testosterone declined slightly in Pima Indian women, whereas there was no significant decrease in these androgens in the Caucasian population for this age range.

A study by Weiss et al[35] analyzed reproductive histories and androgen concentrations from stored serum samples of hyperinsulinemic (high insulin range, 301.140–685.884–685.884 pmol/L × 180 minutes) and relatively non-hyperinsulinemic (low insulin range, 42.390–134.730 pmol/L × 180 minutes) Pima Indian women ($n = 20$ per group, 18–45 years). Hyperinsulinemic women had significantly higher BMI ($p = 0.002$), and 50% reported irregular menses compared with no reports among non-hyperinsulinemic women ($p = 0.004$). Serum DHEAS was significantly lower in hyperinsulinemic women ($p = 0.006$); however, there were no significant differences for testosterone or androstenedione between groups. Among the hyperinsulinemic women, those with irregular menses had significantly higher testosterone levels than women with regular menses ($p = 0.05$). When stratified into low and high groups according to testosterone and BMI, a high testosterone and a high BMI were associated with a 3.5- ($p = 0.03$) and 1.6-fold ($p = 0.32$) increased risk, respectively, of having irregular menses as compared with the low groups.

Building on the earlier study by Weiss et al,[35] Roumain et al[32] examined the relationship between menstrual irregularity and T2DM in nonpregnant Pima Indian women ($n = 695$). A history of menstrual irregularity was reported in 21% of women (145/695) and was significantly associated with a high prevalence of T2DM (33 vs. 24%; $p < 0.05$) and a higher BMI (38.7 vs. 35.4 kg/m^2; $p < 0.05$), compared with women with regular menses. Age-adjusted analysis demonstrated women with a history of menstrual irregularity had a significantly higher ($p < 0.05$) BMI, waist circumference, WHR, waist-to-thigh (WTR) ratio, FPG, 2-hour plasma glucose, hemoglobin A1C, mean BP, prevalence of T2DM, as well as significantly decreased gravidity. After additional adjustment for obesity, T2DM was significantly associated with menstrual irregularity for the least obese group of women (BMI < 30). Among the least obese women, menstrual irregularity was associated with a significantly higher WTR ($p < 0.05$), reflecting central fat distribution. When adjusted for age and BMI within this least obese group of women, history of menstrual irregularity was still significantly associated with a high prevalence of diabetes; however, when adjusted for WTR, the association was no longer significant.

A report by Legro et al[38] has described the methods of a RCT assessing ovulation induction treatment methods for 626 women self-reporting infertility and diagnosed with PCOS using the NIH (1990) criteria, aged 18 to 39 years. Within this study, markers of hyperandrogenism, IR, and BMI were examined according to ethnicity, including American Indian or Alaskan Native (Native Americans; $n = 72$), Caucasian ($n = 435$), African American ($n = 109$), and Asian ($n = 17$). Analysis of biometric variables by race reported Native Americans had a higher BMI (34.3 ± 8) than the Asian group (29.1 ± 6.3), but less than the Caucasian (35.4 ± 8.8) and African American groups (36.0 ± 8.4). Native Americans were more hirsute than other groups. Patient files showed Native Americans had the lowest diagnosis of prior infertility (44/72; 61.1%) and ovulatory dysfunction (43/72; 59.7%) and, in terms of the biochemical measures of PCOS, had the second lowest levels of testosterone. There were no significant ethnic differences in FAI, glucose, insulin, proinsulin, and SHBG, but Native Americans had the highest proportion of women with bilateral PCO. The authors concluded that ethnicity influenced the phenotype to a mild degree.

A cross-sectional retrospective analysis by Afifi et al[27] examined the prevalence, pattern, and severity of hirsutism in a cohort of American patients recruited from a multidisciplinary PCOS clinic, according to patient-reported ethnicity and skin type. The evaluation of hirsutism was conducted with the modified Ferriman–Gallwey (mFG) visual scoring method. A total of 341 women met the study inclusion criteria, of whom 276 were diagnosed with PCOS as per the Rotterdam criteria. Ethnic subgroups included Middle Eastern, Ashkenazi Jew, Caucasian, African American, South Asian, East/Southeast Asian, Hispanic, mixed/other, and Native American. Independent analysis by ethnicity showed Native American women with PCOS had the highest BMI (38.8 ± 4.83) and the lowest severity, as indicated by mFG scores, and prevalence rates of hirsutism (total mFG score >8) compared with other ethnic subgroups. No distinct patterns in anatomic distribution of hirsutism were seen in Native American women, with low mFG scores in all areas (facial: 1 ± 1.41; trunk: 1.5 ± 0.707; extremity: 1.5 ± 2.12). By comparison, a higher facial mFG score was found in African American patients and higher mFG scores in the truncal and extremity regions observed in Middle Eastern patients.

Discussion

We identified limited research on the prevalence of PCOS among indigenous women, including in populations with known elevated risks of related metabolic diseases such as T2DM. There is evidence that PCOS is increased in Australian Indigenous women compared with other Australian women, though this was not evident in indigenous populations from other countries. While prevalence may not be increased, our findings suggest that clinical features of PCOS may be more severe in certain groups of indigenous women from New Zealand and the United States, compared with nonindigenous populations. These findings suggest a more severe phenotype and may reflect reduced access to care. However, small sample sizes and data quality issues impede our ability to draw reliable conclusions.

Of the four studies assessing PCOS prevalence among indigenous women, only one compared results against reference nonindigenous (or national) populations. This was conducted at a clinical setting in New Zealand and reported that the proportion of women with PCOS who were from Maori or Pacific Islander background was similar to the reference population, which was also the case for women of European background.[34] In contrast, women of Indian (South Asian) background were overrepresented. There are no national data of PCOS in New Zealand to compare this to; however, national data report nearly half of all Maori adults are obese (BMI > 30 kg/m^2), with a self-reported prevalence

of diabetes among Maori twice that of non-Maori.[40] Given the interrelationship between PCOS, obesity, and diabetes, it was anticipated that a higher proportion of the women with PCOS would have been Maori or Pacific Islander women.

Of the studies without nonindigenous comparison data, prevalence was reported as 3.0% for Indigenous Sri Lankan women,[36] distinctly lower than the 6.3% reported in the general Sri Lankan population.[41] This surprisingly low prevalence may reflect sampling bias, as study participants were women who had previously given birth, and given the high (70–80%) prevalence of infertility in women with PCOS, are unlikely to be representative of the wider Sri-Lankan population. PCOS prevalence in Indigenous Australian women ranged between 15.3%[29] and 26%,[30] more common than the 8 to 13% reported among all Australian women.[9] This is likely due to many risk factors related to PCOS being more common among Australian Indigenous women, including obesity, hyperinsulinism, T2DM, dyslipidemia, and a history of low birth weight.[42]

This review therefore suggests that PCOS may be more prevalent among particular indigenous population groups, for example, Indigenous Australian women, but that is not universal. Given the paucity of studies and lack of firm comparative data, high-quality targeted research is required to understand the epidemiology of PCOS in indigenous women.

All thirteen studies reported on the clinical presentation of PCOS. Only four studies included a nonindigenous comparison group.[27,31,34,38] Results varied, reporting better and worse metabolic profiles, and occurrences of presentation of clinically severe PCOS among indigenous women compared with nonindigenous populations. Indigenous women from New Zealand, both Maori and Pacific Islander women, demonstrated the highest prevalence of obesity and significantly elevated levels of androgens, triglycerides, LDL cholesterol, fasting insulin, and systolic BP compared with nonindigenous ethnic groups (European, Indian, and "other").[34] This may not reflect specific ethnic difference in PCOS, as national health reports also describe increased obesity and MetS in Maori and Pacific Islander people compared with other New Zealanders.[43] Maori women were also more likely to present with hirsutism than other ethnicities and Pacific Islander women were most likely to present with infertility.

In obese Pima Indian women (19–44 years), concentrations of androgens, androstenedione, testosterone, and DHEA-S decreased significantly with age, compared with normal-weight Caucasian women.[31] This is likely a result of the normal, age-associated decline in androgen levels,[44] exacerbated by the effects of excess adiposity on androgen concentrations and metabolism.[45]

One study reported American Indian and Alaskan Natives were less likely to be morbidly obese (BMI $\geq$ 35) than Caucasians and African Americans, but more likely to have a higher BMI than Asians, and least likely to have a diagnosis of infertility.[38] They also had significantly lower total testosterone levels and FAI than all other racial groups except Asians, perhaps related to lower BMI and unmeasured cardiovascular risk factors such as inflammatory markers and adverse lipids. However, despite the absence of biochemical signs of hyperandrogenism, American Indian and Alaskan Natives were attempting conception for the longest period, were more hirsute, and a greater proportion had ultrasound evidence of PCOS.[38] In contrast, another study reported Native American women had the highest BMI and lowest severity and prevalence rates of hirsutism relative to several major ethnic groups.[27] The difference in findings may be due to the use of various definitions of the syndrome and validity of diagnostic criteria, BMI and metabolic profile of study cohorts, and types of recruitment and sampling. Long duration of infertility may reflect issues related to cost of treatment, decreased access to appropriate services, adherence to treatment, or the diversity of Native American groups with respect to social and cultural values.

The findings of these studies are in contrast to most of the literature, which shows prevalence of obesity, hyperinsulinemia, and metabolic risk associated with PCOS to be higher in indigenous populations than in nonindigenous populations.[46] Hirsutism is more prevalent in obese women; however, this relationship may differ between ethnic groups.[45] The unexpected findings of this review may suggest that there is selection bias among existing studies, reflecting barriers to healthcare for indigenous people and patterns of access to care, or diagnostic limitations on the characterization of clinical features (e.g., subjective scoring systems to grade hirsutism and untimely progesterone measurements).

There are several factors contributing to why some indigenous populations have a higher PCOS prevalence or more severe clinical presentation than their respective nonindigenous populations. Due to the ongoing trauma of colonization, dispossession, and dislocation, many indigenous populations continue to suffer disproportionately from poor health and a high burden of disease.[19,20] This includes increased risks of obesity and diabetes, as well as adverse perinatal outcomes (low birth weight and diabetes in pregnancy) or environmental risk factors (e.g., diet, physical activity, and smoking)[18] potentially involved in the etiology, prevalence, and modulation of the PCOS phenotype. Despite having higher healthcare needs, indigenous people often face several barriers when accessing health care services (i.e., lack of culturally appropriate healthcare services, discriminatory behavior by healthcare staff, geographical isolation and remoteness, unaffordable cost, and lack of time or ability to attend appointments).[47] Limited access to healthcare leads to delays in diagnosis and disease management and ultimately poorer outcomes representing significant health inequities.[48] There is also a need to improve health literacy to increase awareness of the signs and symptoms of PCOS which may permit more timely diagnosis.

Overall, the methodological quality of the 13 studies was moderate to high, and several studies reached the maximum total score. Where studies were not assigned the maximum score, primary concerns were the representativeness of study samples, with some studies drawing samples from clinical populations (rather than the whole population) and others using volunteers, as well as nonresponse rates being either unsatisfactory or inadequately described. Quality of

future studies may be strengthened by use of representative community-based samples of indigenous women, as well as appropriate comparison groups and by exploring any differences in the characteristics of responders and response rates.

There are several strengths of this review. Our search strategy was comprehensive, incorporated multiple global health databases, and was conducted in duplicate to reduce potential for random errors and bias. This study is also the first to synthesize and critically appraise the burden of PCOS among indigenous people globally. There were also limitations to this study. Few studies included a group of nonindigenous women from the same country. Failure to include a nonindigenous comparison group makes it difficult to draw inferences about in-country differences and to monitor this over time. We also found no studies that specifically examined differences between indigenous and nonindigenous comparisons. While we acknowledge that direct indigenous versus nonindigenous comparisons must be made with caution, they can be useful for identifying continuing disparity in needs and better targeting of resources. We did not perform a meta-analysis due to significant variation in study populations across very specific clinical (e.g., infertility, gynecological endocrine, and postpartum with and without GDM) and community settings, as well as a variation in PCOS diagnostic criteria used (NIH, Rotterdam, and other, e.g., menstrual irregularity and IR), study design, and statistical methods employed. This significant clinical and statistical heterogeneity meant that a combined analysis would be difficult to interpret meaningfully. Additionally, there were small numbers in most studies. Despite estimates that indigenous populations live in more than 90 countries around the world,[17] retrieved studies were limited to 4 countries. A particular gap is the lack of reports on PCOS from Canada which has indigenous populations with similar rates of early-onset type 2 diabetes and obesity to Australian Indigenous people.[49]

The heterogeneous nature of PCOS makes it challenging to research. Considering the additional challenges associated with researching scattered, mobile populations in remote locations and inherent cultural barriers of mostly nonindigenous researchers conducting studies in an indigenous domain, the lack of available and/or reliable evidence-based data is unsurprising. Existing literature on prevalence and clinical manifestations of PCOS among indigenous populations globally is extremely limited with much variation between study findings. Given the disproportionately larger impact of inflammation, obesity, and metabolic disease, including diabetes on indigenous populations, it is important to determine whether PCOS remains under-recognized in indigenous women, as it has been the case in general populations, or if there are clear differences between indigenous groups in prevalence and phenotype. For indigenous women where PCOS seems prevalent, increased awareness in community and health care providers, culturally appropriate resources, health promotion, and health care should be available to help prevent and manage symptoms.

Conclusions

This review highlights a gap in the knowledge about PCOS in indigenous women. It appears that PCOS is more common in Australian Indigenous women highlighting a need for awareness among community and health providers to support timely diagnosis and management. However, the paucity of good-quality research supports the need for future studies understanding the natural history of PCOS with nonindigenous populations from sample countries, so that accurate conclusions can be drawn and appropriate recommendations for healthcare can be made. Future research should explore specific genetic and environmental factors that contribute to variations in prevalence and phenotype of PCOS among indigenous populations compared with nonindigenous populations. It is essential that all future research is conducted in a culturally competent way in partnership with indigenous communities, organizations, and participants.

Authors' Contributions

Conceptualization: E.G., S.C., A.R., and J.B.; data curation: E.G. and J.A.; formal analysis: E.G., J.A., and R.B.; investigation: E.G., J.A., and J.B.; methodology: A.R. and J.B.; supervision: S.C., A.R., and J.B.; writing—original draft: E.G. and J.B.; writing—reviewing and editing: E.G., J.A., R. B., S.C., A.J., A.R., and J.B.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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