International Journal of Women's Health

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REVIEW

Effectiveness of long-term (twelve months) nonsurgical weight loss interventions for obese women with polycystic ovary syndrome: a systematic review

This article was published in the following Dove Press journal:
International Journal of Women's Health
9 November 2010
Number of times this article has been viewed

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Abstract: Polycystic ovary syndrome (PCOS) affects 2%–26% of women of reproductive age and is often accompanied by obesity. Modest weight loss reduces health risks and ameliorates effects of the syndrome. Weight loss interventions are mainly of short duration and have limited success. A systematic review of the literature was carried out to assess the efficacy of long-term (12 months), nonsurgical weight loss interventions for women with PCOS. Fifteen databases were searched, resulting in eight papers that met the search criteria. Comparison of results and meta-analysis was difficult due to heterogeneity of studies. Behavioral components of interventions were poorly described, and compliance was difficult to ascertain. The results suggested that the inclusion of a lifestyle component improves outcomes, but protocols must be clearly described to maintain study validity and to identify successful behavioral strategies.

Keywords: obesity, polycystic ovary syndrome, weight loss

Introduction

Polycystic ovary syndrome (PCOS) involves a spectrum of endocrine and metabolic abnormalities, affecting an estimated 2%–26% of the women of reproductive age,[1,2] depending on the ethnicity and on the diagnostic criteria used. Clinical features of PCOS include hyperandrogenism, infertility, and insulin resistance. Approximately 50% of women with PCOS are obese, with associated increased risks of diabetes, cardiovascular disease, and obesity-related comorbidities.[3,4] These risks appear to be significantly reduced, and clinical features are improved by even modest weight loss of 5%–10%.[5]

Traditional nonsurgical approaches to weight loss interventions have been based on diet and pharmacotherapy and have shown limited success, with weight being regained rapidly, and with high attrition rates.[6] In recent decades, the development of behavioral approaches to weight management, alone or in combination with diet, has provided evidence that inclusion of a behavioral change element can enhance weight loss outcomes and improve completion rates.[7] Behavioral and lifestyle modification is important in the management of overweight and obesity, as a chronic condition, in the longer term.[8] A multidisciplinary approach is essential to prevent weight gain and to achieve and sustain weight loss, particularly when fertility is impaired.[9] This requires consideration of psychosocial and practical factors in addition to physiological influences.[10] However, multidisciplinary interventions are resource intensive and are

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submit your manuscript | www.dovepress.com
Dovepress
DOI: 10.2147/IJWH.S13456

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commonly delivered for short periods only. Further, counseling and lifestyle strategies, and the protocols for delivery are often poorly described.[11]

There is little evidence that short-term interventions are effective, in either health or economic terms over longer periods following completion. It is important to evaluate long-term (≥12 months), nonsurgical weight loss interventions, with and without behavioral or lifestyle counseling and support, and to identify effective counseling strategies for the development of standard counseling protocols for comparison.

The aim of this study was to systematically review the efficacy of long-term (12 months), nonsurgical weight loss interventions and to identify specific behavioral weight loss strategies for obese women with PCOS.

Materials and methods

A systematic review was undertaken to evaluate the success of long-term (≥12 months), nonsurgical weight loss interventions for women with PCOS and to identify counseling strategies used in these interventions. The protocol for this review was based on the methods recommended by the Cochrane Collaboration.[12]

A comprehensive search was performed using 15 online databases: AMED, ASLIB, ASSIAnet, Blackwell Synergy, CAB abstracts, CINHAL, Cochrane Library, IngentaConnect, MetaPress, MEDLINE, Oxford University Press, Science Citation Index, Social Sciences Citation Index, ScienceDirect, SAGE Journals Online. Articles, in English, published between January 1998 and June 2008 were reviewed. Inclusion criteria were all prospective long-term (12 months) studies of women with a diagnosis of PCOS and mean body mass index (BMI) ≥28 kg/m^2, where weight loss was a primary or secondary outcome measure. Participant criteria were restricted to those conducted in adult populations with a minimum age >18 years and no ethnic groups were excluded. The review included randomized controlled trials and cohort studies.

The initial search was conducted by one researcher, who performed a search of databases to identify relevant articles from titles and abstracts. Those articles that appeared to meet search criteria were retrieved and examined as full copies to determine which ones met standardized eligibility criteria. Search terms included *weight loss*, *obesity, obes*, polycystic ovar* syndrome* according to specific requirements for advanced search in each database. Wildcards and Boolean operators were used to ensure inclusion of various forms for each search term. The publication *Human Reproduction*, which yielded two eligible studies, was hand-searched during the period January 2003–June 2008, and the reference lists of all included studies were searched for further relevant articles.

Two researchers independently assessed full copies of the selected studies to establish methodological quality using a standardized form. Agreement was ensured by discussion. Neither researcher was blinded to author, publication, or institution. Data were abstracted by one researcher using a standardized form and independently checked for accuracy by the second researcher. Data were entered into a software package, Review Manager 4.2.2, for analysis.

The review evaluated interventions including diet, pharmacotherapy, and behavioral or lifestyle intervention in which weight loss was a primary or a secondary outcome. The included interventions were as follows:

- Pioglitazone + metformin in women with PCOS nonresponsive to metformin + diet[13]
- Spironolactone with and without diet[14]
- Metformin + diet vs diet[15]
- Metformin with diet[16]
- Rosiglitazone + oral contraceptive[17]
- Flutamide, metformin, and combination therapy + diet[18]
- Diet + exercise[19]
- Metformin vs lifestyle + placebo vs metformin + lifestyle vs placebo[20]

Out of 71 studies initially identified, only eight met the inclusion criteria for this review. Reasons for the exclusion of these studies are detailed in Table 1.

Studies reviewed included three randomized controlled trials (RCTs), with the remaining five being prospective cohort studies. The RCTs are described in Table 2.

One RCT was of 48 weeks duration, and a further study included patients who were followed up for only 40 weeks.

Of the five cohort studies, one lasted for 4 years, but only data obtained within 1 year is reported here; three were carried out by the same principal author. In only three studies, weight loss was the primary outcome. Details of cohort studies are described in Table 3.

Table 1 Excluded studies

Reasons for exclusion	Number
Study duration <40 wk	34
Minimum age <18 y	7
Review articles	22

Note: This table indicates the reasons for excluding published studies that were initially identified in a systematic review of the literature.

Table 2 Randomized controlled trials

Principal author	Study design	Participants	Intervention
Hoeger[20]	Prospective randomized trial over 48 wk	38 obese women with PCOS, whose insulin failed to normalize after 4 mo on the diet	Metformin (n = 9) vs Lifestyle modification + placebo (n = 11) vs Metformin + lifestyle modification (n = 9) vs Placebo (n = 9)
Lemay[17]	Prospective randomized cross-over trial over 12 mo following 4 mo diet	28 overweight or obese women with PCOS (23 completers)	Group A: rosiglitazone + diet for 6 mo (n = 15) Group B: oral contraceptive (EE/CPA) + diet for 6 mo (n = 13) At 6 mo, groups A and B commenced rosiglitazone + EE/CPA for further 6 mo
Gambineri[18]	Prospective randomized controlled trial over 12 mo	80 overweight or obese women with PCOS (76 completers)	Diet + placebo (n = 19) vs Diet + metformin (n = 20) vs Diet + flutamide (n = 17) vs Diet + metformin + flutamide (n = 20)

Note: This table provides intervention details for the three randomized controlled trials that were included in this review.
Abbreviation: PCOS, polycystic ovary syndrome.

Results

Results for all studies are summarized in Table 4. It was not possible to perform a meaningful meta-analysis of weight loss outcomes due to the heterogeneous nature of these studies. Of the three RCTs, only one study by Hoeger et al[20] included a lifestyle counseling component consisting of prescribed diet and exercise plan with initial (24-week duration) weekly support, education and monitoring, and subsequent biweekly monitoring. In this study, significant weight loss was seen in groups receiving lifestyle education and support, with and without metformin (–8.9 ± 2.9 kg and –6.8 ± 3.8 kg, respectively), and in the group receiving only metformin (–6.5 ± 3.7 kg), but not in the placebo group (–0.2 ± 0.8 kg). Thus, intensive lifestyle counseling enhanced weight loss, with or without metformin. Of the 38 participants (metformin group 4, lifestyle + placebo group 5, lifestyle + metformin group 4, and placebo group 2), 13 failed to complete the intervention, resulting in an overall attrition rate of 39.5%.

In a RCT by Gambineri et al,[18] which compared diet+flutamide and metformin alone and combined, the diet+placebo group achieved a weight loss comparable to Hoeger's[20] lifestyle + placebo group, with –5 ± 16 kg vs –6.8 ± 3.8 kg,

Table 3 Cohort studies

Principal author	Study design	Participants	Intervention
Glueck[16]	Prospective cohort study	23 obese women with PCOS and idiopathic intracranial hypertension	Metformin + hypocaloric diet (n = 20) Hypocaloric diet (n = 3)
Zulian[14]	Prospective cohort study	25 lean and overweight women with PCOS	Group A (BMI < 25) received spironolactone 12 mo (n = 13) Group B (BMI > 25) received spironolactone 12 mo + dietary restriction (n = 12) Completers: Group A (n = 5) Group B (n = 7)
Glueck[13]	Prospective cohort study	39 obese women with PCOS	After 12 mo of metformin: group A (nonresponsive to metformin) received pioglitazone in addition for 10 mo (n = 13) Group B (responsive to metformin) on metformin (n = 26)
Glueck[15]	Prospective cohort study	89 obese women with PCOS, treated with metformin + diet targeted to entry weight	Metformin + annual dietary instruction (n = 89) Dietary adherence was not assessed
Crosignani[19]	Prospective cohort study	33 obese women with PCOS and chronic anovulation	1200 kcal/d diet + physical exercise (n = 33) Completers (n = 11)

Note: This table provides intervention details for the five cohort studies that were included in this review.
Abbreviations: PCOS, polycystic ovary syndrome; BMI, body mass index.

Table 4 Trials of nonsurgical, long-term weight loss interventions and their impact on weight change

Principal author	Intervention	Group A results	Group B results	Group C results	Group D results
Hoeger[20]	Metformin (n = 9) Lifestyle change + placebo (n = 11) Metformin + lifestyle change (n = 9) Placebo (n = 9)	M: –6.5% weight	LC + Pl: –6.8% weight	LC + M: –8.9% weight	Pl: –0.2% weight
Lemay[17]	Group A: rosiglitazone + diet for 6 mo (n = 15) Group B: oral contraceptive (EE/CPA) + diet for 6 mo (n = 13) At 6 mo, groups A and B commenced rosiglitazone and EE/CPA	No significant weight change	No significant weight change		
Gambineri[18]	Diet + placebo (n = 20) Diet + metformin (n = 20) Diet + flutamide (n = 20) Diet + metformin + flutamide (n = 20)	D + Pl: –5 ± 16 kg	D + M: –4 ± 13 kg	D + F: –9 ± 9 kg	D + M + F: –10 ± 14 kg
Glueck[16]	Metformin + diet (n = 20) Diet (n = 3)	M + D: –7.7% weight	D: –3.3% weight		
Zulian[14]	Group A (BMI < 25): spironolactone for 12 mo (n = 5) Group B (BMI > 25): spironolactone + diet for 12 mo (n = 7)	No weight loss	Mean BMI: –2 ± 4.7 kg		
Glueck[13]	Groups A and B: metformin for 12 mo Group A: pioglitazone for 10 mo (n = 13) Group B: metformin for 10 mo (n = 26)	No weight loss	Median: –6 kg weight		
Glueck[15]	Metformin + dietary advice (n = 89)	Mean: (8.9% weight			
Crosignani[19]	Diet + physical exercise (n = 33)	76% (n = 25): ≥–5% weight 33% (n = 11): ≥–10% weight			

Note: This table displays the results for each study included in the systematic review. The first three articles presented here are randomized controlled trials and the latter five are prospective cohort studies.
Abbreviations: M, metformin; LC, lifestyle change; Pl, placebo; D, diet; F, flutamide; BMI, body mass index.

but with a large standard deviation. The diet + metformin group achieved <50% of the weight loss found in Hoeger's comparable group (–4 ± 13 kg vs –8.9 ± 2.9 kg). However, Gambineri et al's diet + flutamide group achieved a weight loss of –9 ± 9 kg, and the diet + flutamide + metformin achieved most weight loss, –10 ± 14 kg, but with a wide range of individual results. Reported attrition was only 5% in this study and, in part, due to pregnancy.

In the third RCT with cross-over design, Lemay et al[17] found no significant weight loss in the groups that received rosiglitazone, oral contraceptive (EE/CPA), and a combination of the two drugs, and these data were not reported in the article. Weight loss was not a principal aim of this study. In the group that initially commenced rosiglitazone + diet, 33.4% of participants dropped out, whereas in the group that initially commenced EE/CPA + diet, the attrition rate was 46.2%. In the remaining studies, dropout data were not provided. It was not possible to compare weight loss results between the RCTs and cohort studies as the remaining studies reported only percentage change in either weight or BMI, with insufficient data to make relevant calculations.

In Crosignani et al's[19] cohort study of diet and physical exercise, it was unclear when weight loss of 5% and 10% was achieved either as a group mean or as individual results; therefore, it can be assumed that some participants were not followed up for a full 40-week period. However, this diet + exercise intervention resulted in 76% (n = 25) women losing ≥5% weight, and 33% (n = 11) women losing 10% weight within the 40-week period. There was sparse description of intervention strategies. A 1200-kcal diet was prescribed, and aerobic exercise such as swimming or aerobics was recommended, but without prescribed duration or frequency. Compliance was ascertained only by weight loss. This was an unobtrusive intervention, therefore, with progress monitoring every 6–8 weeks.

The results of Crosignani et al study compared favorably with Glueck's[15] cohort study of sustainability of weight loss on metformin + diet, in which at 12 months, weight loss of −8.1% was found in 89 participants who completed the intervention. This was also a nonintensive study, in which participants were initially provided with dietary instruction and received annual dietary follow-up. Progress was monitored at 2-month intervals throughout the study. Sustainability of weight loss was a primary aim.

In another cohort study by Glueck et al[13] on the effects of metformin + diet vs metformin + diet + pioglitazone in metformin nonresponders, pioglitazone had little effect on weight loss. Non metformin-responsive participants showed no weight change even with the addition of pioglitazone, whereas in the metformin-responsive group, significant weight loss (median 6 kg) was achieved with metformin + diet. Progress was monitored at 2-month intervals, but dietary support was not described.

Glueck et al's[16] third cohort study that sought to improve clinical signs and symptoms of idiopathic intracranial hypertension (IIH) in a group of 20 women with PCOS involved the use of diet and metformin. A weight change of −7.7% was achieved within 10 months in women receiving a 1500-kcal/d high-protein diet plus metformin therapy. There was no description of weight monitoring or support for this group. In the three studies reported by Glueck et al, only data from participants who completed the intervention were included.

In Zulian et al's[14] comparison of spironolactone vs spironolactone + lifestyle modification, only participants in the latter group lost significant weight. Only 12 participants were overweight or obese and were assigned as a cohort to one of the following two groups: those who received spironolactone only (mean BMI, 28.6 ± 4.7 kg/m^2; n = 5) and those who received lifestyle modification + spironolactone (mean BMI, 30.3 ± 3.5 kg/m^2; n = 7). Weight measurements were not given. In the former group, final BMI was 29 ± 5.4 kg/m^2, and in the latter group, final BMI was 26.3 ± 3.4 kg/m^2, $P < 0.05$. Lifestyle modification was described only as food restriction, 1400 kcal/d, and there was no description of monitoring or support.

Discussion

Two studies, by Gambineri et al,[18] and Hoeger et al,[20] reported similar results for their diet and lifestyle + placebo arms; however, Gambineri et al's[18] results indicated a wide range of individual results. Gambineri et al's[18] diet + metformin group achieved <50% of the weight loss found in Hoeger et al's[20] comparable group, which perhaps reflected the benefits of intensive lifestyle support in the early weeks, with less intensive early support for participants potentially affecting individual motivation.

Reported dropout in Gambineri et al's[18] study was only 5%, and possible reasons for this unusually low attrition rate were not discussed by the authors, but may be attributable to a lesser emphasis on weight loss and thus less restrictive dietary prescription and monitoring. The inclusion of a qualitative investigative component in studies of this type, to ascertain participant experiences and perceptions of weight loss interventions, could provide insight into the underlying causes for attrition and ways of enhancing the patient experience to improve compliance.

Lemay et al's[17] study of rosiglitazone + diet vs oral contraceptive (EE/CPA) + diet was not primarily aimed at weight loss, and this lack of emphasis may explain the lack of weight change. However, there was a notable difference in attrition rates in each arm of this study with the EE/CPA group having a higher noncompletion rate than in the rosiglitazone arm. Possible reasons for this difference were not discussed, but may reflect lesser participant satisfaction with EE/CPA during the first stage of the study when attrition rate is traditionally higher and benefits have yet to be seen. Alternatively, EE/CPA might cause more unpleasant side effects, affecting compliance unfavorably in the initial stages. Again, an investigation of participants' experiences and perceptions of this intervention may have provided useful insight into patients' failure to complete.

All but two studies used the ESHRE-ASRM (2003) consensus criteria for diagnosis of PCOS, which stipulates the presence of at least two of three of the following:

- Presence of clinical or biochemical hyperandrogenism
- Ovarian dysfunction – oligo-anovulation or polycystic ovaries
- Exclusion of other etiologies related to hyperandrogenism or infertility

However, Hoeger et al[20] used the National Institutes of Health 1990 consensus criteria of chronic anovulation and clinical or biochemical signs of hyperandrogenism, with exclusion of other etiologies, whereas Crosignani et al[19] used the criteria of chronic anovulation and polycystic ovaries, with exclusion of other etiologies. As discussed by March et al,[2] this may have led to the inclusion of different phenotypic groups in the reviewed studies. It is difficult to assess whether the use of differing diagnostic criteria for PCOS affected the results reviewed here. However, the use of different diagnostic criteria limits the interpretation of study results.

The results of this review, particularly for the study by Hoeger et al,[20] support the view expressed by Brown et al[7] that ongoing support and education is an important component of a weight loss intervention, enhancing the effects of drug therapies. Norman et al[9] argue that weight management should be a first-line treatment option for overweight or obese women seeking fertility, and this should comprise a range of strategies including diet, exercise, and behavior modification. However, in this review, the lack of description of support strategies, lifestyle counseling, and educational focus renders comparisons difficult. Furthermore, Dombrowski et al[11] suggests that failure to detail the intervention protocol and to ensure intervention delivery according to protocol renders the investigation invalid. This review highlights the importance of a clear, detailed description of intervention protocols, including the use of specific counseling, behavioral and educational strategies, and the need to use consistent diagnostic criteria.

Of the drugs reviewed, in one study, the antiandrogen flutamide appeared more successful in supporting weight loss, although historically, metformin appears to be the more popular treatment choice, and further comparison of the relative efficacy of these drugs in regulating weight might be helpful. However, it must be noted that neither metformin nor flutamide, per se, is a weight loss drug. Spironolactone and pioglitazone were not helpful in supporting weight loss in this patient group in these single studies. This highlights a need for further investigation of the role and efficacy of drugs used in weight loss interventions aimed specifically at women with PCOS.

Comparison of study results within this review is difficult due to heterogeneity of approaches to weight loss, differences in diagnostic tools, and poor description of lifestyle components of such interventions. This review fails to provide supportive evidence for specific lifestyle and behavioral strategies due to poor description of these and how they were used. Furthermore, only 2 RCTs had placebo controls and 5 studies compared treatment regimens with no control group. Two studies offered all participants the same intervention, although one had a cross-over design.

It can be concluded that there is a poor evidence base for current nonsurgical approaches to weight loss in obese women with PCOS due to poor description of interventions and lack of comparable weight loss data from longer-term (>12 months) studies. The relatively poor completion and success rates suggest a need for evidence-based practices that better engage obese participants in the process of long-term behavior change and to empower them to manage their weight successfully in the longer term.

The fidelity of adherence to behavioral and lifestyle change protocols by weight management staff remains unclear. Approaches to weight loss interventions remain variable, and intervention strategies have been poorly described in the literature. Reported interventions were based on an expert-led, directive medical model of obesity, which may fail to address the emotional aspects of obesity or to fully utilize individual agency for behavioral change for effective, long-term self-management of weight.

In view of the chronic nature of obesity, effective, long-term self-management of weight must be the key to reducing costs, in health and in social and economic terms of this burgeoning pandemic. It is difficult to ascertain from the existing literature which behavioral change strategies are most successful and ultimately offer best value per unit resource. However, this review highlights the lack of nonpharmacological-based trials to evaluate treatment for obese women with PCOS. There is a need for further investigation and comparison of weight loss interventions based on behavioral change, with and without concurrent drug therapy. Future studies of weight loss interventions should adopt a standardized diagnostic approach, with careful reporting of weight change data, and provision of detailed descriptions of lifestyle intervention protocols and behavioral change strategies.

Acknowledgment

The authors wish to thank Dr Peter Wimpenny, School of Nursing and Midwifery, Robert Gordon University for his advisory input into this study.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Knochenhauer ES, Key TJ, Kahsar-Miller M, Waggoner W, Boots LR, Azziz R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. *J Clin Endocrinol Metab*. 1998;83:3078–3082.
2. March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Hum Reprod*. 2010;25(2):544–551.
3. Must A, Spadano J, Coakley E, Field A, Colditz G, Dietz W. The disease burden associated with obesity. *JAMA*. 1999;282:1523–1529.
4. Boeka AG, Lokken KL. Neuropsychological performance of a clinical sample of extremely obese individuals. *Arch Clin Neuropsychol*. 2008;23:467–474.
5. Scottish Intercollegiate Guidelines Network. Management of obesity. A national clinical guideline. Edinburgh, Scotland: Scottish Intercollegiate Guidelines Network. Available from: http://www.sign.ac.uk/guidelines/fulltext/115/index.html. Accessed 2010 Apr 4 .
6. Avenell A, Broom J, Brown TJ, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess*. 2004;8:1–182.

7. Brown J, Wimpenny P, West B, Broom J. Differences in physical, emotional and social factors with weight change in adults seeking treatment for their obesity. *Int J Obes*. 2004;28(1): S133.
8. Wing RR. Behavioural treatment of severe obesity. *Am J Clin Nutr*. 1992;55 Suppl 2;S545–S551.
9. Norman RJ, Noakes M, Ruijin W, Davies MJ, Moran L, Wang JX. Improving reproductive performance in overweight/obese women with effective weight management. *Hum Reprod Update*. 2004;10(3): 267–280.
10. Moran L, Lombard CB, Lim S, Noakes M, Teede HJ. Polycystic ovary syndrome and weight management. *Womens Health (London Engl)*. 2010;6(2):271–283.
11. Dombrowski SU, Sniehotta FF, Avenell A. Current issues and future directions in psychology and health: towards a cumulative science of behaviour change: do current conduct and reporting of behavioural interventions fall short of best practice? *Psychology and Health*. 2007;22(8):869–874
12. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions*. London, UK: The Cochrane Collaboration and Wiley Blackwell; 2008.
13. Glueck CJ, Moreira A, Goldenberg N, Sieve L, Wang P. Pioglitazone and metformin in obese women with polycystic ovary syndrome not optimally responsive to metformin. *Hum Reprod*. 2003;18(8): 1618–1625.
14. Zulian E, Sartorato P, Benedini S, et al. Spironolactone in the Treatment of polycystic ovary syndrome: effects on clinical features, insulin sensitivity and lipid profile. *J Endocrinol Invest*. 2005;28(1): 49–53.
15. Glueck CJ, Aregawi D, Agloria M, Winiarska M, Sieve L, Wang P. Sustainability of 8% weight loss, reduction of insulin resistance and amelioration of atherogenic-metabolic risk factors over 4 years by metformin-diet in women with polycystic ovary syndrome. *Metabolism*. 2006;55(12):1582–1589.
16. Glueck CJ, Golnik KC, Aregawi D, Goldenberg N, Sieve L, Wang P. Changes in weight, papilledema, headache, visual field, and life status in response to diet and metformin in women with idiopathic intracranial hypertension with and without concurrent polycystic ovary syndrome or hyperinsulinaemia. *Transl Res*. 2006;148(5):215–222.
17. Lemay A, Dodin S, Turcot L, Dechene F, Forest J-C. Rosiglitazone and ethinyl estradiol/cyproterone acetate as single and combined treatment of overweight women with polycystic ovary syndrome and insulin resistance. *Hum Reprod*. 2006;21(1):121–128.
18. Gambineri A, Patton L, Vaccina A, et al. Treatment with flutamide, metformin and their combination added to a hypocaloric diet in overweight-obese women with polycystic ovary syndrome: a randomized, 12 month placebo-controlled study. *J Clin Endocrinol Metab*. 2006;91(10):3970–3980.
19. Crosignani PG, Colombo M, Vegetti W, Somigliana E, Gessati A, Ragni G. Overweight and obese anovulatory patients with polycystic ovaries: parallel improvements in anthropometric indices, ovarian physiology and fertility rate induced by diet. *Hum Reprod*. 2003;18(9):1928–1932.
20. Hoeger KM, Kochman L, Wixom N, Craig K, Miller RK, Guzick DS. A randomised 48 week placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertil Steril*. 2004; 82(2):421–429.

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