

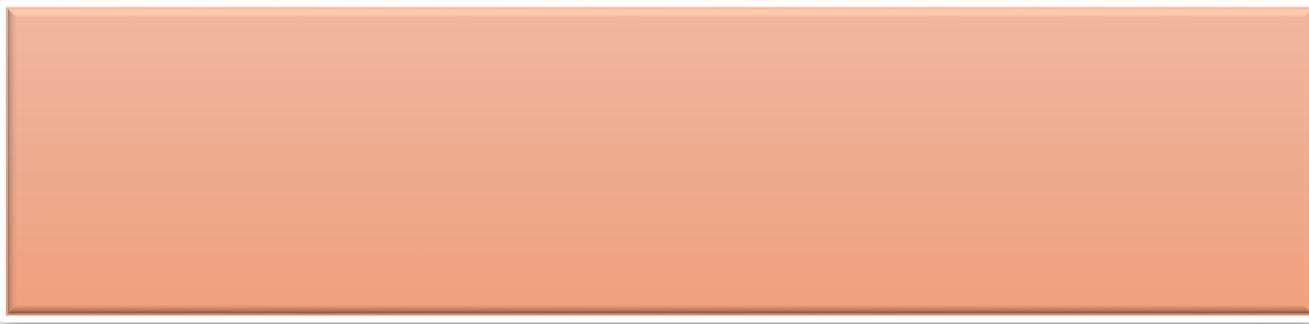
Surgical Indications In PCO

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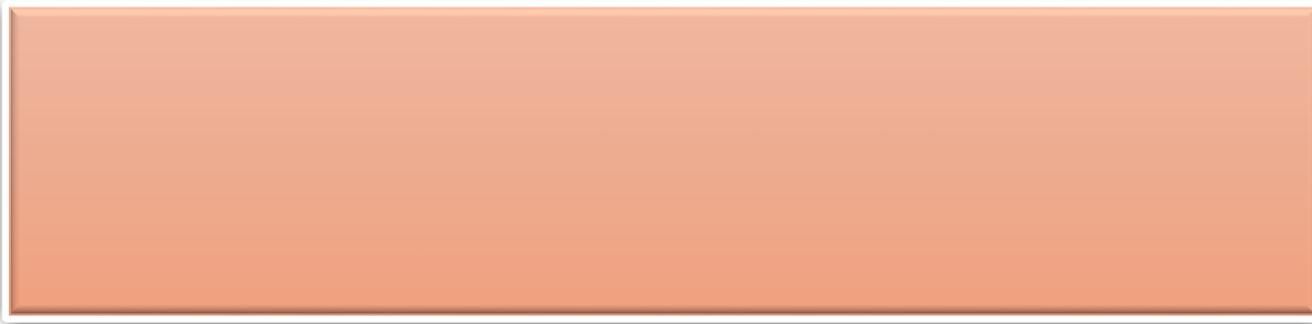
Fellowship in Infertility and Reproductive Medicine



- PCO as is arguably one of the most common endocrine disorders in women of reproductive age, affecting **5% to 10%** of women worldwide.
- It is characterized by a combination of hyperandrogenism (either clinical or biochemical), chronic anovulation, and polycystic ovaries.
- It is frequently associated with insulin resistance and obesity.



- Polycystic ovary syndrome (PCOS) is a common **polygenic multifactorial** condition, affecting a wide population.
- First described in 1935 by **Stein and Leventhal** : who recognized that **enlarged ovaries, amenorrhea, infertility, and hirsutism** could be collated together.



- PCOS is now recognized as a **spectrum disorder ranging** from ultrasound features of polycystic ovarian morphology to anovulatory infertility.
- **Obesity, hyperandrogenemia, and insulin resistance** are all key factors that influence the expression and symptoms of the condition .

Rotterdam



- Since the Rotterdam consensus, there has been further debate about the definitions of both **the syndrome** and the **morphology** of the PCO.
- No single diagnostic criterion is sufficient for the clinical diagnosis of PCOS. **Two of** the following are required:
 - 1.** oligo and/or anovulation,
 - 2.** clinical and/or biochemical signs of hyperandrogenism, and
 - 3.** polycystic ovary morphology on ultrasound.

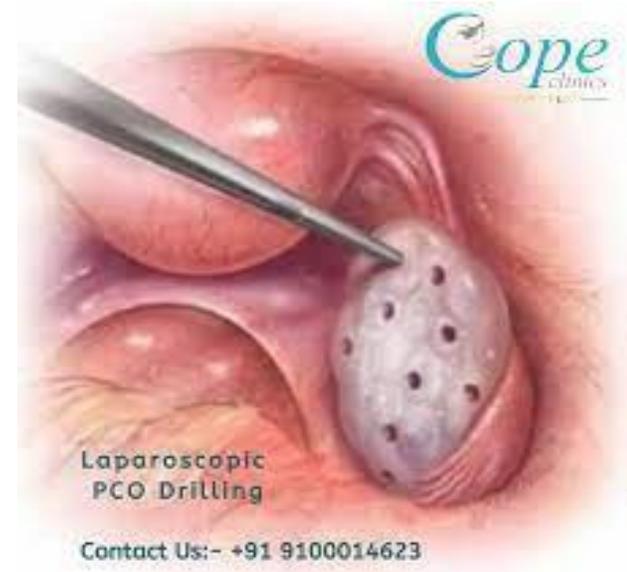


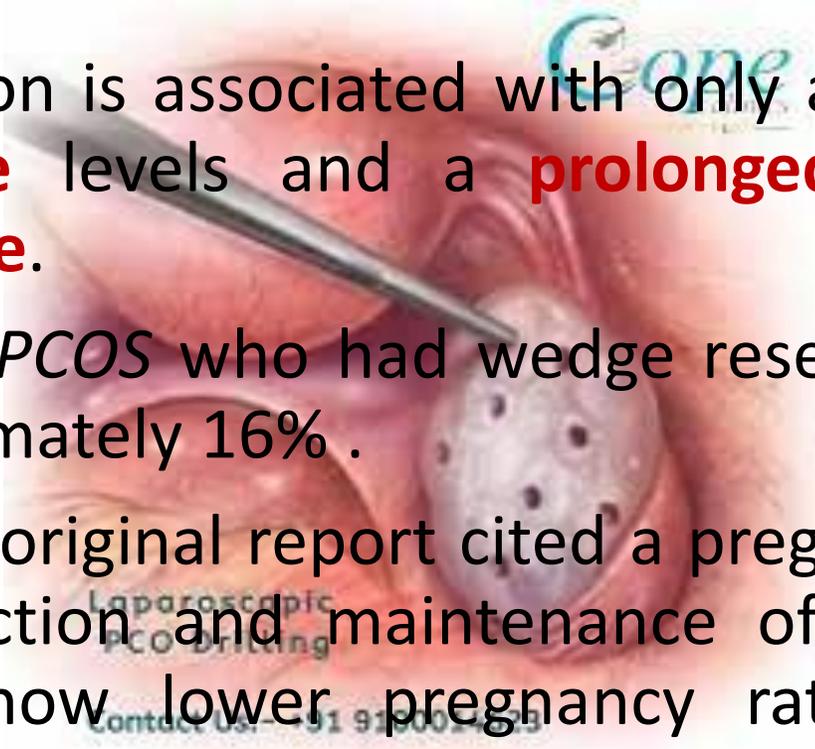
- PCOS receives considerable attention because of its high prevalence and possible **reproductive metabolic**, and **cardiovascular** consequences.
- It is the most common cause of hyperandrogenism, hirsutism, and anovulatory infertility in developed countries .



- **Macroscopically** : ovaries in women with PCOS are two to five times the normal size. A cross-section of the surface of the ovary discloses a white, thickened cortex with multiple cysts that are typically less than a centimeter in diameter.
- **Microscopically:** The superficial cortex is fibrotic and hypocellular and may contain prominent blood vessels. In addition to smaller atretic follicles, there is an increase in the number of follicles with luteinized theca interna. The stroma may contain luteinized stromal cells.
- **1.** Lifestyle modification is the first form of therapy, combining behavioral, dietary, and exercise management.

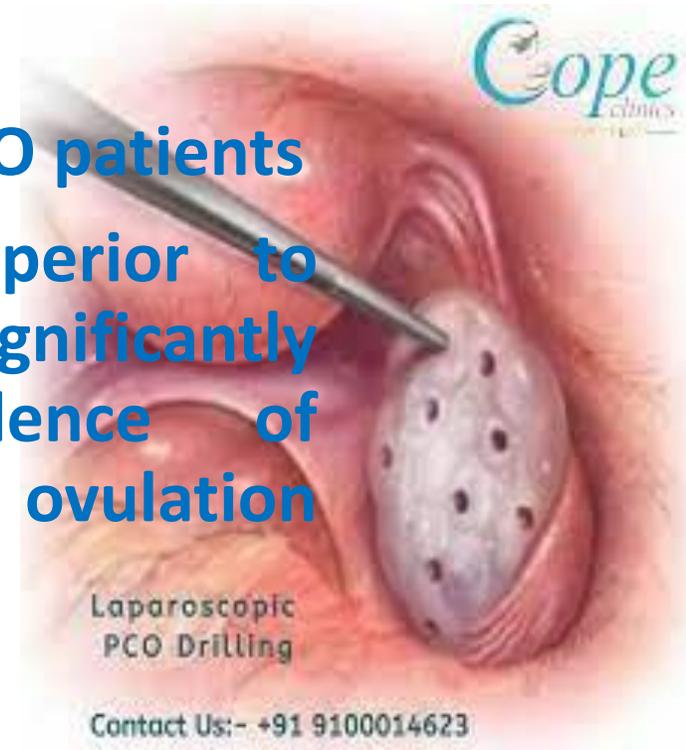
- **Observations that women** with PCOS resumed following ovarian biopsies, led to development of surgical wedge resection via laparotomy .
- Observational data looked promising, but surgery was surpassed by ovulation induction agents, until less invasive laparoscopic surgery with potential for less adhesions and lower cost.
- Minor methodological variations are reported (electrocautery, laser vaporization, multiple ovarian biopsies and others), all seemingly with effects on the endocrine profile.
- OHSS and multiple pregnancy risks are lower than with other options, but other risks potentially are higher, and clarification of the role of LOS, particularly in comparison to other treatments, is needed in infertile women with PCOS.



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- A laparoscopic view of an ovary during a wedge resection procedure. A surgical instrument is visible, performing the resection. The background is a reddish-pink color, typical of the laparoscopic field. There is some faint text overlaid on the image, including "Cone" in blue, "Laparoscopic PCO Drilling" in yellow, and "Contact Us: +91 910001475" in white.
- Bilateral ovarian wedge resection is associated with only a **transient reduction in androstenedione** levels and a **prolonged minimal decrease in plasma testosterone**.
 - In patients with hirsutism and *PCOS* who had wedge resection, hair growth was reduced by approximately 16% .
 - Although Stein and Leventhal's original report cited a pregnancy rate of 85% following wedge resection and maintenance of ovulatory cycles, subsequent reports show lower pregnancy rates and a concerning incidence of periovarian adhesions.
 - Instances of premature ovarian failure and infertility were reported.

Monopolar versus bipolar laparoscopic ovarian drilling in clomiphene-resistant polycystic ovaries (PCO): a preliminary study

- **2016**
- **Eighty clomiphene-resistant PCO patients**
- **Utilizing bipolar LOD is superior to monopolar LOD due to a significantly higher postoperative incidence of resumption of spontaneous ovulation and spontaneous pregnancy.**
- **less adhesion formation**



The Effect of Laparoscopic Ovarian Drilling on Anti-Müllerian Hormone, LH/FSH Ratio and Inhibin B

- 2021
- **AMH level before the operation:** 6.9 ± 1.4 ng/ml and 8.2 ± 1.4 ng/ml for the patients who got pregnant and those who did not get pregnant.
- **AMH level after 3 months of the operation:** 5.1 ± 1.1 ng/ml and 6.3 ± 1.4 ng/ml
- **LH/FSH ratio before :** 2.04 ± 0.5 and 3.02 ± 0.6
- **LH/FSH ratio after 3 months:** 1.15 ± 0.2 and 1.93 ± 0.6 for the patients who got pregnant and those who did not get pregnant respectively.
- **Inhibin B level before :** 52.5 ± 2.2 pg/ml and 52.6 ± 3.9 pg/ml
- **Inhibin B level after:** 48.3 ± 2.1 pg/ml and 49.1 ± 3.6 pg/ml f

• Conclusion:

- Pregnancy rates were significantly related to the preoperative LH/FSH ratio and AMH levels when comparing the cases that got pregnant with the cases who did not conceive postoperatively in patients of polycystic ovary syndrome (PCOS), whereas preoperative Inhibin B level had no relation to pregnancy rates.



Impact of transvaginal hydrolaparoscopy ovarian drilling on ovarian stromal blood flow and ovarian volume in clomiphene citrate-resistant PCOS patients: a case-control study

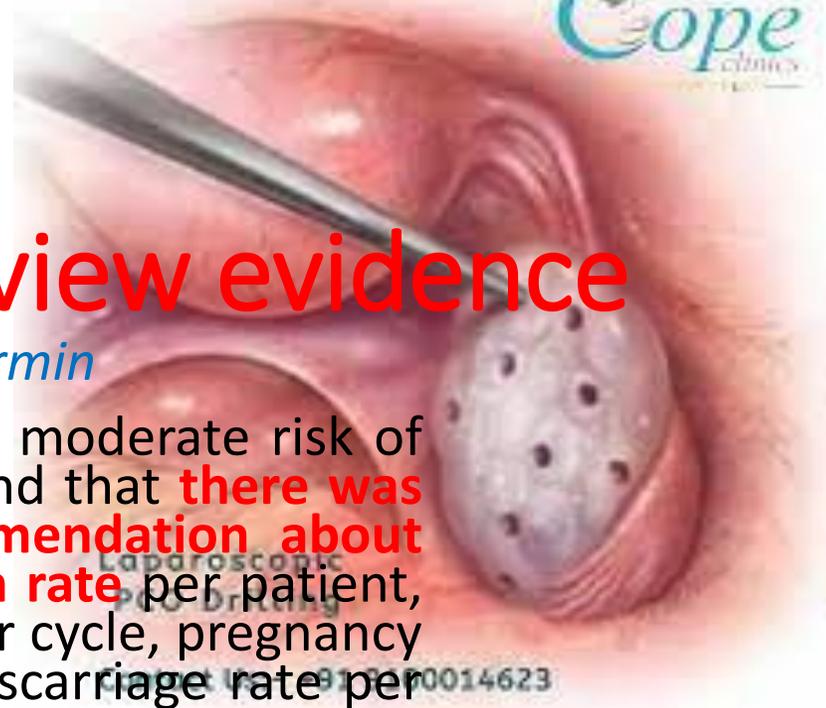
- 2017
- A case-control study on 123 CC-resistant PCOS
- **In conclusion:**
- THL ovarian drilling seems to reduce OV(ovarian volume) and 3D power Doppler indices, and could therefore be a viable alternative to LOD in PCOS patients resistant to medical therapy.



*Laparoscopic ovarian surgery versus
metformin*

Summary of systematic review evidence

- *Laparoscopic ovarian surgery versus metformin*
- Two medium quality RCTs (level II) with a moderate risk of bias compared LOS to metformin and found that **there was insufficient evidence to make a recommendation about LOS compared to metformin for live birth rate** per patient, ovulation rate per cycle, pregnancy rate per cycle, pregnancy rate per patient, multiple pregnancies, miscarriage rate per pregnancy, adverse effects.
- One RCT reported that LOS was better than metformin for ovulation ($p=0.001$) and pregnancy rate ($p=0.03$) and the other study reported that metformin was better than LOS for live birth rate ($p<0.05$), pregnancy rate per cycle (metformin: 18.6%, LOS: 13.4%, $p<0.05$), and miscarriage rate (metformin: 15.4%, LOS: 29.0%, $p<0.05$).
- Both medium quality single centre studies had a small sample size and moderate risk of bias and therefore need to be interpreted with caution.



*Laparoscopic ovarian surgery versus
clomiphene citrate*

Summary of systematic review evidence

- *Laparoscopic ovarian surgery versus clomiphene citrate*
- Two high quality RCTs (level II) with a low risk of bias compared LOS to CC and found that there was **no difference between LOS and CC** for live birth rate per patient and pregnancy rate per patient, ovulation rate per patient and miscarriage rate per pregnancy .There was insufficient evidence to support or refute the use of LOS over CC for multiple pregnancies.



*Laparoscopic ovarian surgery versus
clomiphene citrate + metformin*

Summary of systematic review evidence

- *Laparoscopic ovarian surgery versus clomiphene citrate + metformin*
- Three low to moderate quality RCTs with low to moderate risk of bias compared LOS to CC plus metformin (all three studies reported in Farquhar 2012 systematic review).
- **Meta-analyses found that CC plus metformin (CC+M) was better than LOS for live birth rate**, but there was no difference for pregnancy rate per patient, multiple pregnancy rate, or miscarriage rate per pregnancy .
- There was **insufficient evidence** to support or refute the use of LOS over CC plus metformin for ovulation rate per patient, and OHSS.



*Laparoscopic ovarian surgery
versus aromatase inhibitors*

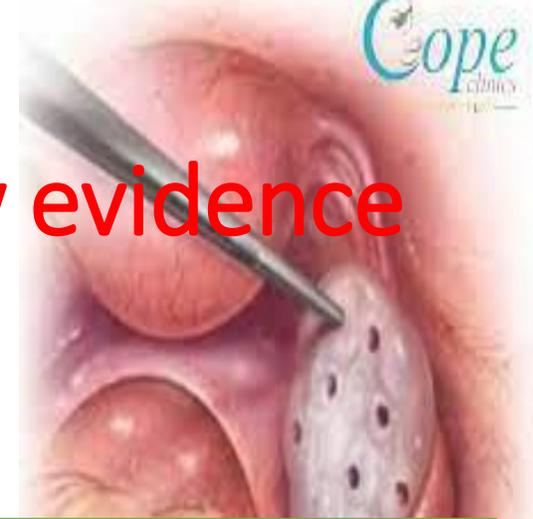
Summary of systematic review evidence



- *Laparoscopic ovarian surgery versus aromatase inhibitors*
- Three RCTs with low risk of bias compared letrozole to LOS and found that there was insufficient evidence of a difference between letrozole and LOS. One of the RCTs in 147 women with CC resistance found that **letrozole was better than LOS** for **ovulation rate** per cycle ,however the evidence is of low certainty.
- The systematic review by Farquhar 2012 combined these studies in meta-analysis for pregnancy rate per patient, multiple pregnancy rate per pregnancy and miscarriage rate per pregnancy and **there was no statistical difference between the two interventions.**
- One low quality RCT with moderate risk of bias compared **LOS with letrozole plus metformin** and found that there was insufficient evidence of a difference between the two interventions for ovulation, pregnancy and miscarriage rate per pregnancy.

*Laparoscopic ovarian surgery
versus gonadotrophins*

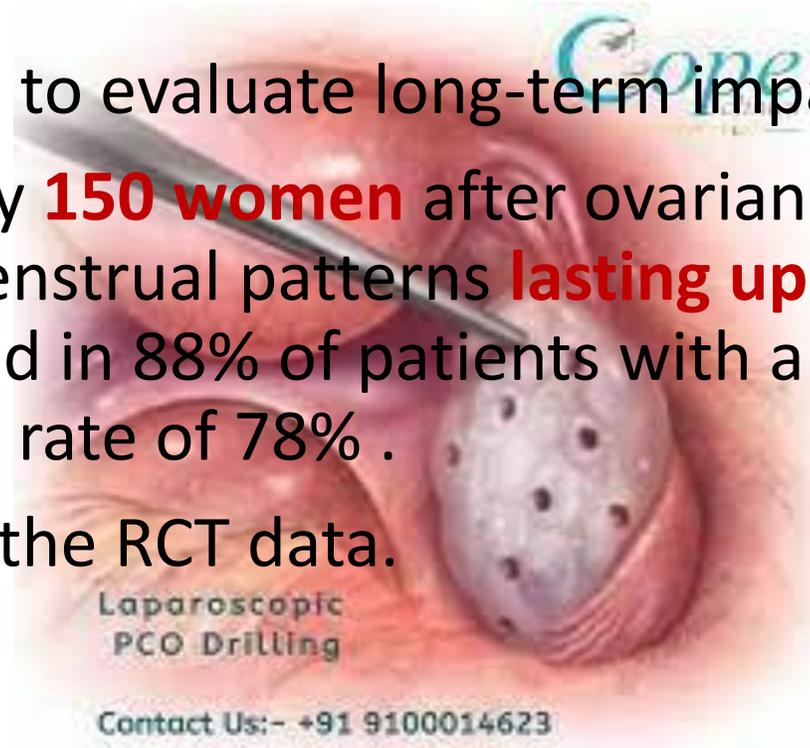
Summary of systematic review evidence



- *Laparoscopic ovarian surgery versus gonadotrophins*
- One high quality systematic review of RCTs (level I) with low risk of bias compared LOS to FSHs and found that **there was no difference** between the interventions for live birth rate per patient and pregnancy rate per patient, ovulation rate per patient and miscarriage rate per pregnancy, but **LOS was better than FSH for multiple pregnancy rate** (OR 0.13 ,4 studies, 303 participants).

Summary of systematic review evidence

- Observational data was sourced to evaluate long-term impacts.
- A **15-25 year follow-up** of nearly **150 women** after ovarian wedge resection shows that regular menstrual patterns **lasting up to 25** years after surgery were restored in 88% of patients with a cumulative pregnancy/live birth rate of 78% .
- This was considered along with the RCT data.



Recommendations

5.7.1 EBR Laparoscopic ovarian surgery could be second line therapy for women with PCOS, who are clomiphene citrate resistant, with anovulatory infertility and no other infertility factors. ◆◆◆
⊕⊕○○

5.7.2 CCR Laparoscopic ovarian surgery could potentially be offered as first line treatment if laparoscopy is indicated for another reason in women with PCOS with anovulatory infertility and no other infertility factors. ◆◆◆

5.7.3 CPP Risks need to be explained to all women with PCOS considering laparoscopic ovarian surgery.

5.7.4 CPP Where laparoscopic ovarian surgery is to be recommended, the following need to be considered:

- comparative cost
- expertise required for use in ovulation induction
- intra-operative and post-operative risks are higher in women who are overweight and obese
- there may be a small associated risk of lower ovarian reserve or loss of ovarian function
- periadnexal adhesion formation may be an associated risk.

Recommendations

- **Justification**

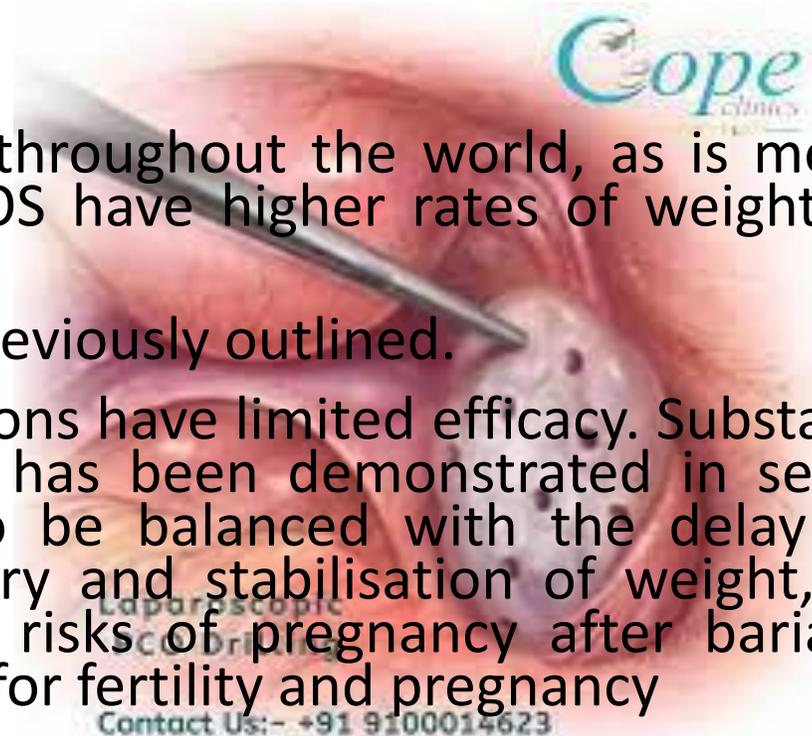
- LOS is an intervention that can lead to a **singleton birth** in women with PCOS. There is no convincing evidence of inferiority over other common ovulation induction agents, there is no need for monitoring (because of mono-ovulation) and only a background risk of multiple pregnancy.
- However, it is important to note that LOS is an invasive surgical intervention; there is a small risk of reduced ovarian reserve or loss of ovarian function; and adhesion formation should be considered.
- Issues covered in the clinical practice points should be carefully considered.

Bariatric surgery

- **Clinical need for the question**

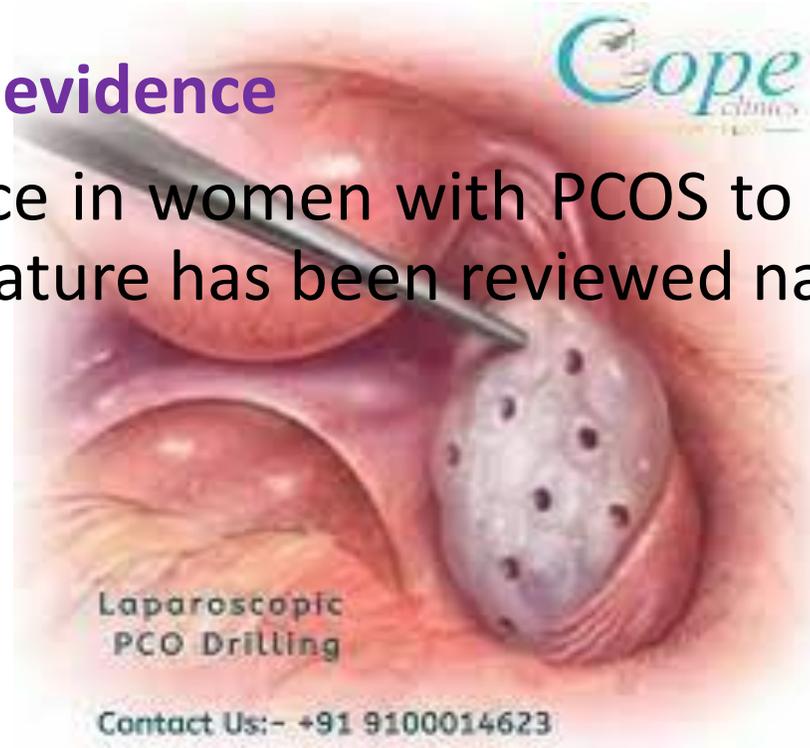
- Obesity is increasing in prevalence throughout the world, as is morbid obesity (BMI ≥ 40 kg/m²). Women with PCOS have higher rates of weight gain and of obesity, adversely affecting fertility.
- Weight loss improves outcomes as previously outlined.
- In **severe obesity**, lifestyle interventions have limited efficacy. Substantial efficacy of bariatric surgery on weight loss has been demonstrated in severely obese women. Potential benefits need to be balanced with the delay in infertility treatment and pregnancy for surgery and stabilisation of weight, the risks of bariatric surgery and the potential risks of pregnancy after bariatric surgery. Controversy persists around efficacy for fertility and pregnancy

outcomes, optimal timing, adverse effects and comparative efficacy with other treatments, as well as on adverse effects on subsequent pregnancies.



Bariatric surgery

- **Summary of systematic review evidence**
- We did not identify any evidence in women with PCOS to answer the question and therefore the literature has been reviewed narratively.



An advertisement for laparoscopic PCO drilling. It features a close-up of a surgical instrument with a circular, perforated tip. The background is a soft-focus, reddish-pink hue. Text elements include the 'Cope' logo in the top right, the title 'Laparoscopic PCO Drilling' in the center, and a contact number '+91 9100014623' at the bottom.

Bariatric surgery

- Bariatric surgery can cause malabsorption and psychological issues including disordered eating and may adversely affect maternal and neonatal health.
- Adequate intake and absorption of iron, folate, iodine and other
- nutrients are of concern. While supplement use is widely recommended following bariatric surgery especially for pregnant women, there are reports of poor compliance and challenges tolerating fortified foods such as bread.
- National registries (surgery, pregnancy, infants) show that obese women who undergo bariatric surgery and conceive compared to similarly obese controls, had more small for gestational age babies, shorter gestations, and a trend towards increased neonatal mortality, with similar findings in retrospective studies.
- Benefits have included less GDM and large for gestational age babies.



- **UK clinical guidelines** for obesity management in the general population recommend considering bariatric surgery with a **BMI $\geq 35\text{kg/m}^2$** with one or more severe complications, expected to improve with weight loss and failure of structured lifestyle intervention .
- Obesity surgery can be considered after non-surgical treatment has failed with a BMI $\geq 40\text{kg/m}^2$ and obesity surgery can be **first line** treatment with a **BMI $\geq 50\text{kg/m}^2$** .

Bariatric surgery



- **Summary of narrative review evidence**

- Other guidelines recommend lower barriers to surgery .For type of surgery, Vertical Sleeve Gastrectomy (VSG) has overtaken the Roux-en-Y Gastric Bypass (RYGB) and gastric band surgery as the most commonly performed bariatric surgery with lower operative morbidity .
- Adjustable gastric banding, once the choice for women planning pregnancy is now less common given complications and overall lower long-term weight loss.
- High quality RCTs of bariatric surgery versus medical management in DM2 show persistent benefits and superiority of weight loss and bariatric surgery in curing or ameliorating diabetes .Yet these studies are absent in PCOS for fertility and pregnancy outcomes, with current PCOS studies poorly designed ,and with failure to report key perinatal outcomes to inform risk to benefit ratio. In PCOS, the balance between delaying infertility treatment and pregnancy whilst undertaking bariatric surgery and attaining stable post-operative weight, is also unclear ,as is the optimal type of bariatric surgery.

Recommendations

5.8.1 CCR Bariatric surgery should be considered an experimental therapy in women with PCOS, for the purpose of having a healthy baby, with risk to benefit ratios currently too uncertain to advocate this as fertility therapy. ❖

5.8.2 CPP If bariatric surgery is to be prescribed, the following needs to be considered:

- comparative cost
- the need for a structured weight management program involving diet, physical activity and interventions to improve psychological, musculoskeletal and cardiovascular health to continue post-operatively
- perinatal risks such as small for gestational age, premature delivery, possibly increased infant mortality
- potential benefits such as reduced incidence of large for gestational age fetus and gestational diabetes
- recommendations for pregnancy avoidance during periods of rapid weight loss and for at least 12 months after bariatric surgery with appropriate contraception.

If pregnancy occurs, the following need to be considered:

- awareness and preventative management of pre-and post-operative nutritional deficiencies is important, ideally in a specialist interdisciplinary care setting
- monitoring of fetal growth during pregnancy.

THANK YOU

