The 2023 Digital Learning Journey on Diabetes and Thyroid Disorders

Clinical considerations of endocrine disorders in pregnancy: from planning through birth

Obesity and fertility: from planning through birth

Anja Pinborg, Professor and medical director, Rigshospitalet – Copenhagen University Hospital, Denmark

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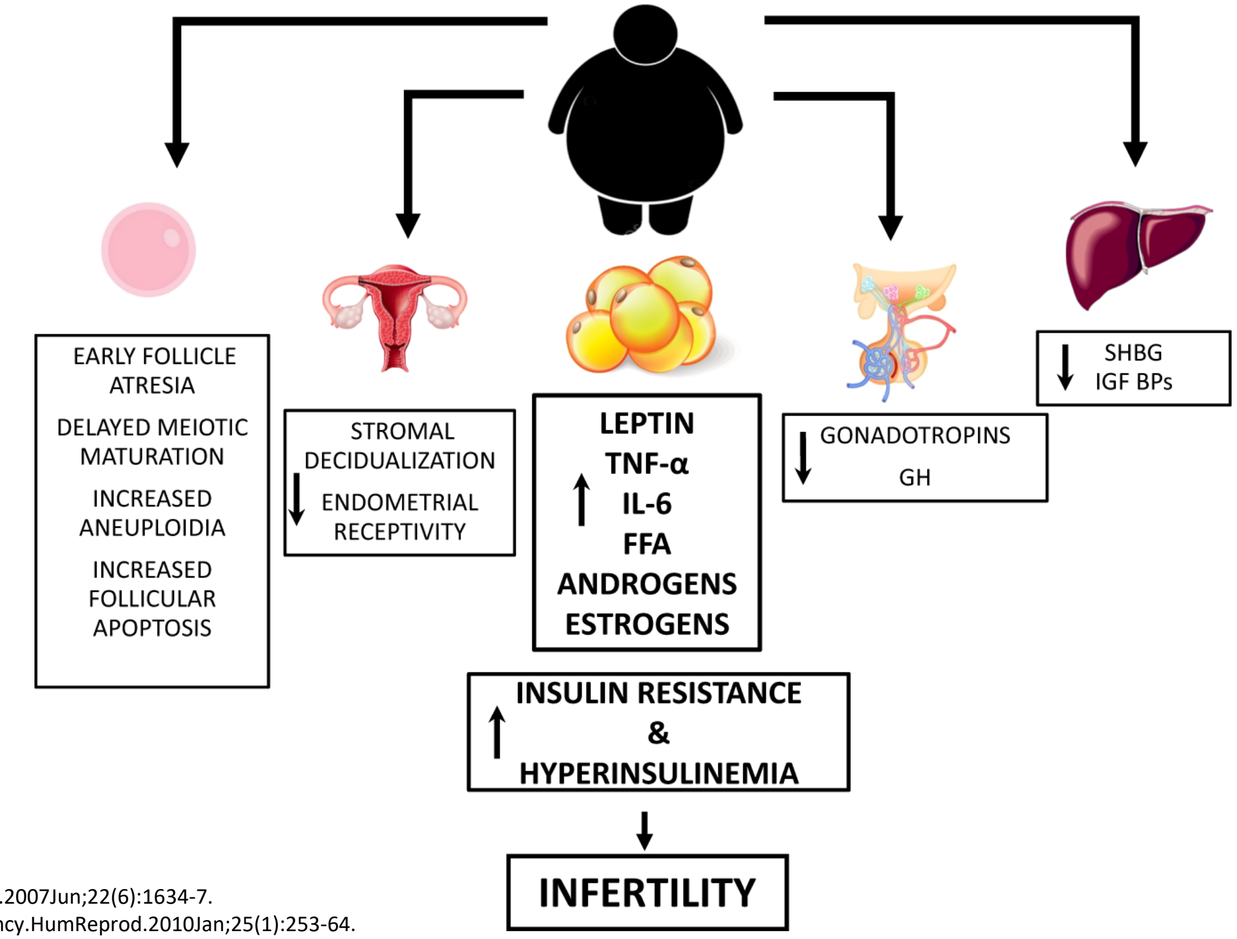
The 2023 Digital Learning Journey on Diabetes and Thyroid Disorders

Obesity and fertility: from planning through birth

- Obesity is associated with a lower fecundity caused by altered secretion of pituitary gonadotrophins and steroids
- Oligo- or amenorrhea due to anovulation
- Increased time-to-pregnancy (TTP)



Ramlau-Hansen CH,ThulstrupAM,NohrEA,BondeJP,SørensenTI,OlsenJ.Subfecundityinoverweightandobesecouples.HumReprod.2007Jun;22(6):1634-7.
WiseLA,RothmanKJ,MikkelsenEM,SørensenHT,RiisA,HatchEE.Aninternet-basedprospectivestudyofbodysizeandtime-to-pregnancy.HumReprod.2010Jan;25(1):253-64.
GesinkLaw DC,MaclehoseRF,LongneckerMP.Obesityandtimetopregnancy.HumReprod.2007Feb;22(2):414-20.
vanderSteegJW,SteuresP,EijkemansMJ,HabbemaJD,HompesPG,BurggraaffJM.Obesityaffectsspontaneouspregnancychancesinsubfertile,ovulatorywomen.HumReprod.2008Feb;23(2):324-8.

Influence of female bodyweight on IVF outcome: a longitudinal multicentre cohort study of 487 infertile couples

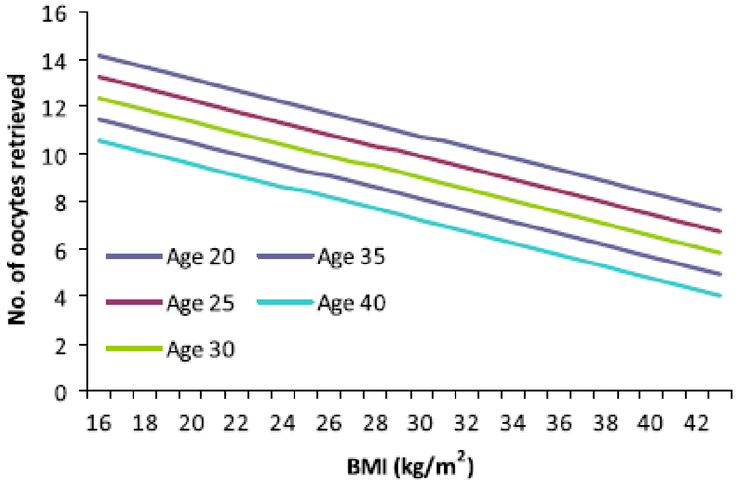


Figure 2 The expected number of oocytes retrieved related to women's body mass index (BMI) and female age. Multiple linear regression analysis only including the first IVF or intra-cytoplasmic sperm injection cycle showed a significant negative association between the number of collected oocytes and BMI ($P < 0.001$, $B = -0.243$, SE = 0.059) and women's age ($P = 0.014$, $B = -0.179$, SE = 0.073).

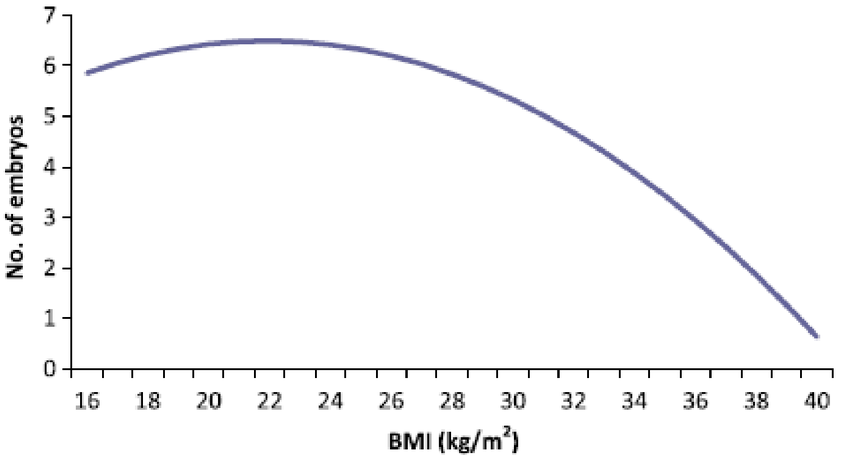


Figure 3 The expected number of embryos related to women's body mass index (BMI). The association between BMI and the number of embryos showed a quadratic relationship with an inverse U-formed curve with fewer embryos among the low-weight and the obese women ($P = 0.03$, $B = -0.018$, SE = 0.008).

Pinborg et al., Reproductive BioMedicine Online (2011) **23**, 490–499

The influence of female and male body mass index on live births after ART treatment 2006 to 2010: a nationwide register-based cohort study

Live birth rate per IVF/ICSI cycle (n = 25 191 cycles):

Women with ovulation (n = 12 566):

Normal weight	64%	Reference*	
Overweight:	23.5%	aOR 0.91 (95% CI 0.84-0.99)* -	9% reduced chance
Obese	9.2%	aOR 0.84 (95% CI 0.74-0.95)* -	16% reduced chance

Men (n = 774):

Normal weight	47.5%	Reference*	
Overweight	38.9%	aOR 0.92 (95%CI 0.72-1.16)*	
Obese	13.1%	aOR 0.69 (95% CI 0.48-0.98)* -	31% reduced chance

*Adjusted odds ratio ~ aOR. Adjustments were made for female and male age and smoking status

(Petersen GL et al., Fertil Steril 2013;99:1654–62)

Weight reduction intervention for obese infertile women prior to IVF: a randomized controlled trial

(Einarsson et al., Human Reproduction, Vol.32, No.8 pp. 1621–1630, 2017)

RESULTS

- 12 weeks of a low-calorie liquid formula diet (LCD) of 880 kcal/day
- Live birth rate: 29.6% (45/152) in the weight reduction and 27.5% (42/153) in controls
- Difference 2.2%, 95% CI: 12.9 to −8.6, P = 0.77)
- Mean weight change was −9.44 (6.57) kg in the weight reduction group as compared to +1.19 (1.95) kg in the controls (P < 0.0001).

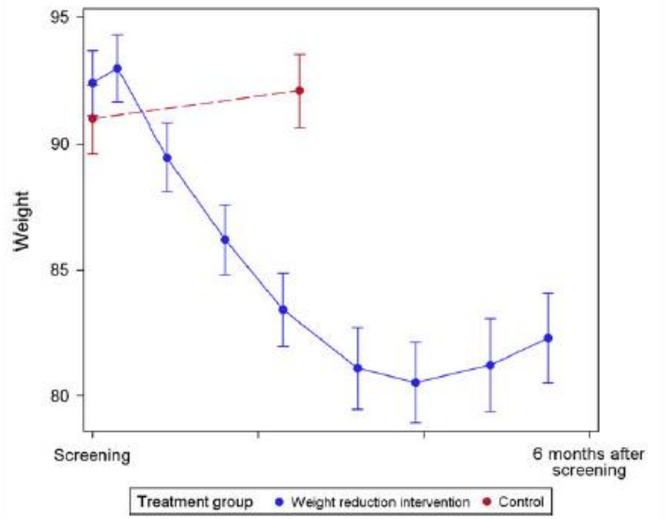


Figure 2 Graph of weight change for the two study groups from randomization to oocyte retrieval.

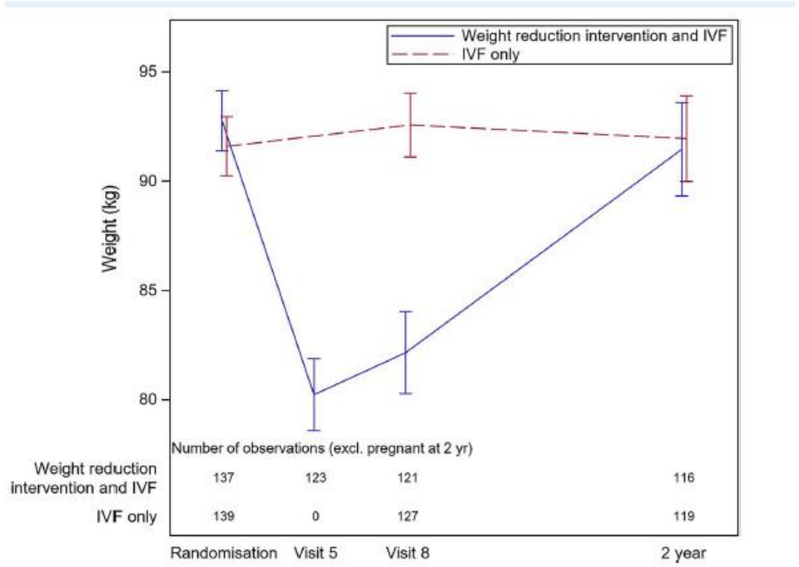
IMPLICATIONS OF THE FINDINGS

- Weight loss for obese women (BMI: 30–34.9 kg/m2) may not rectify the outcome in IVF cycles
- Higher number of spontaneous conceptions leading to live birth in the weight loss group (10.5% vs. 2.6% P = 0.009).
- Intensive weight reduction with *Low Calorie Diet* treatment does not negatively affects results

Cumulative live birth rates after weight reduction in obese women scheduled for IVF: follow-up of an RCT

(Kluge et al., Hum Reprod Open 2019)

- 42 additional live births were achieved during the follow-up in the weight reduction groups and 40 additional live births in the control group
- Cumulative Live Birth Rate (CLBR) of weight loss group: 57.2% (87/152) and controls: 53.6% (82/153)(*P* =0.56; odds ratio (OR) 1.16, 95% CI: 0.74–1.52).
- Most had regained their pre-study weight after 2 years: Mean weight gain over the 2 years was 8.6 kg, while women in the control group had a mean weight loss of 1.2 kg.



Obesity and fertility: from planning through birth

Male overweight and fertility

- Higher risk of low semen quality at increasing BMI > 25
- Lower fecundity at increasing BMI > 25
- There is a lack of evidence that the chance of live birth after IUI or IVF/ICSI is influenced by male obesity

Sermondade N, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Human Reprod. 2013, 19(3):221-231.
Hammiche F, et al. Body mass index and central adiposity are associated with sperm quality in men of subfertile couples. Human Reprod. 2012, 27(8):2365-2372.
Ma J, et al. Association between BMI and semen quality: an observational study of 3966 sperm donors. Human Reprod. 2019, 34(1):155-162.
Sundaram R, et al. Couples' body composition and time-to-pregnancy. Hum Reprod 2017;32(3):662-668.
Hernáez A, et al. Body mass index and subfertility: multivariable regression and Mendelian randomization analyses in the Norwegian Mother, Father and Child Cohort Study. Hum Reprod 2021;36(12):3141-3151.
Mushtaq R, et al. Effect of male body mass index on assisted reproduction treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online 2018;36:459-471.

Female Overweight and obesity
Reproductive and obstetric outcomes

- Fecundity is lower
- The chance of live birth after IUI and IVF/ICSI is lower
- The risk of pregnancy complications such as miscarriage, gestational DM and preeclampsia, thrombo-embolic event and stillbirth increases
- The risk of thrombo-embolic disease in IVF-pregnancies is higher
- The risk of obstetric complications such as shoulder dystocia, the use of vacuum extraction, forceps and Caesarean section is higher
- Increased risk of *stillbirth* at maternal BMI > 30

Maheshwari A, Stofberg L, Bhattacharya S: Effect of overweight and obesity on assisted reproductive technology—a systematic review. Human reproduction update 2007, 13(5):433-444.
Sermondade N, Huberlant S,Bourhis-Lefebre, Arbo E, Gallot V, Columbani M, Fréour T: Female obesity is negatively associated with live birth rate following IVF: a systematic review and meta-analysis. Human Reprod update 2019, 25(4):439-451.
Ovesen P,Rasmussen S,Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. Obstet Gynecol. 2011 Aug; 118(2Pt1):305-312.
Blondon M,Harrington LB,Boehlen F,Robert-Ebadi H,Righini M,Smith NL.Pre-pregnancy BMI,delivery BMI ,gestational weight gain and the risk of postpartum venous thrombosis.Thromb Res 2016;145:151-6.

Female overweight and obesity
Health in the offspring

- Higher risk of congenital anomalies in the children (neuraltube defects, cardiac malformations and palate-cleft anomalies)
- Increased risk of *cardiovascular and respiratory disease* in children, if maternal BMI > 35
- Increased risk of altered *neuro-psychological development* (schizophrenia, ADHD, compromised learning, lower IQ and emotional problems) in children at increasing maternal BMI > 25

Carmichael SL, Rasmussen SA, Shaw GM. Prepregnancy obesity: a complex risk factor for selected birth defects. *Birth Defects Res A Clin Mol Teratol*. 2010;88(10):804-810.
Rasmussen SA, Chu SY, Kim SY, Schmid CH, Lau J. Maternal obesity and risk of neural tube defects: a metaanalysis. *Am J Obstet Gynecol*. 2008;198(6):611-619.
Razaz N, Villamor E, Muraca GM, Bonamy AKE, Cnattingius S. Maternal obesity and risk of cardiovascular diseases in offspring: a population-based cohort and sibling-controlled study. *Lancet Diabetes Endocrinol*. 2020;8(7):572-581.
Buss C, Entringer S, Davis EP, et al. Impaired executive function mediates the association between maternal pre-pregnancy body mass index and child ADHD symptoms. *PLoS One*. 2012;7(6):e37758.

Conclusions

- Weight loss in women prior to IVF increases the chance of natural conception in all intervention studies
- No evidence of increased live birth rate after life-style intervention among women prior to IVF
- Weight loss in women lower the risk of miscarriage, malformation, obstetric complications, stillbirth and child morbidity
- Males with BMI > 25 has lower semen quality and fecundity

Recommendations
Danish IVF guidelines

Weight loss to BMI < 30, if the female age is ≤ 30 years

Weight loss to BMI < 35, if the female age is > 30 years

IVF is not recommended if BMI > 40

(www.fertilitetsselskab.dk)

THANK YOU

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