# PMS, PCOS and Nutrition

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# Premenstrual Syndrome

# Premenstrual Syndrome (PMS)

1) Symptoms
2) Definition and prevalence
3) Nutrition and management of PMS
   - Å Evening primrose oil, calcium, magnesium, Vitamin B6, Vitamin E
4) Conclusion

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# Premenstrual symptoms – Luteal phase of cycle

- Premenstrual symptoms **begin at or after ovula**tion (mid-way through the cycle) and **gradually worsen during the luteal phase** (i.e. the second half of the cycle)

# Premenstrual symptoms – Affective/emotional

- Irritability
- Angry outbursts
- Depression
- Anxiety
- Confusion
- Social withdrawal
- Oversensitivity

# Premenstrual symptoms – Somatic/physical

- Breast tenderness
- Abdominal bloating
- Headache
- Swelling of extremities
- Lower limb pain
- Acne
- GI upset

# Premenstrual symptoms – Somatic/physical ctd.

- Appetite changes
- Food cravings

# Premenstrual syndrome – Definition & Prevalence

- **Definition:** a consistent pattern of emotional and physical symptoms occurring only during the luteal phase of the menstrual cycle that are of sufficient severity to interfere with some aspects of life.
- **Prevalence:**
  - up to 85% of women experience premenstrual symptoms
  - estimated prevalence of PMS is 2-10%

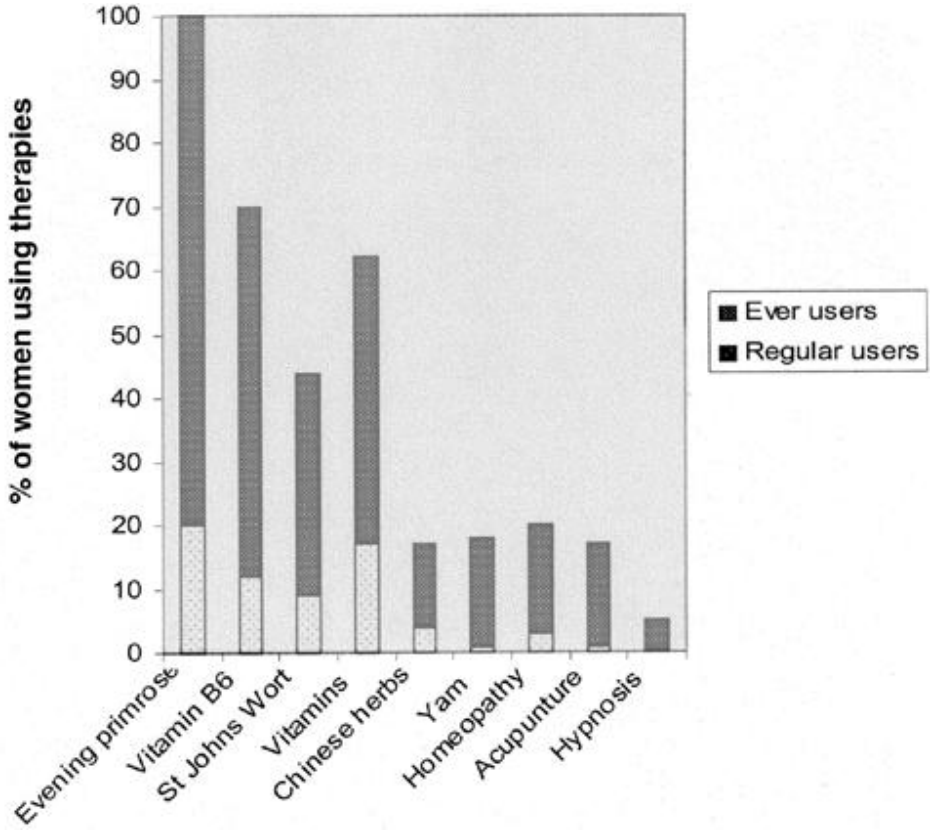
# Diagnosis of PMS

- Requires tracking symptoms for at least two consecutive cycles

- .....looking for a consistent pattern of emotional and physical symptoms occurring only during the luteal phase of the menstrual cycle that are of sufficient severity to interfere with some aspects of life.

# Management of PMS: Use of conventional and complementary therapy

- Anonymous questionnaire, 100 women attending a specialist PMS clinic in UK
- 91% had used at least one form of complementary therapy for the mgt of PMS symptoms
- Mean no. of therapies was 3.2
- Half felt that these therapies had been of benefit..... (but there is a strong placebo effect in PMS)




**Domoney et al. Gynecol Endocrinol 2003; 17: 13-18**

# Management of PMS – the nutrition evidence base

## HERBS, VITAMINS AND MINERALS IN THE TREATMENT OF PREMENSTRUAL SYNDROME: A SYSTEMATIC REVIEW

Anne Marie Whelan[1,2], Tannis M Jurgens[1], Heather Naylor[1]

[1]College of Pharmacy, Dalhousie University, Halifax, Nova Scotia; [2]Department of Family Medicine, Dalhousie University, Halifax, Nova Scotia

*Corresponding Author:* Anne.Marie.Whelan@Dal.Ca

Can J Clin Pharmacol Vol 16 (3) Fall 2009:e407-e429; October 29, 2009

(Last search date for evidence - April 2008)

# Whelan et al. Can J Clin Pharmacol 2009;16:e430-e431

Identified 62 vitamins, minerals or herbs for which some claims of benefit for PMS had been made in the literature

**TABLE 1** Herbs, vitamins and minerals advocated for treatment of premenstrual syndrome/premenstrual dysphoric disorder

| | | |
|---|---|---|
| 1. Alfalfa | 23. Garlic | 45. Potassium |
| 2. Belladonna | 24. Ginger | 46. Pycnogenol |
| 3. Birch Leaf | 25. **Ginkgo** | 47. Raspberry Leaf |
| 4. Black Cohosh | 26. Goldenseal | 48. Red Clover |
| 5. Black Haw | 27. Hawthorn | 49. Rosemary |
| 6. Blessed Thistle | 28. Hops | **50. Saffron** |
| 7. Blue Cohosh | 29. Kava | 51. Sarsaparilla Root |
| 8. Borage Oil | 30. Lavender | 52. Skull Cap |
| 9. Burdock | 31. Lemon Balm | 53. **Soy** |
| 10. **Calcium*** | 32. Licorice Root | 54. Squaw Vine |
| 11. Chamomile | 33. Lilium | 55. Stinging Nettle |
| 12. Chaparral | 34. **Magnesium** | 56. **St. John's Wort** |
| 13. **Chasteberry** | 35. Manganese | 57. Valerian |
| 14. Copper | 36. Milk Thistle | 58. **Vitamin B6** |
| 15. Corn Silk | 37. Motherwort | 59. **Vitamin E** |
| 16. Cramp Bark | 38. Niacin | 60. Wild Yam |
| 17. Dandelion | 39. Pantothenic Acid | 61. Yarrow |
| 18. Dong Quai | 40. Parsley | 62. Zinc |
| 19. **Evening Primrose Oil** | 41. Pennyroyal | |
| 20. False Unicorn | 42. Peony | |
| 21. Fennel | 43. Peppermint | |
| 22. Flaxseed Oil | 44. Pomegranate | |

* Items in bold are herbs, vitamins or minerals for which randomized controlled trials that met inclusion criteria were found.

# Whelan et al. 2009: Summary

**TABLE 5** Summary of Evidence of Benefit of Herbs, Vitamins and Minerals in Premenstrual Syndrome/Premenstrual Dysphoric Disorder

| | | |
|---|---|---|
| EPO (3 RCTs) | Not effective | -No benefit shown in 2 good quality studies[19, 20] or in 1 study of poor quality[18] |
| Vitamin B6 (13 RCTs) | Possibly effective | -Benefit shown in one good quality study [15] and in 3 studies of average quality[26, 32, 33]; the remaining 2 beneficial studies were of poor quality [28, 36]<br>-Symptoms relieved in studies: mood symptoms<br>-Dose used in effective trials: 100-500mg/day.[15, 26, 28, 32, 33, 36] Data suggests that 100mg per day is sufficient to observe any benefit while minimizing adverse effects[45] |
| Vitamin E (2 RCTs) | Limited evidence; more study warranted | -Benefit shown in one study of average quality[37] while trend to improvement observed in a poor quality study[38]<br>-Symptoms relieved in study: mood, physical and depressive symptoms<br>-Dose used in effective trial: 150-300 IU per day[37] |
| Calcium (2 RCTs) | Effective | -Benefit shown in 2 good quality studies[39, 40]<br>-Symptoms relieved in studies: negative affect, water retention, food cravings and pain<br>-Dose used in effective trials: 1000-1200mg elemental calcium per day[39, 40] |
| Magnesium (3 RCTs) | Limited evidence; more study warranted | -Benefit shown for magnesium pyrrolidone carboxylic acid in one study of average quality. [41] No benefit seen with magnesium oxide in one study of average quality[35] and one study of poor quality[42]<br>-Symptoms relieved in studies: negative affect and overall symptoms<br>-Dose used in effective trial: 360mg/d of magnesium pyrrolidone carboxylic acid[41] |

# RCTs since the Whelan systematic review....

Rocha Filho *et al. Reproductive Health* 2011, **8**:2
http://www.reproductive-health-journal.com/content/8/1/2

REPRODUCTIVE HEALTH

RESEARCH Open Access

## Essential fatty acids for premenstrual syndrome and their effect on prolactin and total cholesterol levels: a randomized, double blind, placebo-controlled study

Edilberto A Rocha Filho*, José C Lima, João S Pinho Neto, Ulisses Montarroyos

# Rocha-Filho et al. Reproductive Health 2011

- Randomised, double-blind, placebo-controlled trial
- Two doses of essential fatty acids and a placebo
- For 6 consecutive cycles
- 1g capsules containing: 210 mg gamma linoleic acid; 175 mg oleic acid; 345mg linoleic acid, 250mg other PUFAs, 20mg Vitamin E
- Recruited 120 women with PMS
- Randomised to 1g EFAs/d; 2g EFAs/d; or placebo (1g mineral oil)

# Rocha-Filho et al. Reproductive Health 2011

- Administration of 1g or 2g EFAs resulted in a significant decrease in symptom scores
- There was a statistically significant difference between the 1g or 2g EFAs compared to placebo
- The difference was already evident at 3 months and became more apparent after 6 months
- Change noted in placebo gp reached plateau at 3 months

# Chocano-Bedoya et al. Dietary B vitamin intake and incident PMS. Am J Clin Nutr 2011; 93(5):1080-6

- Nurses Health Study II cohort
- Nested case control
- Intakes B1 and B2 from food sources inversely associated incidence PMS:
  - B1: 25% reduced risk
  - B2: 35% reduced risk
- Supplemental B vitamin intake not associated with lower risk PMS
- Low-fat dairy  good source Ca + B2

# Conclusion

- Based on evidence from randomised controlled trials conducted to date:
  - Effective for PMS: Calcium - 1000-1200mg/d ï all symptom domains ï equates to approx 4 servings dairy/d
  - Equivocal evidence: Vitamin B6
  - Limited evidence but warranting further study: Vitamin E, magnesium, essential fatty acids
  - Not effective: Evening primrose oil
- Recent nested case-control study indicates vitamin B1 and vitamin B2 may be worthy of investigation ï evidence indicates food sources most important

# Polycystic Ovary Syndrome (PCOS)

# Polycystic Ovary Syndrome (PCOS)

- Prevalence
- Clinical features
- Diagnosis
- Lifestyle management
- Conclusion

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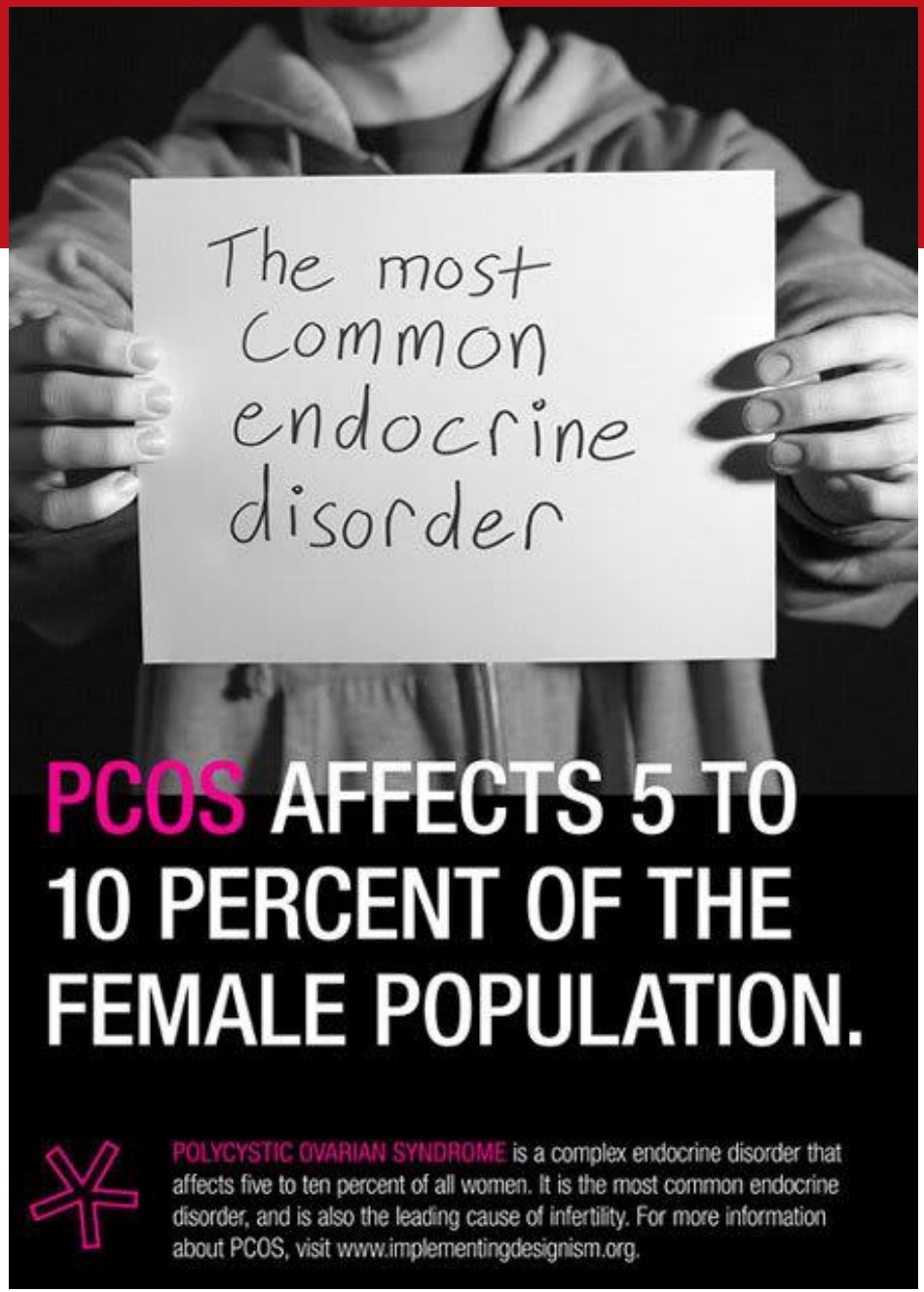
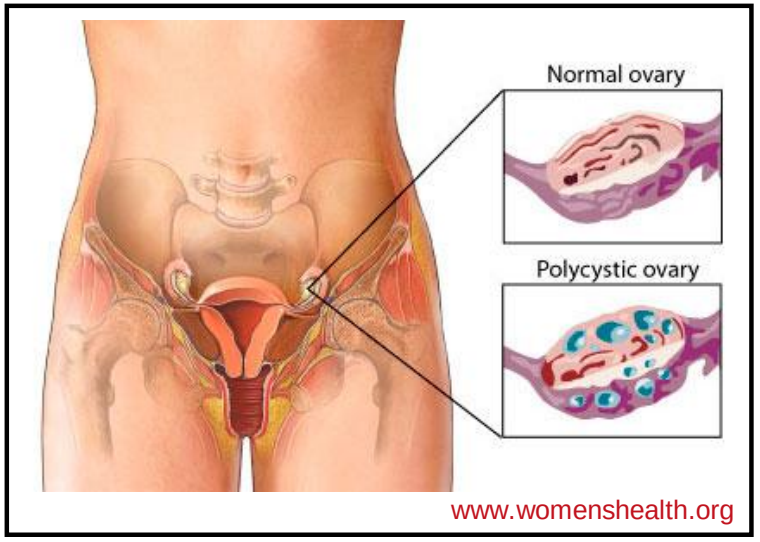

The most common endocrine disorder
PCOS AFFECTS 5 TO 10 PERCENT OF THE FEMALE POPULATION.
POLYCYSTIC OVARIAN SYNDROME is a complex endocrine disorder that affects five to ten percent of all women. It is the most common endocrine disorder, and is also the leading cause of infertility. For more information about PCOS, visit www.implementingdesignism.org.

# Clinical features PCOS: Reproductive

- **Reproductive features include:**
  - Polycystic ovaries
  - Anovulation (lack of ovulation)
  - Irregular menstrual cycles
  - Clinical hyperandrogenism (elevated circulating male hormones or androgens such as testosterone)
  - Biochemical hyperandrogenism (effects of androgens on body tissues including hirsutism or excess hair growth; acne)
  - Infertility



# Clinical features PCOS: Metabolic

- **Metabolic features include:**
  - Obesity ~50% PCOS pts obese (exacerbates biochemical & clinical abnormalities of PCOS)
  - Insulin resistance  strong association with PCOS
  - Increased risk (3-7 times) of type 2 diabetes
  - Increased risk cardiovascular disease (CVD)?
    - More atherogenic lipid profile [ HDL cholesterol; total cholesterol triglycerides); high blood pressure; worsened blood vessel function]
  - Increase in the prevalence of the metabolic syndrome (a clustering of risk factors for CVD)
  - Pregnancy complications:
    - Spontaneous abortions (high BMI/PCOS pts); small for gestational age
    - Impaired glucose tolerance; gestational diabetes; hypertension

# Clinical features PCOS: Psychosocial ï  body image, self esteem, depression, anxiety

## Polycystic ovary syndrome is associated with negatively variable impacts on domains of health-related quality of life: evidence from a meta-analysis

*Yanan Li, M.M.,[a] Yan Li, M.D., Ph.D.,[a] Ernest Hung Yu Ng, M.D.,[b] Elisabet Stener-Victorin, Ph.D.,[a,c] Lihui Hou, M.D.,[a] Taixiang Wu, M.D., Ph.D.,[d] Fengjuan Han, M.D., Ph.D.,[a] and Xiaoke Wu, M.D., Ph.D.[a]*

⇨ PCOS has a significant negative impact on health-related quality of life

⇨ PCOS affects women both psychologically and physically

Fertility and Sterility. 2011; 6(2):452-8.

# PCOS Diagnosis

- **Difficult to diagnose**
  - Heterogeneous endocrine disorder
  - Symptoms vary over time
- Syndrome ï no single criteria sufficient for diagnosis ï **polycystic ovaries are not enough to diagnose PCOS**
- **Rotterdam criteria, 2003:**

  Based on presentation with any two of the three criteria of:
  - hyperandrogenism
  - irregular anovulatory periods (menstrual dysfunction)
  - or polycystic ovaries on ultrasound, with exclusion of related reproductive disorders

Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Fertility and Sterility 2004;;81:19-25.

# Management of PCOS

- **Management of PCOS**
  - Restore regular menstruation
  - Treat hirsutism/acne
  - Restore fertility
  - Manage insulin resistance (continuous life-long management approach required)
- **Lifestyle modification** emphasised as first line treatment  may have beneficial effect on all aspects of management

# Lifestyle changes in women with polycystic ovary syndrome (Review)

Moran LJ, Hutchison SK, Norman RJ, Teede HJ

Cochrane Database Syst Rev. 2011 Feb 16;(2):CD007506.

THE COCHRANE COLLABORATION®

# Cochrane Review - Moran et al (2011): Aim

- **Aim:**
  - To assess the effect of lifestyle treatment (defined as a dietary, exercise or behavioural intervention, or a combination) on anthropometric, reproductive, metabolic and quality of life factors in women with PCOS.
- Randomised controlled trials (RCTs) that compare lifestyle intervention to minimal treatment.
- **Up-to-date as at:** 07 Sept 2010

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

# Cochrane Review - Moran et al (2011): Outcomes

- **Primary outcomes - Reproductive factors**
  - fertility outcomes (pregnancy, live birth, miscarriage)
  - menstrual regularity (an initiation of menses or significant shortening of cycle length where possible)
  - ovulation (number of ovulatory menstrual cycles where possible)
- **Secondary outcomes:**
  - **Reproductive factors -** Total testosterone, sex hormone binding globulin, estimates of free testosterone clinical hyperandrogenism (hirsutism)
  - **Anthropometric factors -** Weight, BMI, adiposity distribution (waist circumference, waist-to-hip ratio)
  - **Metabolic factors -** Oral glucose tolerance test (OGTT), glucose, lipid profile, fasting glucose and insulin, surrogate measures of insulin resistance (OGTT insulin)
  - **Quality of life and participant satisfaction**

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

# Cochrane Review Moran et al (2011): RCTs included

- **Six RCTs met inclusion criteria :** USA (N=4); Sweden (n=1); or Italy (n=1)
- **Duration:** 12 weeks (n=3);16 weeks (n=1); 24 weeks (n=1); 48 weeks (n=1)
- **Lifestyle intervention was either :**
  - a structured physical activity intervention - not specifically designed to induce weight loss (n=1) or designed to be weight maintenance (n=2)
  - or a combined dietary, exercise and behavioural intervention designed to specifically induce weight loss (n=3)
- The studies assessing structured physical activity interventions consisted of:
  - **Study 1:** three supervised 40-minute training sessions/week
  - **Study 2:** individualized prescriptions (average of 228 minutes/week)
  - **Study 3:** advice of 30 to 45 minutes of moderate exercise beyond daily physical activity

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

# Cochrane Review Moran et al (2011): RCTs included

**For studies assessing combined lifestyle intervention (n=3):**

- **Study 1:** meal replacement formula diet (Optifast) with meals and multivitamin supplements (energy intake 1000 -1200 kcal/d), behavioural modification training and individualized energy expenditure goals in a non-supervised environment.
- **Study 2:** Dietary, exercise and behavioural intervention:
  - aiming for a 7% to 10% weight loss through
  - individual and group dietitian and exercise physiologist meetings weekly from weeks 0 to 24 and bi-weekly from weeks 25 to 48
  - individualised meal (500 to 1000 kcal/d energy deficit) and exercise plans (150 minutes/week)
- **Study 3:** As above but with weekly group or individual training classes for diet, exercise and behavioural modification skills with overall therapy goals of a weight loss of 5% to 7%

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

# Primary outcomes ï Reproductive factors

- **Fertility outcomes**: No data were available for analysis on pregnancy outcomes, live birth or miscarriage.

- **Menstrual regularity and ovulation:**
  - No studies reported menstrual regularity/ovulation as defined in the reviewôs methods (initiation of menses or significant shortening of cycle length; number of ovulatory menstrual cycles respectively).

- Lack of reporting/variable reporting means that no statement can be made as to the effects of lifestyle treatment on these outcomes.

Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506

# Secondary outcomes: Hyperandrogenism

- Biochemical hyperandrogenism (high male hormone levels)
  - greater reduction in total testosterone for lifestyle treatment compared to minimal treatment
  - no effect for sex hormone binding globulin (SHBG) or free androgen index (FAI; bioavailable testosterone  a more valid marker of hyperandrogenism)
- Clinical hyperandrogenism
  - greater reduction in Ferriman-Gallwey score (evaluates extent and pattern of hirsutism) for lifestyle treatment compared to minimal treatment
  - No data available for acne vulgaris

# Figure 4. Forest plot of lifestyle intervention versus minimal treatment: Secondary anthropometric outcomes (adiposity)

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

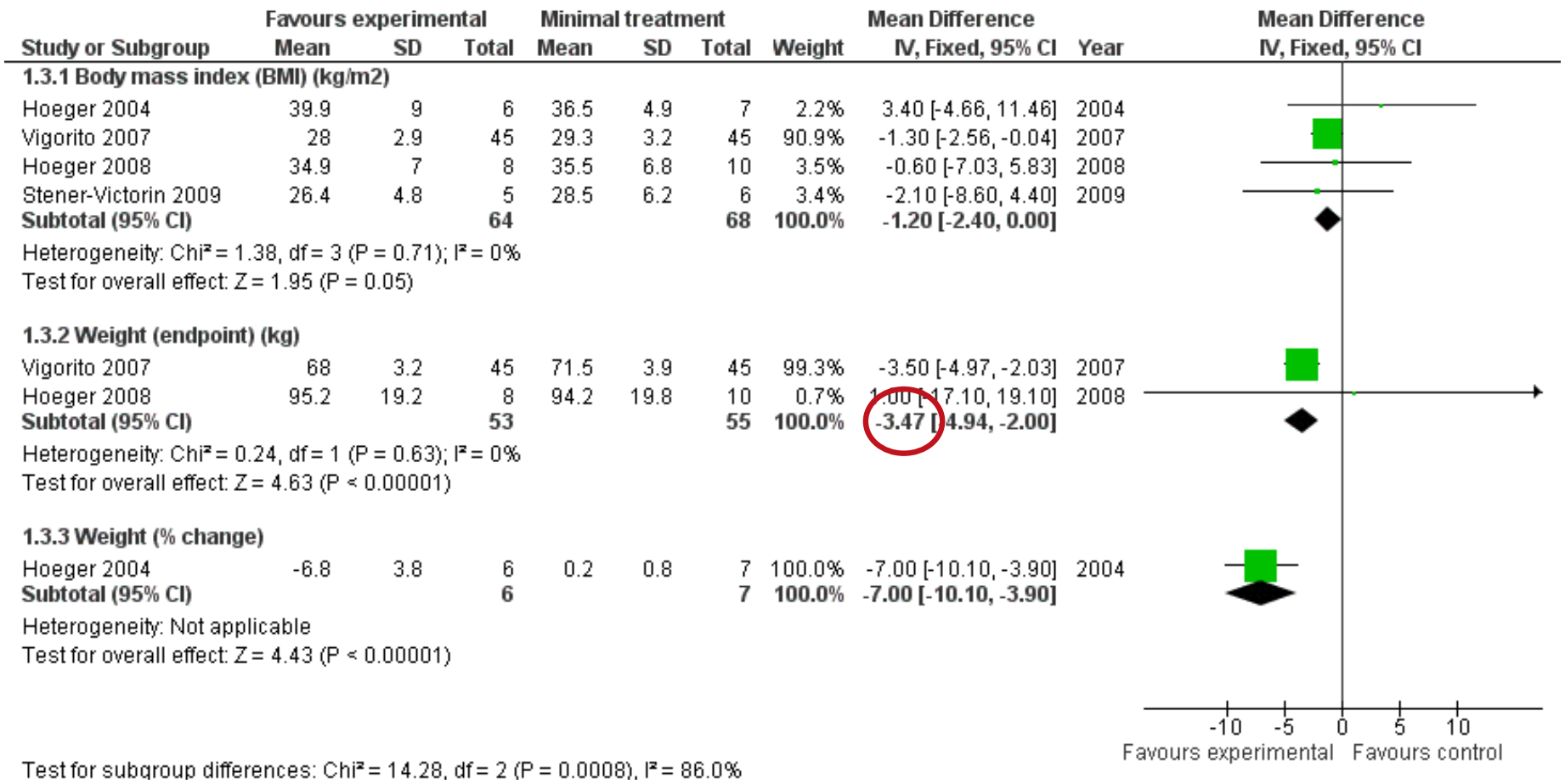
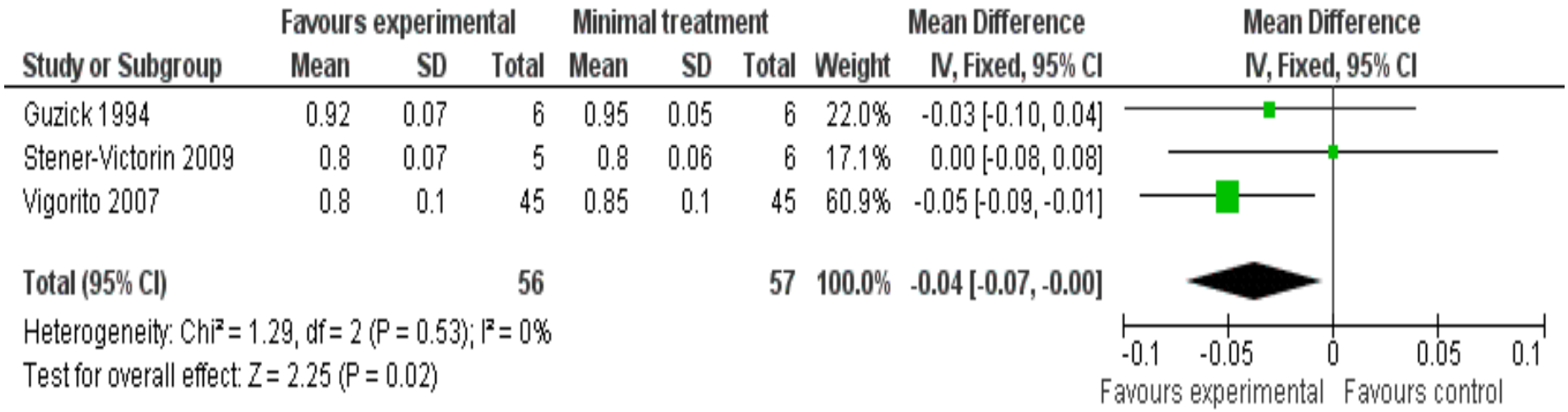


Figure 5. Forest plot of comparison lifestyle intervention versus minimal treatment: Secondary outcome: Adiposity distribution (waist-to-hip ratio (WHR)).




Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506

# Secondary endpoints: Metabolic & other outcomes

**Metabolic outcomes:**

- Surrogate measures of insulin resistance:
  - greater reductions in fasting insulin & OGTT insulin for lifestyle treatment compared to minimal treatment.
- Glucose tolerance - no evidence of effect for fasting glucose or OGTT glucose.
- Lipid profile - no evidence of effect for lipids (total cholesterol, HDL-C or triglycerides).

**Other outcomes:**

- Quality of life  not reported.

# Cochrane Review - Moran et al (2011): Quality of evidence and bias

- 5/6 studies had small sample sizes (11 to 20) - ? power of all analyses
  - only 2 studies had pre-defined power calculations
- No studies carried out ITT analyses
- High drop-out rates in majority of studies - ? methodological weaknesses in study protocols
- Inconsistent outcomes were reported between studies
- Risk of bias:
  - lack of evidence of adequate allocation concealment: n=3
  - lack of evidence of adequate clinician, outcome or data analyst blinding: n=2
  - selective outcome reporting: n=3

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

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- No studies carried out ITT analyses
- High drop-out rates in majority of studies - ? methodological weaknesses in study protocols
- Inconsistent outcomes were reported between studies
- Given the limited number of studies and small sample sizes, subgroup analysis [by intervention duration, type and participants] was not feasible
- Risk of bias:
  - lack of evidence of adequate allocation concealment: n=3
  - lack of evidence of adequate clinician, outcome or data analyst blinding: n=2
  - selective outcome reporting: n=3

**Overall, quality evidence = low - moderate**

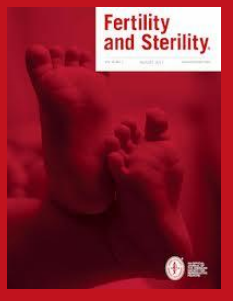
**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

# Cochrane Review - Moran et al (2011): Implications for practice

- Limited well-designed studies available to guide clinical practice
- Current evidence - medium to long-term lifestyle intervention results in reduced weight with associated improvements in the key pathological features in PCOS of abdominal obesity, biochemical and clinical hyperandrogenism and surrogate markers of insulin resistance.
- No existing RCT for reproductive outcomes (fertility, menstrual regularity or ovulation)
- Given the positive effects of diet or exercise on achieving weight loss, reducing risk factors for CVD and type 2 diabetes and improving quality of life in the general population, these interventions should be advocated for women with PCOS
- Issues - ability to translate research findings into clinical practice

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**

Fertility and Sterility 2010; 94: 1812-1816




# Lifestyle management improves quality of life and depression in overweight and obese women with polycystic ovary syndrome

*Rebecca L. Thomson, Ph.D.,*[a,b] *Jonathan D. Buckley, Ph.D.,*[a] *Siew S. Lim, MND.,*[b] *Manny Noakes, Ph.D.,*[b] *Peter M. Clifton, Ph.D.,*[b] *Robert J. Norman, Ph.D.,*[c] *and Grant D. Brinkworth, Ph.D.*[b]

[a] Australian Technology Network Centre for Metabolic Fitness & Nutritional Physiology Research Centre, Sansom Institute for Health Research, University of South Australia; [b] Preventative Health Flagship, Commonwealth Scientific and Industrial Research Organisation, Food and Nutrition Sciences; and [c] Research Centre for Reproductive Health, Robinson Institute, University of Adelaide, Adelaide, South Australia, Australia

# Thomson et al, Fertility and Sterility 2010; 94: 1812-1816

**TABLE 1**

**Depression scores from the center of epidemiologic studies depression scale (CES-D) and polycystic ovary syndrome questionnaire (PCOSQ) for women with polycystic ovary syndrome at baseline and after 10 and 20 weeks of diet only (DO), diet and aerobic exercise (DA), or diet and combined aerobic-resistance exercise (DC).**

| | Week 0 | Week 10 | Week 20 | Time | Time × treatment |
|---|---|---|---|---|---|
| CES-D | | | | | |
| DO | 18.2 ± 2.5 | 13.0 ± 2.7[a] | 16.6 ± 3.3 | | |
| DA | 18.6 ± 2.2 | 10.6 ± 1.8[a] | 14.0 ± 2.4 | <.001 | .86 |
| DC | 13.4 ± 1.7 | 9.3 ± 1.5[a] | 12.8 ± 1.8 | | |
| PCOSQ | | | | | |
| Emotion score | | | | | |
| DO | 4.1 ± 0.4 | 4.6 ± 0.3[a] | 4.7 ± 0.4[a] | | |
| DA | 4.3 ± 0.2 | 5.2 ± 0.2[a] | 4.9 ± 0.3[a] | <.001 | .33 |
| DC | 4.8 ± 0.2 | 5.2 ± 0.2[a] | 5.3 ± 0.2[a] | | |
| Body hair score | | | | | |
| DO | 3.1 ± 0.4 | 3.4 ± 0.4 | 3.3 ± 0.3 | | |
| DA | 3.1 ± 0.3 | 3.2 ± 0.3 | 3.4 ± 0.3 | .10 | .69 |
| DC | 3.3 ± 0.3 | 3.3 ± 0.3 | 3.5 ± 0.3 | | |
| Weight score | | | | | |
| DO | 1.9 ± 0.2 | 2.5 ± 0.3[a] | 2.9 ± 0.3[a] | | |
| DA | 1.9 ± 0.2 | 3.4 ± 0.3[a] | 3.3 ± 0.3[a] | <.001 | .10 |
| DC | 2.2 ± 0.2 | 3.2 ± 0.2[a] | 3.5 ± 0.3[a] | | |
| Infertility problems score | | | | | |
| DO | 4.4 ± 0.5 | 4.7 ± 0.6[a] | 4.8 ± 0.5[a] | | |
| DA | 4.5 ± 0.4 | 5.4 ± 0.4[a] | 5.3 ± 0.4[a] | <.001 | .54 |
| DC | 4.5 ± 0.3 | 5.1 ± 0.3[a] | 5.2 ± 0.3[a] | | |
| Menstrual problems score | | | | | |
| DO | 3.5 ± 0.3 | 3.7 ± 0.4[a] | 4.1 ± 0.4[a] | | |
| DA | 3.8 ± 0.3 | 4.4 ± 0.3[a] | 4.4 ± 0.3[a] | .001 | .15 |
| DC | 3.7 ± 0.3 | 4.4 ± 0.2[a] | 4.6 ± 0.3[a] | | |

*Note:* Values are mean ± SE; n = 49.

[a] Significantly different from week 0 ($P \leq .001$) as determined by repeated measures ANOVA and pairwise comparisons with Bonferroni corrections.

*Thomson. Quality of life and depression in PCOS. Fertil Steril 2010.*

# Thomson et al, Fertility and Sterility 2010; 94: 1812-1816

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| DA | 18.6 ± 2.2 | 10.6 ± 1.8[a] | 14.0 ± 2.4 | <.001 | .86 |
| DC | 13.4 ± 1.7 | 9.3 ± 1.5[a] | 12.8 ± 1.8 | | |
| PCOSQ | | | | | |
| Emotion score | | | | | |
| DO | 4.1 ± 0.4 | 4.6 ± 0.3[a] | 4.7 ± 0.4[a] | | |
| DA | 4.3 ± 0.2 | 5.2 ± 0.2[a] | 4.9 ± 0.3[a] | <.001 | .33 |
| DC | 4.8 ± 0.2 | 5.2 ± 0.2[a] | 5.3 ± 0.2[a] | | |
| Body hair score | | | | | |
| DO | 3.1 ± 0.4 | 3.4 ± 0.4 | 3.3 ± 0.3 | | |
| DA | 3.1 ± 0.3 | 3.2 ± 0.3 | 3.4 ± 0.3 | .10 | .69 |
| DC | 3.3 ± 0.3 | 3.3 ± 0.3 | 3.5 ± 0.3 | | |
| Weight score | | | | | |
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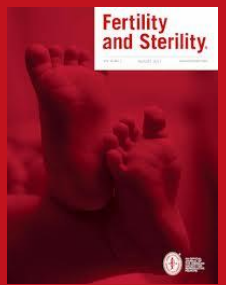
*Note:* Values are mean ± SE; n = 49.

[a] Significantly different from week 0 ($P \leq .001$) as determined by repeated measures ANOVA and pairwise comparisons with Bonferroni corrections.

*Thomson. Quality of life and depression in PCOS. Fertil Steril 2010.*

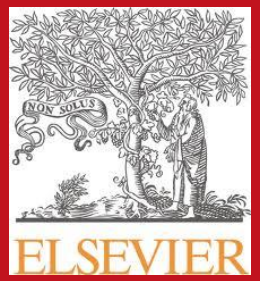
Fertility and Sterility 2011;96:1508-1513



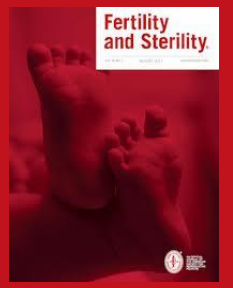

# Randomised comparison of the influence of dietary management and/or physical exercise on ovarian function and metabolic parameters in overweight women with polycystic ovary syndrome.

*Nybacka A, Carlstrom K, Stahle A, Nyren S, Hellstrom PM, Hirschberg AL.*

*Karolinska University Hospital, Sweden*

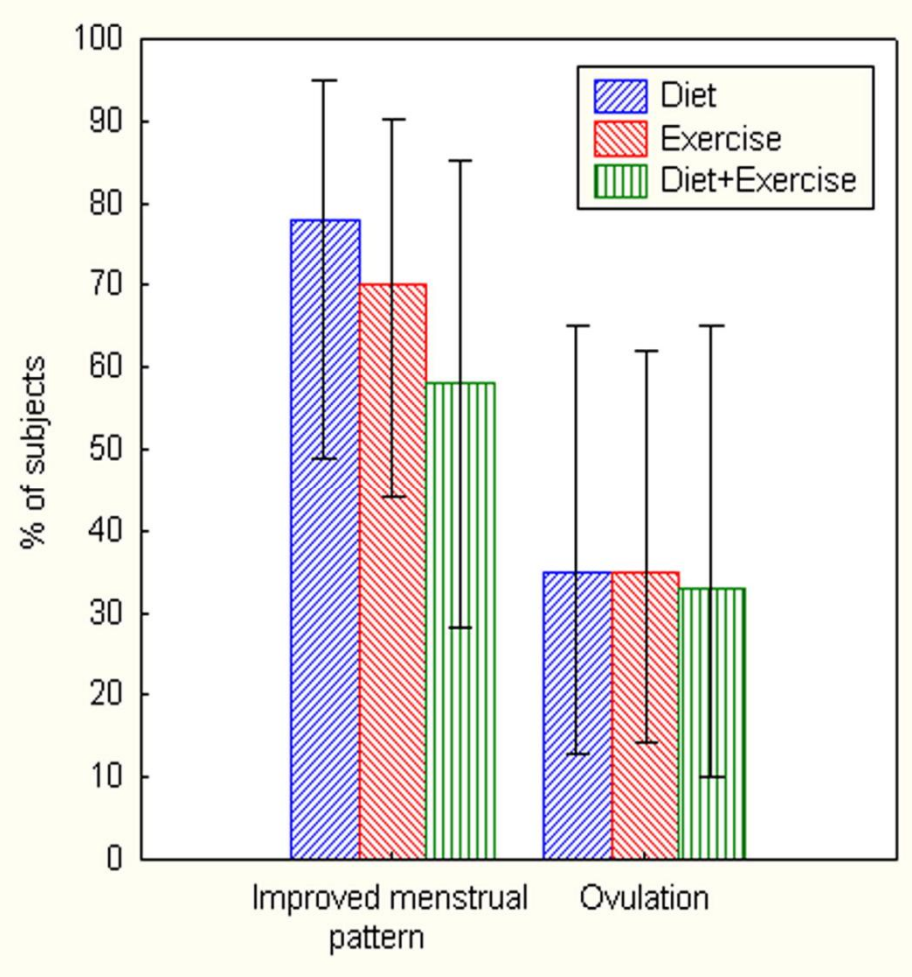



**Nybacka et al. Fertility and Sterility 2011;96:1508-1513**




- 4- month trial + long-term follow-up
- 57 overweight/obese women with PCOS randomised to:
  - Diet (n=19; *14 completed*)
  - Exercise (n=19; *17 completed*)
  - Diet and exercise (n=19; *12 completed*)
- BMI reduced by:
  - 6% diet
  - 3% exercise
  - 5% combined interventions
  - No difference between gps

## Nybacka et al. Fertility and Sterility 2011;96:1508-1513



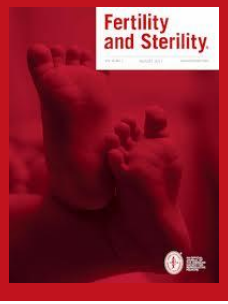

- Menstrual pattern improved in 69% (30 out of 43)
- Ovulation confirmed in 34% (15 out of 43)
- No differences between gps

- Followed up n=7/gp, median 2.8 yrs;

⇨ sustained weight reduction +

⇨ improved menstrual pattern (11/17 not using OCs had regular menstruation)

Nybacka et al. Fertility and Sterility 2011;96:1508-1513




## Å Conclusion:

- ï Dietary management and physical activity, alone or in combination, is equally effective in improving reproductive function in overweight/obese women with PCOS.
- ï Underlying mechanisms appear to involve enhanced insulin sensitivity.
- ï Supportive individualised programs for lifestyle change could exert long-term beneficial effects.

Mutsaerts *et al. BMC Women's Health* 2010, **10**:22
http://www.biomedcentral.com/1472-6874/10/22

BMC Women's Health

STUDY PROTOCOL Open Access

# The LIFESTYLE study: costs and effects of a structured lifestyle program in overweight and obese subfertile women to reduce the need for fertility treatment and improve reproductive outcome. A randomised controlled trial

Meike AQ Mutsaerts*[1], Henk Groen[2], Nancy CW ter Bogt[3], Johanna HT Bolster[1], Jolande A Land[1], Wanda JE Bemelmans[4], Walter KH Kuchenbecker[5], Peter GA Hompes[6], Nick S Macklon[7], Ronald P Stolk[2], Fulco van der Veen[8], Jacques WM Maas[9], Nicole F Klijn[10], Eugenie M Kaaijk[11], Gerrit JE Oosterhuis[12], Peter XJM Bouckaert[13], Jaap M Schierbeek[14], Yvonne M van Kasteren[15], Annemiek W Nap[16], Frank J Broekmans[7], Egbert A Brinkhuis[17], Carolien AM Koks[18], Jan M Burggraaff[19], Adrienne S Blankhart[20], Denise AM Perquin[21], Marie H Gerards[22], Robert JAB Mulder[23], Ed TCM Gondrie[24], Ben WJ Mol[25] and Annemieke Hoek[1]

# LIFESTYLE study protocol

- **Hypothesis** – the intervention will decrease the need for fertility Rx, diminish overweight-related pregnancy complications, and improve perinatal outcomes
- **Methods/design:** Multicenter RCT in subfertile women (age 18-39) with a BMI 29-40 kg/m$^2$
  - Conventional fertility care vs lifestyle intervention (n=285/gp)
  - Intervention gp – aim wt loss at least 5-10% in 6 mth period (diet, physical activity, behaviour modification)
  - Fertility Rx given after 6 mths if no conception
- **Outcomes:**
  - 1$^o$ – healthy full-term singleton
  - 2$^o$ – pregnancy outcome and complications; % women needing fertility Rx, clinical and ongoing pregnancy rates, body weight, QOL and costs

# Conclusion

- PCOS is the most common endocrine disorder among young women .
- PCOS is a heterogeneous condition that is associated with a range of metabolic abnormalities which can lead to long term health problems .
- Medium to long-term lifestyle intervention results in reduced weight with associated improvements in the key pathological features in PCOS of abdominal obesity, biochemical and clinical hyperandrogenism and surrogate markers of insulin resistance.
- Lifestyle management should be advocated patients with PCOS.
- More research required.....

# Further research

- **More research needed into lifestyle intervention in PCOS:**
  - well-designed, adequately powered studies, sufficient duration (lifestyle treatment needs to be maintained long term for improvements in a range of outcomes ï lack of long-term studies);
  - address the gaps in the literature with respect to ovulation, menstrual and fertility outcomes, and lipid and glucose levels and quality of life;
  - determine optimal weight loss for all clinical improvements;
  - perform cost-benefit analysis compared to other commonly used pharmacological and surgical treatments;
  - investigate strategies to minimise drop outs.

**Moran et al. Cochrane Database Syst Rev 2011 Feb 16;(2):CD007506**