Prevalence of acne vulgaris among women with polycystic ovary syndrome: a systemic review and meta-analysis

Tehrani, F. R., Behboudi-Gandevani, S., Yarandi, R. B., Naz, M. S. G. & Carmina, E.

Published in: Gynecological Endocrinology
DOI: 10.1080/09513590.2020.1859474

Available online: 23 December 2020

Citation:

Tehrani, F. R., Behboudi-Gandevani, S., Yarandi, R. B., Naz, M. S. G. & Carmina, E. (2020). Prevalence of acne vulgaris among women with polycystic ovary syndrome: a systemic review and meta-analysis. Gynecological Endocrinology. doi: 10.1080/09513590.2020.1859474

Title Page

Prevalence of acne vulgaris among women with polycystic ovary syndrome: A systemic review and meta-analysis

Short running title**: Acne in PCOS**

Authors

Fahimeh Ramezani Tehrani, MD [1], Samira Behboudi-Gandevani, PhD [2], Razieh Bidhendi Yarandi 1, Marzieh Saei Ghare Naz [1], Enrico Carmina [3].

[1] Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2] Faculty of Nursing and Health Sciences, Nord University, Bodø, Norway.

[3] Department of Health Promotion, Mother and Child Care and General and Specialist Medicine, University of Palermo Medical School, Palermo, Italy

Corresponding Author: Fahimeh Ramezani Tehrani, Professor

Email: ramezani@endocrine.ac.ir, fah.tehrani@gmail.com

a. Tel: +98-021-22432500

b. P.O.Box: 19395-4763,

c. Address: Research Institute for Endocrine Sciences, No 24, Parvane Street, Yaman Street, Velenjak, Tehran, Iran.

d. Email: ramezani@endocrine.ac.ir, fah.tehrani@gmail.com

ABSTRACT

Objective: The aim of this meta-analysis was to evaluate the prevalence of acne among women with PCOS worldwide, and in subgroups of patients with different age, geographical-region and PCOS definition-criteria, compared to healthy non-PCOS counterparts.

Method: A comprehensive literature search was performed in PubMed [including Medline], Web of Science, and Scopus databases for retrieving articles in English investigating the prevalence of PCOS. "Meta-prop" method was applied to estimate pooled prevalence of acne in both groups. Meta-regression was conducted to find the association between acne in women with and without PCOS.

Results: We used 60 studies, included data of 240,213 women with PCOS and 1,902,022 healthy-controls for the meta-analysis. The overall pooled prevalence of acne among women with and without PCOS, was 43% (95% CI: 41–45%) and 21% (95% CI: 19–22%), respectively, which was 1.6 fold significantly higher than among healthy-controls. The pooled prevalence of acne in adults, and in adolescents PCOS patients were 42% and 59%, respectively, which were significantly higher than non-PCOS counterparts. The pooled estimated prevalence of acne in adults PCOS women was 76% using the NIH definition and 36% by Rotterdam-criteria, both were significantly higher than non-PCOS counterparts, respectively. In subgroups of adults, who used Rotterdam-definition, the highest prevalence of acne in PCOS patients was reported in east Asia and were significantly 3.5 fold higher than non-PCOS counterparts.

Conclusion: Based on the available data, acne is one of the most prevalent cutaneous features of PCOS patients. In addition, results highlight geographical differences among PCOS patients.

Key words: Acne, Meta-analysis, Polycystic ovary syndrome, Prevalence.

Background

Polycystic ovary syndrome (PCOS) with a prevalence of 6-10% is one of the most common endocrinopathies among women in the reproductive age [1]. Hyperandrogenism and/or hyperandrogenemia, chronic oligo-ovulation and polycystic ovaries morphology are the main characteristics of this syndrome. The exact underlying pathogenic mechanisms of PCOS are not clearly understood, but it is believed that insulin resistance (IR) with compensatory hyperinsulinemia and hyperandrogenemia are the cornerstones of its pathogenesis [2-4].

PCOS presents with a wide spectrum of common cutaneous manifestations, such as hirsutism, acne, seborrheic dermatitis, and hyperandrogenic female pattern hair loss (androgenetic alopecia) [5,6].

Acne vulgaris (acne) is an extremely common inflammatory skin disorder that, presenting in different periods of the life, but mainly during adolescence, affects approximately 30-85 % of women [7,8]. In general population prevalence of acne id very variable depending not only on age but also on ethnicity, nutrition habits, emotional stress and smoking [9].

Hyperandrogenism is associated to increased acne development. Evidence showed that androgens directly or indirectly, determine increased and altered sebum production [10] and it is often the first step of the acne development.

Because hyperandrogenism is one of the main characters of PCOS, it is not surprising that acne is one of the main cutaneous manifestations of the syndrome [11]. Conversely, it seems that 20% to 40% of patients with acne may suffer from PCOS [12].

Nevertheless, the prevalence of acne in PCOS patients has not been fully quantified and it is unclear whether it affects mainly adolescent patients or presents with the characters of adult acne. Therefore, the aim of this systematic review and meta-analysis hence was to evaluate the prevalence of acne among women with PCOS worldwide compared to healthy non-PCOS population.

Materials and methods

The ethics committee of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, approved this study. This systematic review and meta-analysis was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13] to assess the following objectives:

- To study the pooled prevalence of acne among women with PCOS, compared to non-PCOS population.
- To study the pooled prevalence of acne among women with PCOS based on various age groups of adolescents, adults older than 19 years and in reproductive age (adults and adolescents) compared to non-PCOS women;
- To study the pooled prevalence of acne among women with PCOS based on age group and various PCOS diagnostic criteria, compared to non-PCOS women.
- To study the pooled prevalence of acne among women with PCOS based on age group, various PCOS diagnostic criteria and different geographic regions, compared to non-PCOS women.

Search strategy

A comprehensive literature search was conducted in PubMed [including Medline], Web of Science, and Scopus databases for retrieving original articles published in English language on the prevalence of acne among women with

PCOS from Jan 1990 up to April 2020. Further, a manual search in the references list of studies included and other relevant reviews was used to maximize the identification of eligible studies. Since the acne mostly clinically determined as baseline characteristics of women with PCOS or secondary outcome measures, two set of following terms keywords, alone or in combination, were used for the search: (i) 'polycystic Ovarian Syndrome' OR 'polycystic Ovary Syndrome' OR 'PCOS' AND 'acne' OR 'acne vulgaris' AND "incidence" OR "prevalence" OR "epidemiology"; (ii) polycystic Ovarian Syndrome' OR 'polycystic Ovary Syndrome' OR 'PCOS' AND "incidence" OR "prevalence" OR "epidemiology".

Selection criteria, study selection and data extraction

Studies were eligible if they assessed the prevalence of acne in both PCOS and healthy non-PCOS. We excluded non-original studies including reviews, commentaries, editorials, letters, meeting abstracts, case reports, brief reports or any papers that did not provide accurate and clear data. Full text of all articles was conducted independently by authors, for determining final eligibility criteria, in close consultation with the second one reviewer. The general characteristics of the studies including "the first author name, journal, publication year, country of study, years of sampling, study design, sample size, population characteristics including age and BMI, PCOS definition, acne definition, prevalence of acne and its severity were extracted from the studies included and assessed. To prevent extraction and data entry errors, a control check between the final data used in the meta-analysis and the original publications was performed by all authors.

Quality assessment and risk of bias

Quality of the studies was critically appraised for their methodology and results presentation. Two reviewers (SBG and MS) who were blinded to study author, journal name and institution evaluated the quality of the studies independently. The quality of observational studies was also assessed using the modification of the Newcastle– Ottawa Quality Assessment scale for nonrandomized studies (NRS) [14] which evaluates the quality of published nonrandomized studies in terms of selection, comparability and outcomes. Studies with scores above 6 were considered as high quality, 3-5 as moderate and those with scores below than 3 as low quality. The modified Consolidated Standards of Reporting Trials (CONSORT) was used as a validated quality assessment checklist for clinical trials [15]. Studies with a score $\geq$ 70% of the highest level of the CONSORT checklist score were considered as high quality, those with 40–70% of the score as moderate, and those with 20–40% of the score as low quality and with < 20% of the score as very low quality.

We also evaluated risk of bias for studies. The risk of bias of NRS and other methodological studies was assessed using the ROBINS [16] and Cochrane Collaboration's tool, respectively [17]. In this respect, authors' judgments were categorized as of low-, moderate-, critical- and unclear risk of bias.

Statistical Analysis

The software package STATA (version 12; STATA Inc., College Station, TX, USA) was applied to conduct statistical analysis. Heterogeneity between studies was assessed using chi-squared statistics and $P > 0.05$ was interpreted as heterogeneity. Heterogeneous and non-heterogeneous results were analyzed using the fixed effects and random effects inverse variance models for calculating the pooled effect. "Meta-prop" method was applied to estimate pooled prevalence of acne in both groups in different subgroup of age, PCOS diagnostic criteria and region. Sensitivity analysis was done to assess the reliability of the estimate obtained in the Meta-prop analysis. Moreover, meta-regression was conducted to find the association between acne in women with and without PCOS. In this respect publication bias was assessed by Begg's test. In publication bias cases, the trim and fill method were conducted to correct. Forest plot was also drawn to summarize the result of each study's effect sizes and its 95% confidence intervals (CIs). $P > 0.05$ was set as significance level.

Results

Search results, study selection, study characteristics, and quality assessment

Figure 1 illustrates the flow diagram of the search study selection. The search strategy yielded 5326 potentially relevant articles. Since the acne mostly clinically determined as baseline characteristics of women with PCOS or secondary outcome measures, which did not present in the title or abstract, all articles were identified for further full-text assessment. Finally, we included 60 studies which included data of 240,213 women with PCOS and 1,902,022 healthy controls without PCOS for the meta-analysis. Table 1 presents the summary of studies assessing the prevalence of acne in both groups.

Details of the quality assessment of studies included are presented in supplementary tables 1-4. A total of 10 (16.6%) studies were classified as high [18-27], 46 (76.6%) as moderate [28-73]; and 4 (6.6%) had low quality [74-77].

A total of 7 studies conducted among adolescents [20, 25-27, 47, 62, 65], 31 in adults [14, 18, 19, 22-24, 28-39, 42-44, 64, 66-70, 72, 73, 75-77] and 22 in reproductive age of adults and adolescents [21, 40, 41, 45, 46, 48-61, 63, 71, 74]. A total of 34 (56.7%) studies were cross-sectional [20, 24, 27-57, 77], 11 (18.3%) case-control [21, 65-69, 71-74,

76], 14 (23.3%) prospective or retrospective cohorts [18, 19, 22, 23, 25, 26, 58-64, 75] and 1 (1.6%) interventional study [70] published between 2004 and 2019.

In addition, 3 studies were conducted in the Australia [26, 55, 77], eight in USA and Canada [18, 19, 35, 43, 44, 51, 58, 62], one in chile [42], 7 in Europe including Denmark, Finland, Greece, Italy and UK [22, 23, 29, 34, 36, 64, 75], two in southeast Asia including Thailand and Vietnam [27, 30], 12 in east Asia including China and Taiwan [21, 31, 33, 39, 45, 47, 56, 59-61, 73], 5 in south Asia including India and Pakistan [28, 50, 52, 68, 76] and 22 in west Asia including Iran, Jordan, Oman, Palestine, Qatar and Turkey [20, 24, 25, 32, 37, 38, 40, 41, 46, 48, 49, 53, 54, 63, 65-67, 69-72, 74]. Most of the studies (76.7%) used Rotterdam diagnostic criteria for PCOS definition [20-24, 27-33, 36, 39-42, 44, 45, 47-54, 56, 57, 59-61, 63-66, 68-77], 11.7% NIH criteria [25, 26, 37, 38, 43, 55, 58], 6.7% AES criteria [35, 46, 62, 67], 3.3% ICD-9 [18, 19, 61] and also one study did not present PCOS diagnostic criteria [34].

Meta-analysis and meta-regression of outcomes

The results of all meta-analysis and meta-regression in different subgroups are presented in table 2. The overall pooled prevalence of acne among women with and without PCOS, regardless of age groups, PCOS diagnostic criteria and geographical region, was 43% (95% CI: 41–45%) and 21% (95% CI: 19–22%), respectively (Table 2, and Fig 2A and B). In this respect, the odds of acne among women with PCOS was 1.6-fold higher than among healthy controls (Pooled overall OR:1.67, 95% CI: 1.52, 1.83) (Table 2).

However, the pooled prevalence of acne in adults, older than 19 years and in adolescents PCOS patients were 42% and 59%, respectively, which were significantly higher than non-PCOS counterparts (Pooled P in adults: 42% vs. 17%, Pooled OR=1.58, 95% CI: 1.44, 1.75) and (Pooled P in adolescents: 59% vs. 39%, Pooled OR=2.77, 95% CI: 1.32, 5.83), (Figure 3 A&B). The pooled prevalence of acne in reproductive age group was close to adult group and was 40% in PCOS and 19% in non-PCOS counterparts, which was significantly 2.88 higher than non-PCOS group.

The pooled estimated prevalence of acne in adults PCOS women was 76% (95% CI: 66-86%) using the NIH definition and 36% (95% CI: 33-39%) by Rotterdam criteria, both were significantly higher than non-PCOS counterparts (Pooled OR=3.09, 95% CI: 1.88, 5.06) and (Pooled OR=1.60, 95% CI: 1.39, 1.85), respectively.

The pooled prevalence of acne in adolescents PCOS patients was 66% (45-87%) by NIH criteria and 60% (48-73%) using Rotterdam definition, both are significantly higher than non-PCOS counterparts (Pooled OR=2.84, 95% CI: 1.12, 7.20) and (Pooled OR=3.50, 95% CI: 1.67, 7.32), respectively.

Moreover, we performed a subgroup analysis in adult population, based on diagnostic criteria in different geographic regions. Based on available data, in subgroup of adults, who used Rotterdam definition for PCOS, the highest prevalence of acne was reported in east Asia PCOS patients. The pooled prevalence of acne among women with vs. without PCOS in these geographical regions were 48% vs. 17% respectively, which were significantly 3.5 fold higher than non-PCOS counterparts, (Pooled OR=3.55, 95% CI: 1.30, 9.67). The pooled prevalence of acne in adults women with vs. without PCOS population in other region was 29% (26, 32%) vs. 21% (18, 24%) in Europe, 42% (28-57%) vs. 19% (9-28%) in west Asia and finally 23% (9-36%) vs. 9% (1-17%) south Asia and all of them were significantly higher than non-PCOS population (Table 2). Due to lack of sufficient studies, we could not perform the subgroup meta-analyses based on all geographical regions, other PCOS diagnostic criteria and in other age groups.

Publication bias and risk of bias

We have done sensitivity analysis to assess the reliability of our results in estimate the pooled prevalence (Figure 3 A&B). We have excluded each study one by one and looked for any significant change in the results. The analysis did not find any influence of a single study on the overall estimates obtained, therefore none of studies has been excluded. However, there was substantial publication bias for most of analyses based on the Begg's test (Tables 2). Therefore, trim and fill method were used for publication bias correction. In addition, Logit transformation was used for single proportion.

Overall most of studies were judged as having low risk of bias for the evaluated domains; details are presented in Supplementary figure 1-4, as shown as shown most cross-sectional and case–control studies had a low risk of bias in the assessment of exposure, development of outcome of interest in case and controls and control of prognostic variable, and high risk of bias in selection of cases and controls. In addition, cohort studies had a low or probability risk of bias for all domains of selection of exposed and non-exposed cohorts, assessment of exposure, presence of outcome of interest at start of study, outcome assessment, and assessment of the presence or absence of prognostic factors; however approximately, half of them had a probability high risk of bias in controlling prognostic variables and adequacy of follow up of cohorts. However, one interventional study had low or probability low risk of bias in all domain.

Discussion

Our findings indicate that the acne is one of the most common cutaneous features of PCOS. Approximately half of PCOS patients have suffered from acne, significantly 1.6-fold higher than non-PCOS women. In addition, 60 percent

of adolescent PCOS patients has experienced the acne, significantly 2.7-fold higher than non-PCOS adolescents. As expected, prevalence of acne was higher by using NIH definition for PCOS.

Polycystic ovary syndrome is a complex disorder affecting reproductive and metabolic systems [78, 79]. It also has cutaneous manifestations such as acne, classically associated with excessive androgen secretion [51]. Acne is a multifactorial, inflammatory disease of the pilosebaceous unit with lesions, mostly on the face. Although, acne is often overlooked as an expression of excessive androgen secretion [80], the importance of androgens in the pathogenesis of acne is well documented. It has been known that sebaceous glands are androgen target tissues [81]. Androgen hormones may promote follicular epidermal hyperproliferation and plugging, increase sebum production and cause abnormal desquamation of follicular epithelial cells. In addition, sebaceous glands contain most of the steroidogenic enzymes for the conversion of inactive adrenal precursors including dehydroepiandrosterone (DHEA), DHEA-sulfate (DHEA-S), and androstenedione into potent androgens, including testosterone and dihydrotestosterone (DHT) that could enhance sebaceous gland activity [82, 83]. Because the effects of testosterone and DHT are mediated by binding to the nuclear androgen receptor (AR), also expressed in human sebaceous gland cells. hypersensitivity of the androgen receptor may be one of the mechanisms determining acne lesions in women [84].

Because of the underlying role of hyperandrogenism in pathophysiology of PCOS, an increase prevalence of acne in these patients is expected. It can negatively influence feelings of well-being and quality of life and also cause additional psychological distress to women who are probably coping with other PCOS problems [85].

The results of current meta-analysis demonstrated that acne affected approximately half of patients with PCOS [1], which is much higher than previous report. In this respect, Bozdag et al. (2016) in a meta-analysis of limited 12 trials reported that the prevalence of acne in women with PCOS was 16% (8–26%) [1]. The differences may be due the acne was the secondary outcome in mentioned study, and therefore the inclusion criteria were different from our study, consequently, leads to different type and number of studies included.

Notably, although, acne is a common problem in adolescents [86], our study showed that prevalence of acne in adolescents PCOS patients was more than 2.7 fold higher than non-PCOS adolescents. Physiological elevation of adrenal and ovarian androgens during the onset of puberty [87], in addition to pathological androgen excess of PCOS, might be related to the higher prevalence of acne in those subgroups of population.

Changes in the diagnostic criteria greatly affect the prevalence of acne in PCOS patients. When the studies evaluating prevalence of acne using NIH and Rotterdam criteria were considered, overall higher prevalence rates of acne were

found. There were no data available for AE-PCOS Society criteria. In relation to this finding, since the all PCOS patients with NIH definition had hyperandrogenism, it is hypothesized that acne as signs of cutaneous hyperandrogenism in these patents are more prevalent.

Interestingly, heterogeneity regarding rates of acne was obvious among the various regions. With regard to available studies, the data generated for east Asia, including China and Taiwan suggested a highest prevalence of 48% for acne in adult PCOS patients, where it was 3.5-fold higher than non-PCOS women. However, we did not have enough data for estimation the prevalence of acne in north America and Africa regions. It should be noted that the prevalence of acne in adult PCOS patients in Asia had high heterogenicity and the overall reported CI in those regions were quite wide, pointing to the complexity of data. Limited number of studies included in those region and small sample size may affect the results.

The strength and limitation of current study should be addressed. The main strength of this meta-analysis was performing the critical appraisal of quality which showed that more than 90% of included studies had high or moderate quality and overall judged low risk of bias. Therefore, the results of meta-analysis would be reliable. In terms of drawbacks, although, it is unclear whether the prevalence of acne is significantly increased in clinical-based studies over that observed in the general-population, potential selection bias of including population and non-population based studies in current meta-analysis cannot be ruled out. Most studies conducted across the world are limited by small sample size, selection bias, and lack of comparability across studies. However, since there has not yet been a study generated for all geographical region, such as Africa, and in various age-groups, and even with different diagnostic criteria, we were unable to produce acne prevalence rate to incorporate into the meta-analysis. Moreover, although the scientific societies recommended for using strict criteria for the diagnosis of PCOS in adolescent, however, most available data used the adults PCOS definition for adolescents population that may affect the results.

In addition, the exclusion of non-English articles might also have influenced the reported proportions and result in underrepresentation of some populations. However, there was significant heterogeneities among studies. This heterogeneous finding highlights the importance of ethnic variation in the prevalence of acne among PCOS patients. From the perspective of methodology, this finding may once again be seen to underline the importance of screening an unselected population, rather than acquiring the selected cohort of women. In addition, the variability in diagnostic criteria for PCOS, BMI, race, and ethnicity of participants may play a role. Reciprocally, we used random effect analysis to deal with these issues. In addition, publication bias, most common sources for errors in metanalysis was

found in our study. However, we conducted trim and fill correction to minimize those effect. All these limitations should be considered to interpretations of the findings.

Conclusions

In conclusion, based on the available data, acne is one of the most prevalent cutaneous features in PCOS patients. In addition, results highlight geographical differences in participant-reported acne among PCOS patients, physicians should be sensitive to these issues and approach patients in a caring and sympathetic manner. Further study is needed to provide data in various geographical region.

List of abbreviations

PCOS: Polycystic ovary syndrome; IR: insulin resistance; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; P: prevalence; BMI: body mass index; NIH: National Institutes of Health; OR: odds ratio.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The current study was based on results of relevant published studies.

Competing interests

The authors have no conflict of interest to declare.

Funding

None.

Authors' contribution

SBG was involved in study design, search in databases, quality assessment, study selection, data extraction, manuscript drafting and critical discussion. FRT conceptualized the study and was involved in study design, revising manuscript, and critical discussion. MSQ contribute in quality assessment and critical discussion. RBY contributed in statistical analysis, interpreting data and manuscript drafting. EC conceptualized the study and was involved in study design, revising manuscript, and critical discussion. All authors read and approved the final manuscript.

Acknowledgments

None.

Authors' information

[1] Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2] Faculty of Nursing and Health Sciences, Nord University, Bodø, Norway.

[3] Department of Health Promotion, Mother and Child Care and General and Specialist Medicine, University of Palermo Medical School, Palermo, Italy

References:

1. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2016;31:2841-55.

2. Behboudi-Gandevani S, Ramezani Tehrani F, Rostami Dovom M, Farahmand M, Bahri Khomami M, Noroozzadeh M, et al. Insulin resistance in obesity and polycystic ovary syndrome: systematic review and meta-analysis of observational studies. Gynecol Endocrinol. 2016;32:343-53.

3. Behboudi-Gandevani S, Tehrani FR, Yarandi RB, Noroozzadeh M, Hedayati M, Azizi F. The association between polycystic ovary syndrome, obesity, and the serum concentration of adipokines. J Endocrinol Invest. 2017;40:859-66.

4. Amiri M, Tehrani FR, Bidhendi-Yarandi R, Behboudi-Gandevani S, Azizi F, Carmina E. Relationships between biochemical markers of hyperandrogenism and metabolic parameters in women with polycystic ovary syndrome: A systematic review and meta-analysis. Horm Metab Res. 2019;51:22-34.

5. Chuan SS, Chang RJ. Polycystic ovary syndrome and acne. Skin Therapy Lett. 2010;15:1-4.

6. Ramezani Tehrani F, Behboudi-Gandevani S, Simbar M, Azizi F. A population-based study of the relationship between idiopathic hirsutism and metabolic disturbances. J Endocrinol Invest. 2015;38:155-162.

7. Tan A, Schlosser BJ, Paller A. A review of diagnosis and treatment of acne in adult female patients. Int J Womens Dermatol. 2018;4(2):56-71.

8. Bhate K, Williams H. Epidemiology of acne vulgaris. Br J Dermatol. 2013;168:474-85.

9. Ghodsi SZ, Orawa H, Zouboulis CC. Prevalence, severity, and severity risk factors of acne in high school pupils: a community-based study. J Invest Dermatol. 2009;129:2136-41.

10. Arora MK, Yadav A, Saini V. Role of hormones in acne vulgaris. Clin Biochem. 2011;44:1035-40.

11. Carmina E. Cutaneous manifestations of Polycystic ovary syndrome. Curr Opinion Endocr Metab Res. 2020.

12. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009;91:456-88.

13. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS med. 2009;6:e1000097.

14. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute; 2009. Available in March 2016.

15. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux P, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg. 2012;10:28-55.

16. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. bmj. 2016;355:i4919.

17. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Bmj. 2011;343:d5928.

18. Bird ST, Hartzema AG, Brophy JM, Etminan M, Delaney JA. Risk of venous thromboembolism in women with polycystic ovary syndrome: a population-based matched cohort analysis. CMAJ. 2013;185:E115-E20.

19. Bird ST, Hartzema AG, Etminan M, Brophy JM, Delaney JA. Polycystic ovary syndrome and combined oral contraceptive use: a comparison of clinical practice in the United States to treatment guidelines. Gynecol Endocrinol. 2013;29:365-9.

20. Esmaeilzadeh S, Delavar MA, Amiri M, Khafri S, Pasha NG. Polycystic ovary syndrome in Iranian adolescents. Int J Adolesc Med Health. 2014;26:559-65.

21. Zhang J, Liu Y, Liu X, Xu L, Zhou L, Tang L, et al. High intake of energy and fat in Southwest Chinese women with PCOS: a population-based case-control study. PloS one. 2015;10.

22. Balachandran K, Sumilo D, O'Reilly MW, Toulis KA, Gokhale K, Wijeyaratne C, et al. Increased risk of obstructive sleep apnoea in women with polycystic ovary syndrome: a population-based cohort study. Eur J Endocrinol. 2019; 180: 265–272.

23. Kumarendran B, O'Reilly MW, Manolopoulos KN, Toulis KA, Gokhale KM, Sitch AJ, et al. Polycystic ovary syndrome, androgen excess, and the risk of nonalcoholic fatty liver disease in women: a longitudinal study based on a United Kingdom primary care database. PLoS Med. 2018 Mar 28;15:e1002542.

24. Tehrani FR, Rashidi H, Khomami MB, Tohidi M, Azizi F. The prevalence of metabolic disorders in various phenotypes of polycystic ovary syndrome: a community based study in Southwest of Iran. Reprod Biol Endocrinol.2014;12:89.

25. Ates S, Aydın S, Ozcan P, Soyman Z, Gokmen Karasu AF, Sevket O. Clinical and metabolic characteristics of Turkish adolescents with polycystic ovary syndrome. J Obstet Gynaecol. 2018;38:236-240.

26. Hickey M, Sloboda D, Atkinson H, Doherty D, Franks S, Norman R, et al. The relationship between maternal and umbilical cord androgen levels and polycystic ovary syndrome in adolescence: a prospective cohort study. J Clin Endocrinol Metab. 2009;94:3714-20.

27. Kaewnin J, Vallibhakara O, Arj-Ong Vallibhakara S, Wattanakrai P, Butsripoom B, Somsook E, et al. Prevalence of polycystic ovary syndrome in Thai University adolescents. Gynecol Endocrinol. 2018;34:476-80.

28. Akram M, Roohi N. Endocrine correlates of polycystic ovary syndrome in Pakistani women. J Coll Physicians Surg Pak. 2015;25:22-6.

29. Belosi C, Selvaggi L, Apa R, Guido M, Romualdi D, Fulghesu A, et al. Is the PCOS diagnosis solved by ESHRE/ASRM 2003 consensus or could it include ultrasound examination of the ovarian stroma? Hum Reprod. 2006;21:3108-15.

30. Cao NT, Le MT, Nguyen VQH, Pilgrim J, Le VNS, Le DD, et al. Defining polycystic ovary syndrome phenotype in Vietnamese women. J Obstet Gynaecol Res. 2019;45:2209-19.

31. Chen C-H, Wang P-H, Hsieh M-T, Tzeng C-R, Wu Y-H, Lee C-S, et al. Sexual orientations of women with polycystic ovary syndrome: Clinical observation in Taiwan. Taiwan J Obstet Gynecol. 2014;53:542-6.

32. Ercan C, Coksuer H, Aydogan U, Alanbay I, Keskin U, Karasahin K, et al. Sexual dysfunction assessment and hormonal correlations in patients with polycystic ovary syndrome. Int J Impot Res. 2013;25:127-32.

33. Feng Jg, Guo Y, Ma La, Xing J, Sun Rf, Zhu W. Prevalence of dermatologic manifestations and metabolic biomarkers in women with polycystic ovary syndrome in north China. J Cosmet Dermatol. 2018;17:511-7.

34. Hart K, Barr S, Reeves S, Sharp K, Jeanes Y. Suboptimal dietary intake is associated with cardiometabolic risk factors in women with polycystic ovary syndrome. Nutr Diet. 2016;73:177-83.

35. Kazemi M, Pierson RA, Lujan ME, Chilibeck PD, McBreairty LE, Gordon JJ, et al. Comprehensive evaluation of type 2 diabetes and cardiovascular disease risk profiles in reproductive-age women with polycystic ovary syndrome: a large Canadian cohort. J Obstet Gynaecol Can. 2019;41:1453-60.

36. Lauritsen MP, Bentzen J, Pinborg A, Loft A, Forman JL, Thuesen L, et al. The prevalence of polycystic ovary syndrome in a normal population according to the Rotterdam criteria versus revised criteria including anti-Müllerian hormone. Hum Reprod. 2014;29:791-801.

37. Musmar S, Afaneh A, Mo'alla H. Epidemiology of polycystic ovary syndrome: a cross sectional study of university students at An-Najah national university-Palestine. Reprod Biol Endocrinol. 2013;11:47.

38. Sharif E, Rahman S, Zia Y, Rizk NM. The frequency of polycystic ovary syndrome in young reproductive females in Qatar. Int J Womens Health. 2017;9:1.

39. Tan J, Wang Q-Y, Feng G-M, Li X-Y, Huang W. Increased risk of psychiatric disorders in women with polycystic ovary syndrome in Southwest China. Chin Med J. 2017;130:262.

40. Al-Jefout M, Alnawaiseh N, Al-Qtaitat A. Insulin resistance and obesity among infertile women with different polycystic ovary syndrome phenotypes. Sci Rep. 2017;7:1-9.

41. Erdoğan M, Karadeniz M, Alper G, Tamsel S, Uluer H, Cağlayan O, et al. Thrombin-activatable fibrinolysis inhibitor and cardiovascular risk factors in polycystic ovary syndrome. Exp Clin Endocrinol Diabetes. 2008;116:143-7.

42. Villarroel C, Trejo L, Muñoz A, Kohen P, Fuentes A, Devoto L. Assessment of diagnostic competence of plasmatic androgens on polycystic ovary syndrome based on receiver operator characteristic curves. Gynecol Endocrinol. 2010;26:600-6.

43. Welt C, Arason G, Gudmundsson J, Adams J, Palsdottir H, Gudlaugsdottir G, et al. Defining constant versus variable phenotypic features of women with polycystic ovary syndrome using different ethnic groups and populations. J Clin Endocrinol Metab. 2006;91:4361-8.

44. Welt C, Gudmundsson J, Arason G, Adams J, Palsdottir H, Gudlaugsdottir G, et al. Characterizing discrete subsets of polycystic ovary syndrome as defined by the Rotterdam criteria: the impact of weight on phenotype and metabolic features. J Clin Endocrinol Metab. 2006;91:4842-8.

45. Chun-Sen H, Chien-Hua W, Wan-Chun C, Ching-Tzu L, Chun-Jen C, Ming-I H. Obesity and insulin resistance in women with polycystic ovary syndrome. Gynecol Endocrinol. 2011;27:300-6.

46. Köşüş N, Köşüş A, Turhan NÖ, Kamalak Z. Do threshold values of ovarian volume and follicle number for diagnosing polycystic ovarian syndrome in Turkish women differ from western countries? Eur J Obstet Gynecol Reprod Biol. 2011;154:177-81.

47. Li L, Chen X, He Z, Zhao X, Huang L, Yang D. Clinical and metabolic features of polycystic ovary syndrome among Chinese adolescents. J Pediatr Adolesc Gynecol. 2012;25:390-5.

48. Moini A, Eslami B. Familial associations between polycystic ovarian syndrome and common diseases. J Assist Reprod Genet. 2009;26:123-7.

49. Öztürk A, Kucur SK, Seven A, Deveci E, Şencan H, Yilmaz O, et al. Temperament and character differences of patients with polycystic ovary syndrome. J Gynecol Obstet Hum. 2019;48:255-9.

50. Rashid A, Bhat JA, Ganie MA, Wani IA, Bhat MH, Shah ZA, et al. Evaluation of serum anti-nuclear antibody among women with PCOS: a hospital based single center cross sectional study. Gynecol Endocrinol. 2018;34:965-9.

51. Schmidt TH, Khanijow K, Cedars MI, Huddleston H, Pasch L, Wang ET, et al. Cutaneous findings and systemic associations in women with polycystic ovary syndrome. JAMA dermatol. 2016;152:391-8.

52. Shabir I, Ganie MA, Praveen EP, Khurana ML, John J, Gupta N, et al. Morning plasma cortisol is low among obese women with polycystic ovary syndrome. Gynecol Endocrinol. 2013;29:1045-7.

53. Shahrami SH, Ranjbar ZA, Milani F, Kezem-Nejad E, Rad AH, Heirat SFD. The relation between diverse phenotypes of PCOS with clinical manifestations, anthropometric indices and metabolic characteristics. Acta Med Iran. 2016:134-9.

54. Sulaiman MA, Al-Farsi YM, Al-Khaduri MM, Waly MI, Saleh J, Al-Adawi S. Psychological burden among women with polycystic ovarian syndrome in Oman: a case–control study. Int J Womens Health. 2017;9:897.

55. Varanasi LC, Subasinghe A, Jayasinghe YL, Callegari ET, Garland SM, Gorelik A, et al. Polycystic ovarian syndrome: prevalence and impact on the wellbeing of Australian women aged 16–29 years. Aust N Z J Obstet Gynaecol. 2018;58:222-33.

56. Zhang H, Zhu F, Xiong J, Shi X, Fu S. Characteristics of different phenotypes of polycystic ovary syndrome based on the Rotterdam criteria in a large- scale Chinese population. BJOG. 2009;116:1633-9.

57. Zhao Y, Ruan X, Mueck AO. Clinical and laboratory indicators of polycystic ovary syndrome in Chinese Han nationality with different Rotterdam criteria-based phenotypes. Gynecol Endocrinol. 2016;32:151-6.

58. DeUgarte CM, Bartolucci AA, Azziz R. Prevalence of insulin resistance in the polycystic ovary syndrome using the homeostasis model assessment. Fertil Steril. 2005;83:1454-60.

59. Hsu M-I, Liou T-H, Liang S-J, Su H-W, Wu C-H, Hsu C-S. Inappropriate gonadotropin secretion in polycystic ovary syndrome. Fertil Steril. 2009;91:1168-74.

60. Lam P, Raine-Fenning N, Cheung L, Haines C. Three-dimensional ultrasound features of the polycystic ovary in Chinese women. Ultrasound Obstet Gynecol. 2009;34:196-200.

61. Liou T-H, Yang J-H, Hsieh C-H, Lee C-Y, Hsu C-S, Hsu M-I. Clinical and biochemical presentations of polycystic ovary syndrome among obese and nonobese women. Fertil Steril. 2009;92:1960-5.

62. Roe AH, Prochaska E, Smith M, Sammel M, Dokras A. Using the Androgen Excess–PCOS Society criteria to diagnose polycystic ovary syndrome and the risk of metabolic syndrome in adolescents. J Pediatr. 2013;162:937-41.

63. Sahin M, Demircioglu D, Oguz A, Tuzun D, Sarica MA, Inanc E, et al. Does insulin resistance increase thyroid volume in patients with polycystic ovary syndrome? Arch Endocrinol Metab. 2017;61:145-51.

64. Taponen S, Ahonkallio S, Martikainen H, Koivunen R, Ruokonen A, Sovio U, et al. Prevalence of polycystic ovaries in women with self-reported symptoms of oligomenorrhoea and/or hirsutism: Northern Finland Birth Cohort 1966 Study. Hum Reprod. 2004;19:1083-8.

65. Cankaya S, Demir B, Aksakal SE, Dilbaz B, Demirtas C, Goktolga U. Insulin resistance and its relationship with high molecular weight adiponectin in adolescents with polycystic ovary syndrome and a maternal history of polycystic ovary syndrome. Fertil Steril. 2014;102:826-30.

66. Eser A, Erpolat S, Kaygusuz I, Balci H, Kosus A. Investigation of Demodex folliculorum frequency in patients with polycystic ovary syndrome. An Bras Dermatol. 2017;92:807-10.

67. Hosseini MS, Dizavi A, Rostami H, Parastouei K, Esfandiari S. Healthy eating index in women with polycystic ovary syndrome: A case-control study. Int J Reprod Biomed. 2017;15:575.

68. Mangalath AAM, Alias A, Sajith M, Nimbargi V, Kumdale S. Sociodemographic characteristics and clinical presentation of infertile women with polycystic ovary syndrome in a tertiary care hospital. Int J Infertil Fetal Med. 2018;9:14-8.

69. Rashidi BH, Shams S, Shariat M, Jaliseh HK, Mohebi M, Haghollahi F. Evaluation of serum hepcidin and iron levels in patients with PCOS: a case-control study. J Endocrinol Invest. 2017;40:779-84.

70. Shishehgar F, Mirmiran P, Rahmati M, Tohidi M, Tehrani FR. Does a restricted energy low glycemic index diet have a different effect on overweight women with or without polycystic ovary syndrome? BMC Endocr Disord. 2019;19:93.

71. Sulaiman MA, Al-Farsi YM, Al-Khaduri MM, Saleh J, Waly MI. Polycystic ovarian syndrome is linked to increased oxidative stress in Omani women. Int J Womens Health. 2018;10:763.

72. Vural B, Caliskan E, Turkoz E, Kilic T, Demirci A. Evaluation of metabolic syndrome frequency and premature carotid atherosclerosis in young women with polycystic ovary syndrome. Hum Reprod. 2005;20:2409-13.

73. Zhang HY, Guo CX, Zhu FF, Qu PP, Lin WJ, Xiong J. Clinical characteristics, metabolic features, and phenotype of Chinese women with polycystic ovary syndrome: a large-scale case–control study. Arch Gynecol Obstet. 2013;287:525-31.

74. Anaforoglu I, Algun E, Incecayir O, Ersoy K. Higher metabolic risk with National Institutes of Health versus Rotterdam diagnostic criteria for polycystic ovarian syndrome in Turkish women. Metab Syndr Relat Disord. 2011;9:375-80.

75. Dalamaga M, Papadavid E, Basios G, Vaggopoulos V, Rigopoulos D, Kassanos D, et al. Ovarian SAHA syndrome is associated with a more insulin-resistant profile and represents an independent risk factor for glucose abnormalities in women with polycystic ovary syndrome: A prospective controlled study. J Am Acad Dermatol. 2013;69:922-30.

76. Jacob R, Jude K, Chandrasekhar R, Sasikala K. Prevalence of Acne among women with Poly Cystic Ovarian Syndrome –a clinical study. Scrutiny International Research Journal of Health and Medical Science (SIRJ-HMS). 2014;1.

77. Moran L, Gibson-Helm M, Teede H, Deeks A. Polycystic ovary syndrome: a biopsychosocial understanding in young women to improve knowledge and treatment options. J Psychosom Obstet Gynaecol. 2010;31:24-31.

78. Behboudi- Gandevani S, Amiri M, Bidhendi Yarandi R, Noroozzadeh M, Farahmand M, Rostami Dovom M, et al. The risk of metabolic syndrome in polycystic ovary syndrome: A systematic review and meta- analysis. Clin Endocrinol (Oxf). 2018;88:169-84.

79. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab. 2004;89:2745-9.

80. Carmina E, Lobo RA. A comparison of the relative efficacy of antiandrogens for the treatment of acne in hyperandrogenic women. Clin Endocrinol (Oxf). 2002;57:231-4.

81. Lai J-J, Chang P, Lai K-P, Chen L, Chang C. The role of androgen and androgen receptor in skin-related disorders. Arch Dermatol Res. 2012;304:499-510.

82. Makrantonaki E, Ganceviciene R, Zouboulis C. An update on the role of the sebaceous gland in the pathogenesis of acne. Dermatoendocrinol. 2011;3:41-9.

83. Ebede TL, Arch EL, Berson D. Hormonal treatment of acne in women. J Clin Aesthet Dermatol. 2009;2:16-22.

84. Demirkan S, Sayın DB, Gündüz Ö. CAG polymorphism in the androgen receptor gene in women may be associated with nodulocystic acne. Postepy Dermatol Alergol. 2019;36:173-6.

85. Brady C, Mousa SS, Mousa SA. Polycystic ovary syndrome and its impact on women's quality of life: More than just an endocrine disorder. Drug Healthc Patient Saf. 2009;1:9-15.

86. Lynn DD, Umari T, Dunnick CA, Dellavalle RP. The epidemiology of acne vulgaris in late adolescence. Adolesc Health Med Ther. 2016;7:13-25.

87. Archer JS, Chang RJ. Hirsutism and acne in polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2004;18:737-54.

Table 1. Summary of studies assessing acne prevalence in women with and without PCOS

Author, year	Country	PCOS Diagnostic Criteria	Study Design	Age Group	PCOS characteristics *	Non-PCOS characteristics *	Prevalence of Acne in PCOS	Prevalence of acne in Non-PCOS, N (%)
Akram, et al. 2015	Pakistan	Rotterdam	cross-sectional	Adult	N= 65, Age: 26.71, BMI: 26.23 (4.46)	N= 50, Age: 19.67, BMI: 20.81 (3.01)	21 (32.31)	9 (18)
Al-Jefout, et al. 2017	Jordan	Rotterdam	cross-sectional	Adult and adolescent	N= 159, Age: 24 (22–29), BMI: 28 (4.51)	N= 54, Age: 24 (22.8 – 25.3), BMI: 27.6 (5.4)	9 (5.7)	2 (3.7%)
Anaforoglu, et al. 2011	Turkey	1-Rotterdam 2-NIH	case-control	Adult and adolescent	N1= 54, Age1: 22.5 (5.9), BMI1: 28.1 (6.4) N2= 121, Age2: 23.3 (6.4), BMI2: 30.3 (8.4)	N= 109, Age: 24.5 (6.9), BMI: 27.5 (7)	1- 5 (9.3) 2- 23 (19)	9 (8.3)
Ates, et al. 2018	Turkey	NIH	cohort	Adolescent	N= 77, Age: 17.68 (1.19), BMI: 24.87 (5.03)	N= 33, Age: 17.94 (1.05), BMI: 21.42 (2.73)	43 (55.8)	7 (21.2)
Belosi, et al. 2006	Italy	1- Rotterdam/NIH 2- Rotterdam	cross-sectional	Adult	N1= 273, Age1: 26.38 (5.76), BMI1: 26.86 (6.11) N2= 72, Age2: , BMI2: 24.90 (4.75)	N= 27, Age: 24.81 (5.63), BMI: 21.80 (3.30)	1-10 (28.5) 2- 3 (8.1)	6 (22.2)
Bird, et al. 2013	USA	ICD-9	Population based cohort	Adult	N= 43506, Age: 28.7, BMI: NM	N= 43506, Age: 28.9, BMI: NM	10507 (24.15)	8549 (19.65)
Bird, et al. 2013	USA	ICD-9	Population based cohort	Adult	N= 46867, Age: 28.70, BMI: NM	N= 1585811, Age: 28.60, BMI: NM	11248 (24)	273552 (17.25)
Cankaya, et al. 2014	Turkey	Rotterdam	case-control	Adolescent	N= 39, Age: 17.79 (1.59), BMI: 21.51 (1.92)	N= 40, Age: 17.43 (1.69), BMI: 21.25 (1.75)	15 (38.40)	0
Cao, et al. 2019	Vietnam	Rotterdam	cross-sectional	Adult	N= 479, Age: 29.0 (4.12), BMI: 21.00 (2.83)	N= 422, Age: 31.65 (4.19), BMI: 20.56 (2.20)	114 (23.8)	21 (5)
Chen, et al. 2014	Taiwan	Rotterdam	cross-sectional	Adult	N= 89, Age: 26.5(5.6), BMI: 22.5 (5.2)	N= 78, Age: 30.7 (6.5), BMI: 22.4 (5.0)	54 (60.7)	18 (23.1)
Chun-Sen, et al. 2011	Taiwan	Rotterdam	Retrospective cross-sectional	Adult and adolescent	1: HA+PCOM, N1= 125, Age1: 26.6 (5.8), BMI1: 24.9 (5.9) 2: HA+ANOV, N2= 25, Age2: 26.4 (4.7), BMI2: 25.2 (5.9) 3: HA+PCOM: N3= 37, Age3: 27.1 (4.9), BMI3: 25.0 (4.9) 4: ANOV+PCOM: N4= 46, Age4: 27.4 (4.5), BMI4: 25.1 (6.5)	N= 40, Age: 27.2 (5.2), BMI: 24.3 (4.3)	1-66 (53) 2-17 (68) 3-27 (73) 4-0	0
Dalamaga, et al, 2013	Greece	Rotterdam	Cohort	Adult	1-PCOS with SAHA€ N1= 56, Age1: 24.9 (6.2), BMI1: 28.7 (8.04) B-PCOS without SAHA N2= 260, Age2: 24.8 (5.5), BMI2: 24.9 (6.3)	N= 102, Age: 24.2 (5.7), BMI: 24.6 (4.9)	1-56 (100) 2-126 (48.5)	0
DeUgarte, et al. 2005	USA	NIH	case-control	Adult and adolescent	N= 271, Age: 27.4 (7.5), BMI: 36.4 (9.6)	N= 260, Age: 36.5 (13.8), BMI: 27.8 (6.8)	57 (21)	0
Ercan, et al. 2013	Turkey	Rotterdam	cross-sectional	Adult	N= 32, Age: 27.4 (3.3), BMI: 25.5 (3.0)	N= 32, Age: 27.0 (3.2), BMI: 24.4 (3.6)	14 (43.7)	0
Erdoğan, et al. 2008	Turkey	Rotterdam	cross-sectional	Adult and adolescent	N= 68, Age: 24.27 (5.44), BMI: 24.41 (5.43)	N= 26, Age: 26.41 (5.65), BMI: 23.35 (5.04)	36 (53)	0
Eser, et al. 2017	Turkey	Rotterdam	case-control	Adult	N= 41, Age: 24 (19-40), BMI: 27.3 (5.7)	N= 47, Age: 24 (19-42), BMI: 26.9 (5.7)	29 (70.7)	20 (42.6)
Esmaeilzadeh, et al. 2014	Iran	Rotterdam	Population based cross-sectional	Adolescent	N= 129, Age: 18.0 (1.0), BMI: 22.2 (4.4)	N= 1420, Age: 17.2 (0.84), BMI: 21.8 (4.1)	66 (51.2)	242 (17)

Feng, et al. 2018	China	Rotterdam	Cross-sectional	Adult	N= 186, Age: NM, BMI: NM	N= 113, Age: NM, BMI: NM	Total: 115 (61.8) Mild: 68 (36.6) Moderate: 25 (13.4) Severe: 16 (8.6) Very severe: 6 (3.2)	Total: 50 (44.2) Mild: 32 (28.3) Moderate: 10 (8.8) Severe: 4 (3.5) Verysevere: 4 (3.5)
Hart, et al. 2016	UK	NM	Cross-sectional	Adult	N= 38, Age: 30.8 (5.8), BMI: 24.5 (4.1)	N= 30, Age: 29.3 (6.5), BMI: 23.5 (4.1)	40 (15)	17 (5)
Hickey, et al. 2009	Australia	1-NIH 2- Rotterdam	cohort	Adolescent	N1= 36, Age1: 15.4 (0.55), BMI1: 25.8 (5.6) N2= 66, Age2: 15.3 (0.55), BMI2: 24.3 (5.1)	N1= 190, Age1: 15.2 (0.46), BMI1: 22.1 (3.1) N2= 161, Age2: 15.2 (0.44), BMI2: 22.1 (3.0)	Total1: 28 (77.7) Mild1: 21 (58.3) Moderate1: 7 (19.4) Total2: 47 (71.20) Mild2: 33 (50.0) Moderate2: 14 (21.2)	Total: 124 (65.7) Mild: 86 (45.3) Moderate1: 39 (20.5) Total2: 107 (66.4) Mild2: 86 (45.3) Moderate2: 39 (20.5)
Hosseini, et al. 2017	Iran	AES	Case-control	Adult	N= 99, Age: 29.0 (5.5), BMI: 26.6 (5.0)	N= 198, Age: 29.2 (6.0), BMI: 26.0 (4.0)	30 (30.6)	10 (5.1)
Hsu, et al. 2009	Taiwan	Rotterdam	cohort	Adult and adolescent	N= 251, Age: 27.2 (5.5), BMI: NM	N= 48, Age: 29.2 (5.0), BMI: NM	43 (17)	0
Jacob, et al.	India	Rotterdam	case-control	Adult	N= 75, Age: NM, BMI: NM	N= 75, Age: NM, BMI: NM	21 (27)	7 (9)
Kaewnin, et al. 2017	Thailand	Rotterdam	Cross-sectional	Adolescent	N= 29, Age: 18.66 (0.49), BMI: 12.37 (1.32)	N= ,519 Age: 18.69 (0.47), BMI: 12.55 (1.06)	Total: 23 (79.3) Mild: 11 (37.93) Moderate: 12 (41.38)	Total: 200 (36.50) Mild: 177 (34.10) Moderate: 23 (4.43)
Kazemi, et al. 2019	Canada	AES	Cross-sectional	Adult	N= 237, Age: 27.7 (27.1−28.3), BMI: 32.2 (31.1−33.3)	N= 42, Age: 26.5 (25.3−27.7), BMI: 23.6 (22.4−24.8)	Total: 167 (70.4) Mild: 102 (43.0) Moderate: 52 (21.9) Severe: 13 (5.5)	Total: 28 (66.6) Mild: 21(50.0) Moderate: 7 (16.7) Severe: 0
Köşüş, et al. 2011	Turkey	AES	Cross-sectional	Adult and adolescent	N= 251, Age: 24.9 (6.1), BMI: 27.1 (6.2)	N= 65, Age: 26.7 (5.6), BMI: 20.8 (2.4)	72 (28.7)	0
Kumarendran, et al. 2018	UK	Rotterdam	Population based cohort	Adult	N= 63210, Age: 30.6 (7.1), BMI: NM	N= 121064, Age: 30.8 (7.1), BMI: NM	13,708 (21.69)	19,968 (16.49)
Kumarendran, et al 2019	UK	Rotterdam	Population based cohort	Adult	N= 76978, Age: 30.2 (7.4), BMI: 28.6 (7.6)	N= 143077, Age: 30.4 (7.3), BMI: 27.4 (6.4)	14,589 (19.0)	19,371 (13.5)
Lam, et al. 2009	China	Rotterdam	cohort	Adult and adolescent	1: Caucasian, N1= 40, Age1: 30.8 (5.2), BMI1: 27.35 (4.15) 2: Chinese, N2= 40, Age2: 32.4 (4.7), BMI2: 23.73 (4.49)	N= 40, Age: 32.7 (4.0), BMI: 21.23 (2.85)	Total1: 14 (28) Mild1: 4 (28.6) Moderate1: 7 (50) Severe1: 3 (21.4) Total2: 14 (35.0) Mild2: 4 (28.6) Moderate2: 7 (50) Severe2: 3 (21.4)	0
Lauritsen, et al. 2014	Denmark	Rotterdam	Cross-sectional	Adult	N= 74, Age: 31.5 (3.9), BMI: 24.2 (4.2)	N= 373, Age: 33.9 (3.9), BMI: 22.9 (3.4)	36 (48.6)	185 (49.6)
Li, et al. 2012	China	Rotterdam	Cross-sectional	Adolescent	N= 91, Age: 17.59 (1.36), BMI: 22.00 (4.87)	N= 26, Age: 17.38 (0.75), BMI: 19.73 (1.63)	59 (64)	5 (19)
Liou, et al. 2008	Taiwan	Rotterdam	cohort	Adult and adolescent	N= 295, Age: 26.7 (5.4), BMI: NM	N= 169, Age: 29.8 (5.9), BMI: NM	141 (48)	30 (18)

Mangalath, et al. 2018	India	Rotterdam	Case-control	Adult	N= 75, Age: 25.91 (3.60), BMI: NM	N= 75, Age: 26.16 (3.90), BMI:NM	8 (10.67)	2 (2/67)
Moini, et al. 2009	Iran	Rotterdam	Cross-sectional	Adult and adolescent	N= 273, Age: 27.94 (4.16), BMI: 27.91 (22.81)	N= 276, Age: 31.10 (5.77), BMI: 25.56 (4.35)	70 (25.64)	33 (11.96)
Moran, et al. 2010	Australia	Rotterdam	Cross-sectional	Adult	N= 24, Age: 22.41 (0.39), BMI: 29.17 (1.54)	N= 22, Age: 21.95 (0.47), BMI: 22.05 (0.83)	75 (18)	36 (8)
Musmar, et al. 2013	Palestine	NIH	Cross-sectional	Adult	N=10 , Age: NM, BMI: 23.37 (3.85)	N= 127, Age: NM, BMI: 22.11 (3.06)	8 (80)	43 (33.9)
Öztürk, et al. 2019	Turkey	Rotterdam	Cross-sectional	Adult and adolescent	N= 50, Age: 22.3 (4.2), BMI: 24.17 (5.01)	N= 41, Age: 23.4 (3.5), BMI: 23.21 (4.02)	25 (50%)	9 (22%)
Rashid, et al. 2018	India	Rotterdam	Cross-sectional	Adult and adolescent	N= 88, Age: 22.67 (5.53), BMI: 24.21 (4.56)	N= 87, Age: 22.84 (3.64), BMI: 21.79 (3.94)	40 (45.5)	8 (9.3)
Rashidi, et al. 2017	Iran	Rotterdam	Cross-sectional	Adult	N= 56, Age: 26.84 (4.85), BMI: 26.52 (3.15)	N= 41, Age: 29.39 (4.42), BMI: 25.05 (2.51)	19 (34%)	4 (10.4%)
Roe, et al. 2013	USA	AES	Cohort	Adolescent	N= 148, Age: 16.9 (1.9), BMI: 28.5 (7.4)	N= 57, Age: 16.6 (2.5), BMI: 24.7 (7.1)	55 (37)	28 (50)
Sahin, et al. 2017	Turkey	Rotterdam	Cohort	Adult and adolescent	N= 69, Age: 24.82 (6.17), BMI: 21.86 (2.08)	N= 56, Age: 26.69 (5.25), BMI: 21.48 (2.16)	2 (2.9)	0
Schmidt, et al. 2016	USA	Rotterdam	Cross-sectional	Adult and adolescent	N= 268, Age: 28.1 (6.1), BMI: 30.3 (8.2)	N= 47, Age: 33.0 (9.6), BMI: 28.9 (8.4)	164 (61.2)	19 (40.4)
Shabir, et al. 2013	India	Rotterdam	Cross-sectional	Adult and adolescent	N= 197, Age: 23 (5.6), BMI: 25.8 (4.7)	N= 55, Age: 25 (4.3), BMI: 20.8 (3.2)	121 (61.4)	0
Sharami, et al. 2016	Iran	Rotterdam	Cross-sectional	Adult and adolescent	1: IM+PCO+HA, N= 87, Age: 26.16 (4.81), BMI: 27.86 (6.43) 2: IM+PCO, N= 21, Age: 25.00 (4.79), BMI: 28.39 (6.04) 3: IM+HA, N= 45, Age: 26.00 (4.73), BMI: 28.68 (5.14) 4: PCO+HA, N= 8, Age: 22.12 (2.10), BMI: 26.59 (6.35)	N= 53, Age: 27.23 (5.82), BMI: 26.49 (5.09)	1: 43 (49.4) 2: 7 (33.3) 3: 24 (53.3) 4: 2 (25)	14 (26.4%)
Sharif, et al. 2016	Qatar	NIH	Cross-sectional	Adult	N= 22, Age: 21.00 (20.00–22.00), BMI: 23.93 (19.90–28.48)	N= 98, Age: 22.0 (19.00–22.50), BMI: 23.37 (19.95–24.96)	14 (63.6)	23 (23.5)
Shishehgar, et al. 2019	Iran	Rotterdam	Interventional	Adult	N= 28, Age: 29.7 (5. 2), BMI: 31 (0.93)	N= 34, Age: 30.8 (4.5), BMI: 30.9 (0.5)	14 (50%)	0
Sulaiman, et al. 2018	Oman	Rotterdam	Case-control	Adult and adolescent	N= 51, Age: NM, BMI: NM	N= 45, Age: NM, BMI: NM	15 (29.4)	5 (11.1)
Sulaiman, et al. 2017	Oman	Rotterdam	Cross-sectional	Adult and adolescent	N= 52, Age: NM, BMI: NM	N= 60, Age: NM, BMI: NM	21 (40.4)	10 (16.7)
Tan, et al. 2017	China	Rotterdam	Cross-sectional	Adult	N= 120, Age: 24.8 (3.8), BMI: 21.4 (3.0)	N= 100, Age: 25.0 (3.5), BMI: 20.(1.9)	69 (57.5)	3 (3.0)
Taponen, et al. 2004	Finland	Rotterdam	Population based Cohort	Adult	1: N= HA+ ANOV+ PCO, N= 66, Age: 31, BMI: 25.9 (24.6, 27.1) 2: HA+ ANOV, N= 117, Age: 31, BMI: 24.1 (23.2, 24.9)	N= , Age: 31, BMI: 24.1 (23.2, 25.0)	1: 11 (16.4) 2: 12 (10.3)	12 (18.2)
Tehrani, et al. 2014	Iran	Rotterdam	Population based Cross-sectional	Adult	1: HA+ ANOV+ PCO, N= 11, Age: 25.6 (7.0), BMI: 25.4 (5.0) 2: HA+ ANOV, N= 19, Age: 31.1 (7.8), BMI: 26.4 (4.8) 3: HA+ PCO, N= 42, Age: 30.3 (7.5), BMI: 27.2 (4.4) 4: ANOV+ PCO, N= 13, Age: 24.7 (6.8), BMI: 24.1 (5.5)	N= 517, Age: 33.9 (7.6), BMI: 26.6 (5.0)	1: 4 (36.4) 2: 7 (36.8) 3: 18 (42.9) 4: 4 (30.8)	78(15.1)
Varanasi, et al. 2018	Australia	NIH	Cross-sectional	Adult and adolescent	N= 31, Age: 22 (20 – 24), BMI: 23.2 (20.5 – 27.4)	N= 223, Age: 22 (21 – 24), BMI: 22.9 (21.1 – 25.5)	26 (84)	128 (57)
Villarroel, et al. 2010	Chile	Rotterdam	Cross-sectional	Adult	N= 55, Age: 29.73 (0.50), BMI: 29.17 (0.85)	N= 27, Age: 30.48 (0.86), BMI: 25.70 (0.78)	10 (36.36)	0

Vural, et al. 2005	Turkey	Rotterdam	Case-control	Adult	N= 43, Age: 21.4 (1.8), BMI: 23.4 (4.7)	N= 43, Age: 20.8 (2.2), BMI: 21.5 (3)	8 (18)	6 (14)
Welt, et al. 2006	USA	NIH	Cross-sectional	Adult	1: Iceland, Caucasian, N= 105, Age: 30.2 (6.2), BMI: 31.5 (7.7) 2: Boston, Caucasian, N= 172, Age: 28.8 (5.5), BMI: 30.7 (9.2) 3: Boston, African-American, N= 44, Age: 28.4 (6.7), BMI: 36.3 (7.9) 4: Boston, Hispanic, N= 25, Age: 26.3 (5.2), BMI: 32.3 (10.3) 5: Boston, Asian, N= 21, Age: 25.5 (5.3), BMI: 26.3 (5.9)	N= 32, Age: 32.2 (5.5), BMI: 30.2 (7.5)	1: 59 (62.1) 2: 145 (84.8) 3: 37 (86.0) 4: 20 (87.0) 5: 18 (85.7)	17 (63.0)
Welt, et al. 2006	USA	Rotterdam	Cross-sectional	Adult	1: IM+HA, N= 305, Age: 28.7 (5.6), BMI: 32.0 (8.6) 2: HA+PCOM, N= 77, Age: 29.6 (6.0), BMI: 27.0 (6.8) 3: IM+PCOM, N= 36, Age: 30.2 (6.8), BMI: 24.7 (5.4)	N= 64, Age: 30.8 (6.1) , BMI: 27.3 (6.8)	1: 236 (80.3) 2: 48 (66.7) 3: 31 (88.6)	34 (57.6)
Zhang, et al. 2013	China	Rotterdam	Case-control	Adult	N= 719, Age: 27.54 (3.28), BMI: 23.67 (3.57)	N= 685, Age: 26.56 (3.25), BMI: 21.63 (2.49)	96 (13.3)	22 (3.2)
Zhang, et al. 2009	China	Rotterdam	Cross-sectional	Adult and adolescent	1: ANOV + HA + PCO, N= 193, Age: 26 (4.9), BMI: 36.5 (8.6) 2: ANOV + HA, N= 55, Age: 25 (5.1), BMI: 35.8 (9.3) 3: HA + PCO N= 96, Age: 27 (3.7), BMI: 30.9 (8.3) 4: ANOV + PCO, N= 375, Age: 26 (4.5), BMI: 28.6 ± (6.5)	N= 85, Age: 27 (5.3), BMI: 27.3 (5.2)	1: 158 (82) 2: 33 (66) 3: 60 (62) 4:86 (23)	16 (19)
Zhang, et al. 2015	China	Rotterdam	Population based Case-control	Adult and adolescent	N= 169, Age: 22.07 (6.10), BMI: 20.56 (2.65)	N= 338, Age: 22.08 (6.09), BMI: 20.07 (4.28)	70 (41.4)	120 (35.5)
Zhao, et al. 2016	China	Rotterdam	Cross-sectional	Adult and adolescent	1: HA+ ANOV+ PCO, N=409 , Age: 27.61 (2.26), BMI: 25.73 (5.35) 2: HA+ ANOV, N= 58, Age: 27.47 (4.5), BMI: 25.77 (4.68) 3: HA+ PCO, N= 101, Age: 27.46 (4.13), BMI: 25.72 (5.36) 4: ANOV+ PCO, N= 79, Age: 28.39 (3.51), BMI: 23.24 (5.78)	N= 60, Age: 27.01 (3.23), BMI: 23.35 (4.98)	1: 310 (76) 2: 18 (43.9) 3: 51 (51.5) 4: 0	3 (2.1)

Table 2: Results of heterogeneity and publication bias estimation, subgroup meta-analysis and meta-regression for prevalence of acne based on various subgroups.

				Publication bias Begg's test	Heterogeneity Chi square	P value	Pooled Overall Prevalence (95%CI)	Pooled Overall OR (95%CI) [¥]
PCOS				<0.005*	5448.32	0.001*	0.43 (0.41, 0.45)	1.67 (1.52, 1.83)
Non-PCOS				<0.005*	3668.31	0.001*	0.21 (0.19, 0.22)	Ref
Subgroup analysis based on age group								
Adults	PCOS			<0.005*	3136.71	0.001*	0.42 (0.40, 0.44)	1.58 (1.44, 1.75)
	Non-PCOS			>0.005	2867.34	0.001*	0.17 (0.15, 0.18)	Ref
Adolescents	PCOS			>0.005	59.58	0.001*	0.59 (0.47, 0.70)	2.77 (1.32, 5.83)
	Non-PCOS			>0.005	380.24	0.001*	0.39 (0.22, 0.57)	Ref
Reproductive age	PCOS			<0.005*	1448.59	0.001*	0.40 (0.29, 0.50)	2.88 (1.84, 4.50)
	Non-PCOS			>0.005	294.19	0.001*	0.19 (0.11, 0.28)	Ref
Subgroup analysis based on age group and PCOS diagnostic criteria								
Adults [£]	NIH		PCOS	>0.005	29.68	0.001*	0.76 (0.66, 0.86)	3.09 (1.88, 5.06)
			Non-PCOS	>0.005	27.17		0.45 (0.34, 0.55)	Ref
	Rotterdam		PCOS	<0.005*	1583.97	0.001*	0.36 (0.33, 0.39)	1.60 (1.39, 1.85)
			Non-PCOS	>0.005	1199.47		0.16 (0.14, 0.18)	Ref
Adolescents [£]	NIH		PCOS	>0.005	[€]--	--	0.66 (0.45, 0.87)	2.84 (1.12, 7.20)
			Non-PCOS	>0.005	--	--	0.57 (0.51, 0.63)	Ref
	Rotterdam		PCOS	>0.005	24.22	0.001*	0.60 (0.48, 0.73)	3.50 (1.67, 7.32)
			Non-PCOS	>0.005	225.01	0.001*	0.36 (0.15, 0.57)	Ref
Reproductive age [£]	NIH		PCOS	>0.005	--	--	0.40 (0.12, 0.68)	2.60 (0.77, 8.77)
			Non-PCOS	>0.005	--	--	0.27 (0.23, 0.31)	Ref
	Rotterdam		PCOS	>0.005	1327.09	0.001*	0.40 (0.28, 0.53)	2.85 (1.77, 4.61)
			Non-PCOS	>0.005	125.64	0.001*	0.17 (0.11, 0.23)	Ref
Subgroup analysis based on age group, PCOS diagnostic criteria and geographical region								
Adults [£]	Rotterdam	Europe	PCOS	>0.005	473.73	0.001*	0.29 (0.26, 0.32)	1.48 (1.32, 1.64)
			Non-PCOS	>0.005	630.04	0.001*	0.21 (0.18, 0.24)	Ref
		East Asia	PCOS	<0.005*	288.02	0.001*	0.48 (0.17, 0.80)	[¥]3.55 (1.30, 9.67)
			Non-PCOS	>0.005	91.77	0.001*	0.17 (0.06, 0.28)	Ref
		West Asia	PCOS	<0.005*	53.69	0.001*	0.42 (0.28, 0.57)	[¥]3.08 (1.39, 6.80)
			Non-PCOS	>0.005	75.77	0.001*	0.19 (0.09, 0.28)	Ref
		South Asia	PCOS	<0.005*	--	--	0.23 (0.09, 0.36)	[¥]2.17 (1.34, 3.50)
			Non-PCOS	>0.005	--	--	0.09 (0.01, 0.17)	Ref

[¥] Results obtained from Trim and fill random/fixed effect method

[£] Analysis did not performed in all subgroups due to insufficient data

[€] Insufficient observation

* Statistically significant.

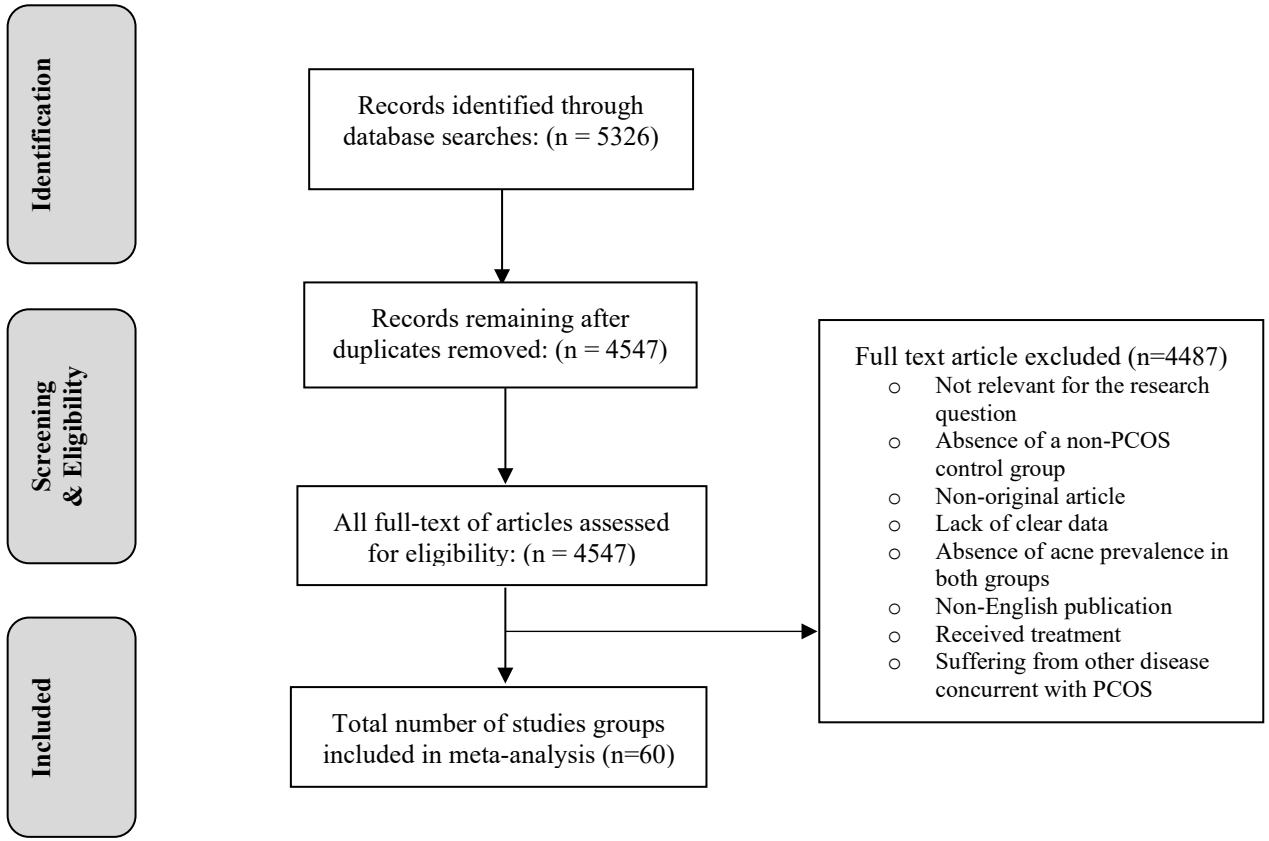
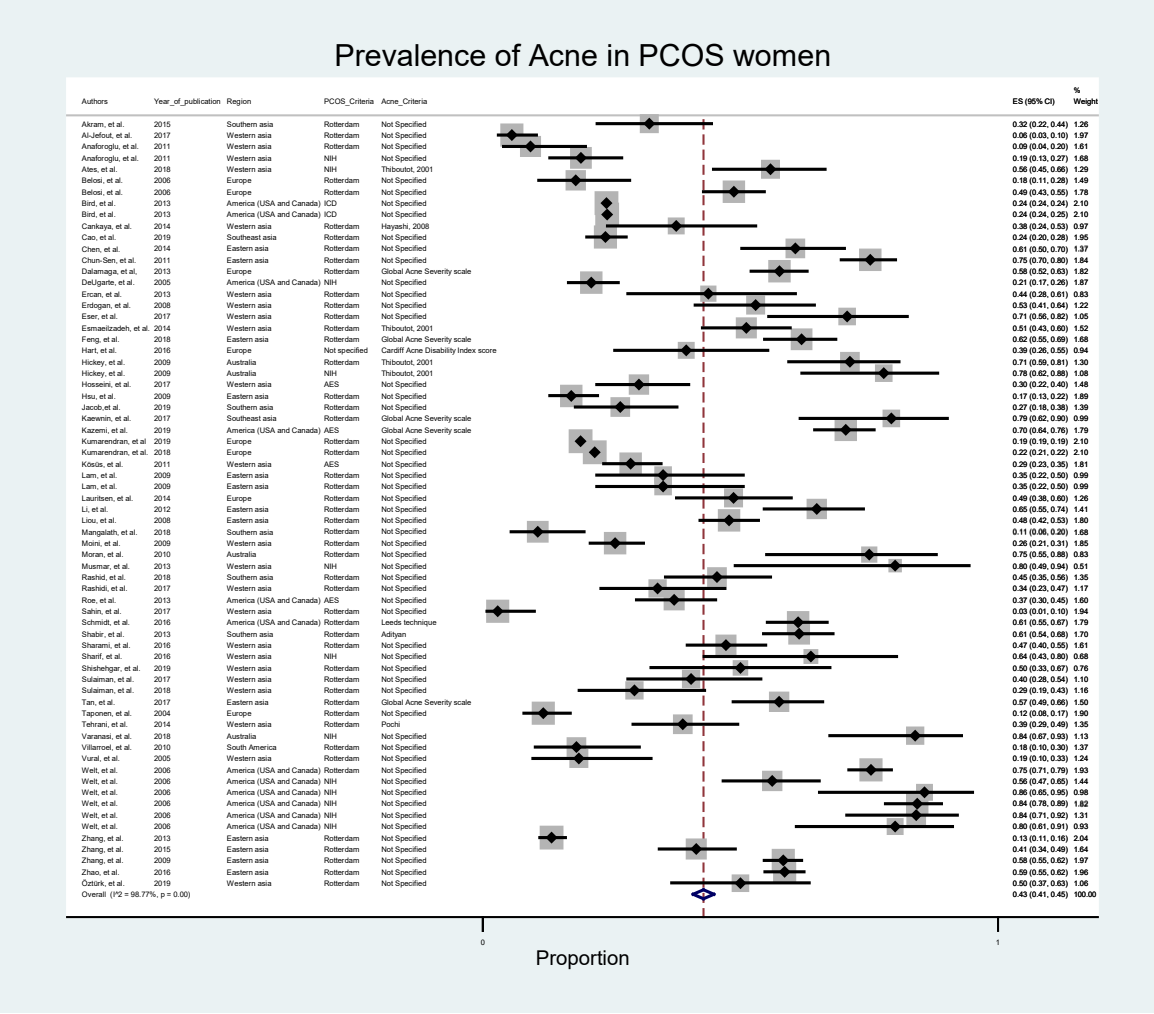


Figure 1. Flow diagram of study selection.

Figure 2: Forest lot for prevalence of acne among women with PCOS (A) and without PCOS (B)

A:



B:

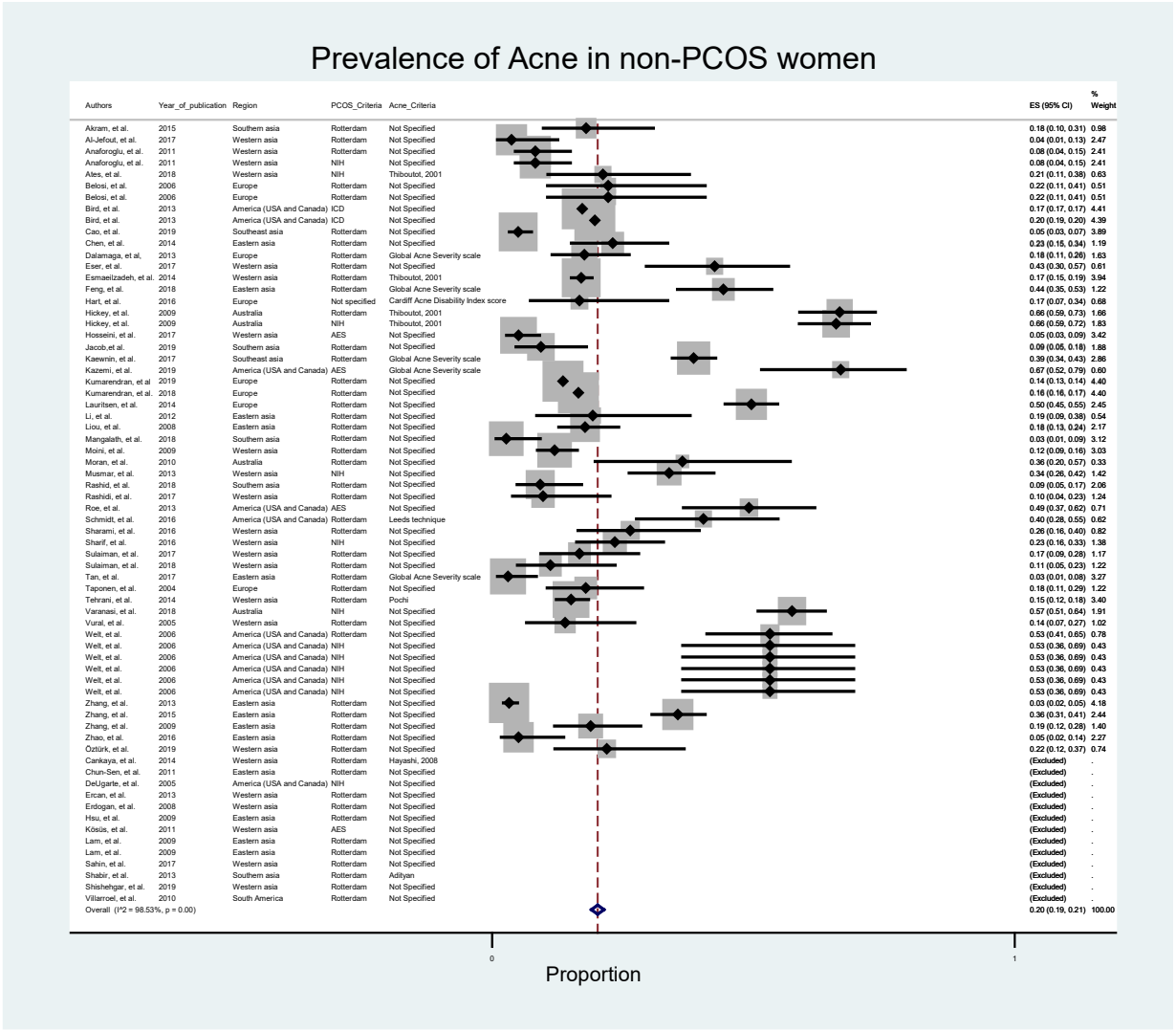
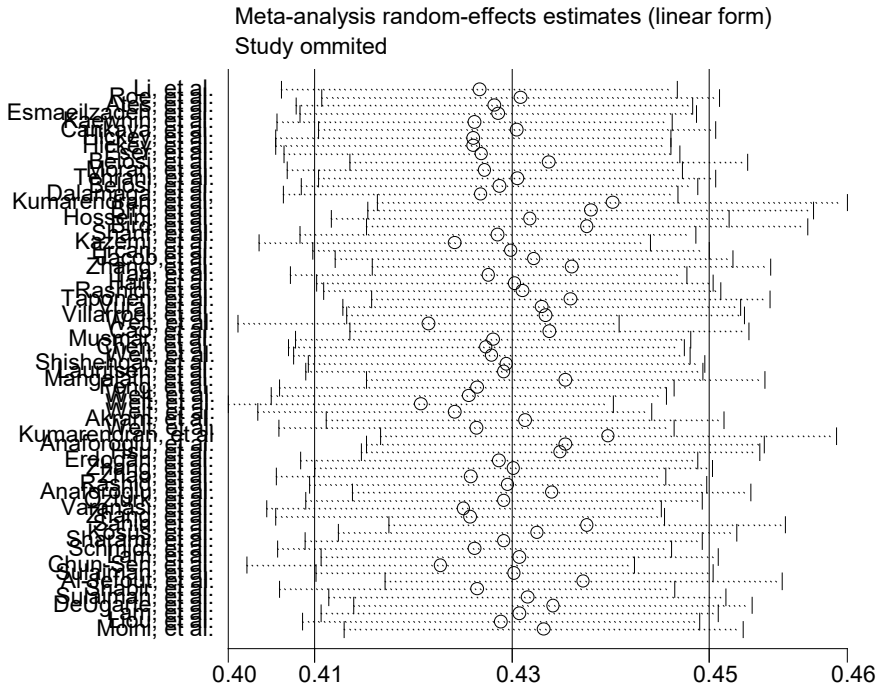
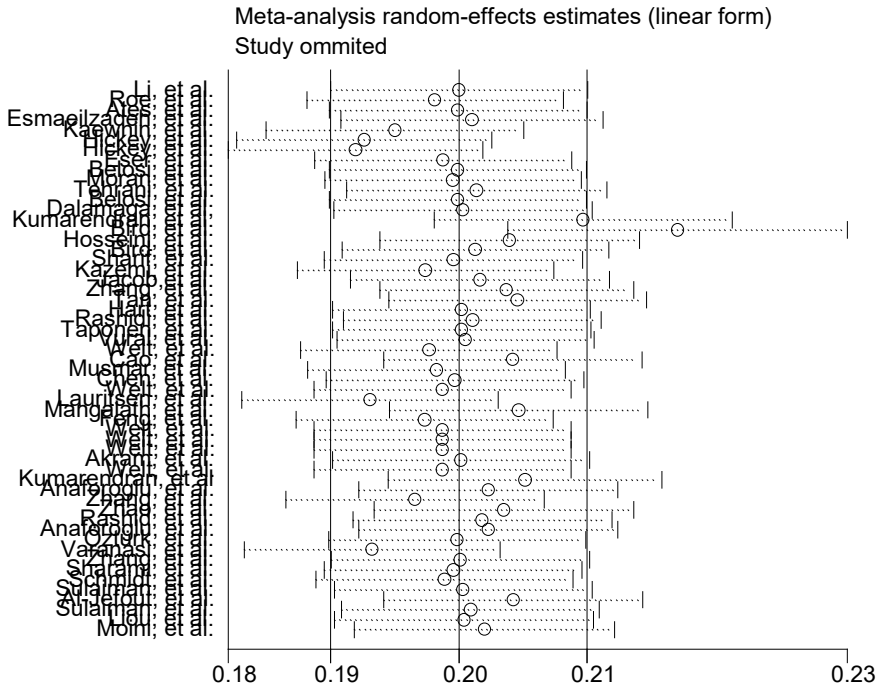

Prevalence of Acne in non-PCOS women
Authors
Year_of_publication
Region
PCOS_Criteria
Acne_Criteria
ES (95% CI)
% Weight
Akram, et al. 2015 Southern asia Rotterdam Not Specified 0.18 (0.10, 0.31) 0.98
Al-Jefout, et al. 2017 Western asia Rotterdam Not Specified 0.04 (0.01, 0.13) 2.47
Anaforoglu, et al. 2011 Western asia Rotterdam Not Specified 0.08 (0.04, 0.15) 2.41
Anaforoglu, et al. 2011 Western asia NIH Not Specified 0.08 (0.04, 0.15) 2.41
Ates, et al. 2018 Western asia NIH Thiboutot, 2001 0.21 (0.11, 0.38) 0.63
Belosi, et al. 2006 Europe Rotterdam Not Specified 0.22 (0.11, 0.41) 0.51
Belosi, et al. 2006 Europe Rotterdam Not Specified 0.22 (0.11, 0.41) 0.51
Bird, et al. 2013 America (USA and Canada) ICD Not Specified 0.17 (0.17, 0.17) 4.41
Bird, et al. 2013 America (USA and Canada) ICD Not Specified 0.20 (0.19, 0.20) 4.39
Cao, et al. 2019 Southeast asia Rotterdam Not Specified 0.05 (0.03, 0.07) 3.89
Chen, et al. 2014 Eastern asia Rotterdam Not Specified 0.23 (0.15, 0.34) 1.19
Dalamaga, et al, 2013 Europe Rotterdam Global Acne Severity scale 0.18 (0.11, 0.26) 1.63
Eser, et al. 2017 Western asia Rotterdam Not Specified 0.43 (0.30, 0.57) 0.61
Esmaeilzadeh, et al. 2014 Western asia Rotterdam Thiboutot, 2001 0.17 (0.15, 0.19) 3.94
Feng, et al. 2018 Eastern asia Rotterdam Global Acne Severity scale 0.44 (0.35, 0.53) 1.22
Hart, et al. 2016 Europe Not specified Cardiff Acne Disability Index score 0.17 (0.07, 0.34) 0.68
Hickey, et al. 2009 Australia Rotterdam Thiboutot, 2001 0.66 (0.59, 0.73) 1.66
Hickey, et al. 2009 Australia NIH Thiboutot, 2001 0.66 (0.59, 0.72) 1.83
Hosseini, et al. 2017 Western asia AES Not Specified 0.05 (0.03, 0.09) 3.42
Jacob,et al. 2019 Southern asia Rotterdam Not Specified 0.09 (0.05, 0.18) 1.88
Kaewnin, et al. 2017 Southeast asia Rotterdam Global Acne Severity scale 0.39 (0.34, 0.43) 2.86
Kazemi, et al. 2019 America (USA and Canada) AES Global Acne Severity scale 0.67 (0.52, 0.79) 0.60
Kumarendran, et al 2019 Europe Rotterdam Not Specified 0.14 (0.13, 0.14) 4.40
Kumarendran, et al. 2018 Europe Rotterdam Not Specified 0.16 (0.16, 0.17) 4.40
Lauritsen, et al. 2014 Europe Rotterdam Not Specified 0.50 (0.45, 0.55) 2.45
Li, et al. 2012 Eastern asia Rotterdam Not Specified 0.19 (0.09, 0.38) 0.54
Liou, et al. 2008 Eastern asia Rotterdam Not Specified 0.18 (0.13, 0.24) 2.17
Mangalath, et al. 2018 Southern asia Rotterdam Not Specified 0.03 (0.01, 0.09) 3.12
Moini, et al. 2009 Western asia Rotterdam Not Specified 0.12 (0.09, 0.16) 3.03
Moran, et al. 2010 Australia Rotterdam Not Specified 0.36 (0.20, 0.57) 0.33
Musmar, et al. 2013 Western asia NIH Not Specified 0.34 (0.26, 0.42) 1.42
Rashid, et al. 2018 Southern asia Rotterdam Not Specified 0.09 (0.05, 0.17) 2.06
Rashidi, et al. 2017 Western asia Rotterdam Not Specified 0.10 (0.04, 0.23) 1.24
Roe, et al. 2013 America (USA and Canada) AES Not Specified 0.49 (0.37, 0.62) 0.71
Schmidt, et al. 2016 America (USA and Canada) Rotterdam Leeds technique 0.40 (0.28, 0.55) 0.62
Sharami, et al. 2016 Western asia Rotterdam Not Specified 0.26 (0.16, 0.40) 0.82
Sharif, et al. 2016 Western asia NIH Not Specified 0.23 (0.16, 0.33) 1.38
Sulaiman, et al. 2017 Western asia Rotterdam Not Specified 0.17 (0.09, 0.28) 1.17
Sulaiman, et al. 2018 Western asia Rotterdam Not Specified 0.11 (0.05, 0.23) 1.22
Tan, et al. 2017 Eastern asia Rotterdam Global Acne Severity scale 0.03 (0.01, 0.08) 3.27
Taponen, et al. 2004 Europe Rotterdam Not Specified 0.18 (0.11, 0.29) 1.22
Tehrani, et al. 2014 Western asia Rotterdam Pochi 0.15 (0.12, 0.18) 3.40
Varanasi, et al. 2018 Australia NIH Not Specified 0.57 (0.51, 0.64) 1.91
Vural, et al. 2005 Western asia Rotterdam Not Specified 0.14 (0.07, 0.27) 1.02
Welt, et al. 2006 America (USA and Canada) Rotterdam Not Specified 0.53 (0.41, 0.65) 0.78
Welt, et al. 2006 America (USA and Canada) NIH Not Specified 0.53 (0.36, 0.69) 0.43
Welt, et al. 2006 America (USA and Canada) NIH Not Specified 0.53 (0.36, 0.69) 0.43
Welt, et al. 2006 America (USA and Canada) NIH Not Specified 0.53 (0.36, 0.69) 0.43
Welt, et al. 2006 America (USA and Canada) NIH Not Specified 0.53 (0.36, 0.69) 0.43
Welt, et al. 2006 America (USA and Canada) NIH Not Specified 0.53 (0.36, 0.69) 0.43
Zhang, et al. 2013 Eastern asia Rotterdam Not Specified 0.03 (0.02, 0.05) 4.18
Zhang, et al. 2015 Eastern asia Rotterdam Not Specified 0.36 (0.31, 0.41) 2.44
Zhang, et al. 2009 Eastern asia Rotterdam Not Specified 0.19 (0.12, 0.28) 1.40
Zhao, et al. 2016 Eastern asia Rotterdam Not Specified 0.05 (0.02, 0.14) 2.27
Öztürk, et al. 2019 Western asia Rotterdam Not Specified 0.22 (0.12, 0.37) 0.74
Cankaya, et al. 2014 Western asia Rotterdam Hayashi, 2008 (Excluded) .
Chun-Sen, et al. 2011 Eastern asia Rotterdam Not Specified (Excluded) .
DeUgarte, et al. 2005 America (USA and Canada) NIH Not Specified (Excluded) .
Ercan, et al. 2013 Western asia Rotterdam Not Specified (Excluded) .
Erdogan, et al. 2008 Western asia Rotterdam Not Specified (Excluded) .
Hsu, et al. 2009 Eastern asia Rotterdam Not Specified (Excluded) .
Kösüs, et al. 2011 Western asia AES Not Specified (Excluded) .
Lam, et al. 2009 Eastern asia Rotterdam Not Specified (Excluded) .
Lam, et al. 2009 Eastern asia Rotterdam Not Specified (Excluded) .
Sahin, et al. 2017 Western asia Rotterdam Not Specified (Excluded) .
Shabir, et al. 2013 Southern asia Rotterdam Adityan (Excluded) .
Shishehgar, et al. 2019 Western asia Rotterdam Not Specified (Excluded) .
Villarroel, et al. 2010 South America Rotterdam Not Specified (Excluded) .
Overall (I^2 = 98.53%, p = 0.00) 0.20 (0.19, 0.21) 100.00
0
1
Proportion

Figure 3: Sensitivity analysis plot for Prevalence of Acne in PCOS (A) non-PCOS (B) women

A:



B:


Meta-analysis random-effects estimates (linear form)
Study ommited
0.18
0.19
0.20
0.21
0.23

Supplementary Table 1. Quality assessment of included studies using the Newcastle–Ottawa Quality Assessment Scale for cross-sectional study.

Author/year	SELECTION								COMPARABILITY		OUTCOME				Total scores	Quality
	Representativeness of the samples		Sample size		Non-responders		Ascertainment of the exposure (risk factor)		A: study controls for age and/or BMI B: control for any additional factor		Assessment of the outcome a) Independent blind assessment** b) Record linkage. ** c) Self report. *		Statistical test			
	location	score	location	score	location	score	location	score	location	score	location	score	location	score		
Akram, et al. (2015)					p.23	*	p.23	*	p.23	*	p.23	*	p.23	*	5*	Moderate
Belosi, et al. (2006)					p.3109	*	p.3109	*			p.3109	*	p.3109	*	4*	Moderate
Cao, et al. (2019)					p.2	*			p.3	*	p.3	*	p.3	*	4*	Moderate
Chen, et al. (2014)					p.544	*	p.543	*			p.543	*	p.543	*	4*	Moderate
Ercan, et al.(2013)					p.2	*	p.2	*	p.3	**	p.2	*	p.2	*	6*	Moderate
Feng, et al.(2018)					p.2	*	p.2-3	*	p.5	*	p.2	*	p.3	*	5*	Moderate
Hart, et al.(2016)					p.178-9	*	p.178	*	p.178	*	p.178	*	p.178	*	5*	Moderate
Kazemi, et al.(2019)					p.4-5	*	p.3	*	p.3	*	p.3	**	p.3	*	6*	Moderate
Lauritsen, et al.(2014)					p.793	*	p.792	*			p.792	*	p.793	*	4*	Moderate
Moran, et al.(2010)					p.26	*					p.25	*	p.26	*	3*	low
Musmar, et al.(2013)			p.2	*	p.3	*	p.2	*	p.3	*	p.2	*	p.3	*	6*	Moderate
Sharif, et al.(2016)			p.3	*	p.3-4	*	p.2	*	p.4	*	p.2	*	p.3	*	6*	Moderate
Tan, et al.(2017)					p.264	*	p.263	*	p.264	**	p.263	*	p.263	*	6*	Moderate
Tehrani, et al.(2014)	p.2	*	p.2	*	p.3	*	p.2	*	p.3	*	p.2	**	p.3	*	8*	High
Villarroel, et al.(2010)			p.601	*	p.603	*	p.602-3	*	p.603	*	p.602	*	p.603	*	6*	Moderate
Welt, et al.(2006) Code:4248					p.4363	*	p.4368	*	p.4362	*	p.4362	*	p.4363	*	5*	Moderate
Welt, et al.(2006) Code:4250					p.4843	*	p.4843	*	p.4843	**	p.4843	*	p.4843	*	6*	Moderate
Al-Jefout, et al.(2017)					p.2	*	p.6	*			p.6-7	*	p.7-8	*	4*	Moderate
Erdoğan, et al.(2008)							p.144	*	p.145	**	p.144	*	p.144	*	5*	Moderate
Esmaeilzadeh, et al.(2014)	p.560	*	p.560	*	p.561	*	p.560	*	p.562	**	560	**	P560	*	9*	High
Chun-Sen, et al. (2011)					p.303	*	p.301	*	p.302	*	p.301	*	p.302	*	5*	Moderate
Kaewnin, et al. (2017)			p.1	*	p.2	*	p.2	*	p.3	*	p.2	**	p.2	*	7*	High
Köşüş, et al.(2011)					p.179	*	p.178	*	p.179	*	p.178	*	p.179	*	5*	Moderate
Li, et al.(2012)					p.392	*			p.391	*	p.391	*	p.391	*	4*	Moderate
Moini, et al.(2009)			p.124	*			p.124	*	p.124	*	p.124	*	p.124	*	5*	Moderate
Öztürk, et al.(2019)							p.256	*	p.256	**	p.256	*	p.256	*	5*	Moderate
Rashid, et al.(2018)					p.2	*	p.1	*	p.1	**	p.1	*	p.2	*	6*	Moderate
Schmidt, et al.(2016)					p.3	*	p.2	*			p.2	**	p.3	*	5*	Moderate
Shabir, et al.(2013)					p.2	*	p.2	*	p.1	*	p.1-2	**	p.2	*	6*	Moderate
Sharami, et al.(2016)					p.136	*	p.135	*			p.135	*	p.135	*	4*	Moderate
Sulaiman, et al.h(2017)			p.898	*	p.899	*	p.898	*	p.900	*	p.899	*	p.899	*	6*	Moderate
Varanasi, et al.(2018)					p.4	*	p.3	*	p.5	*	p.2-3	*	p.3	*	5*	Moderate
Zhang, et al.(2009)					p.1635	*	p.1634	*			p.1634	*	p.1635	*	4*	Moderate
Zhao, et al. (2016)							p.152	*	p.152	*	p.152	*	p.152	*	4*	Moderate

Supplementary Table 2. Quality assessment of studies included using the Newcastle–Ottawa Quality Assessment Scale for cohort studies

	SELECTION								COMPARABILITY		OUTCOME						Total scores	Quality
Author	Representativeness of the exposed cohort		Selection of the non-exposed cohort		Ascertainment of exposure		No outcome of interest at start of study		A: Study controls for age and/or BMI B: Study controls for other confounders		A: Independent blind assessment B: Record linkage		Follow-up long enough for outcomes (at least one year)		A:complete of follow up of cohorts B: lost to follow up less than 20%			
	location	score	location	score	location	score	location	score	location	score	location	score	location	score	location	score		
Bird, et al. (2013) Code.486	p.116	*	p.116	*	p.116	*	p.116	*			p.116	*	p.117	*	p.118	*	7*	High
Bird, et al.(2013) Code:488	p.365	*	p.365	*	p.366	*	p.366	*			p.366	*	p.366	*	p.366	*	7*	High
Dalamaga, et al.(2013)					p.923	*			p.923	*	p.923	*					3*	Low
Kumarendran, et al.(2018)	p.4	*	p.4	*	p.4	*	p.4	*	p.6,9	**	p.4	*	p.7	*	p.6	*	9*	High
Kumarendran, et al. (2019)	p.6	*	p.6	*	p.6	*	p.6	*	p.6	**	p.6	*	p.6	*	p.6	*	9*	High
Taponen, et al.(2004)	p.1084	*	p.1084	*	p.1084	*					p.1084	*	p.1084	*			5*	Moderate
Ates, et al.(2018)					p.2	*	p.3	*	p.3	**	p.2	**			p.3	*	7*	high
DeUgarte, et al.(2005)					p.1455	*	p.14	*	p.1456	**	p.1455	*			p.1456	*	6*	Moderate
Hickey, et al.(2009)					p.3715	*	p.3715	*	p.3715	*	p.3715	**	p.3715	*	p.3715	*	7*	Moderate
Hsu, et al.(2009)					p.1169	*	p.1170	*			p.1169	*			p.1170	*	4*	Moderate
Lam, et al. (2009)					p.197	*	p.197	*			p.197	*			p.197	*	4*	Moderate
Liou, et al.(2008)					p.1961	*	p.1961	*			p.1961	*			p.1961	*	4*	Moderate
Roe, et al.(2013)					p.5	*	p.5	*			p.5	*			p.5	*	4*	Moderate
Sahin, et al.(2017)					p.146	*	p.146	*	p.147	*	p.146	*			p.147	*	5*	Moderate

Supplementary Table 3. Quality assessment of included studies using the Newcastle–Ottawa Quality Assessment Scale for case-control study.

	SELECTION								COMPARABILITY		EXPOSURE						Total scores	Quality
Author	Is the case definition adequate?		Representativeness of the cases		Selection of Controls		Definition of Controls		Comparability of cases and controls on the basis of the design or analysis		Ascertainment of exposure		Same method of ascertainment for cases and controls		Non-Response rate			
	location	score	location	score	location	score	location	score	location	score	location	score	location	score	location	score		
Eser, et al.(2017)	p.808	*					p.808	*	p.808	**	p.808	*	p.808	*			6*	Moderate
Hosseini, et al.(2017)	p.576	*					p.576	*	p.576	*	p.576	*	p.576	*	p.577	*	6*	Moderate
Rashidi, et al.(2017)	p.2	*					p.2	*				*	p.2	*			4*	Moderate
Vural, et al.(2005)	p.2409	*					p.2410	*	p.2410	*	p.2410	*	p.2410	*			5*	Moderate
Zhang, et al.(2013)	p.526	*					p.526	*	p.528	*	p.526	*	p.526	*			5*	Moderate
Jacob, et al.(2014)	p.8	*									p.8	*	p.8	*			3*	Low
Mangalath, et al.(2018)	p.15	*							p.16	*	p.15	*	p.15	*			4*	Moderate
Anaforoglu, et al.(2011)	p.376-8	*									p.376	*	p.376	*			3*	Low
Cankaya, et al.(2014)	p.825	*					p.825	*	p.825	*	p.825	*	p.8.26	*	p.828	*	6*	Moderate
Sulaiman, et al.(2018)	p.764	*					p.765	*	p.766	*	p.765	*	p.765	*	p.766	*	6*	Moderate
Zhang, et al.(2015)	p.3	*	p.2	*	p.3	*	p.3	*	p.3	**	p.3	*	p.3	*	p.5	*	9*	High

Supplementary Table 4. Quality assessment of included studies using the Consort Assessment Scale for interventional studies

Author	Methods																	
	Trial design		Participants		Interventions	Outcomes		Sample size		Randomization		Allocation concealment mechanism	Implementation	Blinding		Statistical methods	
	a	b	a	b		a	b	a	b	a	b			a	b	a	b
Shishehgar , et al. (2019)	-	-	+	+	+	+	-	-	-	-	-	-	-	-	-	+	-

Author	Results									Total	**Quality**
	Participant flow (a diagram is strongly recommended)		Recruitment		Baseline data	Numbers analyzed	Outcomes and estimation		Ancillary analyses	Harms		
	a	b	a	b			a	b				
Shishehgar , et al. (2019)	+	-	+	-	+	+	+	-	-	-	10	moderate

Supplementary Figure 1: Risk of bias in cross-sectional studies

A:

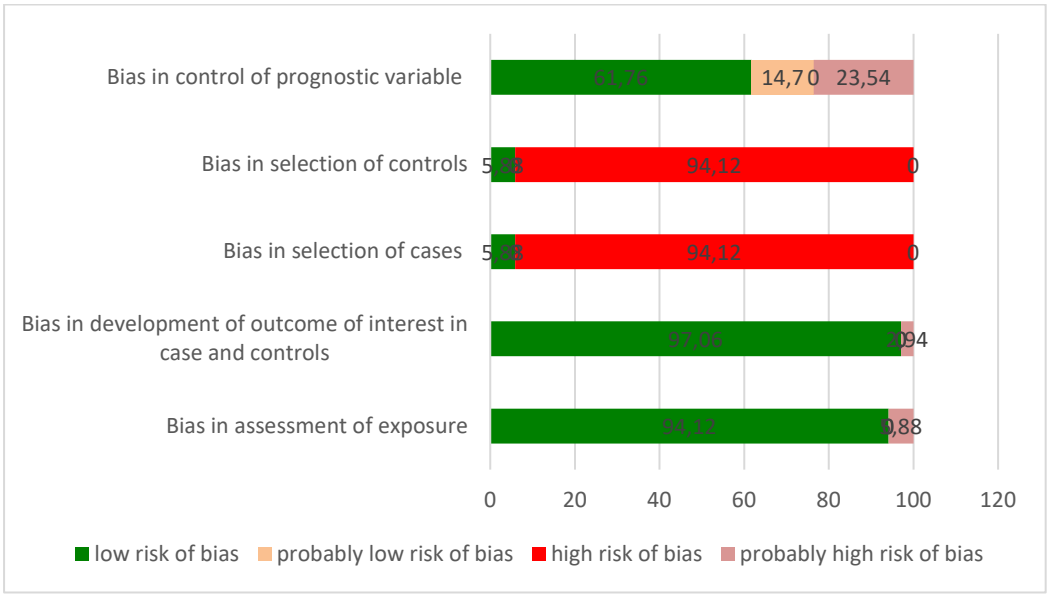
Author, date	Bias in assessment of exposure	Bias in development of outcome of interest in case and controls	Bias in selection of cases	Bias in selection of controls	Bias in control of prognostic variable (without case and control matching or adjustment in statistical methods)
Akram, et al. (2015)					
Belosi, et al. (2006)					
Cao, et al. (2019)					
Chen, et al. (2014)					
Ercan, et al.(2013)					
Feng, et al.(2018)					
Hart, et al.(2016)					
Kazemi, et al.(2019)					
Lauritsen, et al.(2014)					
Moran, et al.(2010)					
Musmar, et al.(2013)					
Sharif, et al.(2016)					
Tan, et al.(2017)					
Tehrani, et al.(2014)					
Villarroel, et al.(2010)					
Welt, et al.(2006) Code:4248					
Welt, et al.(2006) Code:4250					
Al-Jefout, et al.(2017)					
Erdoğan, et al.(2008)					

Author, date	Bias in assessment of exposure	Bias in development of outcome of interest in case and controls	Bias in selection of cases	Bias in selection of controls	Bias in control of prognostic variable (without case and control matching or adjustment in statistical methods)
Esmaeilzadeh, et al.(2014)					
Chun-Sen, et al. (2011)					
Kaewnin, et al. (2017)					
Köşüş, et al.(2011)					
Li, et al.(2012)					
Moini, et al.(2009)					
Öztürk, et al.(2019)					
Rashid, et al.(2018)					
Schmidt, et al.(2016)					
Shabir, et al.(2013)					
Sharami, et al.(2016)					
Sulaiman, et al.(2017)					
Varanasi, et al.(2018)					
Zhang, et al.(2019)					
Zhao, et al. (2016)					

Definitely No (low risk of bias) **probably no**

Definitely yes (high risk of bias) **probably Yes**

B:


Bias in control of prognostic variable
61,76
14,7 0
23,54
Bias in selection of controls
5,88
94,12
0
Bias in selection of cases
5,88
94,12
0
Bias in development of outcome of interest in case and controls
97,06
2,94
Bias in assessment of exposure
94,12
5,88
0
20
40
60
80
100
120
low risk of bias
probably low risk of bias
high risk of bias
probably high risk of bias

Supplementary Figure 2: Risk of bias in cohort studies

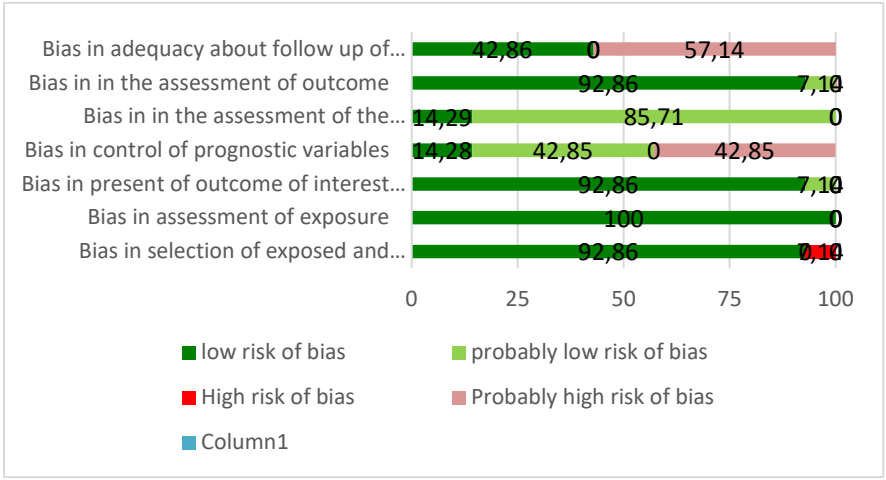
A:

First Author, date	Bias in selection of exposed and non-exposed cohorts	Bias in assessment of exposure	Bias in present of outcome of interest at start of study	Bias in control of prognostic variables (with matching or adjusting)	Bias in the assessment of the presence or absence of prognostic factors	Bias in the assessment of outcome	Bias in adequacy about follow up of cohorts
Bird, et al. (2013)/Code.486							
Bird, et al.(2013)/Code:488							
Dalamaga, et al.(2013)							
Kumarendran, et al.(2018)							
Kumarendran, et al. (2019)							
Taponen, et al.(2004)							
Ates, et al.(2018)							
DeUgarte, et al.(2005)							
Hickey, et al.(2009)							
Hsu, et al.(2009)							
Lam, et al. (2009)							
Liou, et al.(2008)							
Roe, et al.(2013)							
Sahin, et al.(2017)							

Definitely No (low risk of bias) Probably no

Definitely yes (high risk of bias) Probably Yes

B:


Bias in adequacy about follow up of...
Bias in in the assessment of outcome
Bias in in the assessment of the...
Bias in control of prognostic variables
Bias in present of outcome of interest...
Bias in assessment of exposure
Bias in selection of exposed and...
42,86
0
57,14
92,86
7,14
14,29
85,71
0
14,28
42,85
0
42,85
92,86
7,14
100
0
92,86
0
0
25
50
75
100
low risk of bias
probably low risk of bias
High risk of bias
Probably high risk of bias
Column1

Supplementary Figure 3: Risk of bias in case-control studies

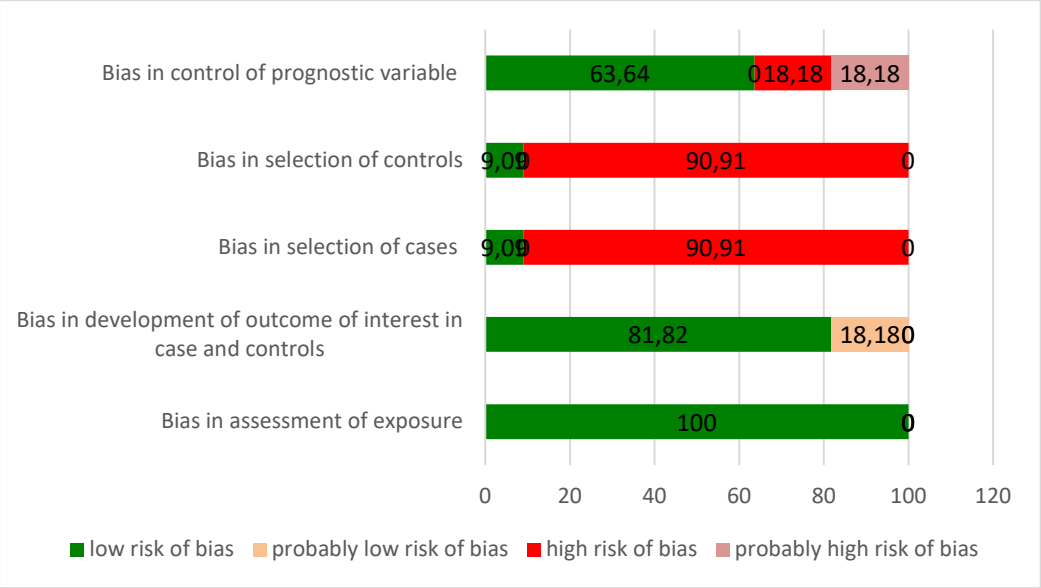
A:

Author, date	Bias in assessment of exposure	Bias in development of outcome of interest in case and controls	Bias in selection of cases	Bias in selection of controls	Bias in control of prognostic variable (without case and control matching or adjustment in statistical methods)
Eser, et al.(2017)					
Hosseini, et al.(2017)					
Rashidi, et al.(2017)					
Vural, et al.(2005)					
Zhang, et al.(2013)					
Jacob, et al.(2014)					
Mangalath, et al.(2018)					
Anaforoglu, et al.(2011)					
Cankaya, et al.(2014)					
Sulaiman, et al.(2018)					
Zhang, et al.(2015)					

Definitely No (low risk of bias) **probably no**

Definitely yes (high risk of bias) **probably Yes**

B:



Supplementary Figure 4: Risk of bias in interventional study

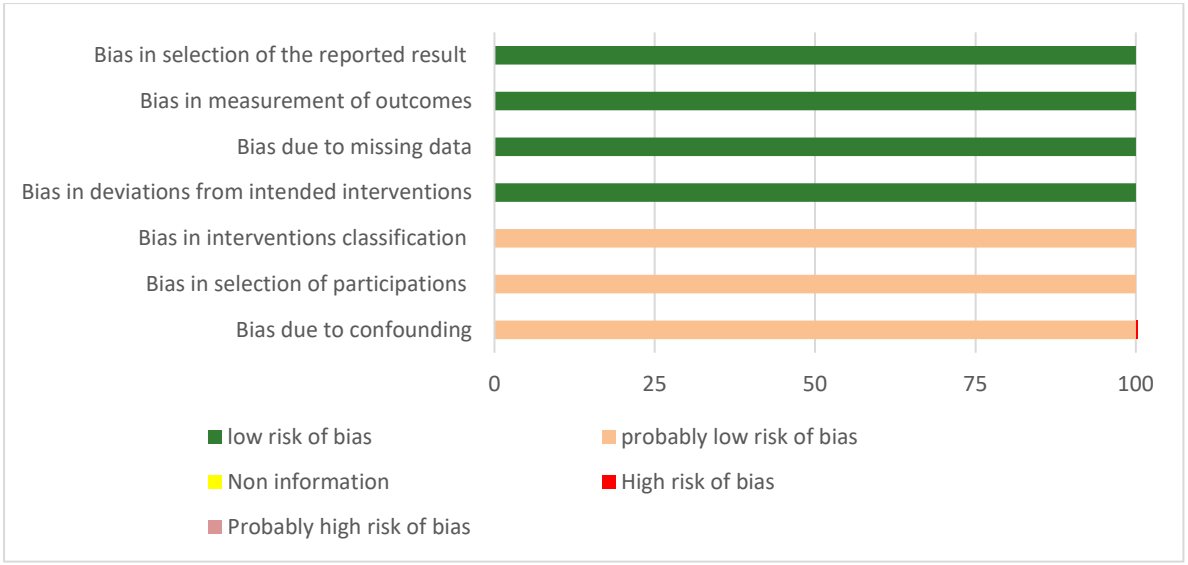
A:

Author, date	Bias due to confounding	Bias in selection of participations	Bias in interventions classification	Bias in deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
Shishehgar, et al. (2019)	○	○	○	●	●	●	●

● **No (low risk of bias)** ○ **probably no** ● **Non information**

● **Yes (High risk of bias)** ○ **Probably yes**

B:


Bias in selection of the reported result
Bias in measurement of outcomes
Bias due to missing data
Bias in deviations from intended interventions
Bias in interventions classification
Bias in selection of participations
Bias due to confounding
0
25
50
75
100
low risk of bias
probably low risk of bias
Non information
High risk of bias
Probably high risk of bias

Supplementary figure 5: Odds ratio od acne based on age groups