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Association of Periodontal Disease and Polycystic Ovarian Syndrome: A Systematic Review and Meta-analysis with Trial Sequential Analysis

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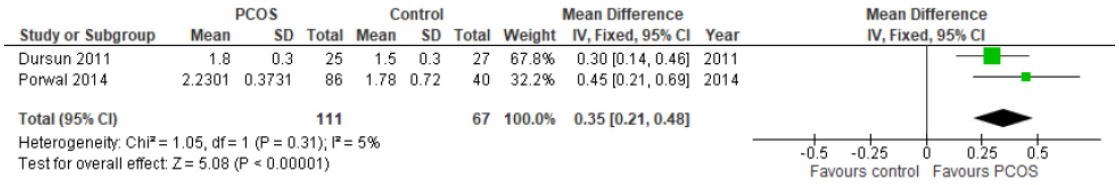
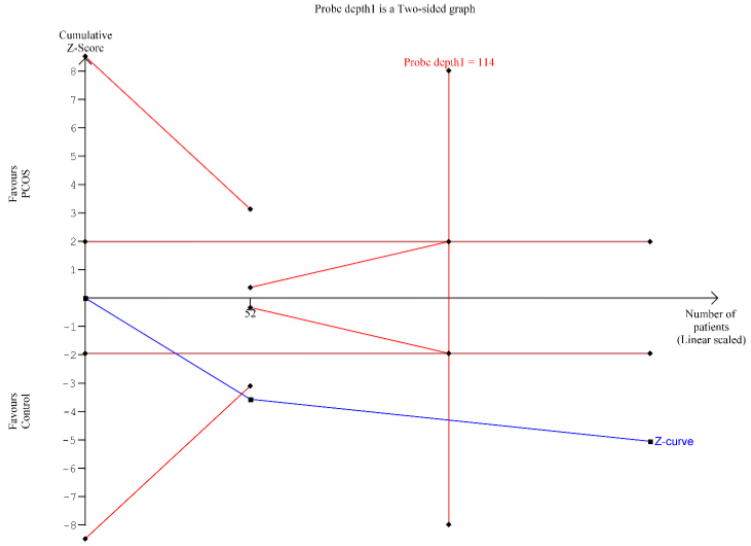
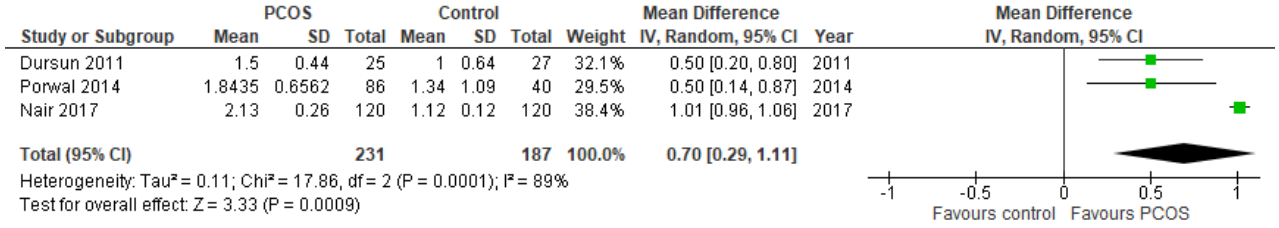
SUPPLEMENTARY TABLE AND FIGURES



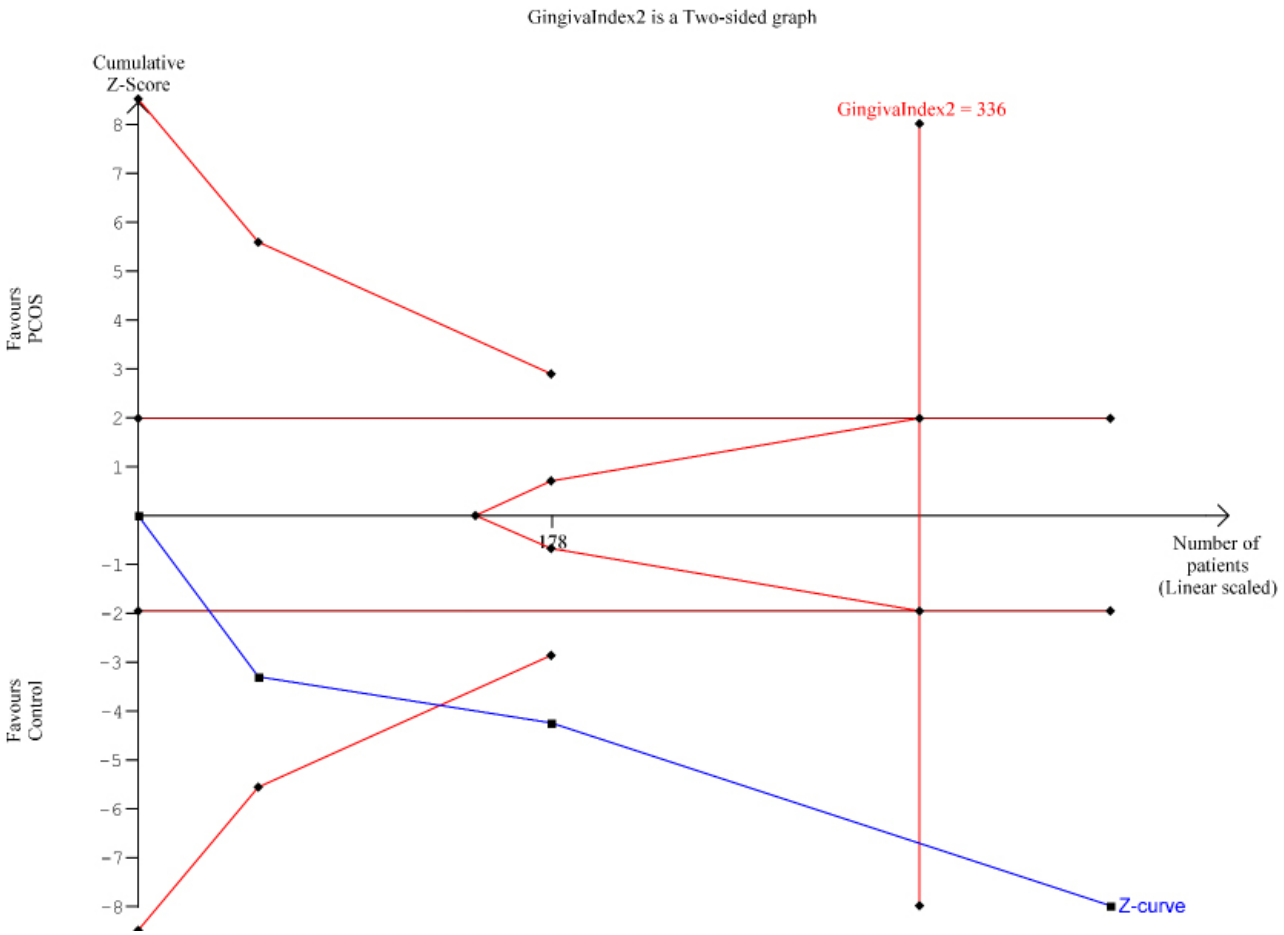
S-Fig. (1). Forest plot of probing depth.



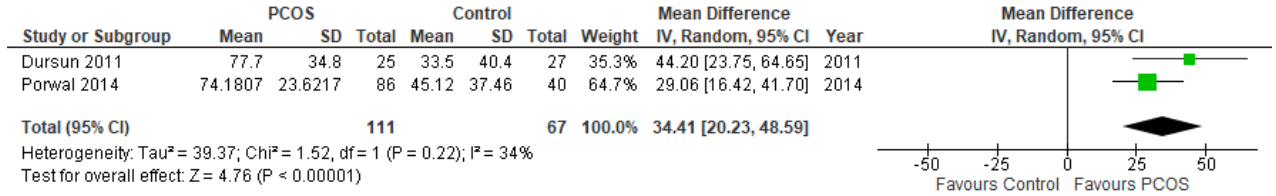
S-Fig. (2). TSA of probing depth.



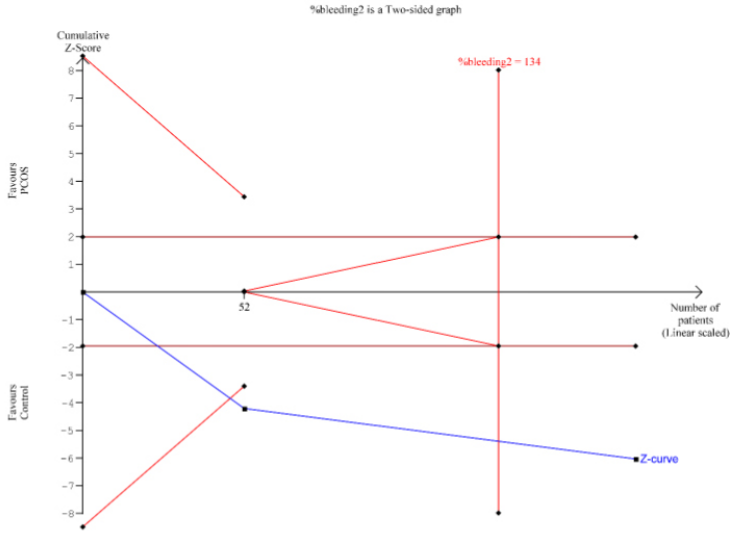
S-Fig. (3). Forest plot of gingival index.



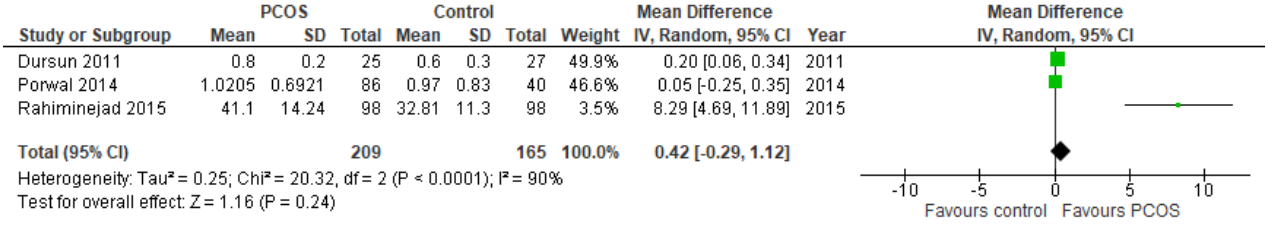
S-Fig. (4). TSA of gingival index.



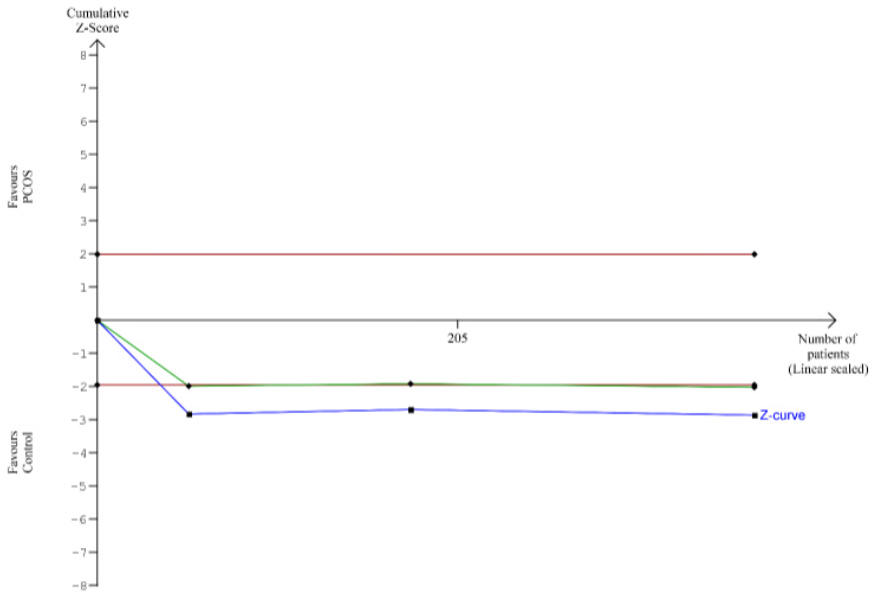
S-Fig. (5). Forest plot of percentage of bleeding on probing.



S-Fig. (6). TSA of percentage of bleeding on probing.



S-Fig. (7). Forest plot of plaque index.



S-Fig. (8). TSA of plaque index.

S-Table 1. PICO table.

Population	Intervention	Control	Outcome
Patients with polycystic ovary syndrome, who were matched with control cohort, having periodontal diseases	Polycystic ovary syndrome	Healthy cohort	Clinical attachment loss Probing indexGingival indexBleeding on probing Plaque index

S-Table 2. Search strategy medline and embase databases.

Step	Search String
1	polycystic ovary syndrome.mp. or exp Polycystic Ovary Syndrome/
2	ovarian cysts.mp. or exp Ovarian Cysts/
3	polycystic ovary disease.mp. or polycystic ovary disease.mp
4	OR (1-3)
5	periodontal disease.mp. or exp Periodontal Diseases/
6	periodontitis.mp. or exp CHRONIC PERIODONTITIS/ or exp AGGRESSIVE PERIODONTITIS/ or exp PERIODONTITIS/ or exp PERIAPICAL PERIODONTITIS/
7	exp GINGIVITIS, NECROTIZING ULCERATIVE/ or exp GINGIVITIS/ or gingivitis.mp.
8	gingival disease.mp. or exp Gingival Diseases/
9	OR (5-8)
10	4 AND 9
11	Limit 10 to humans

CENTRAL:
(periodontal disease OR gingival disease OR periodontitis OR gingivitis) AND (polycystic ovary syndrome OR polycystic ovary disease OR PCOS).

S-Table 3. Characteristics of excluded studies.

No	Study (Year)	Location	Design	Study population	Reason for exclusion
1	Akcali 2014	Turkey	Case-control study	Women with PCOS and healthy periodontium(n=45), women with PCOS and gingivitis(n=35), systemically and periodontally healthy women(n=25), systemically healthy women with gingivitis(n=20)	Selection bias
2	Akcali 2015	Turkey	Case-control study	Same population of Akcal 2014 is included	Selection bias/same population of Akcal 2014
3	Akcali 2017	Turkey	Case-control study	Same population of Akcal 2014 is included	Selection bias/same study population of Akcal 2014
4	Najah 2017	Iraq	Case-control study	Women with PCOS and CP(n=20), systemically healthy women with CP(n=20), systemically and periodontally healthy women(n=20)	Selection bias
5	Deepti 2017	India	Randomised controlled clinical trial	Test group: women with PCOS and periodontitis treated with scaling and root planing along with Myo-inositol supplementation(n=30) Control Group: women with PCOS and periodontitis treated with Myo-inositol along with oral hygiene instructions. (n=30)	Selection bias, Not directly answering the our research question
6	Hameed 2017	Iraq	Case-control study	Women with gingivitis (n=20),women with gingivitis and PCOS (n=20), women with CP (n=20), Women with CP and PCOS (n=20)	Selection bias
7	Ali 2018	Iraq	Case-control study	Women with gingivitis (n=20),women with gingivitis and PCOS (n=20), women with CP (n=20), Women with CP and PCOS (n=20)	Selection bias/ same study population of Hameed 2017
8	Najafi 2017	Iran	Case-control study	Women with PCOS (n=40) and infertile women without PCOS or any biochemical or clinical sign of hyperandrogenism as control(n=40)	CPI is used
9	Özçaka 2012	Turkey	Case-control study	Women with PCOS and healthy periodontium(n=31),women with PCOS and gingivitis(n=30), systemically and periodontally healthy women (n=12)	Selection bias
10	Özçaka 2013	Turkey	Case-control study	Same population as Özçaka 2012	Selection bias/same population as Özçaka 2012
11	Saglam 2017	Turkey	Case-control study	Women with PCOS and CP(n=22), systemically healthy women with CP(n=22), periodontally healthy women with PCOS (n=22), periodontally and systemically healthy women(n=22)	Selection bias

CP: chronic periodontitis, CPI: community periodontal index, PCOS: polycystic ovary syndrome.

S-Table 4. Risk of bias assessment: Newcastle-Ottawa Quality Assessment Scale.

No	Reference	Case-cohort representative	Selection of non-exposed control	Ascertainment of exposure	Outcome negative at start	Comparability by design	Comparability by analysis	Outcome assessment	Duration of follow-up	Score
1	Dursun et al	*	*	*	*	*	*	*	*	8
2	Porwal et al	**	*	*	*	*	*	*	*	9
3	Rahiminejad et al	*	*	*	*	*	*	*	*	8
4	Nair et al	X	*	*	*	*	*	*	*	7

*indicates that the feature is present; x, that the feature is absent. But for comparability by design this checklist awards maximum of two stars (**), one (*) or none if the feature is completely absent.

S-Table 5. Summary of findings.

Certainty Assessment							Nº of Patients		Effect		Certainty	Importance
Nº of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PCOS**	**healthy cohort**	**Relative (95% CI)**	**Absolute (95% CI)**		
Clinical Attachment Loss												
4	observational studies	not serious	very serious [a]	not serious	not serious	none	329 cases 285 controls		**RR 0.27** (0.19 to 0.36)	-	⨁◯◯◯ VERY LOW	
							-	0.0%		**0 fewer per 1,000** (from 0 fewer to 0 fewer)		
Probing depth												
2	observational studies	not serious	not serious	not serious	serious [b]	none	111 cases 67 controls		**RR 0.35** (0.21 to 0.48)	-	⨁◯◯◯ VERY LOW	
							-	0.0%		**0 fewer per 1,000** (from 0 fewer to 0 fewer)		
Gingiva Index												
3	observational studies	not serious	very serious [a]	not serious	not serious	none	231 cases 187 controls		**RR 0.70** (0.29 to 1.11)	-	⨁◯◯◯ VERY LOW	
							-	0.0%		**0 fewer per 1,000** (from 0 fewer to 0 fewer)		
Bleeding on Probing (%)												
2	observational studies	not serious	very serious [a]	not serious	serious [b]	none	0 cases 0 controls		**RR 34.41** (20.23 to 48.59)	-	⨁◯◯◯ VERY LOW	
							-	0.0%		**0 fewer per 1,000** (from 0 fewer to 0 fewer)		
Plaque index												

(S-Table 5) contd.....

Certainty Assessment							Nº of Patients		Effect		Certainty	Importance
3	observational studies	not serious	very serious [a]	not serious	serious [b]	none	209 cases 165 controls -	0.0%	**RR 0.42** (-0.29 to 1.12)	- **0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Substantial heterogeneity

b. Total participants <400

S-Table 6. PRISMA checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3, 4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4, 5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (*e.g.*, Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (*e.g.*, PICOS, length of follow-up) and report characteristics (*e.g.*, years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (*e.g.*, databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5, 6
Study selection	9	State the process for selecting studies (*i.e.*, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6, 7
Data collection process	10	Describe method of data extraction from reports (*e.g.*, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (*e.g.*, PICOS, funding sources) and any assumptions and simplifications made.	5, 6, 7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (*e.g.*, risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (*e.g.*, I^2) for each meta-analysis.	7
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (*e.g.*, publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (*e.g.*, sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8, 9
Study characteristics	18	For each study, present characteristics for which data were extracted (*e.g.*, study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8

(S-Table 6) contd.....

Section/topic	#	Checklist item	Reported on page #
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8, 9, 10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8, 9,10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8, 9, 10
Additional analysis	23	Give results of additional analyses, if done (*e.g*., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (*e.g*., healthcare providers, users, and policy makers).	11, 12, 13, 14
Limitations	25	Discuss limitations at study and outcome level (*e.g*., risk of bias), and at review-level (*e.g*., incomplete retrieval of identified research, reporting bias).	14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	11, 14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (*e.g*., supply of data); role of funders for the systematic review.	15