



# Obstetric complications and management in women with polycystic ovary syndrome



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SUBFERTILITY

INFERTILITY



# Perinatal problems;

## Main Maternal or Paternal causes versus ART ?



Hayashi M, Nakai A, Satoh S, Matsuda Y.

## Fertility and Sterility® Vol. 98, No. 4, October 2012

Adverse obstetric and perinatal outcomes of singleton pregnancies may be **related to maternal factors associated with infertility** rather than the type of assisted reproductive technology procedure used

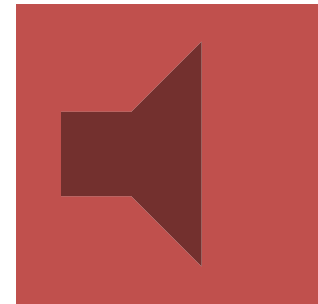
**Comparison of adverse obstetric outcomes between the groups that underwent specific types of ART procedures and the corresponding matched controls.**

| Outcome                 | Ovulation stimulation |           | IUI  |            | IVF-ET |           |
|-------------------------|-----------------------|-----------|------|------------|--------|-----------|
|                         | OR                    | 95% CI    | OR   | 95% CI     | OR     | 95% CI    |
| Pregnancies             |                       |           |      |            |        |           |
| PIH                     | 1.06                  | 0.87–1.28 | 0.88 | 0.70–1.09  | 0.74   | 0.62–0.89 |
| Eclampsia               | 0.65                  | 0.16–2.73 | 0.41 | 0.09–1.85  | 0.31   | 0.08–1.15 |
| Placenta abruption      | 1.35                  | 0.88–2.08 | 0.98 | 0.59–1.62  | 1.21   | 0.79–1.87 |
| Placenta previa         | 1.77                  | 1.24–2.54 | 1.46 | 1.03–2.08  | 2.2    | 1.68–2.87 |
| Placenta accrete        | 0.6                   | 0.28–1.31 | 1.51 | 0.80–2.84  | 2.67   | 1.42–5.03 |
| PTD <37 wk of gestation | 1.29                  | 1.15–1.45 | 1.16 | 1.01–1.33  | 1.29   | 1.16–1.45 |
| PTD <34 wk of gestation | 1.31                  | 1.11–1.54 | 1.22 | 1.01–1.47  | 1.33   | 1.13–1.57 |
| Type of delivery        |                       |           |      |            |        |           |
| Spontaneous cephalic    | 0.91                  | 0.83–0.99 | 0.87 | 0.79–0.96  | 0.75   | 0.69–0.81 |
| Instrumental            | 0.95                  | 0.82–1.11 | 1.07 | 0.91–1.26  | 1.01   | 0.87–1.66 |
| Elective cesarean       | 1.06                  | 0.93–1.20 | 1.09 | 0.95–1.26  | 1.38   | 1.23–1.55 |
| Emergency cesarean      | 1.11                  | 0.99–1.25 | 1.11 | 0.98–1.26  | 1.19   | 1.07–1.32 |
| Others                  | 1.68                  | 1.11–2.55 | 1.2  | 0.66–2.16  | 0.82   | 0.47–1.44 |
| Postpartum hemorrhage   | 1.24                  | 0.99–1.56 | 1.23 | 0.95–1.60  | 1.46   | 1.18–1.81 |
| ICU admission           | 0.36                  | 0.04–3.48 | 0.77 | 0.20–2.98  | 0.19   | 0.02–1.60 |
| Maternal death          | 0.54                  | 0.05–5.99 | 1.13 | 0.10–12.45 | 0.47   | 0.04–5.14 |
| Infants                 |                       |           |      |            |        |           |
| Birth weight, g         |                       |           |      |            |        |           |
| <2,500                  | 1.35                  | 1.21–1.50 | 1.17 | 1.04–1.32  | 1.27   | 1.15–1.40 |
| <1,500                  | 1.36                  | 1.13–1.64 | 1.23 | 0.99–1.52  | 1.3    | 1.08–1.57 |
| <1,000                  | 1.77                  | 1.34–2.32 | 1.38 | 1.01–1.88  | 1.44   | 1.09–1.90 |
| SGA                     | 1.45                  | 1.21–1.73 | 1.27 | 1.04–1.55  | 1.12   | 0.94–1.33 |
| UmA pH <7.00            | 0.6                   | 0.25–1.49 | 1.26 | 0.59–2.70  | 0.93   | 0.45–1.92 |
| Apgar score (5 min) <7  | 1.11                  | 0.87–1.41 | 1.24 | 0.95–1.62  | 1.18   | 0.93–1.49 |
| Neonatal resuscitation  | 1.29                  | 1.17–1.43 | 1.06 | 0.94–1.19  | 1.23   | 1.12–1.35 |
| NICU admission          | 1.1                   | 0.98–1.24 | 0.96 | 0.84–1.11  | 1.12   | 1.00–1.26 |
| Infant death            | 1.23                  | 0.87–1.75 | 1.22 | 0.83–1.80  | 1.25   | 0.89–1.78 |

**Risk of adverse pregnancy outcomes in women with polycystic ovary syndrome: population based cohort study**

Roos N, Kieler H, Sahlin L, et al. *BMJ* 2011;343:d6309

- Population based cohort study
- 1995-2007, Sweden
- N=3787, PCOS pregnancy, Rotterdam criteria
- Results:
  - Nulliparity (P<0.001)
  - ART (P<0.001)
  - >BMI (P<0.001)
  - Age (P<0.001)



Hypertensive disease

GDM

Preterm delivery

# PCOS(1)

- PCOS; menstrual irregularity and hyperandrogenism
  - Irregular menstrual cycle
  - Hirsutism
  - Acne
  - Obesity (more frequently)
- Incidence; 6.5-15%
- Syndrome !(multiple etiology, presentation)



# PCOS(2)

- More frequent gonadotropine dysfunction
- Prenatal androgenisation in female fetus
- Subfertility in PCOS,
- More frequent early pregnancy loss?

Balen AH,et al. Hum Reprod 1993; 8:959.

# PCOS(3)

- More frequent need for ART in PCOS patients

Azziz R, et al. J Clin Endocrinol Metabol 2001;86:1626-32

Lord JM, et al. BMJ 2003;327:951-3

Heijnen E, et al. Hum Reprod Update 2006;12:13-21

- More frequent **PIH** and **IUGR** due to insulin resistance and low levels of IGLGFB-P1

Jensen RB, et al. Horm Res 2003;60(suppl):136-48

Ryan E, et al. Lancet 2003;362:1777

Yogev Y, et al. An J Obstet Gynecol 2004;12:13-21



# PCOS(4)

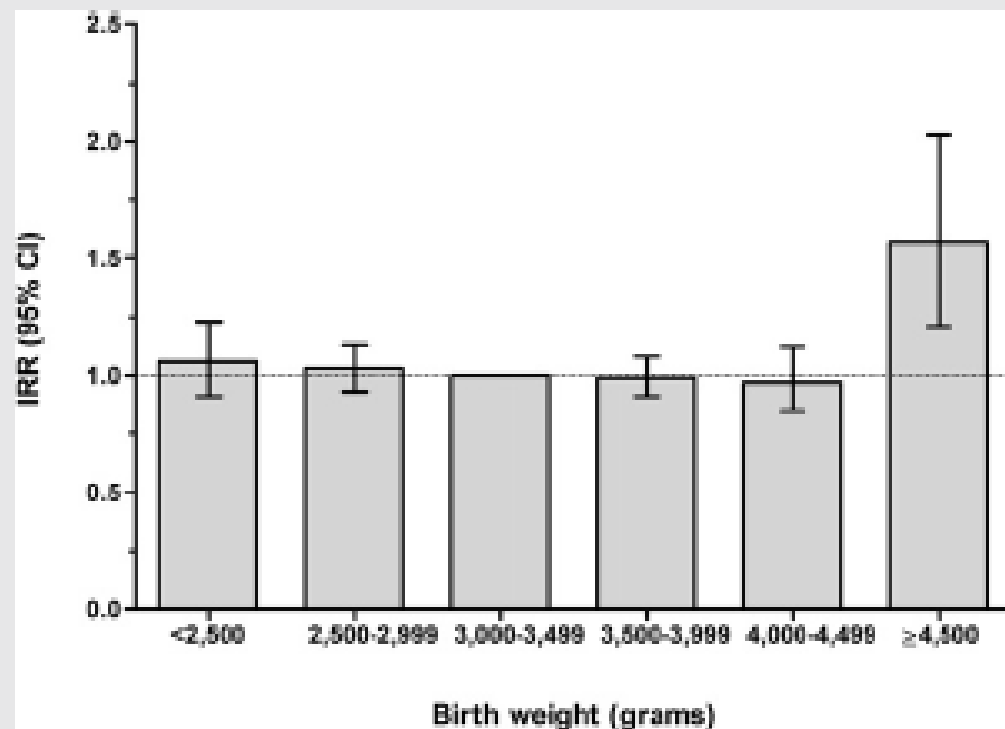
- “NHANES report”, (National Health and Nutrition Examination Survey) :  
The incidence of metabolic syndrome:  
18-19 % in healthy women (20-39y)  
– Higher rate in PCOS (%33-43)  

Apridonidze T, et al. J Clin Endocrinol Metab 2005; 90:1929.  
Dokras A, et al. Obstet Gynecol 2005; 106:131.  
Ehrmann DA, et al. J Clin Endocrinol Metab 2006; 91:48.
- DM, IGT, dyslipidemia,....
- Endothelial dysfunction
- Increase in the rate of VTE????

# Birth weight and polycystic ovary syndrome in adult life: a register-based study on 523,757

Danish women born 1973–1991

Fertility and Sterility® Vol. 99, No. 3, March 1, 2013



Incidence risk ratios (IRR) (95% confidence interval [CI]) of polycystic ovary syndrome (PCOS) in relation to birth weight.

Mumm. Birth weight and risk of PCOS. Fertil Steril 2013.



**Birth weight >4500gr in PCOS**

**Birth weight and polycystic ovary syndrome in adult life: a register-based study on 523,757 Danish women born 1973–1991**

Fertility and Sterility® Vol. 99, No. 3, March 1, 2013

**Number of PCOS cases and IRR of PCOS according to birth weight and maternal diabetes.**

| Birth weight (g) | No diabetes |      |             | Diabetes |      |             |
|------------------|-------------|------|-------------|----------|------|-------------|
|                  | n           | IRR  | (95% CI)    | n        | IRR  | (95% CI)    |
| <2,500           | 190         | 1.04 | (0.89–1.21) | 9        | 3.51 | (1.82–6.75) |
| 2,500–2,999      | 587         | 1.03 | (0.93–1.14) | 10       | 2.07 | (1.11–3.86) |
| 3,000–3,499      | 1,208       | 1.00 | (ref.)      | 23       | 2.54 | (1.68–3.83) |
| 3,500–3,999      | 863         | 1.00 | (0.92–1.09) | 13       | 1.61 | (0.93–2.79) |
| 4,000–4,499      | 235         | 0.97 | (0.85–1.12) | 6        | 1.49 | (0.67–3.32) |
| ≥4,500           | 58          | 1.61 | (1.23–2.09) | 2        | 1.19 | (0.30–4.76) |

Note: CI = confidence interval; IRR = incidence risk ratios; PCOS = polycystic ovary syndrome.

*Mumm. Birth weight and risk of PCOS. Fertil Steril 2013.*

# PCOS & Obstetric-Neonatal Risk

**PCOS is associated with a significantly increased risk of:**

- Maternal:
  - Gestational diabetes †
  - Pregnancy induced hypertension †
  - Preeclampsia
  - Delivery by caesarean section
  
- Neonatal:
  - Admission to a Neonatal Intensive Care Unit
  - Perinatal mortality
  - Premature deliveries

†: Outcome confirmed by subgroup analysis of higher validity studies

# Diagnostic criteria of PCOS

- Problems due to definition:
  - Rotterdam Criteria before 2006
    - oligo/anovulation
    - hyperandrogenism
    - PCO (usg)
  - AE-PCOS (Androgen Excess-PCOS criteria) since 2006
    - hyperandrogenism (+)
    - Other phenotypes

Azziz R, et al Fertil Steril 2009;91:456-88

Lucinda E, et al. Am J Obstet Gynecol 2011;204:558.e1-6

# PCOS & Pregnancy(1)

- Increased risk of adverse pregnancy and neonatal complications observed in PCOS pregnancy.

(2 META-ANALYSIS)

Boomsma CM,et al. Hum Reprod Update. **2006**;12:673–83.

Kjerulff LE,et al. Am J Obstet Gynecol. **2011**;204:558.

- **Perinatal Complications(1):**

- **Early abortion**

- High LH ?
- Hyperandrogenia (HOXA10 gen ?)
- fibrinolysis (PAI-1 aktivitesi?)
- İnsülin resistance
- Endometrial disfunctions
- Obesity

Homburg R. Best Pract Res Clin Endocrinol Metab.2006;20:281–92

Apparao KBC,et al. Biol Reprod. 2002;66:297–304.

Palomba S, et al. Fertil Steril. 2005;84:761–5.

Lee C-L,et al. J Reprod Immunol. 2011;90:29–34.

# PCOS & Pregnancy(2)

- **Perinatal complications(2):**

- **GDM**

- More frequent in PCOS pregnancy (40-50% )
- +/- Obesity

Veltman-Verhulst SM, et al. Hum Reprod. 2010;25:3123–8.

Urman B, et al. J Reprod Med. 1997;42:501–5.

Turhan NO, et al. Int J Gynaecol Obstet. 2003;81:163–8.

- **PIH**

- Prevalence: 8%

Haakova L, et al. Hum Reprod. 2003;18:1438–41.

Mikola M, et al. Hum Reprod. 2001;16:226–9.

Ghazeeri GS, et al. Acta Obstet Gynecol Scand. 2012;91:658–78

Kjerulff LE, et al. Am J Obstet Gynecol. 2011;204:558. e1-6.

# PCOS & Pregnancy(3)

- **Perinatal Complications(3):**

- **Preterm delivery**

- 5-15 % (?)

Boomsma CM, et al. Hum Reprod Update. 2006;12:673–83.

Ghazeeri GS, et al. Acta Obstet Gynecol Scand.2012;91:658–78

Indian J Endocrinol Metab. 2013 Jan;17(1):37-43.



# PCOS pregnancy & Abortion(1)

- Possibility of impaired trophoblastic invasion because of;
  - *insulin resistance*
  - Hyperandrogenism

a role in first trimester abortions?.

Palomba S, Russo T, Falbo A, et al. J Clin Endocrinol Metab 2012;97:2441-9

- Metformine effect in Abortions?

- **17 RCT analysis: No effect**

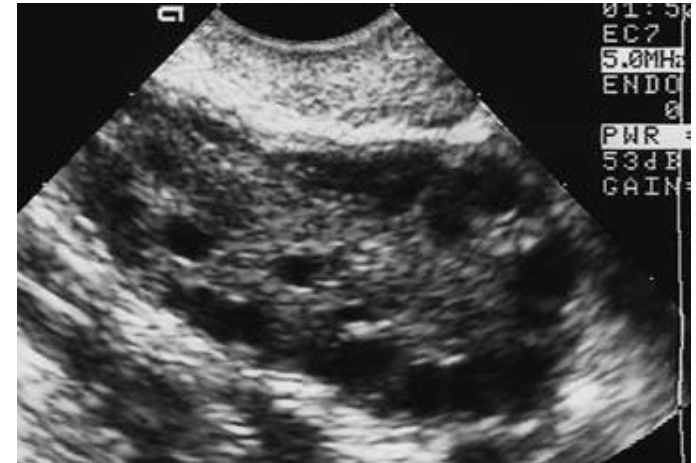
(Palomba S, et al. 2009 fertil Steril)

- Effect in **obesity**

(Morin-Papunen L, et al. J Clin Endocrinol Metab 2012)

# PCOS pregnancy & abortion(2)

- Metformine
  - Pre/post conception effect
    - Oocyte quality
    - Hypofibrinolysis
    - Insuline effects
    - PAI-Fx
    - Ghlicodelin ve ILGBP-1 increase effects



Qublan HS, et al. J Obstet Gynaecol 2009;29:651-5

Wei Z, et al. Fertil Steril 2008;90:1149-54

Glueck CJ, et al. Metabolism 2006;55:345-52

Glueck CJ, et al. Clin Appl Thromb Hemost 2004;10:323-34

Salvesen KA, et al. Ultrasound Obstet Gynecol 2007;29:433-7

Jakubowicz DJ, et al. J Clin Endocrinol Metab 2004; 89:833-9

# Metformin & Perinatal Outcome

- N=197, Rotterdam criteria
- Start Preconceptional, metformine therapy (1500mg)

**Table 3. Secondary outcome comparison in cases and controls**

| Outcome              | Cases<br>(n = 119) | Controls<br>(n = 78) | p<br>value |
|----------------------|--------------------|----------------------|------------|
| Gestational diabetes | 10.4%              | 44.4%                | 0.0021     |
| PIH                  | 16.5%              | 45%                  | <0.002     |
| IUGR                 | 16.5%              | 38.3%                | <0.001     |
| Live birth rate      | 92%                | 70%                  | <0.001     |

p value significant at <0.05.

| Outcome   | Cases (n =119) | Controls (n = 78) | p value |
|---|----------------|-------------------|---------|
| Miscarriage rate                                    | 9/119 = 8.8%   | 23/78 (29.4%)     | <0.002  |
| Rate of EPL in patients with recurrent miscarriages | 2/16 = 12.5%   | 5/11 = 49.4%      | <0.001  |

p value significant at <0.05. Univariate analysis and  $\chi^2$  were used for this analysis.

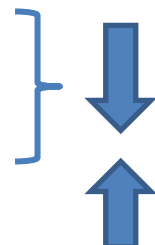
Gynecol Obstet Invest **2010**;69:184–189

Fauzia Haq Nawaz Javed Rizvi

**Continuation of Metformin Reduces Early Pregnancy Loss in Obese Pakistani Women with Polycystic Ovarian Syndrome**

Effects of metformin in women with polycystic ovary syndrome treated with gonadotrophins for in vitro fertilisation and intracytoplasmic sperm injection cycles: a systematic review and meta-analysis of randomised controlled trials

Palomba S, Falbo A, La Sala GB. **BJOG, 2013** Feb;120(3):267-76.

- N=10 RCT, n=845 PCOS pregnancy (+Metformin)
    - Pregnancy Rate : (OR 1.20, 95% CI 0.90-1.61)
    - Live birth Rate : (OR 1.69, 95% CI 0.85-3.34)
    - OHSS : (OR 0.27, 95% CI 0.16-0.46)
    - Abortion Rate : (OR 0.50, 95% CI 0.30-0.83)
    - Implantation : (OR 1.42, 95% CI 1.24-2.75)
- 

- **RESULTS:**

There is **need for more selective studies in different PCOS phenotypes for metformine effects.**

# PCOS pregnancy & Abortions(3)

- **More frequent in PCOS pregnancy:**

- Glueck CJ, et al. Fertil Steril 2001;75:46-52
- Glueck CJ, et al. Hum Reprod 2002;17:2858-64
- Jakubowicz DJ, et al. J Clin Endocrinol Metab 2002;87:524-9
- Vanky E, et al. Hum Reprod 2004;19:1734-40
- De Leo V, et al. Eur J Obstet Gynecol Reprod Biol 2011;157:63-6
- Regan L, et al. BMJ 1989;299:541-5
- Glueck CJ, et al. Metabolism 1999;48: 1589-95

- **No effect:**

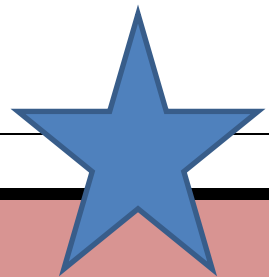
- Kjotrod SB, et al. Hum Reprod 2011;26:2045-53
- Koivunen R, et al. Hum Reprod 2008;23:2134-9

Consensus Statement on PCOS, 2011

Risk is debated

The results are the same in subfertil group

(Fauser BC, et al. Fertil Steril 2012;97:28-38 e25)



# A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome

Before 2006 studies

| Article                       | Definition PCOS  | PCOS group   | Control group   | Study population  | Study design                   | Multiple pregnancies                                 | Note   |
|-------------------------------|--|--|---|---|--------------------------------|--|--|
| Diamant <i>et al.</i> (1982)  | PCO + LH/FSH ↑/<br>androgen level ↑,<br>and ≥2 of:<br>1. Oligomenorrhea<br>2. Hirsutism<br>3. Anovulation  | Ovulation induction (by CC, hMG, dexamethasone, bromocriptine)     | Anovulatory women (non-PCOS). Pregnant by ovulation induction | PCOS: 33 women, 72 pregnancies<br>Control: 39 women, 71 pregnancies<br>Matched for: age, similar parity | Retrospective<br>Single centre | Included. However, equal incidence both study groups | Women were included for ≥1 pregnancy<br>BMI not stated |
| Levrin <i>et al.</i> (1990)   | 1. Oligo-/amenorrhea<br>2. Obesity<br>3. Hirsutism<br>4. PCO<br>5. LH/FSH ratio ↑                          | Pregnant by CC, hMG or spontaneous                                 | Control in hospital. Spontaneous pregnancies                  | PCOS: 76<br>Control: 95<br>Matched for: age, BMI, family and obstetric history (parity)                 | Retrospective<br>Single centre | Not stated   | None   |
| Wortsman <i>et al.</i> (1991) | 1. Oligo-/amenorrhea<br>2. Hirsutism/anovulatory infertility<br>3. LH/FSH ↑/<br>androgen level ↑<br>4. PCO | Pregnant by CC, hMG, dexamethasone, bromocriptine (or spontaneous) | All prenatal patients   | PCOS: 47<br>Control: 2306<br>Not matched  | Retrospective<br>Multi-centre  | Included   | BMI, age, parity not stated                            |
| Cardenas <i>et al.</i> (1996) | 1. Oligo-/amenorrhea<br>2. Androgen level ↑  | Ovulation induction  | Delivered at hospital. Regular menstrual cycles               | PCOS: 31<br>Controls: 78<br>Matched for: age, parity.   | Retrospective<br>Single centre | Not included   | PCOS women significant BMI ↑<br><i>Abstract</i>        |
| Urman <i>et al.</i> (1997)    | Combination of:<br>1. Oligo-/amenorrhea<br>2. Hirsutism<br>3. LH/FSH ↑<br>4. Androgen level ↑              | Pregnant by CC, hMG, dexamethasone, IVF, spontaneous               | Delivered at hospital, randomly selected                      | PCOS: 47<br>Control: 100<br>Not matched. Similar age, parity, history                                   | Retrospective<br>Single centre | Not included   | PCOS women significant BMI ↑                           |

Boomsma CM, Eijkemans MJC, Huges EG, et al

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006

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|---------------------------------|--|--|---|--|--------------------------------|--|---|
| Fridström <i>et al.</i> (1999)  | 1. Oligo-/amenorrhea<br>2. PCO   | Pregnant by IVF, ovulation induction   | Fertility treatment. Pregnant by IVF, ovulation induction           | PCOS: 33<br>Controls: 66<br>Matched for age, BMI, parity, history similar                            | Retrospective<br>Single centre | Included only for GDM, PIH, PE                       | PCOS more multiple pregnancies, not included in all outcomes                            |
| Radon <i>et al.</i> (1999)      | 1. Oligo-/amenorrhea<br>2. Hirsutism<br>3. Androgen level ↑/<br>LH/FSH > 2                   | Pregnant by CC, hMG, IVF, IUI or spontaneous                                 | Delivered in hospital. Spontaneous pregnancies                      | PCOS: 22<br>Control: 66<br>Matched for: age, BMI   | Retrospective<br>Single centre | Not included   | PCOS women significant parity ↓   |
| Kashyap <i>et al.</i> (2000)    | 1. Oligo-/amenorrhea<br>2. Androgen level ↑<br>3. LH/FSH > 2 or PCO                          | Pregnant by hMG ovulation induction  | Pregnant by hMG + IVF/IUI. Regular menstrual cycles                 | PCOS: 22<br>Control: 27<br>Not matched.<br>Similar BMI, age, parity                                  | Retrospective<br>Single centre | Not included   | None  |
| Vollenhove <i>et al.</i> (2000) | 1. Oligomenorrhea or hirsutism<br>2. PCO   | Ovulation induction  | From antenatal care and delivery. Normal fertility                  | PCOS: 60<br>Controls: 60<br>Matched for: age, BMI, ethnicity. Parity similar (raw data)              | Retrospective<br>Single centre | Included. However, equal incidence both study groups | None  |
| Mikola <i>et al.</i> (2001)     | PCO + 2 of:<br>1. Oligo-/amenorrhea, hirsutism<br>2. Androgen level ↑<br>3. LH/FSH > 2       | 72% ovulation induction  | Visit hospital for routine ultrasound. Poorly defined control group | PCOS: 99 pregnancies, 80 women<br>Controls: 737 pregnancies, 712 women<br>Similar age ( $P = 0.05$ ) | Retrospective<br>Single centre | Included only for GDM, PE                            | PCOS women BMI ↑, multiple pregnancies ↑ parity ↓. Women were included for ≥1 pregnancy |
| Bjercke <i>et al.</i> (2002)    | PCO + ≥3 of:<br>1. Oligo-/amenorrhea<br>2. Hirsutism<br>3. Androgen level ↑<br>4. LH/FSH > 2 | Pregnant by CC, hMG, IVF, IUI or spontaneous<br>Poorly defined control group | Conceived following ART   | PCOS: 52<br>Control: 355<br>Not matched<br>Similar parity, age                                       | Prospective<br>Single centre   | Not included   | PCOS women significant BMI ↑  |

# A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome

Before 2006 studies

| Article                            | Definition PCOS   | PCOS group   | Control group   | Study population   | Study design                   | Multiple pregnancies                                 | Note   |
|------------------------------------|---|--|---|--|--------------------------------|--|--|
| Haakova <i>et al.</i> (2003)       | 1. Oligo-/amenorrhea<br>2. PCO<br>3. Androgen level ↑<br>4. Anovulation infertility | Fertility treatment  | From prenatal ultrasound screening                                    | PCOS: 52<br>Controls: 66<br>Matched for: age, BMI                      | Retrospective<br>Single centre | Not included (received data from authors)            | PCOS women parity ↓                                  |
| Turhan <i>et al.</i> (2003)        | 1. Oligo-/amenorrhea or hirsutism<br>2. PCO<br>3. Androgen level ↑                  | Not stated   | Outpatient clinic, randomly selected                                  | PCOS: 38<br>Control: 136<br>Not matched.<br>Similar parity, age        | Retrospective<br>Single centre | Not included   | PCOS women significant BMI ↑, family history of DM ↑ |
| Weerakiet <i>et al.</i> (2004)     | 1. Oligo-/amenorrhea<br>2. Hirsutism/acne<br>3. PCO                                 | Pregnant by CC, metformin, IVF, laparoscopic ovarian drilling, spontaneous | Regular menstrual cycle   | PCOS: 39 women<br>Controls: 219 women<br>Matched for age               | Prospective<br>Single centre   | Not included. Author provided additional information | PCOS significant BMI ↑, parity ↓                     |
| Sir-Petermann <i>et al.</i> (2005) | ESHRE/ASRM PCOS consensus 2004  | Fertility treatment  | From prenatal care unit.<br>Spontaneous pregnancies.<br>Regular cycle | PCOS: 47<br>Control: 180<br>Matched for: age, BMI, socioeconomic class | Prospective<br>Single centre   | Not included   | PCOS women significant parity ↓                      |

Boomsma CM, Eijkemans MJC, Huges EG, et al

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006



# PCOS Pregnancy: perinatal complications

| Outcome                | Study                        |                             |                               |                               |                            |                                |                            |                           |                                  |                             |                              |                              |                             |                                |                                    | Number included studies |
|------------------------|------------------------------|-----------------------------|-------------------------------|-------------------------------|----------------------------|--------------------------------|----------------------------|---------------------------|----------------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------|--------------------------------|------------------------------------|-------------------------|
|                        | Diamant <i>et al.</i> (1982) | Levrán <i>et al.</i> (1990) | Wortsman <i>et al.</i> (1991) | Cardenas <i>et al.</i> (1996) | Urman <i>et al.</i> (1997) | Fridstrom <i>et al.</i> (1999) | Radon <i>et al.</i> (1999) | Kashyap and Claman (2000) | Vollenhoven <i>et al.</i> (2000) | Mikola <i>et al.</i> (2001) | Bjercke <i>et al.</i> (2002) | Haakova <i>et al.</i> (2003) | Turhan <i>et al.</i> (2003) | Weerakiet <i>et al.</i> (2004) | Sir-Petermann <i>et al.</i> (2005) |                         |
| GDM                    |                              | X                           | X                             | X                             | X                          | X                              | X                          |                           | X                                | X                           | X                            | X                            | X                           | X                              | X                                  | 13                      |
| PIH                    |                              |                             |                               |                               | X                          | X                              |                            | X                         | X*                               |                             | X                            | X                            | X                           | X                              |                                    | 8                       |
| PE                     | X                            |                             |                               |                               | X                          | X                              |                            |                           |                                  | X                           | X                            |                              | X                           | X                              | X                                  | 8                       |
| Section rate           | X                            |                             |                               |                               |                            | X                              |                            |                           | X                                | X                           | X                            | X                            | X                           | X                              |                                    | 8                       |
| Vacuum/forceps         | X                            |                             |                               |                               |                            |                                |                            |                           | X                                |                             | X                            |                              |                             |                                |                                    | 3                       |
| Gestation              |                              |                             |                               | X                             |                            | X                              |                            |                           | X*                               | X                           |                              | X                            | X                           | X                              | X                                  | 8                       |
| Preterm birth          |                              |                             |                               |                               | X                          |                                |                            |                           | X*                               | X                           | X                            | X                            | X                           | X                              | X*                                 | 8                       |
| Birthweight            | X                            |                             | X                             | X                             |                            | X                              | X                          |                           | X                                | X                           | X                            | X                            | X                           | X                              | X                                  | 12                      |
| SGA                    |                              |                             |                               |                               | X                          |                                |                            |                           | X*                               |                             |                              | X*                           | X                           |                                | X                                  | 5                       |
| Macrosomia             |                              |                             |                               | X                             | X                          |                                |                            |                           | X*                               | X                           |                              | X*                           | X                           |                                | X                                  | 7                       |
| NICU                   |                              |                             |                               |                               | X                          | X                              |                            |                           |                                  |                             | X                            |                              | X                           |                                | X*                                 | 5                       |
| Neonatal malformations |                              |                             |                               |                               | X                          |                                |                            |                           |                                  |                             |                              |                              | X                           |                                | X*                                 | 3                       |
| Perinatal mortality    |                              |                             |                               |                               | X                          | X                              |                            |                           |                                  | X                           |                              |                              |                             | X*                             | X*                                 | 5                       |

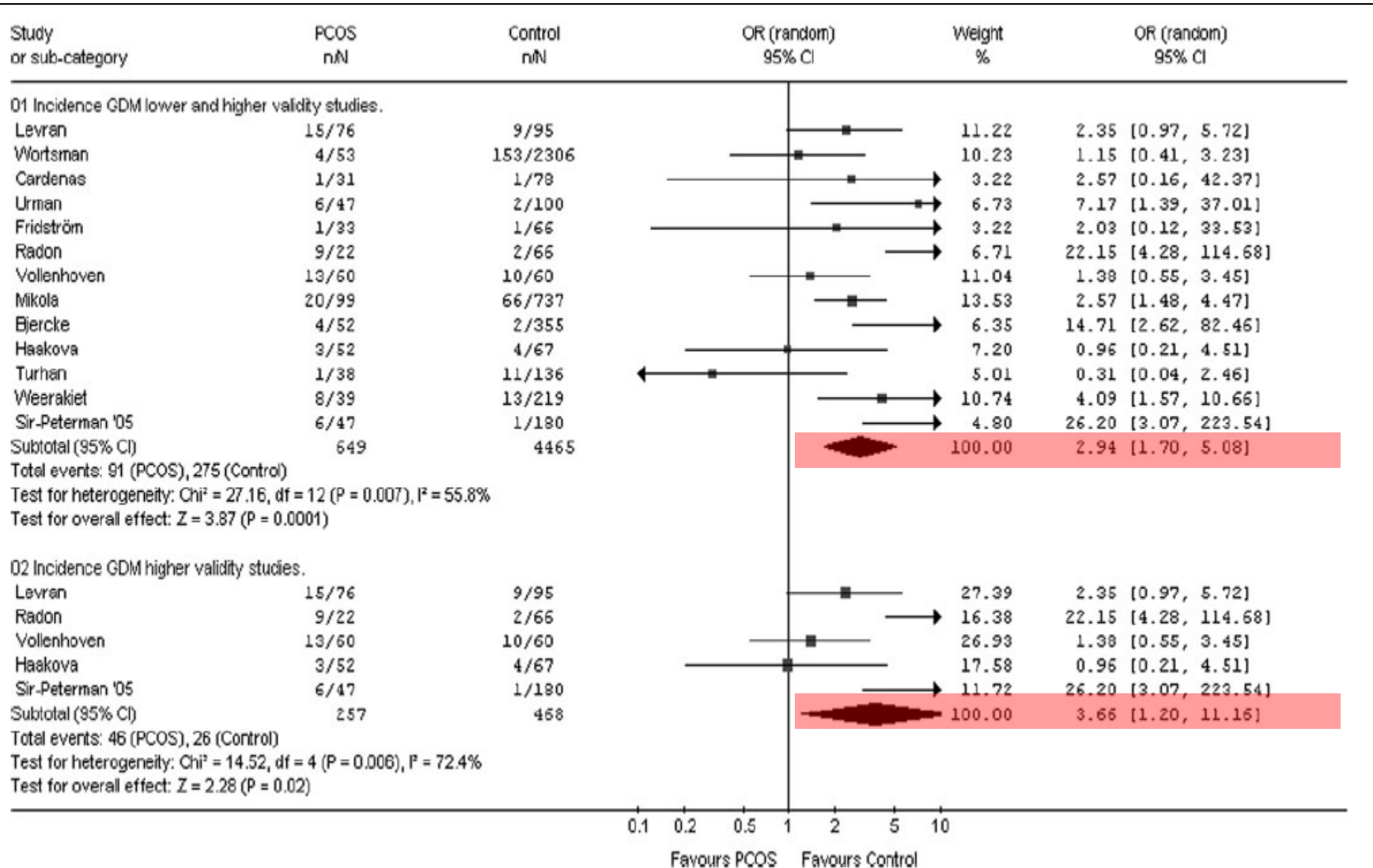
**(15 studies, 720 PCOS pregnancy, Control:4505)**

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006

Boomsma CM, Eijkemans MJC, Huges EG, et al

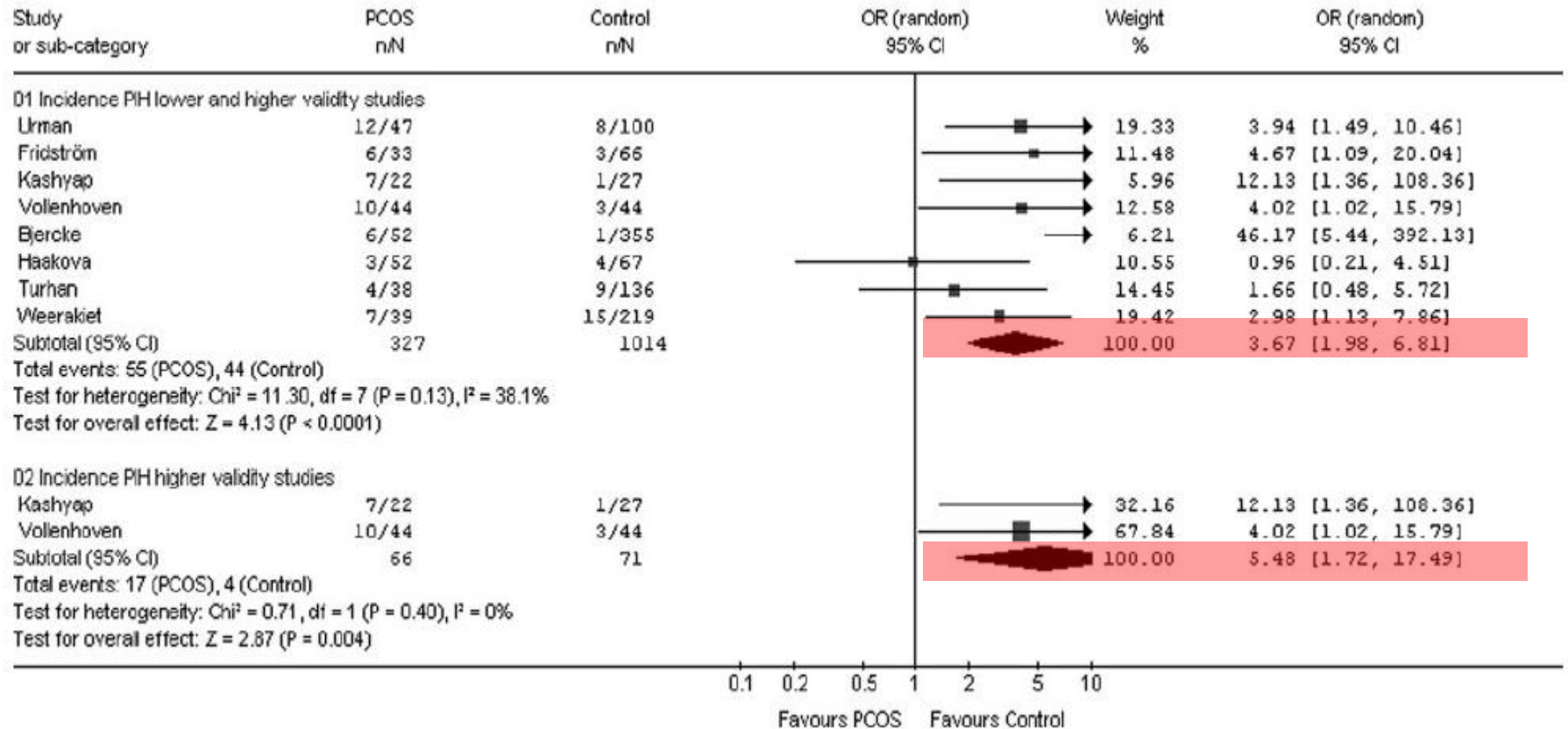
# PCOS pregnancy & GDM

Human Reproduction Update, Vol.12, No.6 pp. 673-683, 2006



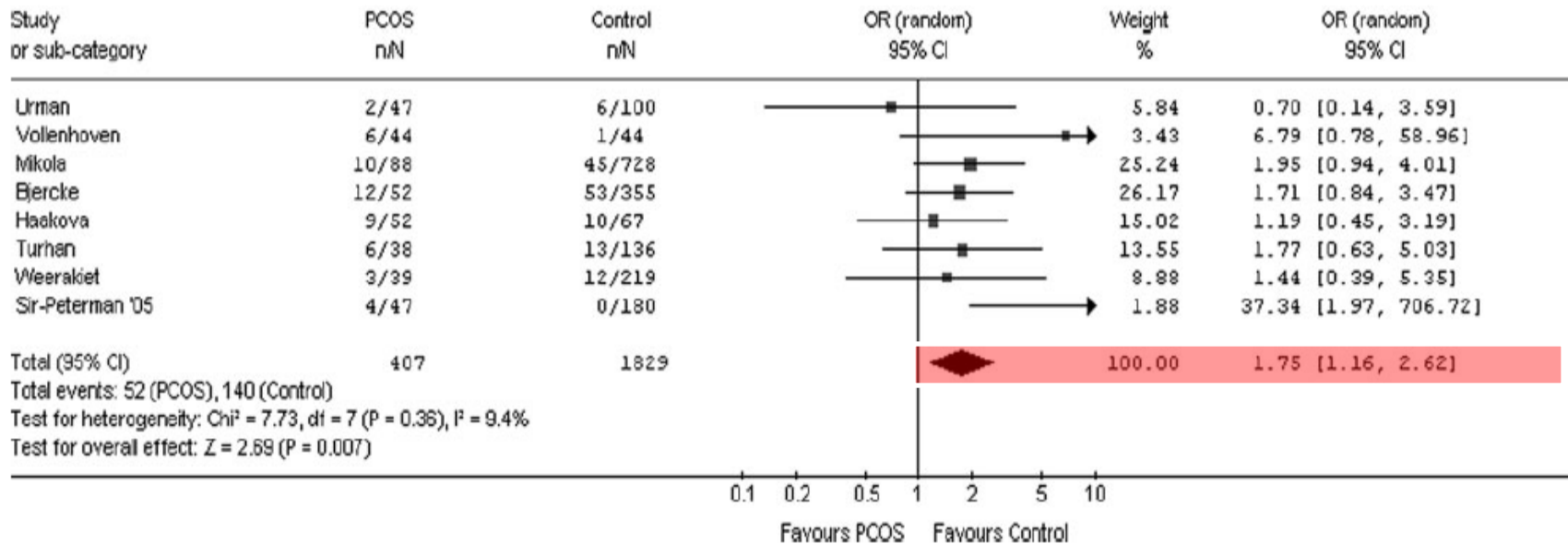
# PCOS pregnancy & PIH

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006



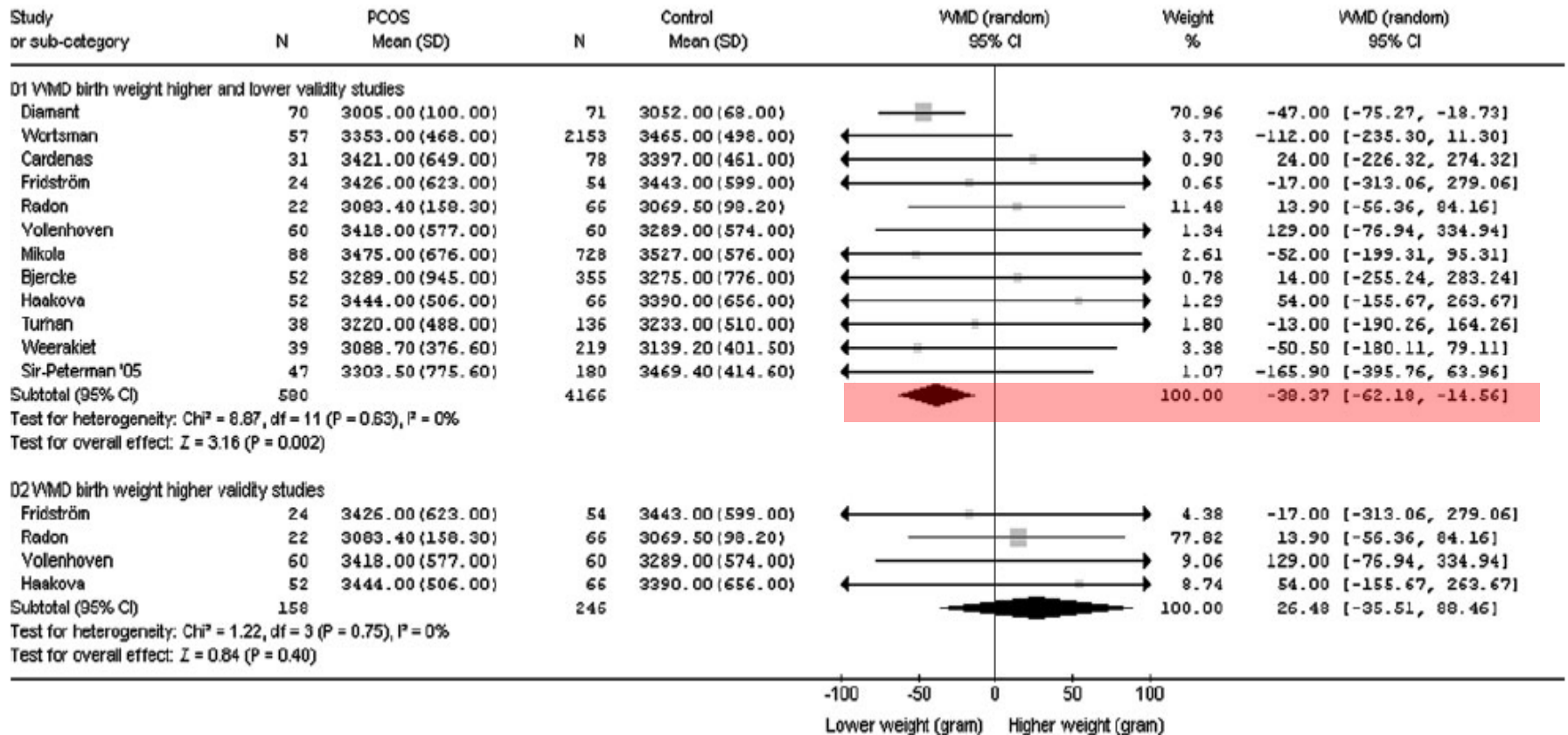
# PCOS pregnancy & PRETERM delivery

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006

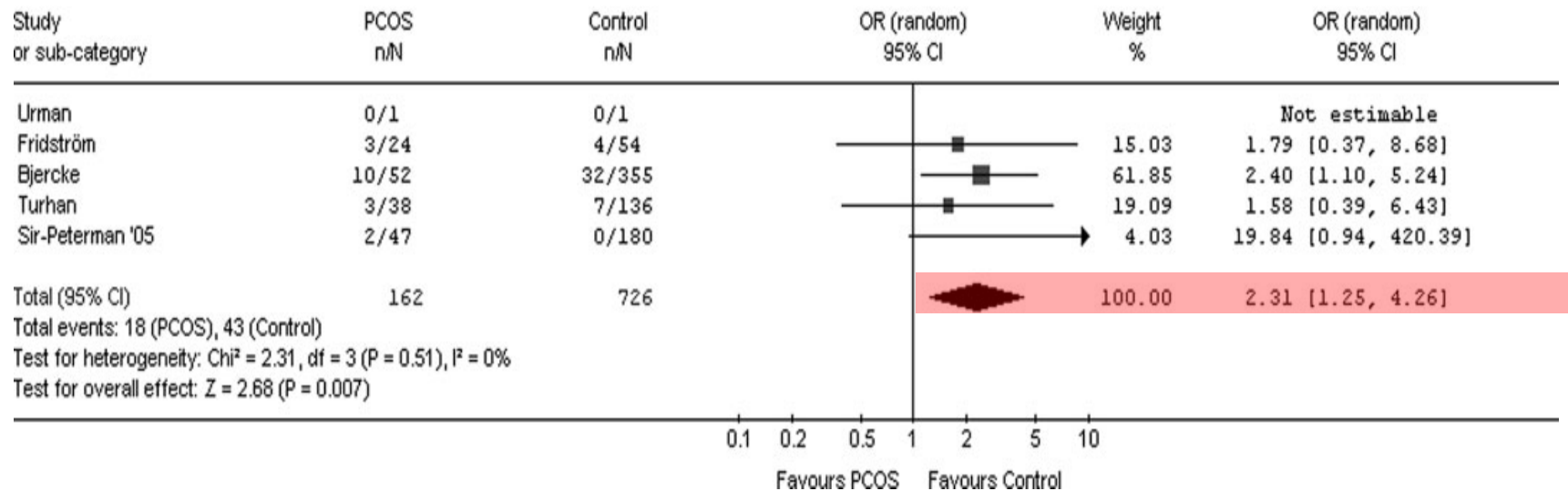


# PCOS pregnancy & Birth weight

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006

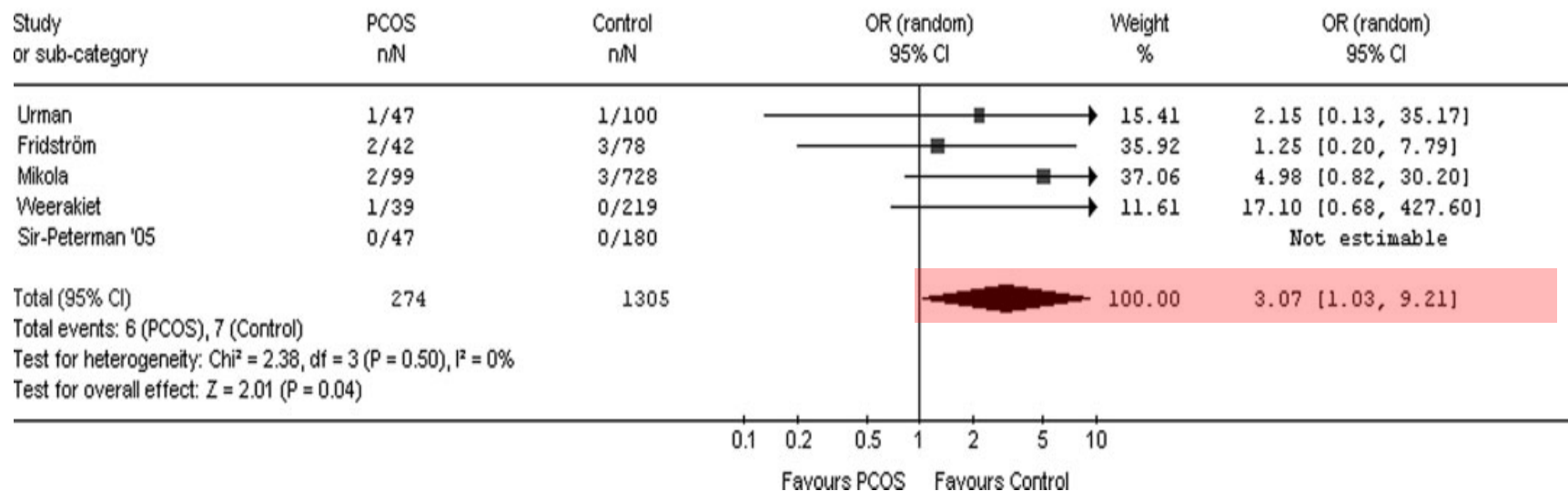


# PCOS pregnancy & NICU



# PCOS pregnancy & Perinatal Mortality

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006



# PCOS & Mode of Delivery

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006

- PCOS pregnancy: High rate of C/S
  - OR 1,56 (%95 CI : 1,20-2,02)
  - In Subgroup analysis : OR 0,92

Haakova L, Cibula D, Rezabek K, et al. (2003) Hum Reprod 18,1438–1441

Vollenhoven B, Clark S, et al. (2000) Aust N Z J Obstet Gynaecol 40,54–58.

- Vacuum – Forceps: no difference



# Risk of adverse pregnancy outcomes in women with polycystic ovary syndrome: population based cohort study

*BMJ 2011;343:d6309 doi: 10.1136/bmj.d6309*

| Pregnancy outcomes                                      | No of births (rate %)       |                                     | Standardised absolute risk difference* (%)<br>in women with PCOS | Crude odds ratio†<br>(95% CI) | Adjusted odds ratio† (95% CI) | P value |
|---|-----------------------------|-------------------------------------|--|-------------------------------|-------------------------------|---------|
|   | Women with PCOS<br>(n=3787) | Women without PCOS<br>(n=1 191 336) |  |                               |                               |         |
| <b>Gestational diabetes:</b>                            |                             |                                     |  |                               |                               |         |
| Yes   | 125 (3.30)                  | 10 672 (0.90)                       | 1.85   | 3.78 (3.16 to 4.52)           | 2.32 (1.88 to 2.88)           | <0.001  |
| No  | 3662 (96.70)                | 1 180 664 (99.10)                   | —  | 1.00                          | 1.00                          |         |
| <b>Pre-eclampsia:</b>                                   |                             |                                     |  |                               |                               |         |
| Yes   | 221 (5.84)                  | 35 129 (2.95)                       | 1.74   | 2.04 (1.78 to 2.34)           | 1.45 (1.24 to 1.69)           | <0.001  |
| No  | 3566 (94.16)                | 1 156 207 (97.05)                   | —  | 1.00                          | 1.00                          |         |
| <b>Antepartum bleeding or placental complications:</b>  |                             |                                     |  |                               |                               |         |
| Yes   | 59 (1.56)                   | 14 490 (1.22)                       | —  | 1.29 (0.99 to 1.66)           | 1.14 (0.85 to 1.53)           | 0.37    |
| No  | 3728 (98.44)                | 1 176 846 (98.78)                   | —  | 1.00                          | 1.00                          |         |
| <b>Caesarean section‡:</b>                              |                             |                                     |  |                               |                               |         |
| Yes   | 846 (22.44)                 | 174 298 (14.68)                     | 2.75   | 1.69 (1.56 to 1.82)           | 1.18 (1.07 to 1.29)           | 0.001   |
| No  | 2924 (77.56)                | 1 013 112 (85.32)                   | —  | 1.00                          | 1.00                          |         |
| Data missing  | 0                           | 30                                  | —  | —                             | —                             |         |
| <b>Very preterm birth (&lt;31+6 weeks)‡:</b>            |                             |                                     |  |                               |                               |         |
| Yes   | 65 (1.73)                   | 7999 (0.67)                         | 0.94   | 2.59 (2.02 to 3.31)           | 2.21 (1.69 to 2.90)           | <0.001  |
| No  | 3701 (98.27)                | 1 178 296 (99.33)                   | —  | 1.00                          | 1.00                          |         |
| Data missing  | 4                           | 1145                                | —  | —                             | —                             |         |
| <b>Moderately preterm birth (32+0 to 36+6 weeks)‡§:</b> |                             |                                     |  |                               |                               |         |
| Yes   | 226 (6.11)                  | 50 352 (4.27)                       | 1.38   | 1.46 (1.28 to 1.67)           | 1.31 (1.13 to 1.53)           | 0.0004  |
| No  | 3475 (93.89)                | 1 127 944 (95.73)                   | —  | 1.00                          | 1.00                          |         |
| Data missing  | 4                           | 1145                                | —  | —                             | —                             |         |
| <b>Post-term birth (&gt;42+0 weeks)‡:</b>               |                             |                                     |  |                               |                               |         |
| Yes   | 252 (6.69)                  | 86 771 (7.31)                       | -1.39  | 0.91 (0.80 to 1.03)           | 0.82 (0.71 to 0.95)           | 0.0069  |
| No  | 3514 (93.31)                | 1 099 524 (92.69)                   | —  | 1.00                          | 1.00                          |         |
| Data missing  | 4                           | 1145                                | —  | —                             | —                             |         |

## Risk of adverse pregnancy outcomes in women with polycystic ovary syndrome: population based cohort study. *BMJ* 2011

**Table 4| Adjusted odds ratios of women with and without polycystic ovary syndrome (PCOS) and singleton preterm births (<37+0 weeks) undergoing assisted reproductive technology in Sweden, 1995 to 2007**

| Preterm birth | Assisted reproductive technology* |                    |      |                               | No assisted reproductive technology* |           |      |                               |
|---------------|-----------------------------------|--------------------|------|-------------------------------|--------------------------------------|-----------|------|-------------------------------|
|               | Women with PCOS                   | Women without PCOS | Rate | Adjusted odds ratio† (95% CI) | Yes                                  | No        | Rate | Adjusted odds ratio† (95% CI) |
| Yes           | 41                                | 1400               | 7.96 | 1.08 (0.76 to 1.53)           | 256                                  | 58 723    | 7.83 | 1.54 (1.33 to 1.79)           |
| No            | 474                               | 16 618             | 7.77 | 1.00                          | 3012                                 | 1 113 426 | 5.01 | 1.00                          |
| Data missing  | 2                                 | —                  | —    | —                             | 4                                    | 1167      | —    | —                             |

\*P=0.055 for interaction analysis for assisted reproductive technology and PCOS in relation to preterm birth.

†Adjusted for maternal age, parity, body mass index, years of education, cigarette consumption, and assisted reproductive technology.

# Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis

Lucinda E. Kjerulff, Luis Sanchez-Ramos, Daniel Duffy

Am J Obstet Gynecol, 2011;204:558.e1-6.

**TABLE 2**  
**Summary of results**

| Variable                       | Group, n                                |       |   |        | Odds ratio (95% CI) |
|--------------------------------|---|-------|---|--------|---------------------|
|                                | Patients with polycystic ovary syndrome | Total | Control patients with polycystic ovary syndrome | Total  |                     |
| Gestational diabetes mellitus  | 340                                     | 2385  | 5263  | 89,669 | 2.82 (1.93–4.10)    |
| Pregnancy-induced hypertension | 84                                      | 521   | 56  | 1317   | 4.07 (2.75–6.02)    |
| Preeclampsia                   | 63                                      | 589   | 57  | 2228   | 4.23 (2.77–6.46)    |
| Preterm delivery               | 76                                      | 565   | 155   | 2129   | 2.20 (1.59–3.04)    |
| Cesarean delivery              | 57                                      | 171   | 201   | 716    | 1.41 (0.96–2.07)    |
| Operative vaginal delivery     | 43                                      | 160   | 62  | 583    | 1.56 (0.93–2.63)    |
| Small-for-gestational age      | 29                                      | 204   | 16  | 353    | 2.62 (1.35–5.10)    |
| Large-for-gestational age      | 32                                      | 204   | 44  | 353    | 1.56 (0.92–2.64)    |

CI, confidence interval.

Kjerulff. Pregnancy outcomes and polycystic ovary syndrome. Am J Obstet Gynecol 2011.

# Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis

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**TABLE 3**

**Odds ratio for incidence of gestation diabetes mellitus of women with polycystic ovary syndrome and control patients**

| Study                             | Group (n/N)                          |                    | Odds ratio (95% CI)     |
|-----------------------------------|--------------------------------------|--------------------|-------------------------|
|                                   | Women with polycystic ovary syndrome | Control patients   |                         |
| Altieri et al <sup>14</sup>       | 3/15                                 | 6/159              | 6.38 (1.41–28.72)       |
| Palomba et al <sup>18</sup>       | 15/93                                | 4/69               | 3.13 (0.99–9.88)        |
| Levrán et al <sup>20</sup>        | 15/76                                | 9/95               | 2.35 (0.97–5.72)        |
| Wortsman et al <sup>21</sup>      | 4/53                                 | 153/2306           | 1.15 (0.41–3.22)        |
| Cardenas et al <sup>22</sup>      | 1/31                                 | 1/78               | 2.57 (0.16–42.37)       |
| Urman et al <sup>23</sup>         | 6/47                                 | 2/100              | 7.17 (1.39–37.01)       |
| Fridstrom et al <sup>24</sup>     | 1/33                                 | 1/66               | 2.03 (0.12–33.54)       |
| Radon et al <sup>25</sup>         | 9/22                                 | 2/66               | 22.15 (4.28–114.68)     |
| Vollenhoven et al <sup>27</sup>   | 13/60                                | 10/60              | 1.38 (0.55–3.45)        |
| Mikola et al <sup>28</sup>        | 20/99                                | 66/737             | 2.57 (1.48–4.47)        |
| Bjercke et al <sup>29</sup>       | 4/52                                 | 2/355              | 14.71 (2.62–82.46)      |
| Haakova et al <sup>30</sup>       | 3/66                                 | 8/66               | 0.36 (0.087–1.36)       |
| Turhan et al <sup>31</sup>        | 1/38                                 | 11/136             | 0.31 (0.038–2.46)       |
| Weerakiet et al <sup>32</sup>     | 8/39                                 | 13/219             | 4.09 (1.57–10.66)       |
| Sir-Petermann et al <sup>33</sup> | 6/47                                 | 1/180              | 26.20 (3.07–223.54)     |
| Lesser and Garcia <sup>34</sup>   | 4/24                                 | 3/44               | 2.73 (0.56–13.40)       |
| Lo et al <sup>35</sup>            | 221/1542                             | 4970/84,882        | 2.69 (2.33–3.11)        |
| Sir-Petermann et al <sup>36</sup> | 6/48                                 | 1/51               | 7.14 (0.827–61.71)      |
| <b>TOTAL</b>                      | <b>340/2385</b>                      | <b>5263/89,669</b> | <b>2.82 (1.94–4.11)</b> |

Heterogeneity  $\chi^2 = 36.19$  (degrees of freedom = 17;  $P = .004$ ); estimate of between-study variance Tau-squared = 0.2369; test of odds ratio = 1:  $z = 5.42$ ;  $P = .000$ .  
 CI, confidence interval.

Kjerulff. Pregnancy outcomes and polycystic ovary syndrome. Am J Obstet Gynecol 2011.

# Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis

Lucinda E. Kjerulff, Luis Sanchez-Ramos, Daniel Duffy

Am J Obstet Gynecol, 2011;204:558.e1-6.

**TABLE 4**

**Odds ratio for incidence of pregnancy-induced hypertension of women with polycystic ovary syndrome and control patients**

| Study                             | Group (n/N)                          |                  | Odds ratio (95% CI)     |
|-----------------------------------|--------------------------------------|------------------|-------------------------|
|                                   | Women with polycystic ovary syndrome | Control patients |                         |
| Altieriat et al <sup>14</sup>     | 2/15                                 | 10/159           | 2.29 (0.45–11.59)       |
| Hu et al <sup>15</sup>            | 6/22                                 | 0/22             | 17.73 (0.93–337.26)     |
| Palomba et al <sup>18</sup>       | 13/93                                | 3/69             | 3.58 (0.98–13.08)       |
| Urman et al <sup>23</sup>         | 12/47                                | 8/100            | 3.94 (1.49–10.46)       |
| Fridstrom et al <sup>24</sup>     | 6/33                                 | 3/66             | 4.67 (1.09–20.04)       |
| Kashyap and Claman <sup>26</sup>  | 7/22                                 | 1/27             | 12.13 (1.36–108.36)     |
| Vollenhoven et al <sup>27</sup>   | 10/44                                | 3/44             | 4.02 (1.02–15.79)       |
| Bjercke et al <sup>29</sup>       | 6/52                                 | 1/355            | 46.17 (5.44–392.13)     |
| Haakova et al <sup>30</sup>       | 5/66                                 | 4/66             | 1.27 (0.33–4.96)        |
| Turhan et al <sup>31</sup>        | 4/38                                 | 9/136            | 1.66 (0.48–5.72)        |
| Weerakiet et al <sup>32</sup>     | 9/41                                 | 14/222           | 4.18 (1.67–10.45)       |
| Sir-Petermann et al <sup>33</sup> | 4/48                                 | 0/51             | 10.42 (0.55–198.83)     |
| <b>TOTAL</b>                      | <b>84/521</b>                        | <b>56/1317</b>   | <b>4.07 (2.75–6.02)</b> |

Heterogeneity  $\chi^2 = 12.64$  (degrees of freedom = 11;  $P = 0.317$ ); test of odds ratio = 1:  $z = 7.03$ ;  $P = .000$ .  
*CI*, confidence interval.

Kjerulff. Pregnancy outcomes and polycystic ovary syndrome. Am J Obstet Gynecol 2011.

# Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis

Lucinda E. Kjerulff, Luis Sanchez-Ramos, Daniel Duffy

Am J Obstet Gynecol, 2011;204:558.e1-6.

TABLE 5

Odds ratio for the incidence of preeclampsia for women with polycystic ovary syndrome and control patients

| Study                             | Group (n/N)               |                  | Odds ratio (95% CI)     |
|-----------------------------------|---------------------------|------------------|-------------------------|
|                                   | Polycystic ovary syndrome | Control patients |                         |
| Altieri et al <sup>14</sup>       | 0/15                      | 2/159            | 2.03 (0.09–44.26)       |
| Li et al <sup>16</sup>            | 6/34                      | 4/70             | 3.54 (0.93–13.51)       |
| Palomba et al <sup>18</sup>       | 9/93                      | 1/69             | 7.29 (0.90–58.94)       |
| Diamant et al <sup>19</sup>       | 20/70                     | 3/71             | 9.07 (2.55–32.20)       |
| Urman et al <sup>23</sup>         | 3/47                      | 4/100            | 1.64 (0.35–7.62)        |
| Fridstrom et al <sup>24</sup>     | 3/33                      | 0/66             | 15.26 (0.76–304.73)     |
| Radon et al <sup>25</sup>         | 5/22                      | 1/66             | 19.12 (2.09–174.70)     |
| Mikola et al <sup>28</sup>        | 4/99                      | 14/737           | 2.17 (0.70–6.74)        |
| Bjercke et al <sup>29</sup>       | 7/52                      | 25/355           | 2.05 (0.84–5.02)        |
| Turhan et al <sup>31</sup>        | 3/38                      | 2/136            | 5.74 (0.92–35.71)       |
| Weerakiet et al <sup>32</sup>     | 1/39                      | 1/219            | 5.74 (0.35–93.70)       |
| Sir-Petermann et al <sup>33</sup> | 2/47                      | 0/180            | 19.84 (0.94–420.39)     |
| <b>TOTAL</b>                      | <b>63/589</b>             | <b>57/2228</b>   | <b>4.23 (2.77–6.46)</b> |

Heterogeneity  $\chi^2 = 10.87$  (degrees of freedom = 11;  $P = .454$ ); test of odds ratio = 1:  $z = 6.69$ ;  $P = .000$ .  
*CI*, confidence interval.

Kjerulff. Pregnancy outcomes and polycystic ovary syndrome. Am J Obstet Gynecol 2011.

# Prevalence of cervical insufficiency in polycystic ovarian syndrome

Feigenbaum SL, et al. Human Reproduction, Vol.27, No.9 pp. 2837–2842, 2012

- Retrospective cohort study
- Rotterdam criteria
- Results:
  - N=999 PCOS                      Cervical incompetence    :%2,9 (P<0,01)
  - N=1020 Control                      “                                      :%0,5
  - More frequent in South Asian and Black population
  - Overall: PCOS, **Cervical incompetence**(Age, parity, race, BMI,fertility therapy) **OD=4,8 CI:1,5-15,4**
  - **In PCOS pregnancy cases, second trimester cervical evaluation should be done for incompetence.**

**Table II** Prevalence of CI among PCOS women by race/ethnicity.

| Race/ethnicity                               | Prevalent CI (current or prior CI <sup>a</sup> ) | CI case description   |
|--|--|---|
| White<br>(N = 413)                           | 1.0% (4/413)                                     | 4 CI cases:<br>2 prior CI, prophylactic cerclage<br>2 new CI in index pregnancy |
| Black<br>(N = 40)                            | 17.5% (7/40)                                     | 7 CI cases:<br>3 prior CI, prophylactic cerclage<br>4 new CI in index pregnancy |
| Hispanic<br>(N = 255)                        | 1.6% (4/255)                                     | 4 CI cases:<br>3 prior CI, prophylactic cerclage<br>1 new CI in index pregnancy |
| East Asian/<br>Pacific Islander<br>(N = 143) | 3.5% (5/143)                                     | 5 CI cases:<br>1 prior CI, prophylactic cerclage<br>4 new CI in index pregnancy |
| South Asian<br>(N = 115)                     | 7.8% (9/115)                                     | 9 CI cases:<br>2 prior CI, prophylactic cerclage<br>7 new CI in index pregnancy |
| Other race<br>(N = 33)                       | 0.0% (0/33)                                      | No cases  |

<sup>a</sup>Prior PCOS-CI cases had a prophylactic cerclage placed during the current (index) pregnancy.

**Table I** Demographic and clinical features of women by polycystic ovarian syndrome (PCOS) and current or prior CI (PCOS-CI) status.

| Patient characteristics                          | Non-PCOS, N = 1020 | PCOS, N = 999 | PCOS-CI, N = 29 |
|--|--------------------|---------------|-----------------|
| Maternal age (years, mean ± SD)                  | 30.9 ± 6.0         | 31.4 ± 4.4**  | 32.1 ± 4.8      |
| Race/ethnicity%                                  |                    | *             | †               |
| White  | 41.1%              | 41.3%         | 13.8%           |
| Black  | 7.1%               | 4.0%          | 24.1%           |
| Hispanic   | 24.0%              | 25.5%         | 13.8%           |
| East Asian                                       | 17.8%              | 14.3%         | 17.2%           |
| South Asian                                      | 6.2%               | 11.5%         | 31.0%           |
| Other  | 3.8%               | 3.3%          | 0.0%            |
| Gravidity (mean ± SD)                            | 2.6 ± 1.6          | 2.1 ± 1.3*    | 2.4 ± 1.4       |
| Obesity (body mass index ≥30 kg/m <sup>2</sup> ) | 16.5%              | 42.9%*        | 44.8%           |
| Obesity (Asian-specific threshold) <sup>a</sup>  | 18.0%              | 46.7%*        | 55.2%           |
| Androgen excess (%) <sup>b</sup>                 | 5.0%               | 78.2%*        | 75.9%           |



# **METFORMINE**

**?**

- **Is effective perinatal complications?**

# Management of perinatal complication in PCOS pregnancy(1)

- Obesity and insulin resistance!!!

- **Metformine** (?)

- FDA “B”
    - MIG Trial (metformin In Gestational Diabetes)
      - Insulin & Metformin (Perinatal outcome)
      - Result is the same

Rowan JA, et al. Diabetes Care. 2010;33:9–16

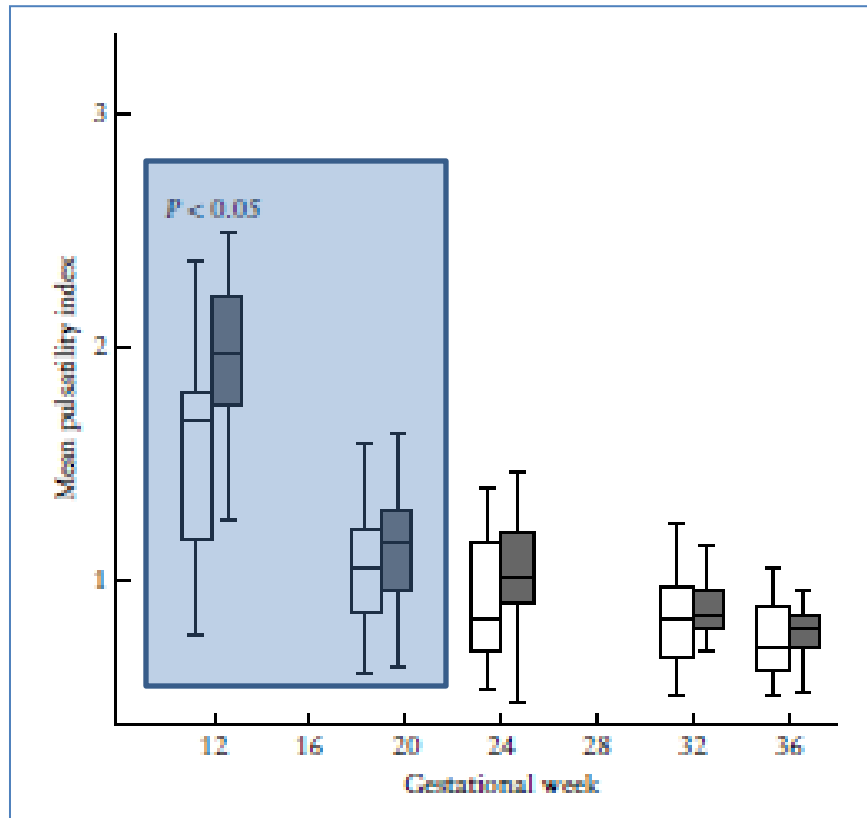
- Metformine: decrease in GDM, no effect of birth weight, No effect of motor activity.

Glueck CJ, et al. Hum Reprod. 2002;17:2858–64.

- “Randomized, placebo-controlled, double-blind, multicenter study”, Vanky E, (J Clin Endocrinol Metab. 2010;95:E448–55):  
PIH, PL, GDM:;

**Placebo-Metformine: no differences**

# Uterine Artery pulsation index Metformin & Plasebo



Metformin effective:12-20W



*Ultrasound Obstet Gynecol 2007; 29: 433–437*

SALVESEN KA, VANKY E, CARLSEN SM.

**Metformin treatment in pregnant women with polycysticovary syndrome –is reduced complication rate mediated by changes in the uteroplacental circulation?**

# The efficacy of metformin in pregnant women with polycystic ovary syndrome: a meta-analysis of clinical trials

Zheg J, Shan PF, Gu W. J Endocrinol Invest.2013 Apr 12.

- Meta- analysis -Medline

- 8 studies , N=1106

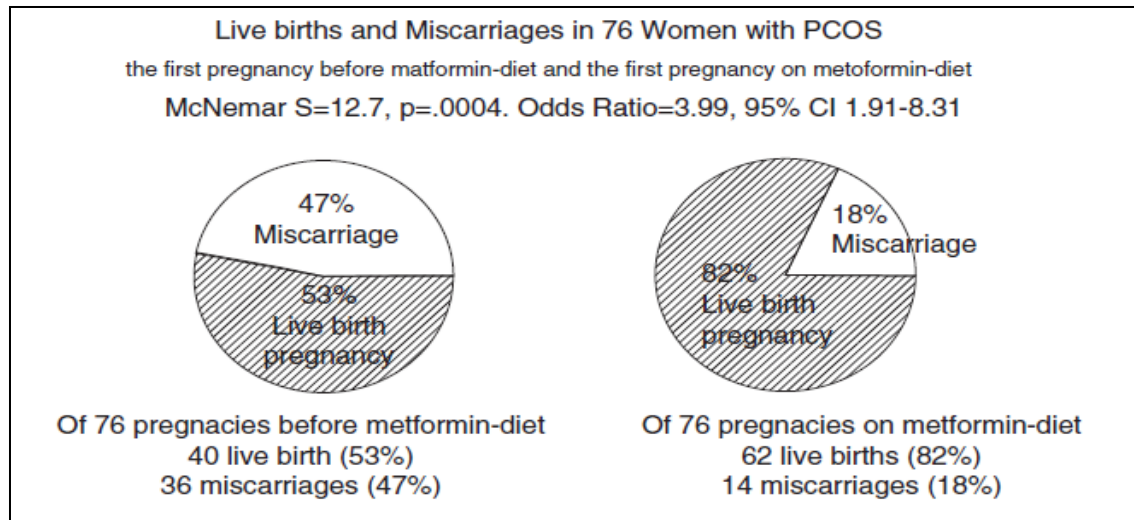
- Metformine in PCOS :

|                        |         |             |
|------------------------|---------|-------------|
| • Early pregnancy loss | OR:0,32 | (0,19-0,55) |
| • GDM                  | :0,37   | (0,25-0,56) |
| • Preeclampsia         | :0,53   | (0,30-0,95) |
| • Premature delivery   | :0,30   | (0,13-0,68) |



Effects of metformin-diet intervention before and throughout pregnancy on obstetric and neonatal outcomes in patients with polycystic ovary syndrome  
Glueck CJ, et al. Current Medical Research & Opinion Vol. 29, No. 1, 2013, 55–62

- N=76
- Metformin(2-2,55g/day)-Diet(low glysemic index) & Control



- In Metformin-Diet group; GDM, PIH, Fetal macrosomi : no differences

# Management of perinatal complications in PCOS pregnancy(2)

- “3. ESHRE/ASRM-sponsored PCOS consensus workshop”:
  - There is no positive decreased effect on perinatal complications results for Metformin.

Fauser BCJM, et al. Fertil Steril. **2012**;97:28–38.



# PCOS pregnancy: RESULTS

- PCOS cases are **subfertile**.
- Highly demanding pregnancies
- Cervical incompetence?
- **Perinatal complications:**
  - Early pregnancy loss
  - Preterm delivery
  - GDM
  - PIH
- Metformin; No effect on perinatal complications

***Thank you,***



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