ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

Terapia dell' Obesità: PCOS

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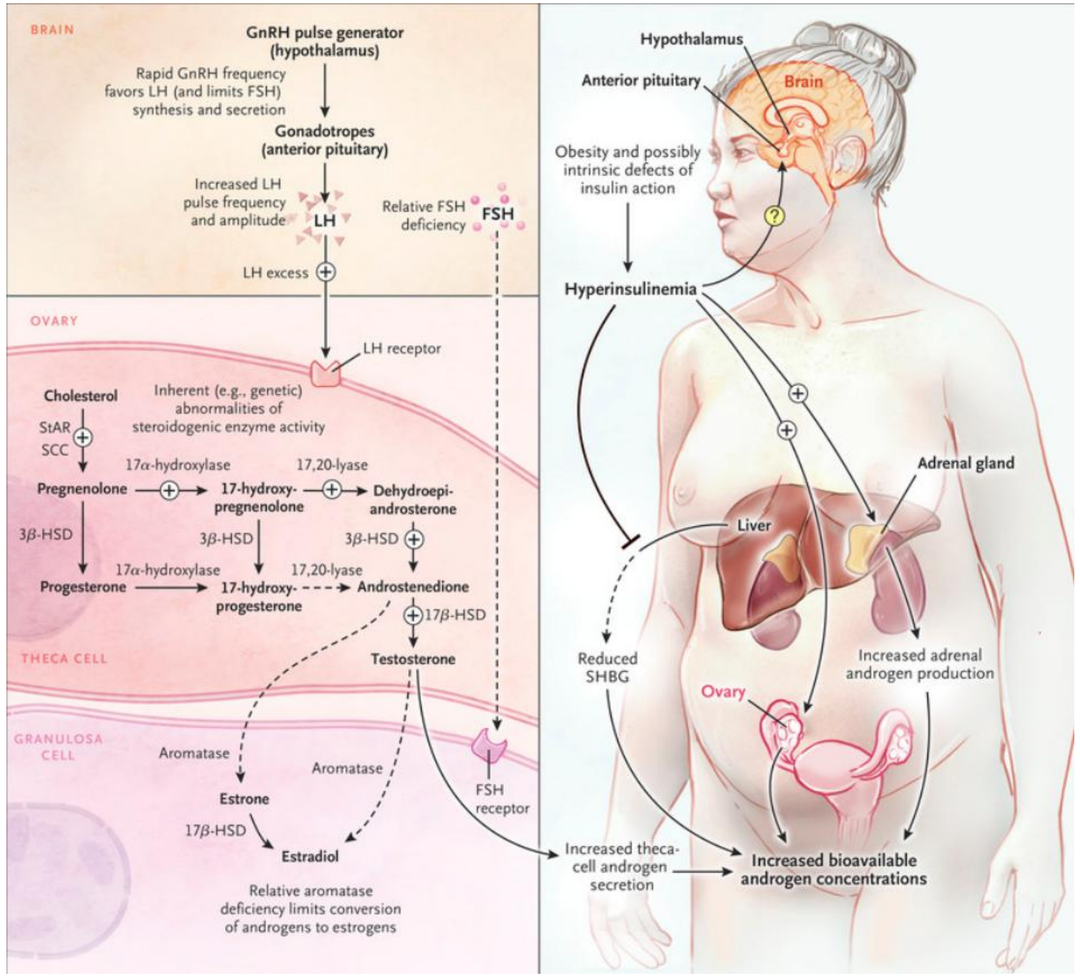
Università di Bologna

DISCLOSURES

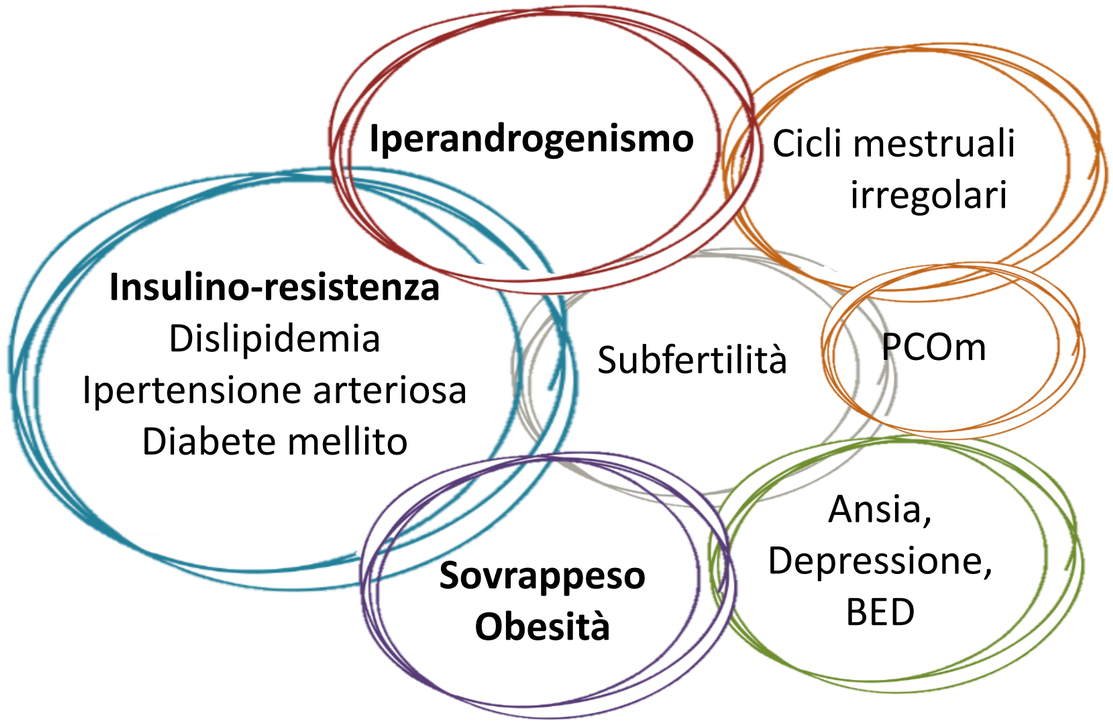
Ai sensi dell'art. 76 del Regolamento applicativo dell'Accordo Stato-Regioni 02.02.2017, dichiaro che negli ultimi DUE ANNI ho avuto i seguenti rapporti anche di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

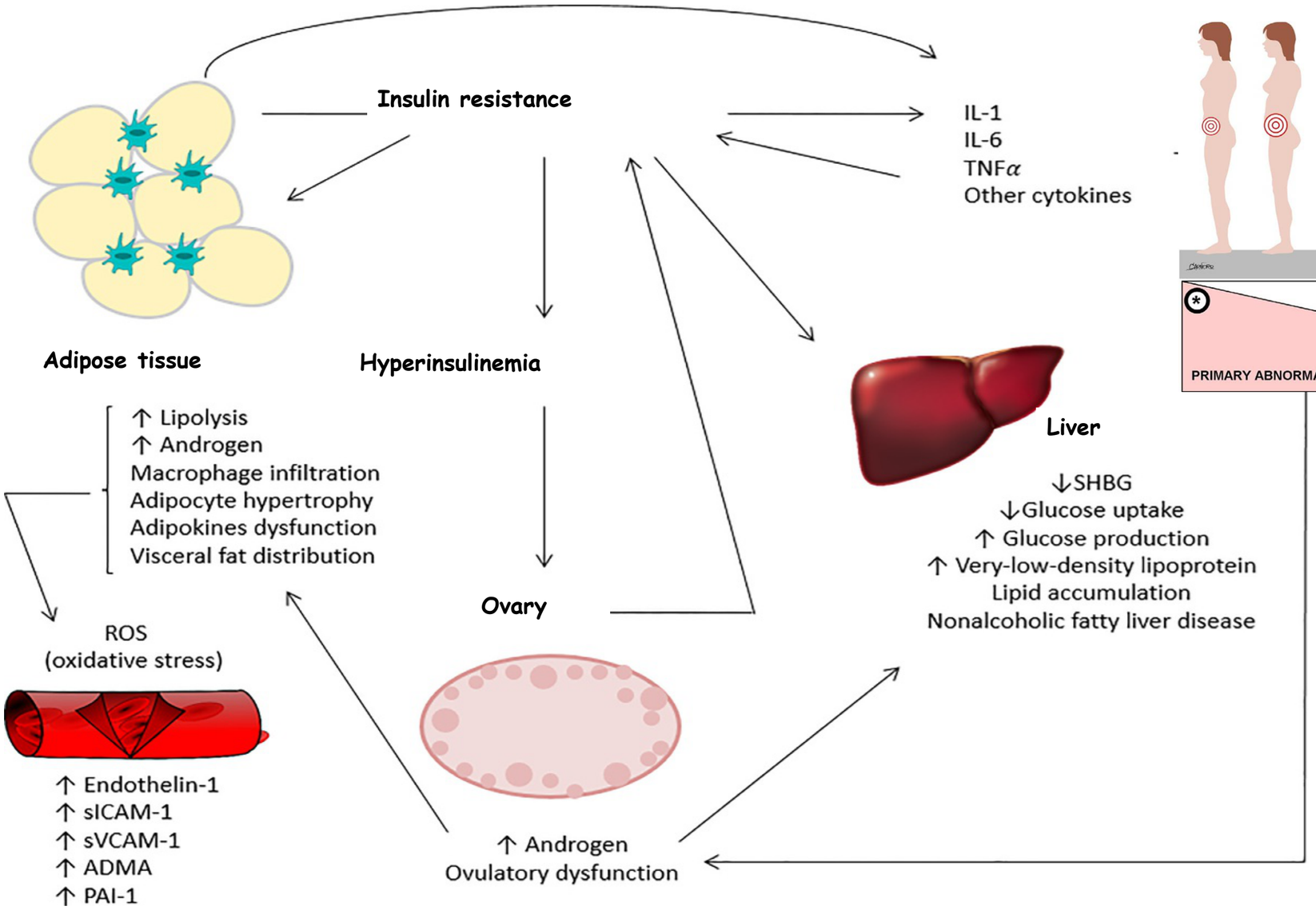
Novo-Nordisk
Sandoz S.p.A.
Neurocrine
Eli Lilly S.p.A.

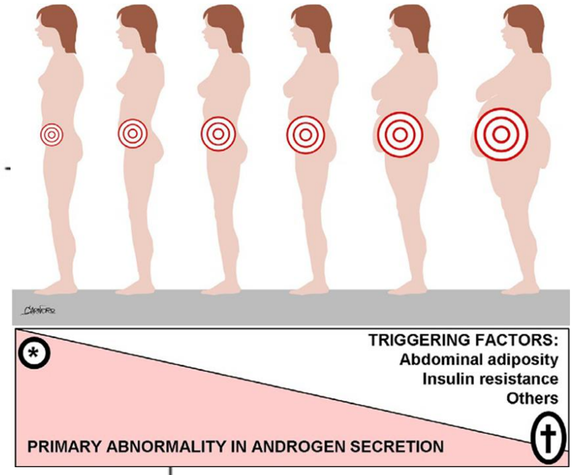
PCOS: DISORDINE ENDOCRINO-METABOLICO COMPLESSO ED ETEROGENEO



McCartney & Marshall *N Engl J Med*. 2016







Escobar-Morreale et al. Trends Endocrinol Metab 2007

Spritzer et al. In: PCOS Challenging Issues in the Modern Era of Individualized Medicine Elsevier 2022

CLUB SIE ENDOCRINOLOGIA DELLA DONNA

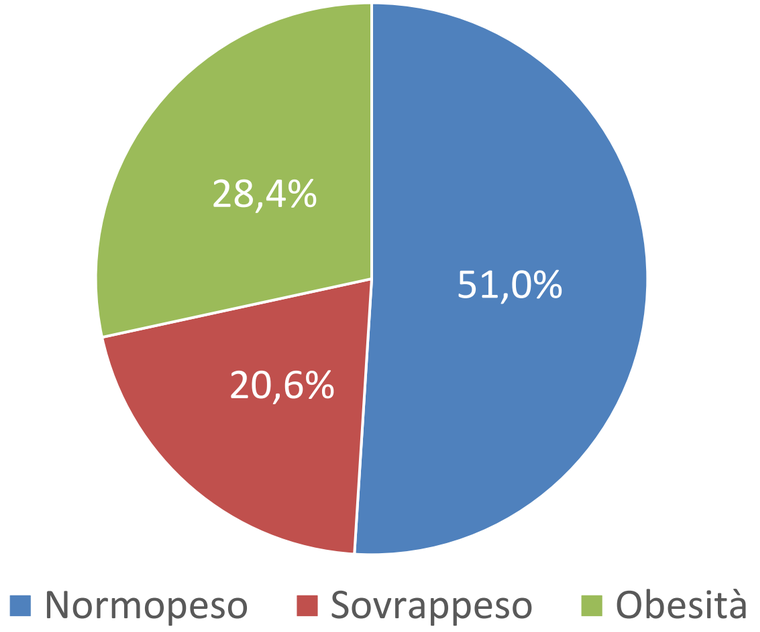
OSSERVATORIO NAZIONALE OVAIO POLICISTICO E SINDROME DA ECCESSO DI ANDROGENI

https://www.pcosoutcome.net/

1464 PCOS in età fertile

1414: Etnia Caucasica

Età (anni): 23.4±6.4



STUDIO OSSERVAZIONALE PROSPETTICO MONOCENTRICO IN UNA POPOLAZIONE ITALIANA CON PCOS

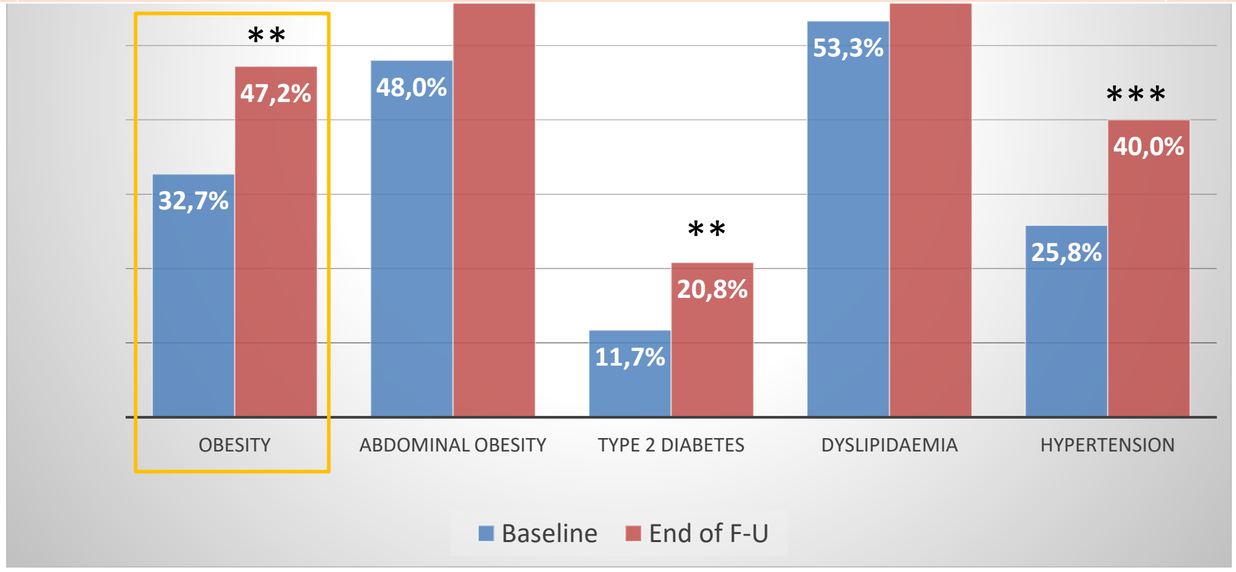
EVOLUZIONE DEI FAT

N = 120	2009 (Baseline)	2021 (End of F-U)	P
Age (years, mean±SD)	39.9±7.7	51.9±7.6	
Menopause (%)	7.5 %	40.8%	**< 0.001**
Drugs for PCOS:			
EP (%)	78.2%	90.8%	**< 0.001**
Years of treatment	8.0±5.5	10.3±8.2	
Metformin (%)	23.3%	29.2%	**0.0233**
Years of treatment	4.1±3.0	6.7±4.5	
Antiandrogens (%)	13.3%	13.3%	1
Years of treatment	2.2±1.7	2.2±1.7	

Gambineri et al Eur J Endocrinol 2025
This study was supported by PRIN 2017 Prot. 2017ATZ2YK

3.5	Factors affecting weight gain in PCOS	
3.5.2	Whilst the specific mechanisms are unclear, it is recognized that many women with PCOS will have underlying mechanisms that drive greater longitudinal weight gain and higher BMI which may • Underpin greater challenges with weight management. • Highlight the importance of lifelong healthy lifestyle strategies and prevention of excess weight gain. • Assist women with PCOS and healthcare professionals in forming realistic, tailored lifestyle goals.	PP

2023 International Evidence-based guideline for PCOS



STUDIO OSSERVAZIONALE PROSPETTICO MONOCENTRICO IN UNA POPOLAZIONE ITALIANA CON PCOS

EVOLUZIONE DEI FATTORI DI RISCHIO CARDIOVASCOLARE

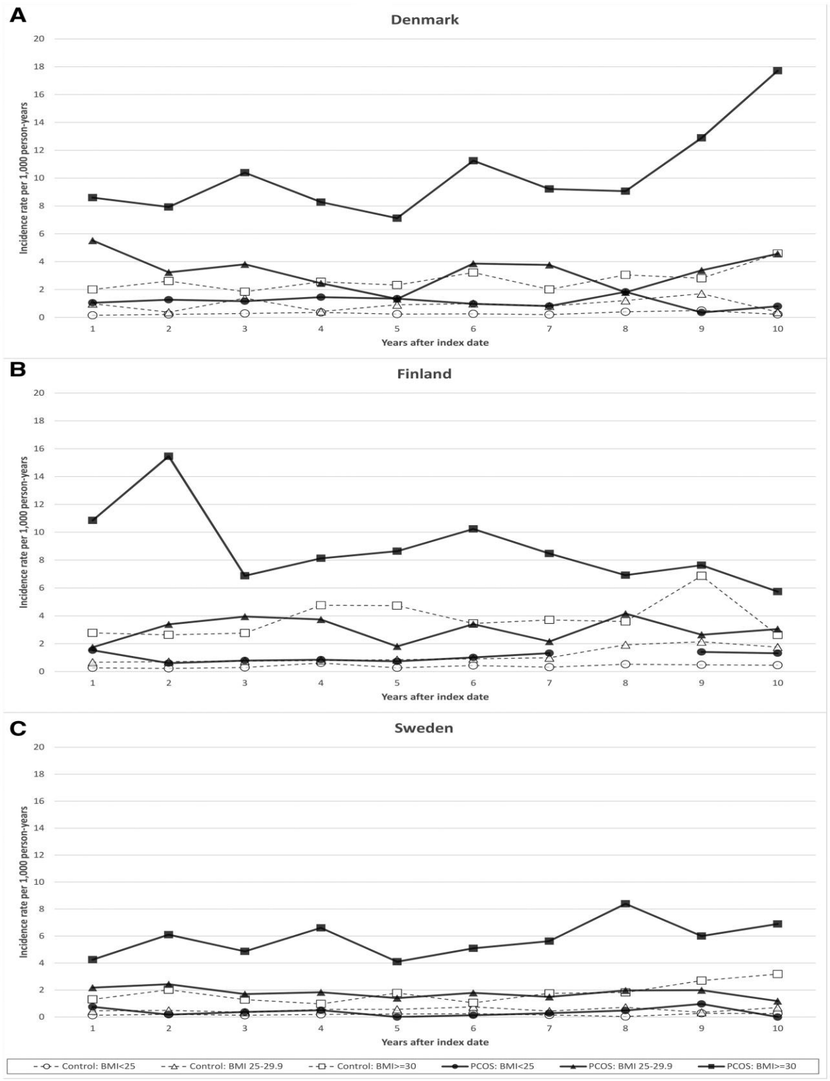
Correlation at the end of Follow-up

	Normalweight	Overweight	Obesity	P value
Type 2 diabetes	**0%**	**7.4%**	**33.3%**	**<0.001**
Dyslipideamia	76.7%	96.3%	90%	NS
Hypertension	**10%**	**29.6%**	**68.6%**	**<0.001**

Gambineri et al Eur J Endocrinol 2025

This study was supported by PRIN 2017 Prot. 2017ATZ2YK

The risk for type 2 diabetes is increased in women with PCOS, and the risk is aggravated in women with BMI ≥30 kg/m^2



STUDY DESIGN, SIZE, DURATION

This national register-based study included women with PCOS and age-matched controls. The main study outcome was T2D diagnosis occurring after PCOS diagnosis. T2D was defined according to ICD-10 diagnosis codes and/or filled medicine prescriptions of anti-diabetic medication excluding metformin.

PARTICIPANTS/MATERIALS, SETTING, METHODS

The study cohort included women originating from Denmark (PCOS Denmark, N = 27 016; controls, N = 133 994), Finland (PCOS Finland, N = 20 467; controls, N = 58 051), and Sweden (PCOS Sweden, N = 52 409; controls, N = 254 010). The median age at cohort entry was 28 years in PCOS Denmark, Finland, and Sweden with a median follow-up time (interquartile range) in women with PCOS of 8.5 (4.0–14.8), 9.8 (5.1–15.1), and 6.0 (2.0–10.0) years, respectively. Cox regression analyses were adjusted for BMI and length of education.

MAIN RESULTS AND THE ROLE OF CHANCE

The crude hazard ratio (HR, 95% CI) for T2D diagnosis in women with PCOS was 4.28 (3.98–4.60) in Denmark, 3.40 (3.11–3.74) in Finland, and 5.68 (5.20–6.21) in Sweden. In adjusted regression analyses, BMI ≥30 vs <25 kg/m^2 was associated with a 7.6- to 11.3-fold risk of T2D. In a combined meta-analysis (PCOS, N = 99 892; controls, N = 446 055), the crude HR for T2D in PCOS was 4.64 (3.40–5.87) and, after adjustment for BMI and education level, the HR was 2.92 (2.32–3.51).

WIDER IMPLICATIONS OF THE FINDINGS

The prospective risk for diagnosis of T2D is increased in women with PCOS, and the risk is aggravated in women with BMI ≥30 kg/m^2.

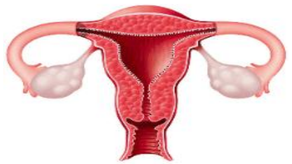
Hum Reprod, Volume 39, August 2024, Pages 1823–1834, https://doi.org/10.1093/humrep/deae124

EARLY FOLLICLE ATRESIA

DELAYED MEIOTIC MATURATION

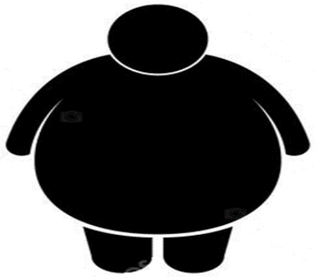
INCREASED ANEUPLOIDIA

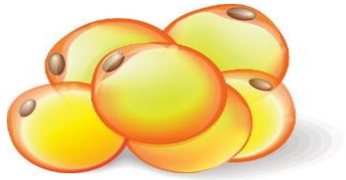
INCREASED FOLLICULAR APOPTOSIS



↓ STROMAL DECIDUALIZATION

↓ ENDOMETRIAL RECEPTIVITY



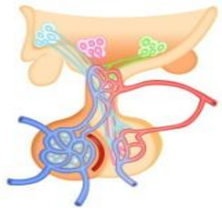


↑ **LEPTIN**
TNF-α
IL-6
FFA
ANDROGENS
ESTROGENS

↑ **INSULIN RESISTANCE & HYPERINSULINEMIA**

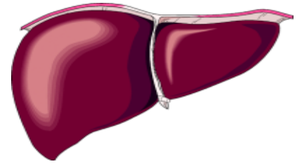
↓

INFERTILITY



↓ GONADOTROPINS

↓ GH



↓ SHBG
IGF BPs

L' Obesità nella PCOS:

- Aggrava l'infertilità, e riduce il tasso di gravidanze e di nati vivi
- Riduce la risposta agli induttori dell'ovulazione, e riduce il tasso di risposta alla ART

Gambineri et al. Int J Obes Suppl 2019

Systematic review and meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome

Nature Communications **2024**

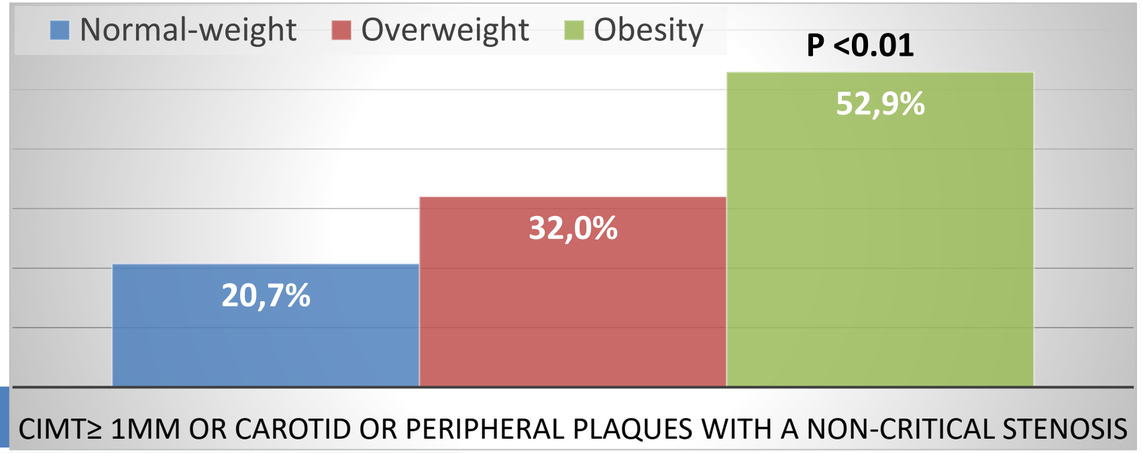
This systematic review and meta-analysis included 104 studies and 106,690 pregnancies in women with and without PCOS from inception until 13th July 2022.
It reported that:

- Women with PCOS have higher body mass index (BMI) around conception and have greater gestational weight gain
- Women with PCOS are more likely to experience pregnancy complications (**Miscarriage, Gestational diabetes, Gestational hypertension, Pre-eclampsia, Delivery by cesarean section**), which are independent of but exacerbated by increased age and BMI

4.10	Pregnancy outcomes	
4.10.7	An OGTT should be considered in all women with PCOS and without pre-existing diabetes, when planning pregnancy or seeking fertility treatment, given the high risk of hyperglycaemia and the associated comorbidities in pregnancy. If not performed preconception, an OGTT could be offered at the first prenatal visit and all women with PCOS should be offered the test at 24-28 weeks gestation	❖❖❖ ⊕◯◯◯
4.10.5	Early lifestyle intervention should be offered to pregnant women with PCOS, given the risk of higher baseline weight, excess gestational weight gain, and pregnancy complications.	PP

2023 International Evidence-based guideline for PCOS

BMI rather than the phenotype impacts precocious ultrasound CV risk markers in PCOS



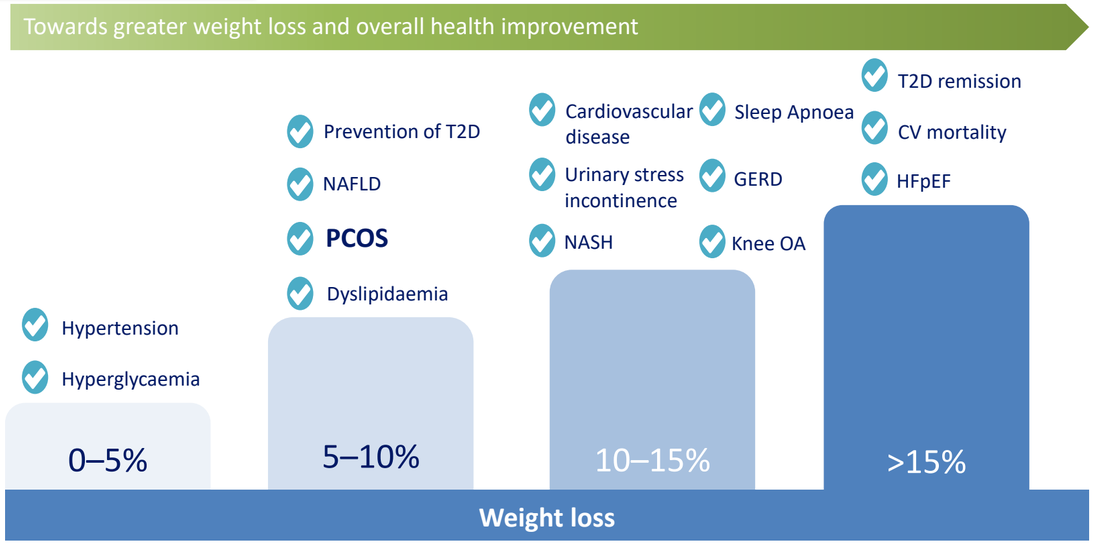
	BMI (kg/m²)			
Variables	***Normal-weight; n=35***	***Overweight; n=29***	***Obese; n=38***	p
cIMT (cm)	**0.49±0.1**	**0.55±0.14**	**0.67±0.17**	**<0.001**
FMD (%)	**12.52±5.23**	**13.66±7.52**	**9.17±4.93**	**0.006**
NGT (%)	26.02±9.26	26.16±8.72	21.85±6.99	0.052
EFT (cm)	**0.63±0.17**	**0.82±0.21**	**1.07±0.4**	**<0.001**

cIMT, carotid intima media thickness; FMD, flow-mediated vessel dilation; NGT, nitroglycerine test; EFT, epicardial fat thickness

This study was supported by PRIN 2017 Prot. 2017ATZ2YK
Pandurevic et al. Eur J Endocrinol 2021

Prevention and management of weight gain, with lifestyle interventions as the initial approach, are recommended as first-line treatments

Most pts with PCOS are unable to engage in sustained dietary changes or exercise regimens, and 15-25% fail to respond. Moreover, some obese PCOS women need to loose more than 5-10% to achieve significant clinical improvement



LCKD/VLCKD

GLP1-RA

GLP1-GIP-RA

Bariatric surgery

2023 International Evidence-based guideline for PCOS; Barbosa-Desongles et al. Am J Physiol Cell Physiol 2013; Blouin et al. Clin Endocrinol (Oxf) 2010; Georgopoulos et al. Fertil Steril 2009; Robinson et al. Clin Endocrinol (Oxf) 1992; Banting et al. BMC Womens Health 2014; Crosignani et al. Hum Reprod 2003

Efficacy of Very Low-Calorie Ketogenic Diet with the Pronokal® method in Obese women with PCOS: a 16-week Randomized Controlled Trial

Summary of main results

	Experimental group	Control group
Body weight & BMI	↓↓	↓
Waist circumferance	↓	≈
Fat mass by BIA	↓	≈
Fasting insulin & HOMA-IR	↓(*)	≈
Free testosterone	↓	≈
SHBG	↑	≈
Ovulation	↑46.1%	↑21.4%

Frequency of WL≥ 5% and 10%
Experimental group: 15.4% and **76.9%**
Control group: 21.4% and 21.4%

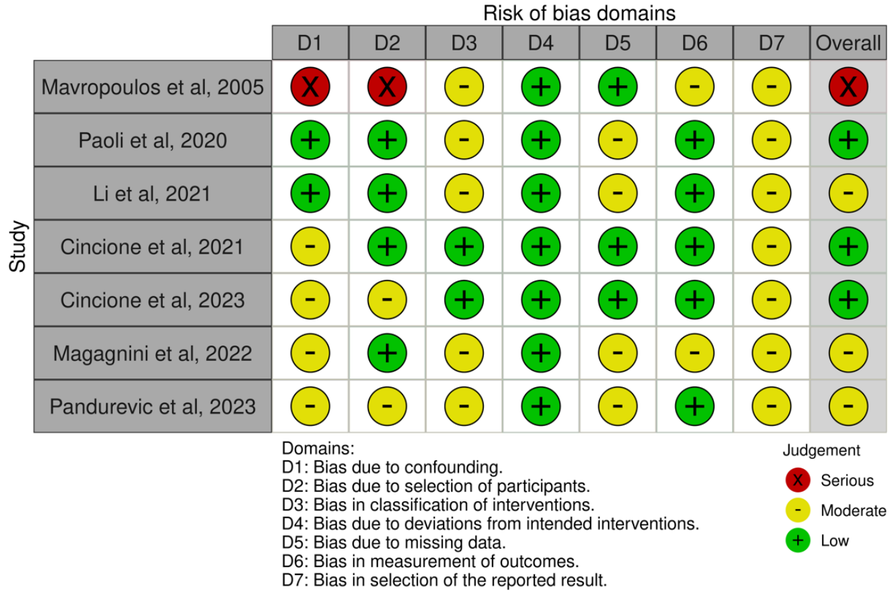
(*) Overall changes did not differ between Experimental and Control group

Pandurevic S et al, Endocr Conect 2023

Gynecol Obstet Invest 2025 Feb 20:1-19. doi: 10.1159/000543941.

Impact of Ketogenic Diet on Weight, Metabolic, and Endocrine Parameters in Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis

Camilla Turetta[1], Andrea Giannini[1], Maria Grazia Tarsitano[2], Daniele Gianfrilli[3], Antonio Paoli[4], Evangelos Kontopantelis[5], Emanuele De Angelis[1], Marianna Minnetti[3], Eleonora Poggiogalle[3], Andrea Colizza[6], Marco De Vincentiis[6], Antonio Simone Laganà[7], Giorgio Bogani[1], Innocenza Palaia[1], Ludovico Muzii[1], Violante Di Donato[1]

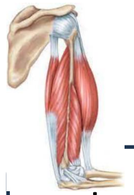


Results: Seven studies were included in the systematic review. The results of the meta-analysis showed that after KD the patients had a significant weight loss (standard mean difference or SMD 1.31 kg [95% CI: 0.45, 2.17] $p = 0.003$) and lower BMI (SMD 1.27 kg/m^2 [95% CI: 0.71, 1.83], $p < 0.001$). Blood glucose (SMD 1.36 mg/dL [95% CI: 1.08, 1.64], $p < 0.001$), insulin (SMD 1.15 µU/mL [95% CI: 0.60, 1.70], $p < 0.001$) and HOMA-IR (SMD 1.84 [95% CI: 0.72, 2.96], $p = 0.001$) were all decreased, and lipid profile was improved with higher HDL (SMD 0.38 mg/dL [95% CI: 1.45, 0.68], $p = 0.48$, not significant), lower LDL (SMD 0.73 mg/dL [95% CI: 0.03, 1.42], $p = 0.04$) and lower triglycerides (SMD 1.11 mg/dL [95% CI: 0.53, 1.68], $p < 0.001$). Moreover, LH concentrations were significantly reduced (SMD 1.12 ng/dL [95% CI: 0.39, 1.84] $p = 0.003$), FSH levels raised (SMD −0.76 ng/dL [95% CI: −1.25, −0.28], $p = 0.002$), the LH/FSH ratio decreased (SMD 2.04 [95% CI: 1.04–3.03], $p < 0.001$); testosterone decreased (free-T SMD 0.57 ng/dL [95% CI: 0.28, 0.86], $p < 0.001$; total-T SMD 0.54 ng/dL [95% CI: 0.28, 0.80] $p < 0.001$), and SHBG levels were significantly increased (SMD 0.79 [95% CI: 1.24–0.34], $p < 0.001$). Data about estrogens, progesterone, DHEAS, and pregnancies were too scarce to allow a comparison in the meta-analysis. ***Conclusion:*** The KD seems to offer a substantial benefit in improving all the anthropometric, metabolic, and hormonal parameters evaluated.

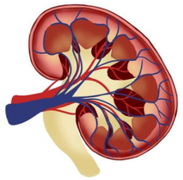
Mechanisms and target tissues for GLP-1R-based therapies

- WAT-lipolysis ↑↑
- WAT-lipogenesis ↓↑
- Fat mass ↓ ↓
- BAT-thermogenesis ↑

- Cardiac protection ↑
- Heart rate ↑



- Insulin sensitivity ↑
- Glucose uptake ↑ ↓



- Albuminuria ↓
- Natriuresis ↓
- Blood pressure ↓

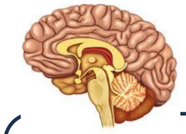
<u>GLP1-RA</u>:
Liraglutide
Semaglutide

<u>GLIP1-GIP-RA</u>:
Tirzepatide

GLP-1

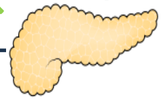
Glucagon

GIP

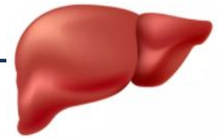


- Satiety ↑↑
- Food intake ↓↓

- Insulin secretion ↑↑↑
- Glucagon secretion ↓↑
- Beta cell survival ↑↑



- Gastric emptying ↓



- Insulin sensitivity ↑
- De novo lipogenesis ↓↓
- Gluconeogenesis ↓↑
- Steatosis ↓

Helvaci & Yildiz 2023

The efficacy and safety of GLP-1 agonists in PCOS women living with obesity in promoting weight loss and hormonal regulation: A meta-analysis of randomized controlled trials

Journal of Diabetes and Its Complications 38 (2024) 108834

Baseline characteristics of included studies

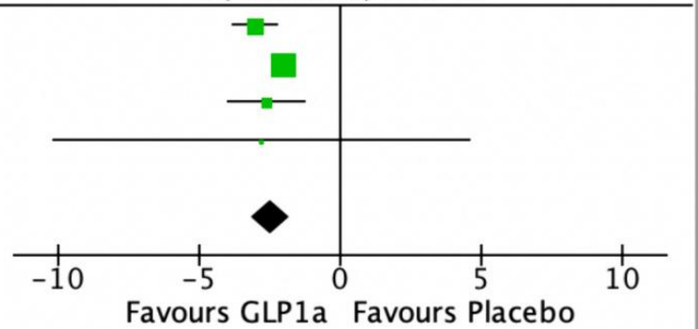
Study	GLP1 agonist	Patients, No
Jensterle 2021	Semaglutide	S: 13 P: 12
Frøssing 2018	Liraglutide	L: 48 P: 24
Elkind-Hirsch 2022	Liraglutide	L: 55 P: 27
Jensterle 2022	Semaglutide	S: 10 P: 10

BMI

	GLP1a			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Elkind-Hirsch 2022	-2.5	1.1	44	0.5	1.749	23	30.9%	-3.00 [-3.79, -2.21]
Frøssing 2018	-1.9	0.3	44	0.1	0.3	21	51.2%	-2.00 [-2.16, -1.84]
Jensterle 2021	-1.9	1.5	13	0.7	1.9	12	17.1%	-2.60 [-3.95, -1.25]
Jensterle 2022	-2.11	7.525	10	0.68	8.743	9	0.8%	-2.79 [-10.16, 4.58]
Total (95% CI)			**111**			**65**	**100.0%**	**-2.42 [-3.10, -1.74]**

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 6.69$, df = 3 (P = 0.08); $I^2 = 55\%$

Test for overall effect: Z = 6.97 (P < 0.00001)

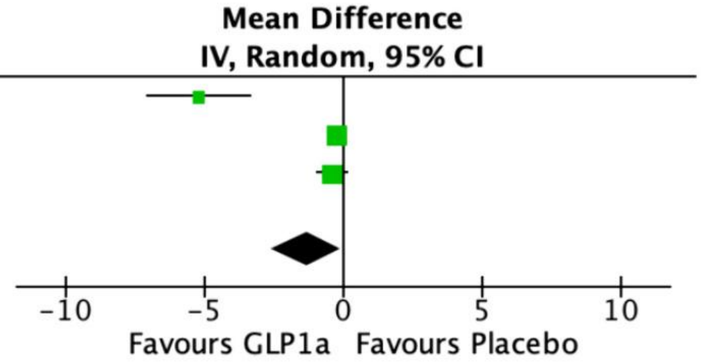


Total testosterone

	GLP1a			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Elkind-Hirsch 2022	-3.6	3.44	44	1.6	3.79	23	21.0%	-5.20 [-7.05, -3.35]
Frøssing 2018	-0.07	0.09	44	0.15	0.12	21	41.1%	-0.22 [-0.28, -0.16]
Jensterle 2022	-0.139	0.604	10	0.263	0.6	9	38.0%	-0.40 [-0.94, 0.14]
Total (95% CI)			**98**			**53**	**100.0%**	**-1.33 [-2.55, -0.12]**

Heterogeneity: $Tau^2 = 0.93$; $Chi^2 = 28.14$, df = 2 (P < 0.00001); $I^2 = 93\%$

Test for overall effect: Z = 2.16 (P = 0.03)



…and greater waist circumference and triglycerides reduction of GLP1-RAs than placebo

OBESITY Reviews WORLD OBESITY

Anti-obesity pharmacological agents for polycystic ovary syndrome: A systematic review and meta-analysis to inform the 2023 international evidence-based guideline

Alyse Goldberg, Sandro Graca, Jing Liu, Vibhuti Rao, Selma Feldman Witchel, Alexia Pena, Rong Li, Aya Mousa, Chau Thien Tay, Loyal Pattuwage, Helena Teede, Bulent O. Yildiz, Carolyn Ee.
***Published**: 14 February **2024** https://doi.org/10.1111/obr.13704*

CONCLUSION

Our findings support the need for further investigations of anti-obesity agents in PCOS. On the basis of our analyses, we cannot provide definitive recommendations at this time due to the small number of trials, short follow-up periods, and overall high or unclear risk of bias in the majority of trials. Given the association of metabolic and reproductive benefits that appear to have a dose response with degree of weight loss, anti-obesity medications including liraglutide, semaglutide, GLP-1 RAs, and orlistat could be considered, in addition to active lifestyle intervention, for the management of higher weight in adult women with PCOS as per general population guidelines. Weight management is an important outcome for those with PCOS, and further studies in this area need to be prioritized. In particular, the need for placebo-controlled trials is urgent. With increasing popularity but limited initial data, more trials to assess the efficacy of these agents are needed, particularly for GLP-1 RAs given their promising benefits and minor AEs. Future research should also examine weight regain in PCOS following cessation of anti-obesity agents and evaluate the impact of anti-obesity agents on quality of life and clinical hyperandrogenism. Longer follow-up periods are also required to demonstrate meaningful clinical benefits. With PCOS currently impacting approximately 10% of reproductive-aged women, this research should be designated as high priority.

Semaglutide and Taste in Women With Obesity and Polycystic Ovary Syndrome: A Randomized Placebo-Controlled Study

Mojca Jensterle , Jernej Kovac , Andrej Vovk , Simona Ferjan , Saba Battelino , Tadej Battelino , Andrej Janez

The Journal of Clinical Endocrinology & Metabolism, https://doi.org/10.1210/clinem/dgaf278 ***Published:*** *09 May* ***2025***

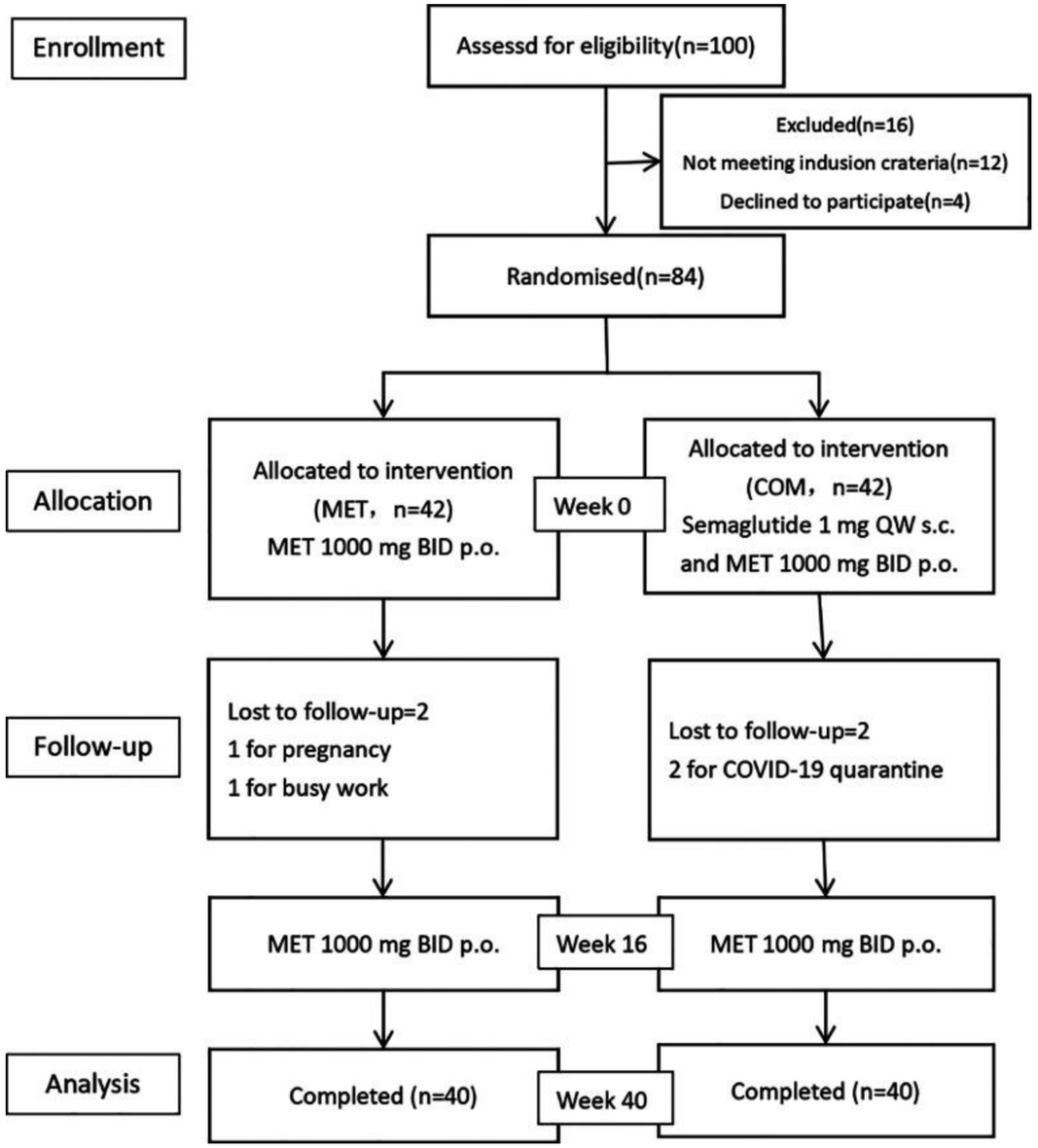
Characteristic	Placebo N = 15	Semaglutide N = 15		
	mean ± SD	mean ± SD	ETD[a]	*P*[b]
BMI (kg/m^2)[c]	0.8 ± 1.9	−2 ± 1.6	−2.8 [−4.1, −1.5]	<.001
Blood pressure:				
Systolic (mm Hg)	0.7 ± 16.9	−4.3 ± 12.7	−5.0 [−16.7, 6.7]	.387
Diastolic (mm Hg)	1.5 ± 8.1	0.2 ± 7.2	−1.3 [−7.2, 4.7]	.658
Heart rate (beats/min)	−2.1 ± 9.7	6.1 ± 11.5	8.1 [−0.1, 16.3]	.053
Waist circ. (cm)	3.2 ± 6.8	−8.2 ± 5.4	−11.5 [−16.1, −6.8]	<.001
DXA total body % fat	0.3 ± 1.7	−0.7 ± 1.9	−1.0 [−2.4, 0.4]	.167
VAT mass (g)	48.5 ± 150.1	−74.9 ± 53.4	−124.0 [−211.4, −36.5]	.007
HbA1c (%)	0.1 ± 0.2	−0.2 ± 0.2	−0.2 [−0.4, −0.1]	.003
Glucose (mmol/L)	0.1 ± 0.4	−0.3 ± 0.6	−0.4 [−0.8, −0.04]	.031
Glucose OGTT				
Glucose 0min OGTT (mmol/L)	0.0 ± 0.4	−0.3 ± 0.4	−0.3 [−0.6, 0.04]	.084
Glucose 120min OGTT (mmol/L)	0.3 ± 1.5	−1.4 ± 1.6	−1.7 [−2.8, −0.6]	.005
HOMA-IR	0.0 ± 2.1	0.2 ± 1.8	0.1 [−1.4, 1.6]	.860
Lipid levels				
Cholesterol (mmol/L)	−0.2 ± 0.8	−0.5 ± 0.5	−0.3 [−0.8, 0.3]	.291
HDL cholesterol (mmol/L)	0.0 ± 0.2	−0.2 ± 0.2	−0.2 [−0.3, −0.03]	.017
LDL cholesterol (mmol/L)	−0.3 ± 0.6	−0.2 ± 0.4	0.1 [−0.3, 0.5]	.727
TG (mmol/L)	0.2 ± 1.0	0.1 ± 0.7	−0.1 [−0.8, 0.5]	.700

Research design and methods: In this 16-week, single-blinded, placebo-controlled study, 30 women with polycystic ovary syndrome (PCOS), aged 33.7 ± 6.1 years with a body mass index of 36.4 ± 4.4 kg/m2 were randomized to semaglutide 1.0 mg QW or placebo. ***Change in taste recognition*** was assessed by 16 strips impregnated with four different concentrations of the four basic tastes. ***Tongue biopsies*** were performed for the ***gene expression analysis***. ***Brain responses to visual cues of sweet and savory foods and to sweet solution*** dripping on the tongue were evaluated by ***functional MRI***.

Results: Semaglutide improved overall taste recognition score from 11.9 ± 1.9 points to 14.4 ± 1.0 points, with an estimated treatment difference of 2.5 points [95% CI, 1.7 to 3.3]. The genes EYA, PRMT8, CRLF1, and CYP1B1, that are associated with taste signaling transduction pathways, neural plasticity, and renewal of taste buds, showed differential RNA expression by a multi-tiered analytical pipeline. Semaglutide decreased activation of putamen in response to visual food cues and increased activity in the angular gyrus of the parietal cortex in response to sweet solution after meal intake (semaglutide vs. placebo, p<0.001).

Conclusions: In women with obesity and PCOS, semaglutide improved an overall taste recognition score, altered RNA expression in the tongue and modified brain activity in response to sweet and savory food cues and to tasting sweet solution.

Chen, H., Lei, X., Yang, Z. *et al.* **Effects of combined metformin and semaglutide therapy on body weight, metabolic parameters, and reproductive outcomes in overweight/obese women with polycystic ovary syndrome: a prospective, randomized, controlled, open-label clinical trial**. *Reprod Biol Endocrinol* **23**, 108 (2025). https://doi.org/10.1186/s12958-025-01447-3



	MET	*COM*	*P*
Weight(kg)	-2.25 ± 4.27	-6.09 ± 3.34	< 0.01
BMI(kg/m^2)	-1.28(-2.37,0.88)	-2.38(-3.40,-1.65)	< 0.01
WHR	-0.02(-0.03,0.02)	-0.04(-0.05,0.00)	< 0.01
TG(mmol/L)	-0.05 ± 0.38	-0.11 ± 0.81	NS
TC(mmol/L)	-0.02 ± 0.21	-0.27(-0.66,-0.09)	< 0.01
HDL-C(mmol/L)	-0.02 ± 0.15	-0.06 ± 0.18	< 0.05
LDL-C(mmol/L)	0.00(-0.12,0.09)	-0.35(-0.63,0.15)	< 0.05
CRP(mg/L)	0.03(-0.47,0.24)	-0.49(-1.29,-0.07)	< 0.05
HbA1c(%)	0.2 ± 0.5	-0.3 ± 0.4	NS
FBG(mmol/L)	-0.18 ± 0.51	-0.41 ± 0.54	NS
FINS(mU/L)	-5.66 ± 6.31	-6.68 ± 11.95	NS
HOMA-IR	-1.40 ± 1.51	-2.05 ± 2.88	NS
SHBG(nmol/L)	11.97 ± 26.49	34.83 ± 33.64	< 0.01
DHEA-S(μg/dL)	-15.93 ± 99.34	-20.75 ± 66.23	NS
E2(pg/mL)	9.06(-11.38,43.41)	9.01(-8.44,40.87)	NS
TEST(ng/dL)	-6.47 ± 14.37	-14.88 ± 16.08	< 0.05
FAI	-2.31(-6.75,0.59)	-6.82(-9.65,-4.97)	< 0.01
LH/FSH	-0.19 ± 1.20	-0.45 ± 1.21	NS
AMH(ng/mL)	-1.40 ± 2.54	-2.39 ± 2.01	NS
Menstrua cycle recovery	17(42.3%)	29(72.5%)	< 0.01

Pregnancy outcome	*MET(n = 40)*	*COM(n = 40)*	*P*
Natural pregnancy	6(15.0%)	14(35.0%)	*P* < 0.05

CASO CLINICO

1 12/2023

2 02/2024

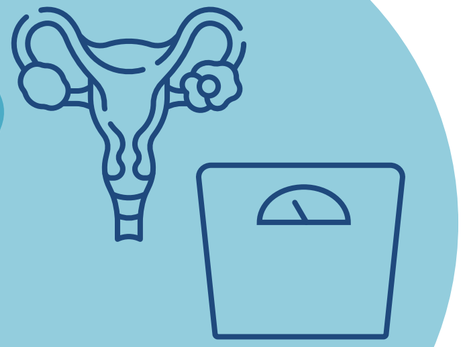
3 06/2024

4 01/2025

C.G.

ANNI 29

DONNA



Giunge in visita per
PCOS, OBESITÀ e INFERTILITA’

1° VISITA ENDOCRINOLOGICA

1 — 12/2023 | 2 — 02/2024 | 3 — 06/2024 | 4 — 01/2025

Giunge in visita per **PCOS, OBESITÀ e INFERTILITA'**

- Familiarità per PCOS (madre), DMT2 ed obesità (padre)
- Non fumatrice
- Menarca a 11.5 aa, ***oligomenorrea***
- In ***terapia E/P*** dai 12 ai 27 anni, sospesa per desiderio di gravidanza. Dalla sospensione ***oligo/amenorrea ed infertilità***
- **Sindrome dell'ovaio policistico**, seguita da ginecologa di fiducia

STORIA PONDERALE

- Inizio di ***aumento ponderale a 10 anni***, seguito da ***graduale incremento*** fino ai 18 anni, quando si è stabilizzato (80kg; BMI 31.2kg/m^2).
- Tentati brevi periodi di LCD con scarsi risultati.
- Non pratica attività fisica strutturata.

ESAMI IN VISIONE (fase follicolare)

- Aumento di testosterone e androstenedione.
- Gonadotropine+ estradiolo regolari.
- Prolattina e TSH nella norma.
- Glicemia venosa a digiuno nella norma.
- Marcata iperinsulinemia basale (HOMA-IR 4.05)

OBIETTIVAMENTE

- ***Irsutismo*** (mFG 10), lieve ***alopecia androgenetica***.
- ***Acanthosis*** nucale e ascellare, assenza di stigmate cushingoidi e lipodistrofiche.
- **BMI: 30.9kg/m²**

TERAPIA DOMICILIARE
Metformina 1000mg/die

ESAMI A COMPLETAMENTO

2° VISITA ENDOCRINOLOGICA

1 12/2023 | 2 02/2024 | 3 06/2024 | 4

Rivalutazione con esami richiesti a completamento

Esami 01/2024	
LH/FSH (U/L)	9.4/7.1
Estradiolo (pg/ml)	39
Testosterone (ng/ml)	**0.93**
Androstenedione (ng/dL)	**428**
DHEAs (ng/dl)	296
17OHP (ng/dl)	72
Glucosio (mg/dl)	94
Insulina (mcUI/ml)	**29.8**
HOMA-IR	**6.91**

Inizia LCD +
attività fisica strutturata

Avvia Metformina RP 750mg
2 cp/die (=1500mg/die)

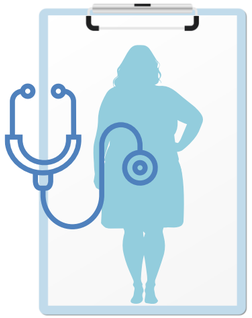
3° VISITA ENDOCRINOLOGICA

1 12/2023 | 2 02/2024 | 3 06/2024 | 4

Esame obiettivo		
Altezza (cm)	160	
Peso (kg)	**79**	(vs 79)
BMI (kg/m^2)	**30.9**	
CV (cm)	**94**	(vs 94)
PA (mmHg)	112/**85**	
FC (bpm)	70	

AVVIA SEMAGLUTIDE:

0.25 mg settimana *(sett. 1-4), poi*
0.5 mg settimana *(sett. 5-8), poi*
1 mg settimana *(sett. 9-12), poi*
1.7 mg settimana *(sett. 13-16), poi*
2.4 mg settimana



- Ben tollerata terapia con metformina RP
- Segue LCD con buona compliance, avviata attività fisica strutturata (palestra 60 min 2 vv/sett.)
- **Amenorrea**
- Avviato minoxidil su indicazione dermatologica per alopecia; persiste irsutismo
- Ecografia pelvica TV: rima endometriale regolare, **PCOm** bilaterale

4° VISITA ENDOCRINOLOGICA

1 12/2023 | 2 02/2024 | 3 06/2024 | 4 01/2025

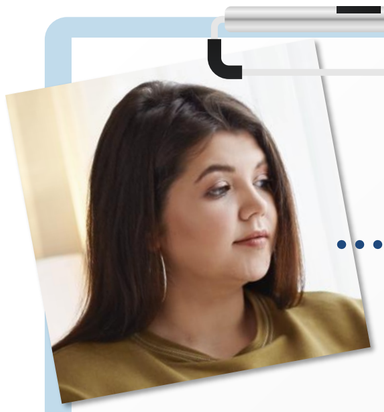
Esame obiettivo		
Altezza (cm)	160	
Peso (kg)	**72 ↓**	(vs 79)
BMI (kg/m^2)	**28.1 ↓**	(vs 30.9)
CV (cm)	**88**	(vs 94)
PA (mmHg)	112/**80**	
FC (bpm)	80	
Glucosio (mg/dl)	73	
Insulina (mcUI/ml)	**10.1 ↓**	(vs 29.8)
HOMA-IR	**1.81 ↓**	(vs 6.91)
Colesterolo tot (mg/dl)	186	
Colesterolo HDL (mg/dl)	53	
Colesterolo LDL (mg/dl)	115.8	

Esame obiettivo		
Trigliceridi (mg/dl)	86	
GOT/GPT (U/L)	17/12	
Testosterone (ng/ml)	**0.62 ↓**	(vs 0.93)
Androstenedione (ng/dL)	**173 ↓**	(vs 428)

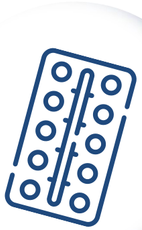
- **Eumenorrea**
- **Remissione HA biochimico**
- Irsutismo stabile

- **Prosegue Semaglutide 2.4 mg sett.**
- **Prosegue Metformina RP 750 mg x2**
- **Prosegue LCD + Attività fisica**

Riassumendo…



- Iperandrogenismo clinico/biochimico
- Irregolarità mestruali
- Infertilità
- Obesità di I grado
- Insulino-resistenza



X Aumento ponderale poi stabilizzato su obesità I grado

X Iperandrogenismo clinico e biochimico dopo la sospensione

X Oligo-amenorrea ed infertilità dopo la sospensione

X Peso stabile

X Persistenza oligo-amenorrea

✓ **Calo ponderale**

✓ **Eumenorrea**

✓ **Risoluzione iperandrogenismo biochimico**

U.O.C Endocrinologia e Prevenzione e Cura del Diabete

(Dir. Prof. Uberto Pagotto)

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Grazie

per l'attenzione!