



24° CONGRESSO NAZIONALE

A.Gi.CO.

Sindrome dell'ovaio policistico
e disturbi metabolici della menopausa:
due facce della stessa medaglia?

19-21
Ottobre
2022

Grand Hotel Excelsior
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Effetti dell'inositolo sulla funzionalità ovarica e sui fattori metabolici nelle donne con PCOS

Concetta Nadia Arico'

U.O.C. Diabetologia ed Endocrinologia

Grande Ospedale Metropolitano Reggio Calabria



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PCOS : APPROCCIO TERAPEUTICO

- **Stile di vita finalizzato alla perdita di peso:** la **perdita del 5% - 10%** del peso corporeo può migliorare l'insulino-resistenza, l'ovulazione e le probabilità di gravidanza anche con un BMI > del normale.
- **Trattamento farmacologico**



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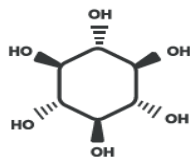
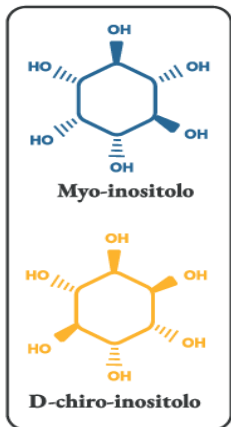
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INSULINOSENSIBILIZZANTI NELLA PCOS

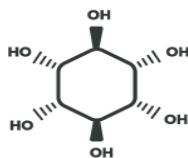
- **La Metformina è stata ed è un punto cardine del trattamento delle PCOS:**
 - **Riduce il siero di androgeni**
 - **Aumenta la frequenza di ovulazione**
 - **Aumenta la fertilità**
 - **Ritarda o previene la progressione al diabete**
 - **Riduce il rischio cardiovascolare**



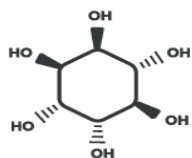
INSULINOSENSIBILIZZANTI: INOSITOLI



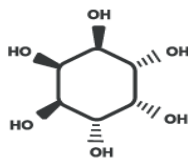
Scyllo-inositol



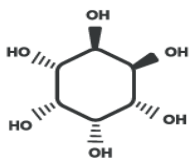
Muco-inositol



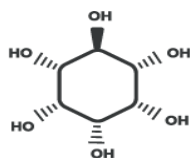
L-Chiro-inositol



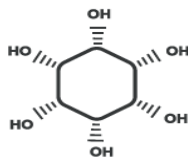
Neo-inositol



Allo-inositol



Epi-inositol



Cis-inositol

DUE MOLECOLE

STRUTTURALMENTE
SIMILI
CON FUNZIONI
FISIOLOGICHE IN PARTE
DIVERSE



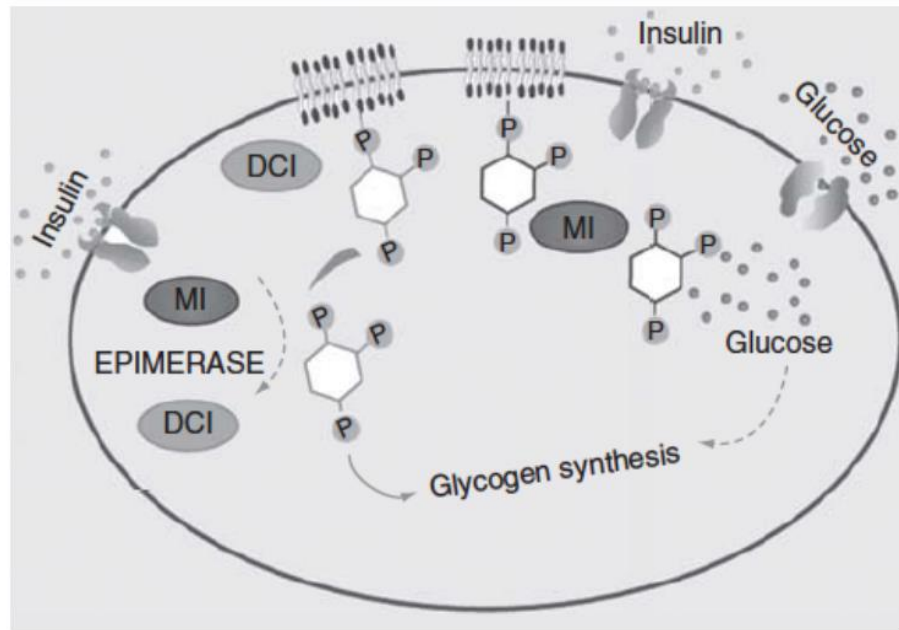
Myo-inositolo e D-chiro-inositolo e insulinosensibilità'

Myo-inositolo

Contribuisce all'**ingresso del glucosio nella cellula** come substrato immediatamente disponibile.

D-chiro-inositolo

Prende parte al **metabolismo ossidativo e non ossidativo cellulare** che porta alla **glicogenosintesi**



Myo-inositolo e D-chiro-inositolo riducono i livelli di insulina circolante



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EVIDENZE CLINICHE INOSITOLI IN PCOS



Myo-inositol effects in women with PCOS: a meta-analysis of randomized controlled trials

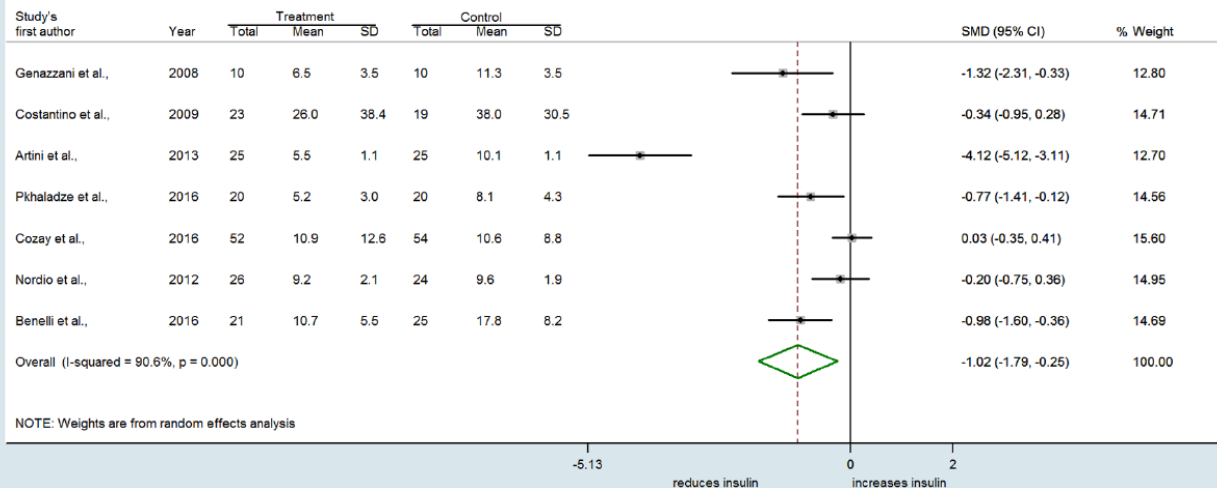
Vittorio Unfer¹, Fabio Facchinetti², Beatrice Orrù³, Barbara Giordani³ and
John Nestler⁴

The daily dose of MI supplementation ranged from 1.1g to 4g,
and the durations of treatment ranged from 12 to 24 weeks

**Il myo-inositolo è in grado di migliorare i parametri
metabolici e riproduttivi delle donne PCOS**



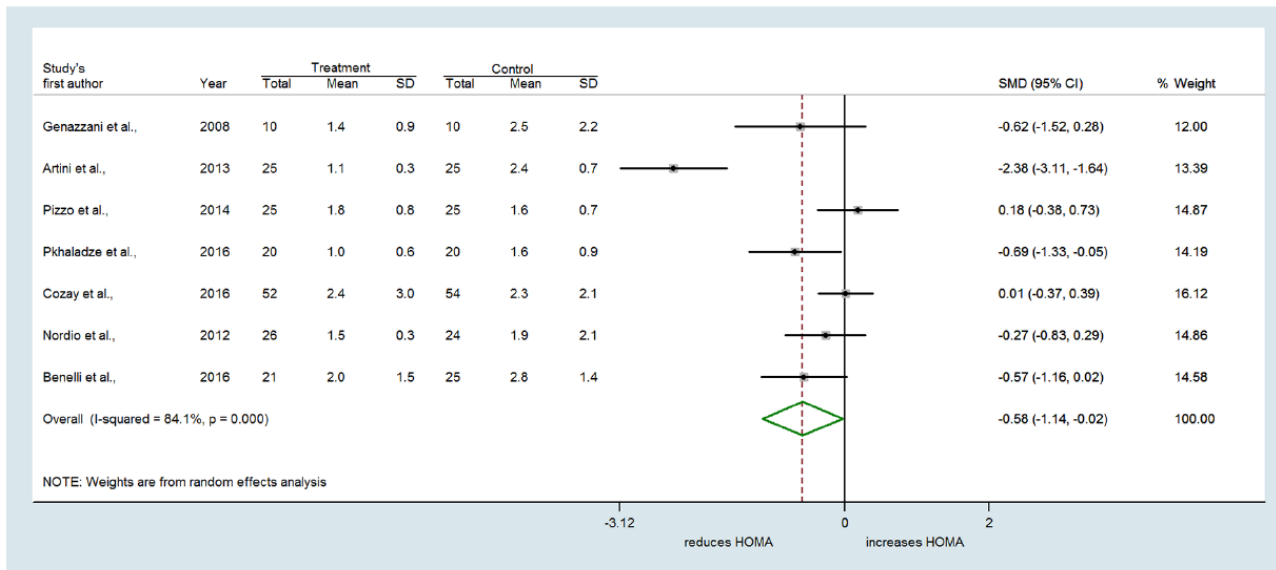
Aspetto metabolico: livelli di insulina a digiuno



**Il myo-inositolo riduce i livelli di insulina nelle
pazienti affette da PCOS**



Aspetto metabolico : HOMA INDEX



The daily dose of MI supplementation ranged from 1.1g to 4g, and the durations of treatment ranged from 12 to 24 weeks

**Il myo-inositolo riduce l'HOMA-index
nelle pazienti affette da PCOS**



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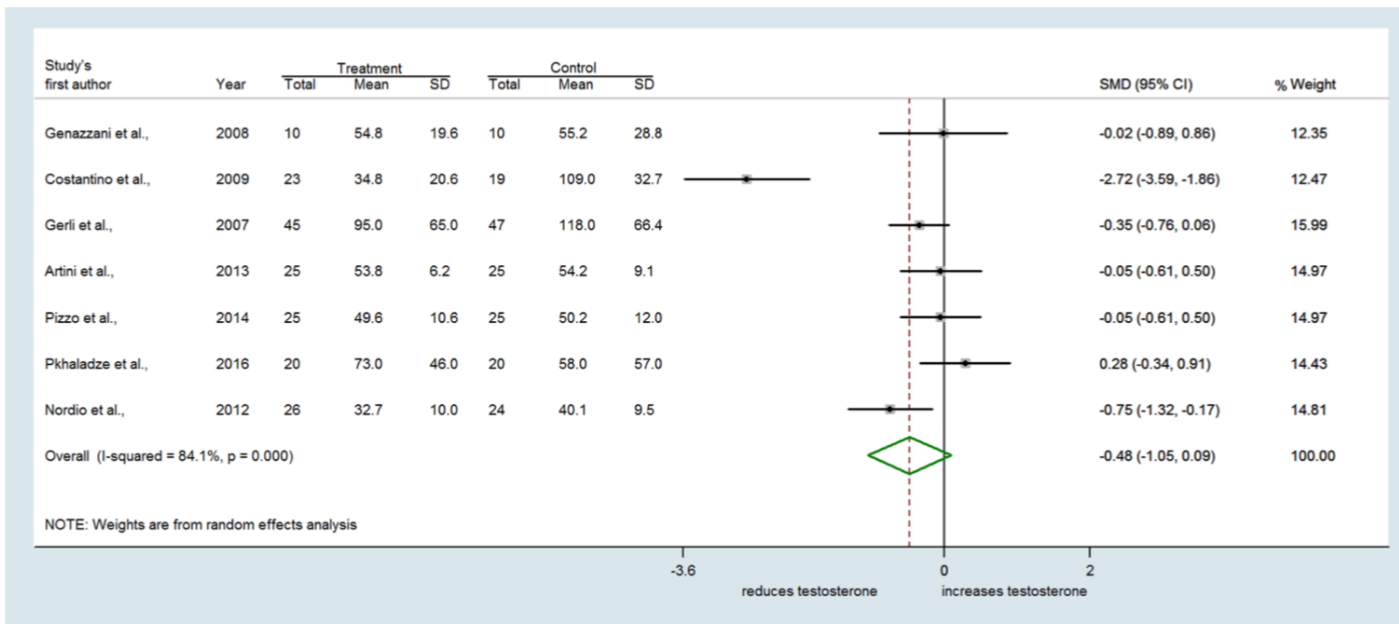
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Aspetto endocrino : livelli di testosterone

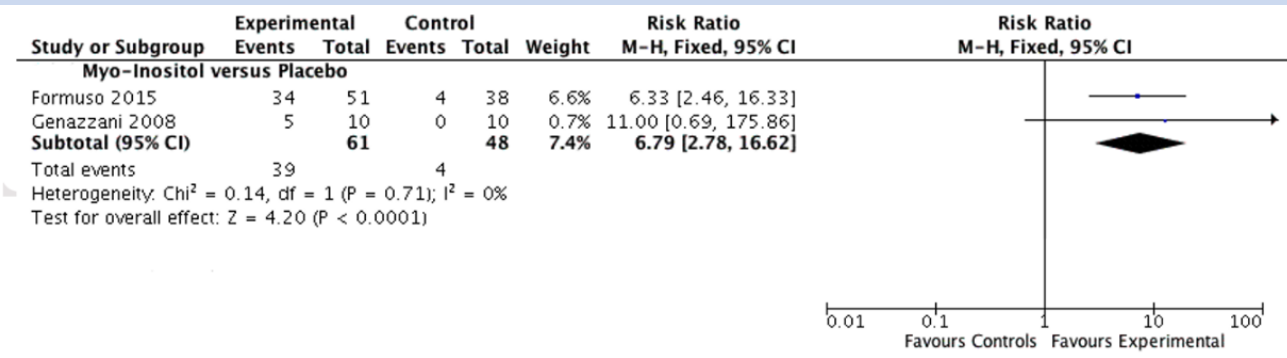


**Il myo-inositolo riduce i livelli di testosterone
nelle pazienti affette da PCOS**



ASPETTO RIPRODUTTIVO

Regolarizzazione dei cicli mestruali



Il myo-inositolo aumenta la frequenza dei cicli mestruali nelle donne PCOS con oligomenorrea o amenorrea



Associazione Ginecologi Consultoriali



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DE GRUYTER

Hormone Molecular Biology and Clinical Investigation. 2018; 20170067

Original Article

Pedro-Antonio Regidor¹ / Adolf Eduard Schindler² / Bernd Lesoine³ / Rene Druckman⁴

Management of women with PCOS using myo-inositol and folic acid. New clinical data and review of the literature

Patients and methods: In an open, prospective, non-blinded, non-comparative observational study, 3602 infertile women used myo-inositol and folic acid between 2 and 3 months in a dosage of 2×2000 mg myo-inositol + 2×200 μ g folic acid per day. In a subgroup of 32 patients, hormonal values for testosterone, free testosterone and progesterone were analyzed before and after 12 weeks of treatment. The mean time of use was 10.2 weeks.

analyses Student's t-test was performed.

Results: Seventy percent of the women had a restored ovulation, and 545 pregnancies were observed. This means a pregnancy rate of 15.1% of all the myo-inositol and folic acid users. In 19 cases a concomitant medication with clomiphene or dexamethasone was used. One twin pregnancy was documented. Testosterone levels changed from 96.6 ng/mL to 43.3 ng/mL and progesterone from 2.1 ng/mL to 12.3 ng/mL in the mean after 12 weeks of treatment ($p < 0.05$) Student's t-test. No relevant side effects were present among the patients. The



Review

Targeting Metabolic Consequences of Insulin Resistance in Polycystic Ovary Syndrome by D-chiro-inositol and Emerging Nutraceuticals: A Focused Review

Author	Intervention	Study Design	Population	Dosage/Duration	Outcomes	Results
Cheang et al. [64]	DCI supplementation	RCT with placebo	11 women (18–40 y) with PCOS	1200 mg twice daily for 6 weeks	Hormones, plasma DCI, DCI-IPG release, insulin sensitivity	Significant relationship between DCI-IPG release and insulin sensitivity
Nestler et al. [65]	DCI supplementation	RCT with placebo	44 obese women (18–40 y) with PCOS	1200 mg/day for 6 to 8 weeks	Hormones, lipid profiles, BP, plasma insulin	Increase of the action of insulin, improvement of ovulatory function and decrease androgens, BP, and TG
Genazzani et al. [66]	DCI supplementation	Intervention trial	22 obese women (age not reported) with PCOS	500 mg/day for 12 weeks	Hormones and plasma insulin	Improvement of hormonal pattern, especially LH and FSH, and restores insulin sensitivity
De Leo et al. [68].	DCI supplementation	Intervention trial	20 women (age not reported) with PCOS	500 mg twice daily for 12 weeks	Oxidative stress on follicular fluids	Reduction of the oxidation of thiol groups



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Clinical Study

A Combined Therapy with Myo-Inositol and D-Chiro-Inositol Improves Endocrine Parameters and Insulin Resistance in PCOS Young Overweight Women

Introduction. We evaluated the effects of a therapy that combines myo-inositol (MI) and D-chiro-inositol (DCI) in young overweight women affected by polycystic ovary syndrome (PCOS), characterized by oligo- or anovulation and hyperandrogenism, correlated to insulin resistance. *Methods.* We enrolled 46 patients affected by PCOS and, randomly, we assigned them to two groups, A and B, treated, respectively, with the association of MI plus DCI, in a 40:1 ratio, or with placebo (folic acid) for six months. Thus, we analyzed pretreatment and posttreatment FSH, LH, 17-beta-Estradiol, Sex Hormone Binding Globulin, androstenedione, free testosterone, dehydroepiandrosterone sulphate, HOMA index, and fasting glucose and insulin. *Results.* We recorded a statistically significant reduction of LH, free testosterone, fasting insulin, and HOMA index only in the group treated with the combined therapy of MI plus DCI; in the same patients, we observed a statistically significant increase of 17-beta-Estradiol levels. *Conclusions.* The combined therapy of MI plus DCI is effective in improving endocrine and metabolic parameters in young obese PCOS affected women.



Clinical Study

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International Journal of Endocrinology Volume 2016

TABLE 2: Baseline and posttreatment endocrine and metabolic parameters of groups A and B of PCOS patients.

	Group A (n = 21)			Group B (n = 25)		
	Baseline	MI plus DCI	p value	Baseline	placebo	p value
FSH (mIU/mL)	5.86 ± 1.75	4.96 ± 1.74	ns	5.67 ± 1.11	5.47 ± 0.63	ns
LH (mIU/mL)	12.5 ± 8	8.5 ± 4.04	p < 0.05	11.27 ± 7.2	11.25 ± 5.35	ns
E (pg/mL)	47.06 ± 18.20	107.42 ± 92.86	p < 0.01	50.37 ± 19.45	52 ± 20.2	ns
Fasting insulin (μU/mL)	20.19 ± 8.14	10.74 ± 5.46	p < 0.001	18 ± 8	17.8 ± 8.2	ns
Fasting glucose (mg/dL)	85 ± 5.96	86 ± 7.12	ns	86.2 ± 9.1	84.73 ± 8.3	ns
Free testosterone (ng/dL)	0.76 ± 0.20	0.62 ± 0.15	p < 0.05	0.85 ± 0.22	0.83 ± 0.2	ns
SHBG (nmol/L)	24.11 ± 10.35	35.85 ± 24.3	p < 0.05	20.44 ± 8.77	21.36 ± 7.57	ns
Androstenedione (ng/mL)	4.25 ± 1.48	4.01 ± 1.70	ns	3.48 ± 1.21	3.12 ± 2.23	ns
DHEAS (μg/dL)	327.32 ± 150.89	347.6 ± 170.98	ns	337.95 ± 155.79	315.83 ± 145.59	ns
HOMA	3.38 ± 1.97	1.97 ± 1.48	p < 0.05	3.48 ± 2.02	2.8 ± 1.4	ns

E, 17-beta-Estradiol; P, progesterone; 17OHP, 17-OH-progesterone; SHBG, Sex Hormone Binding Globulin; DHEAS, dehydroepiandrosterone sulphate.



	Dosage	Effects on Metabolic Abnormalities	Effects on Hyperandrogenism	Effect on Menstrual Cyclicity/Ovulation
MI	1200–4000 mg daily [77,78,81]	<ul style="list-style-type: none"> Improved insulin sensitivity Reduced BMI 	<ul style="list-style-type: none"> Decreased testosterone levels Decreased plasma LH levels and LH/FSH ratio Decreased FG score 	<ul style="list-style-type: none"> Improved menstrual cycle Improved ovulation rate
DCI	1200 mg daily [68]	<ul style="list-style-type: none"> Improved insulin sensitivity Decreased BP Decreased TG concentrations 	<ul style="list-style-type: none"> Decreased serum androgen concentrations 	
MI + DCI 40:1	550 mg + 13.8 mg daily [92–94]	<ul style="list-style-type: none"> Improved insulin sensitivity Decreased BP Decreased TG and TChol concentrations Decreased BMI and fat mass 	<ul style="list-style-type: none"> Decreased serum androgen concentrations Increased SHBG 	<ul style="list-style-type: none"> Improved menstrual cycle Improved ovulation rate
MI + DCI in other ratios	10:1—500 mg + 50 mg [95] 0:1; 1:3.5; 2.5:1; 5:1; 20:1; 80:1 (total daily dose 2000 mg) [112] 2:1 (500 mg + 300 mg) [114] 3:1 (550 mg+150 mg)	<ul style="list-style-type: none"> Decreased blood glucose Decreased insulin levels Decreased BMI 	<ul style="list-style-type: none"> Decreased testosterone levels Decreased FSH, LH levels Increased SHBG concentrations 	<ul style="list-style-type: none"> Higher pregnancy rate positive effect on the “cytoplasm” Higher pregnancy and live birth rates Lower risk of ovarian hyperstimulation syndrome (OHSS)



Review

Inositols in PCOS

Molecules 2020, 25, 5566



INOSITOLI-RESISTENZA

Circa il 30-40% delle donne PCOS non risponde alla terapia con gli inositoli

Studio	Pazienti	Trattamento	EFFETTO
Kamenov et al. <i>Gynecol Endocrinol. 2015</i>	50 pz PCOS con anovulazione e IR	Myo-inositolo (2g due volte die) per 3 mesi	38.3% resistenti
Raffone et al. <i>Gynecol Endocrinol. 2010</i>	60 pz PCOS con irregolarità mestruale	Myo-inositolo (2g due volte die) per 6 mesi	28.3% resistenti
Gerli et al. <i>Eur Rev Med Pharmacol Sci. 2007</i>	45 pz PCOS con oligomenorrea	Myo-inositolo (2g due volte die) per 14 sett.	30% resistenti
Iuorno et al. <i>Endocr Pract. 2002</i>	10 pz PCOS magre	D-chiro-inositolo (600 mg) per 6-8 sett.	40% resistenti



Circa il **30-40%** delle donne PCOS **non risponde** alla terapia con gli inositoli

*È il risultato del **ridotto o mancato assorbimento degli inositoli** dovuto a condizioni non ancora chiare né prevedibili*

Le cause di questa **RESISTENZA** agli inositoli?

- X** **Obesità**
- X** **Malattie croniche intestinali**
- X** **Disbiosi**



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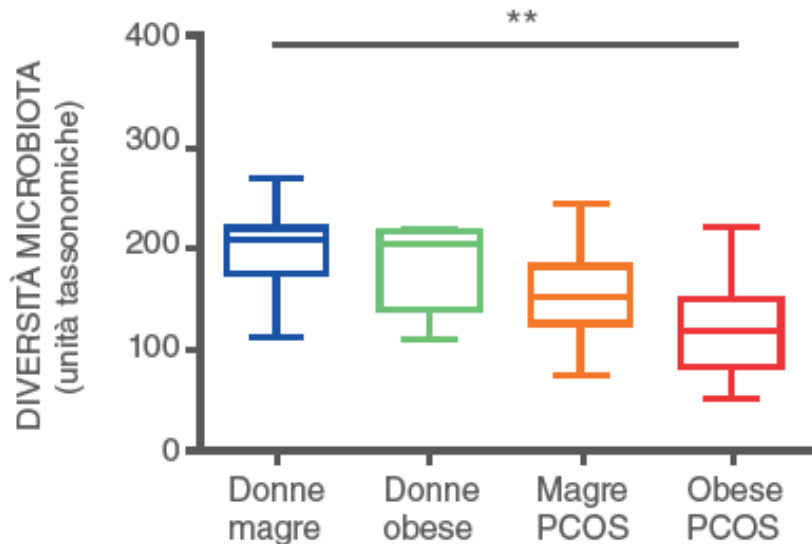
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Check for updates

Dysbiosis of Gut Microbiota Associated with Clinical Parameters in Polycystic Ovary Syndrome

Rui Liu^{1†}, Chenhong Zhang^{1†}, Yu Shi², Feng Zhang¹, Linxia Li³, Xuejiao Wang⁴, Yunxia Ling⁴, Huaqing Fu¹, Weiping Dong⁴, Jian Shen¹, Andrew Reeves⁵, Andrew S. Greenberg⁵, Liping Zhao¹, Yongde Peng^{4*} and Xiaoying Ding^{4*}

frontiers
in Microbiology



IL **MALASSORBIMENTO** È STRETTAMENTE COLLEGATO ALLA PCOS E **PEGGIORA ALL'AUMENTARE DEL BMI**



Review

Polycystic Ovary Syndrome: An Evolutionary Adaptation to Lifestyle and the Environment

Jim Parker ^{1,*}, Claire O'Brien ², Jason Hawrelak ³ and Felice L. Gersh ⁴

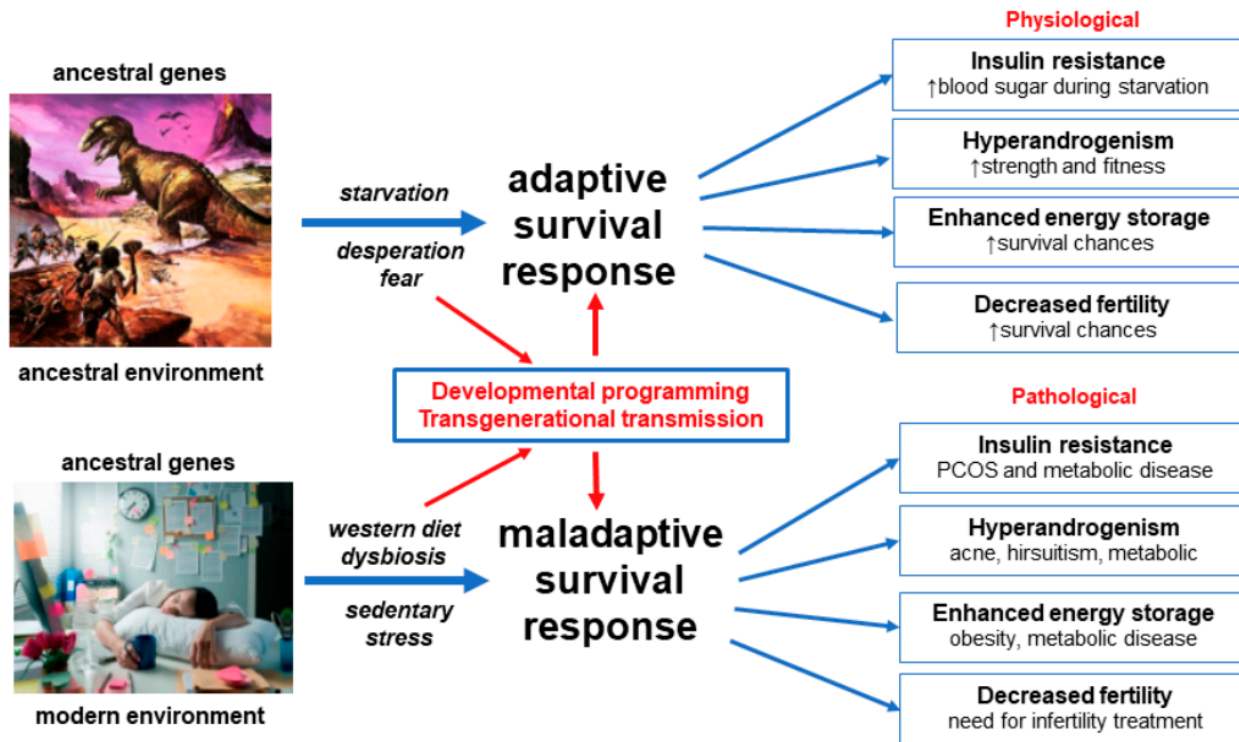


Figure 1. Evolutionary model of the pathogenesis of polycystic ovary syndrome. Adapted with permission from Ref. [12]. 2021 Journal of ACNEM.



Grazie

