



SALUTE E MEDICINA DI GENERE CLINICA

DIFFERENZE DI GENERE NELLE VARIE FASI DELLA VITA



21 ottobre 2025

ore 8.30-14.00

Sala Chiesa "IL FULIGNO"

Firenze, via Faenza 48



Differenze di genere dal periodo pre-concezionale alla gravidanza

Dott.ssa Michela Cirillo, PhD

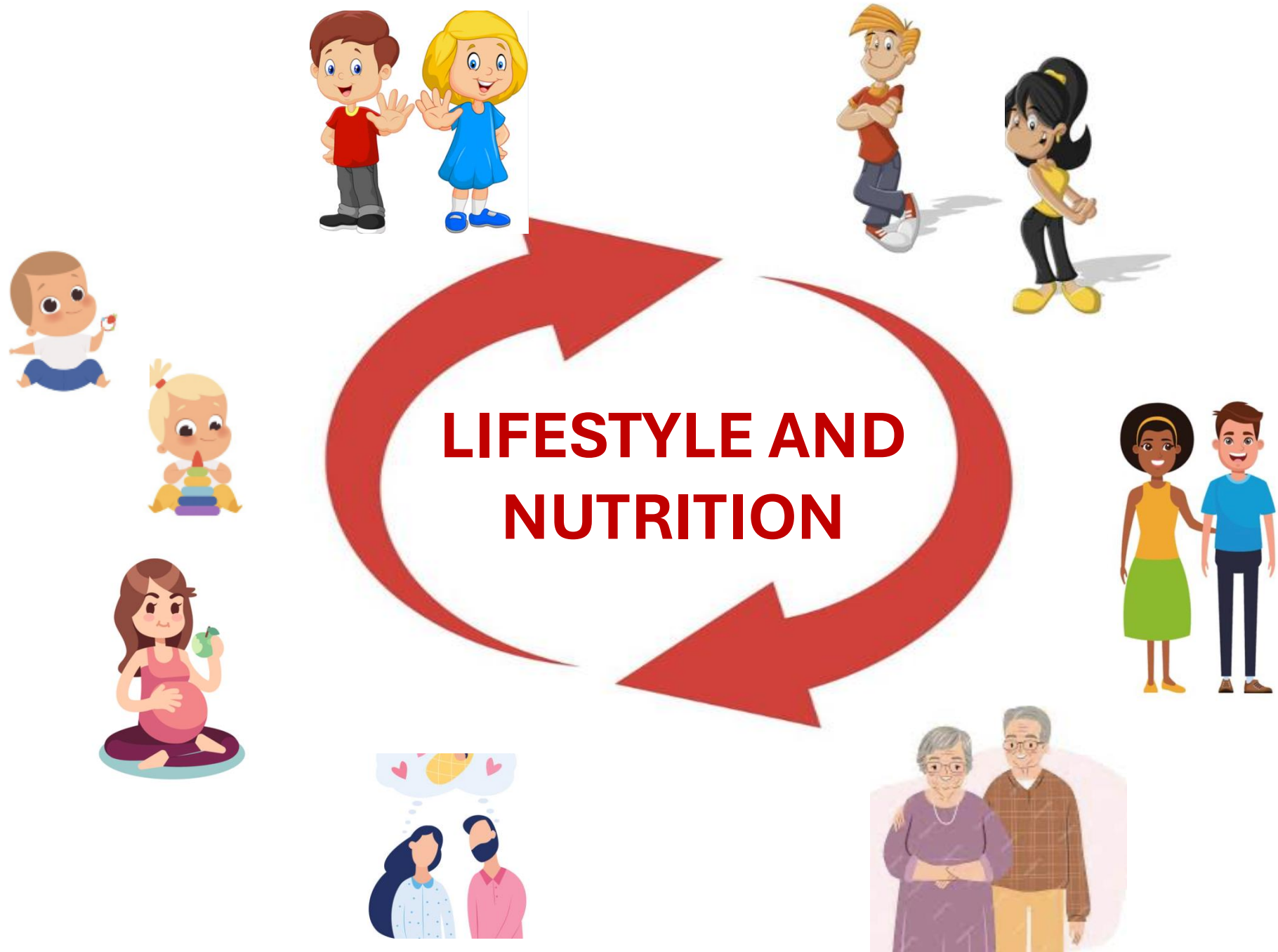
Assegnista di Ricerca presso il Dipartimento di Medicina Sperimentale e Clinica, Università degli Studi di Firenze

SODc Andrologia, Endocrinologia Femminile ed Incongruenza di Genere (Dir. Prof.ssa L. Vignozzi), Azienda Ospedaliero-Universitaria Careggi

Gruppo GISEG Giovani

CISMEG (Centro di ricerca/innovazione e coordinamento aziendale per la Salute e Medicina di genere) Azienda Ospedaliero-Universitaria Careggi

Scuola di Specializzazione in Scienze dell'Alimentazione, Università di Roma Tor Vergata (Dir. Prof.ssa L. Di Renzo)

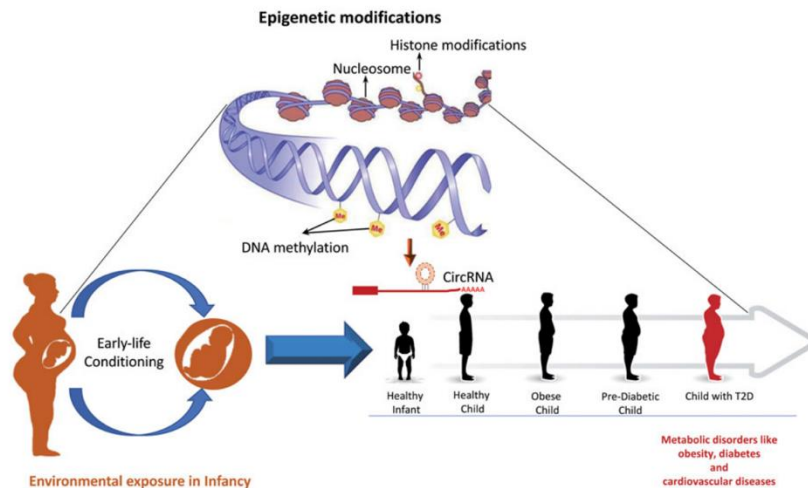


Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health

Defining the preconception period

The preconception period is often defined as the 3 months before conception, possibly because this is the average time to conception for fertile couples. However, a time period before conception can only be identified after a woman has become pregnant.

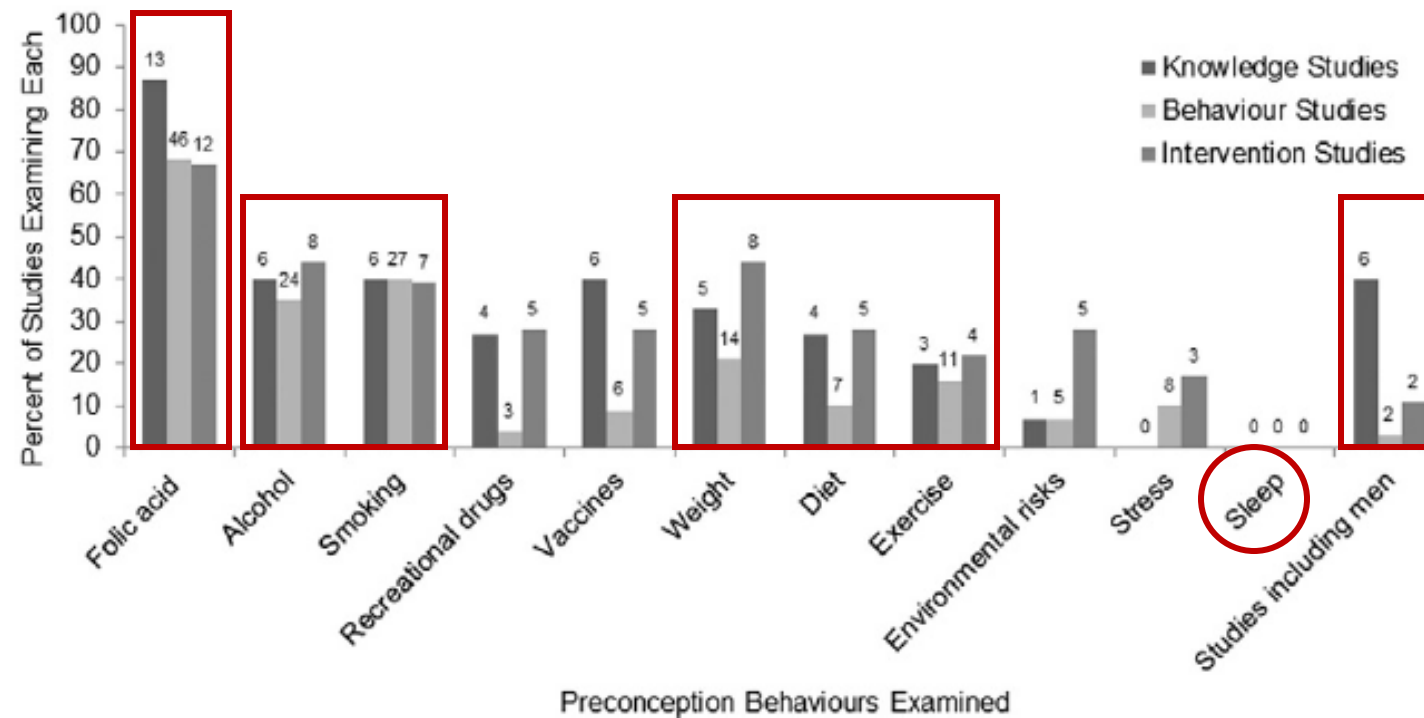
The period around conception is a critical period for optimising gamete function, and early placental development. These preconception risk factors can set patterns that have a cumulative effect on health into adulthood and for future generations, as shown by mounting evidence of the long-term impact of poor maternal nutrition and obesity for the child.



Stephenson et al, Lancet 2018.

Agarwal et al, Crit Rev Clin Lab Sci. 2018.

Preconception health behaviours: A scoping review





Relationships between Women's and Men's Modifiable Preconception Risks and Health Behaviors and Maternal and Offspring Health Outcomes: An Umbrella Review

- **Modifiable preconception health behaviors** in both women and men significantly impact **maternal and offspring health outcomes**.
- **Obesity, smoking, alcohol use, poor diet, and physical inactivity** before conception are linked to increased risks of complications in pregnancy and adverse neonatal outcomes.
- **Paternal health and behaviors**, though less studied, also influence offspring outcomes, highlighting the importance of a **couple-based approach**.
- **Preconception care** should be prioritized in public health strategies and clinical practice to improve lifelong health for both mothers and children.
- There is a need for **more awareness, education, and early interventions** targeting both prospective mothers and fathers.

29 MARZO 2024

INDICATORI DEMOGRAFICI | ANNO 2023

1,20

Il numero medio di figli per donna

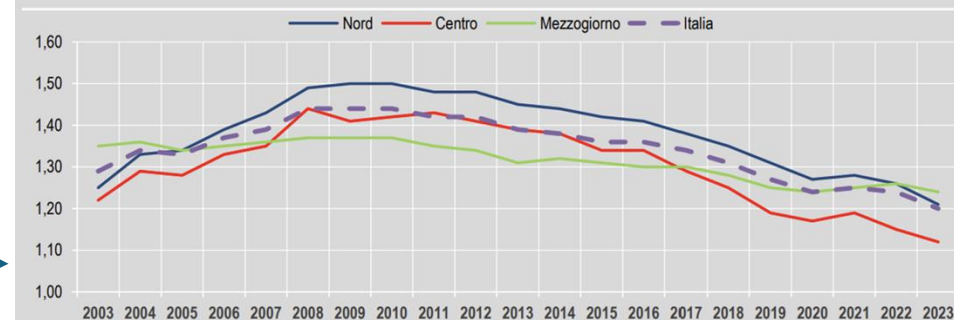
Da 1,24 nel 2022

83,1 anni

La speranza di vita alla nascita (sei mesi di vita in più sul 2022)

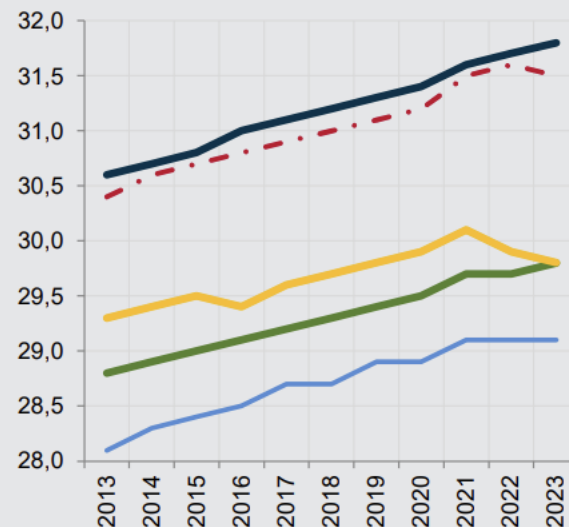
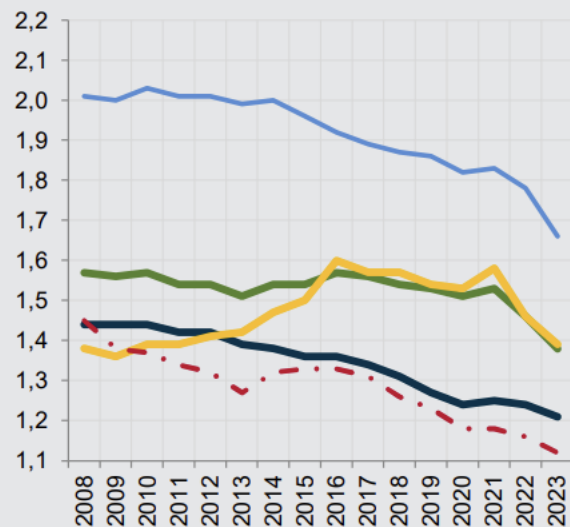


FIGURA 2. NUMERO MEDIO DI FIGLI PER DONNA PER RIPARTIZIONE GEOGRAFICA
Anni 2003-2023.



Fonte: Istat, Rilevazione delle nascite (2003-2022) e Stime anticipatorie degli indicatori demografici e sociali (2023).

UE27 Italia Francia Germania Spagna
Numero medio di figli per donna
Età media al primo figlio

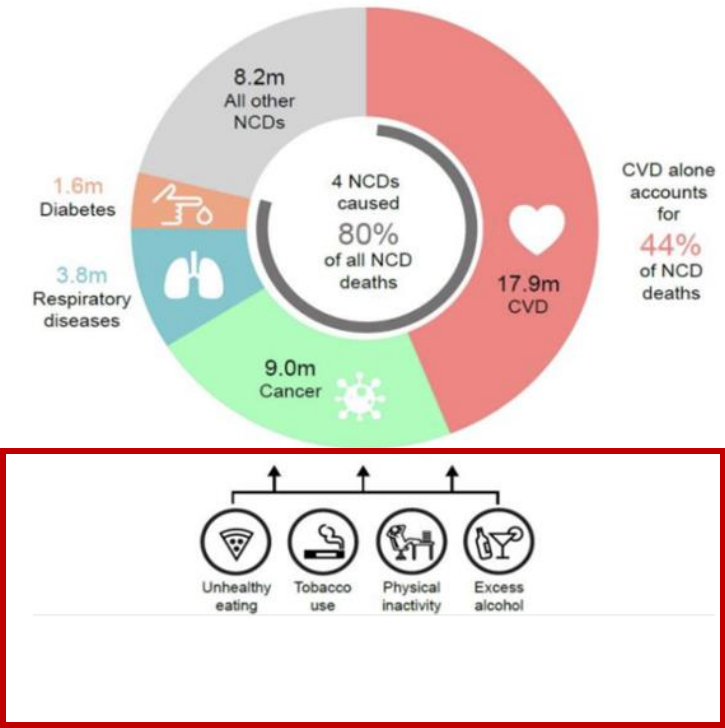


Numero medio di figli per donna (sinistra) ed età media al primo figlio (destra)
nelle maggiori economie dell'UE27. Anni 2008-2023 e 2013-2023 (a) (b)

Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults

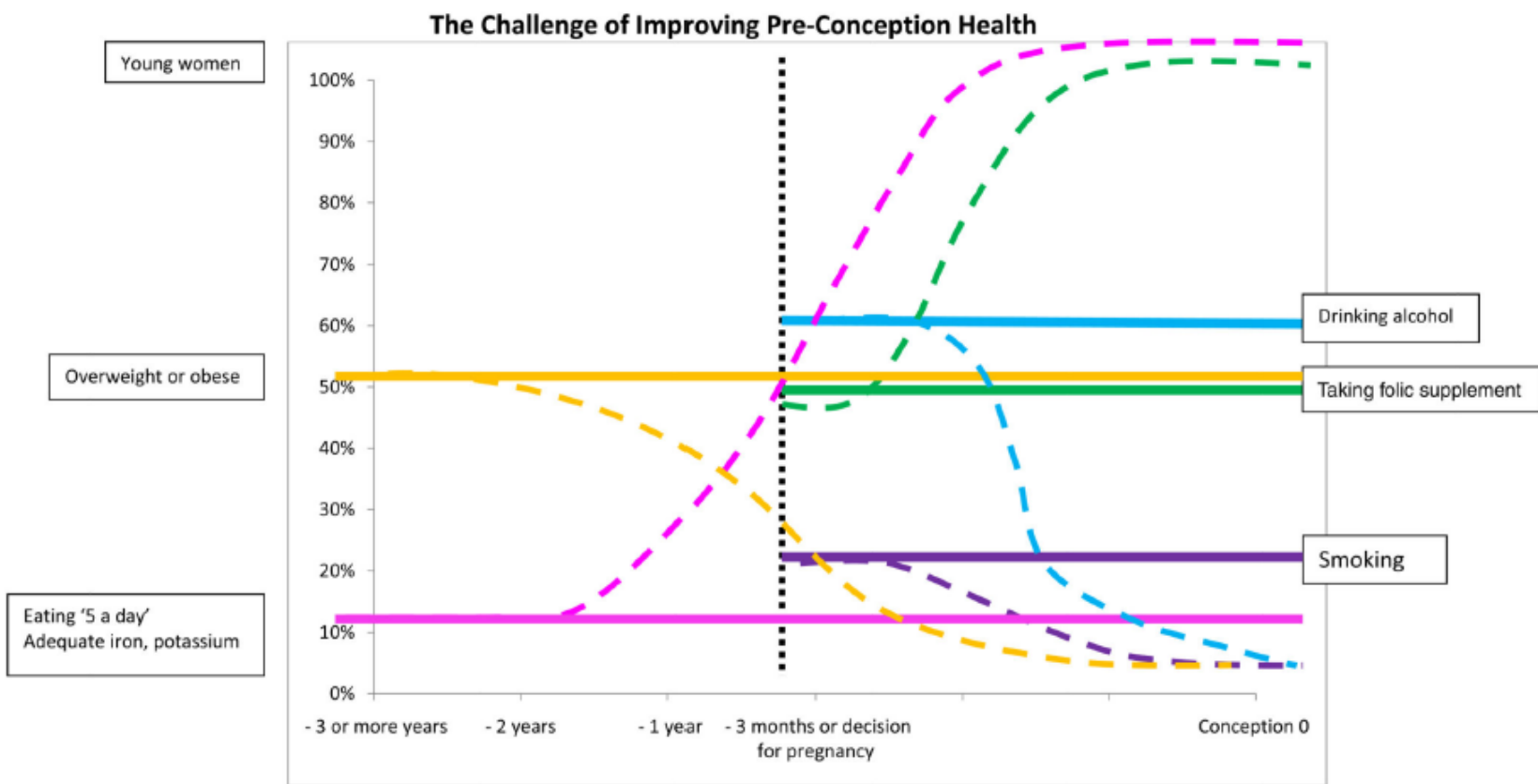
NCD Risk Factor Collaboration (NCD-RisC)*

Nelle persone adulte il tasso di obesità è più che raddoppiato nelle donne e quasi triplicato negli uomini.



Zou KH, et al. *Health Serv Outcomes Res Methodol.* 2021. NCD Risk Factor Collaboration (NCD-RisC). *Lancet.* 2024. WHO 2024.

Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health

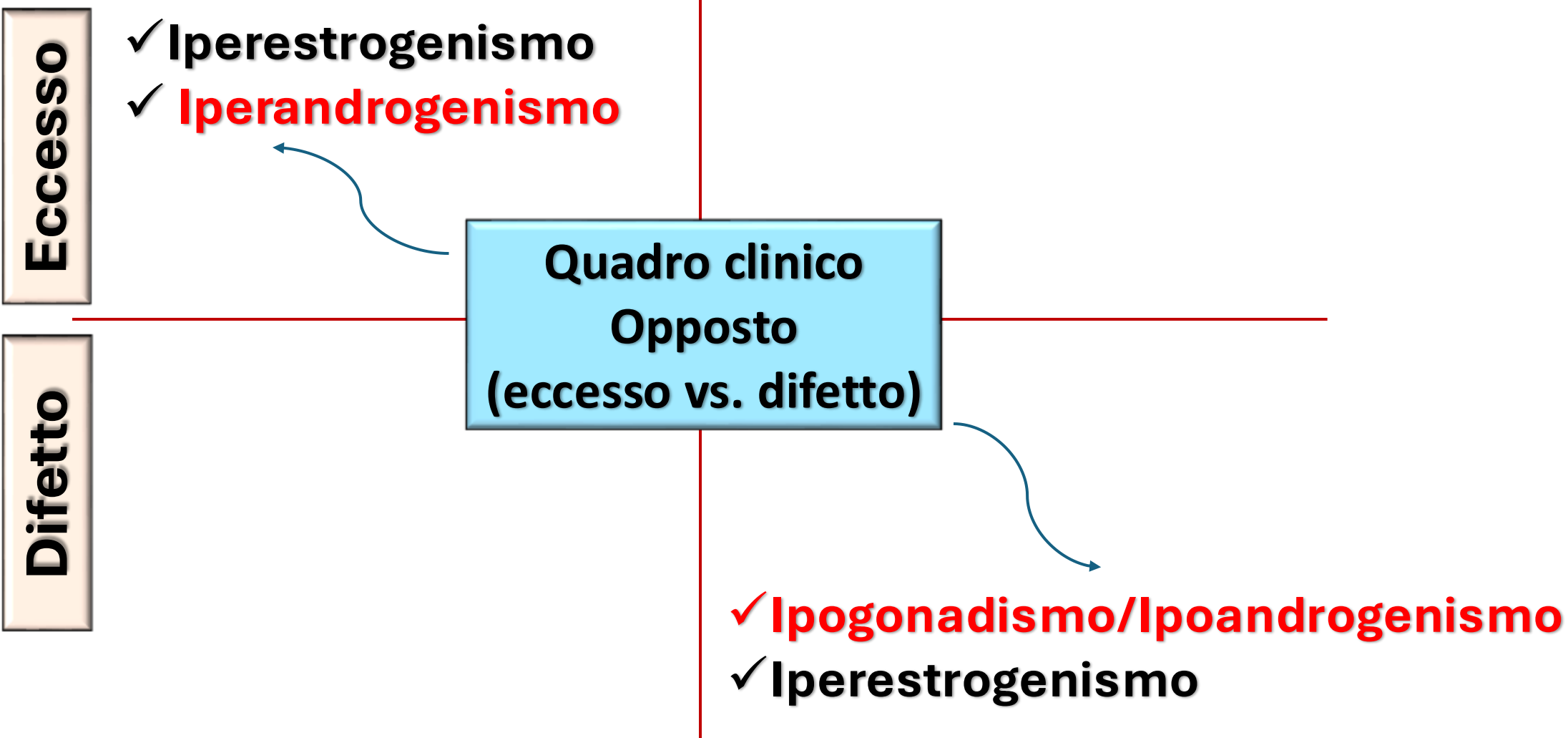


- Eating '5 a day' Adequate iron, potassium
- Overweight or obese
- Drinking alcohol
- Taking folic supplement
- Smoking

Differenze di Genere nel rapporto Obesità e Riproduzione



Differenze di Genere nel rapporto Obesità e Riproduzione

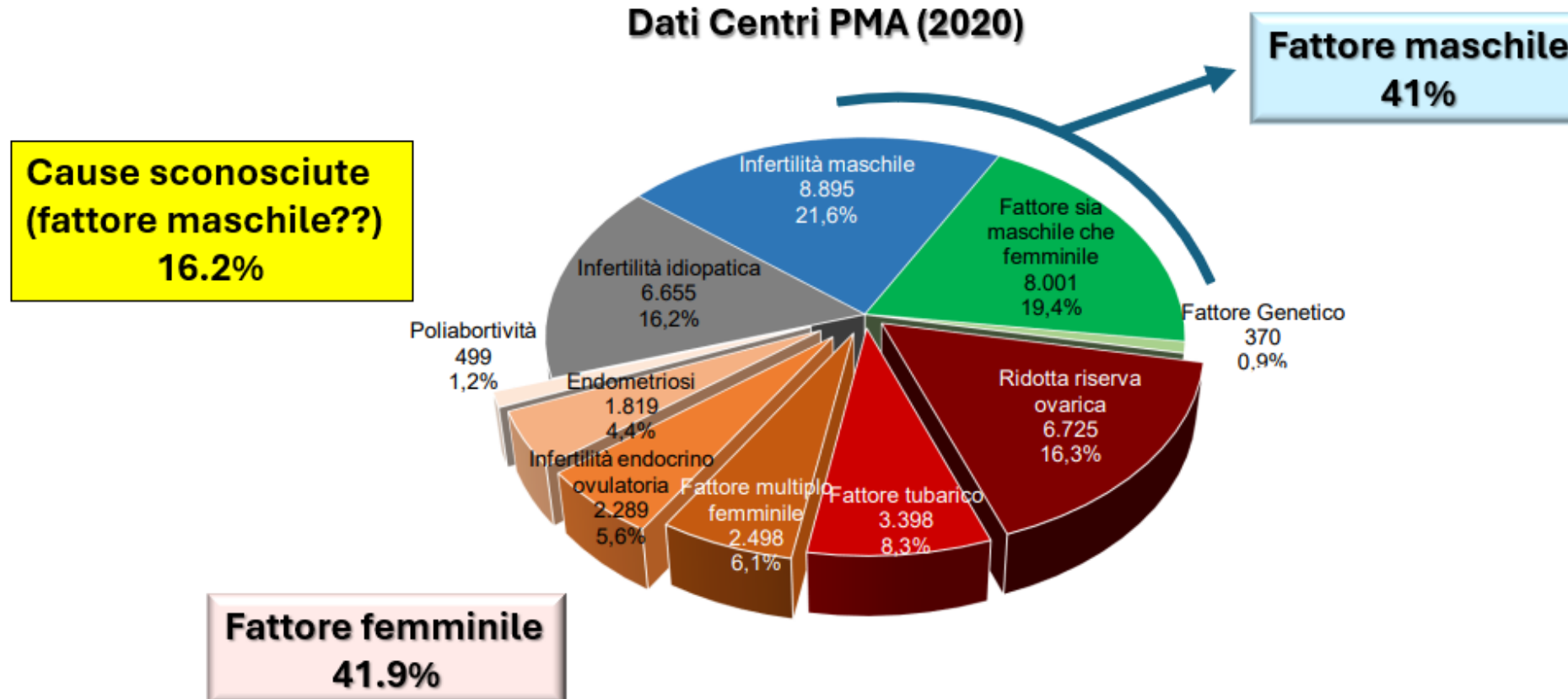




Ministero della Salute

RELAZIONE DEL MINISTRO DELLA SALUTE AL PARLAMENTO SULLO
STATO DI ATTUAZIONE DELLA LEGGE CONTENENTE NORME IN
MATERIA DI PROCREAZIONE MEDICALMENTE ASSISTITA
(LEGGE 19 FEBBRAIO 2004, N. 40, ARTICOLO 15)

Dati Centri PMA (2020)



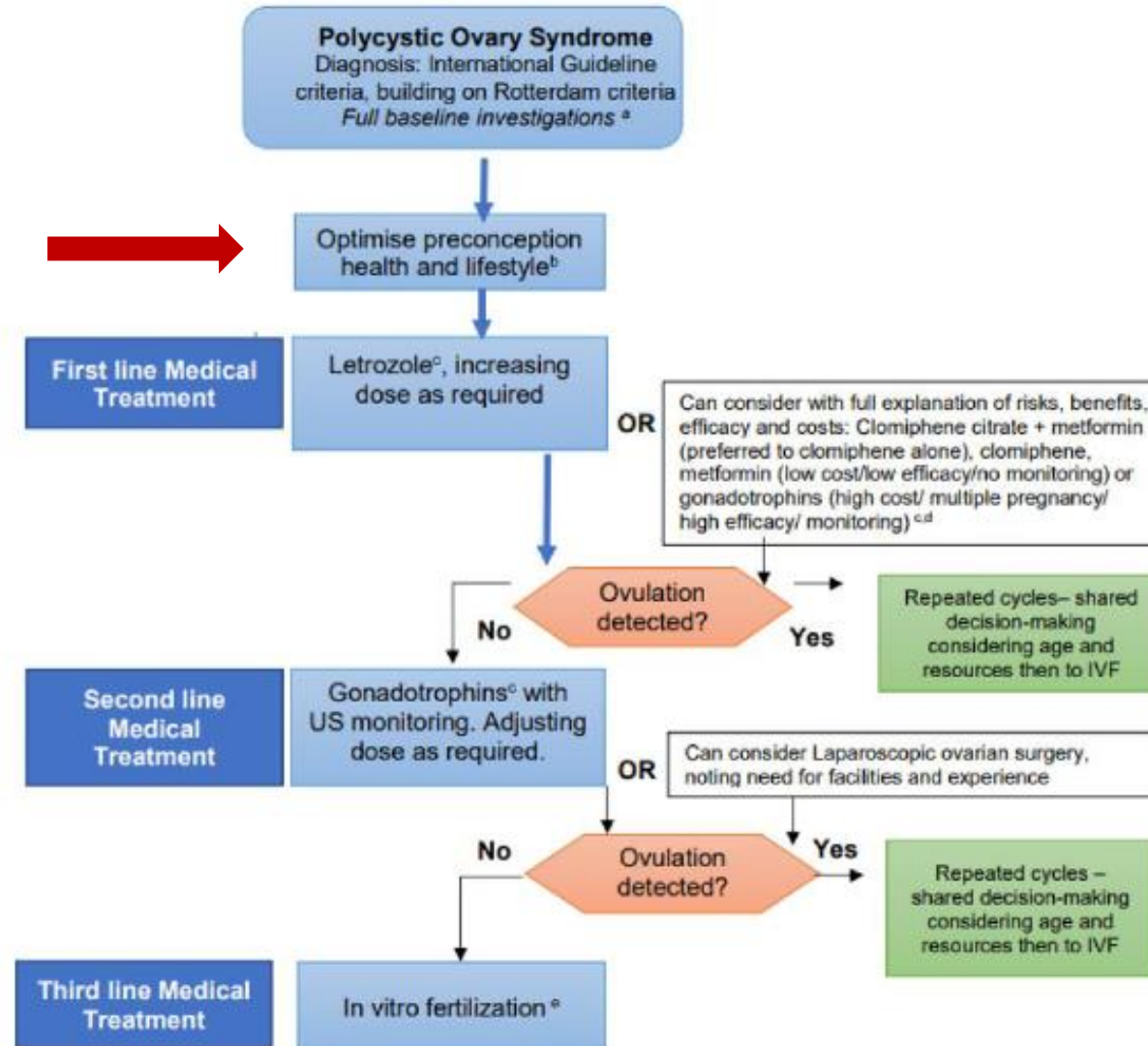
PCOS =

The most common endocrinopathy

Prevalence between 10% to 13%

Algorithm 2: Infertility algorithm for polycystic ovary syndrome (PCOS)

Central Blue Pathway follows best practice evidence and is preferred



J Clin Endocrinol Metab. 2023 Oct; 108(10): 2447–2469.

Published online 2023 Aug 15. doi: [10.1210/clinem/dgad463](https://doi.org/10.1210/clinem/dgad463)

PMCID: PMC10505534

PMID: [37580314](https://pubmed.ncbi.nlm.nih.gov/37580314/)

Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome

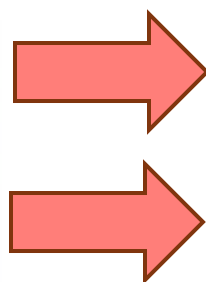
Helena J Teede,²² Chau Thien Tay, Joop J E Laven, Anuja Dokras, Lisa J Moran, Terhi T Piltonen, Michael F Costello, Jacky Boivin, Leanne M Redman, Jacqueline A Boyle, Robert J Norman, Aya Mousa, and Anju E Joham, on behalf of the International PCOS Network

ENDOCRINE
SOCIETY



Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome

Helena J Teede,[✉] Chau Thien Tay, Joop J E Laven, Anuja Dokras, Lisa J Moran, Terhi T Piltonen, Michael F Costello, Jacky Boivin, Leanne M Redman, Jacqueline A Boyle, Robert J Norman, Aya Mousa, and Anju E Joham, on behalf of the International PCOS Network

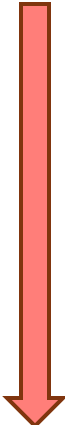


Recommendations

5.1 #		Preconception risk factors	
5.1.1	EBR	Women with PCOS should be counseled on the adverse impact of excess weight on clinical pregnancy, miscarriage and live birth rates, following infertility treatment.	◆◆◆◆ ⊕○○○
5.1.2	CR	Consistent with routine preconception care, in women with PCOS planning pregnancy, weight, blood pressure, smoking, alcohol, diet and nutritional status, folate supplementation (higher dose in those with BMI > 30), exercise, sleep and mental, emotional and sexual health should be considered and optimised to improve reproductive and pregnancy outcomes and overall health.	◆◆◆◆
5.1.3	PP	A reproductive life plan and age appropriate education on optimising reproductive health, is recommended in adolescents and women with PCOS, including healthy lifestyle, prevention of excess weight gain, and optimising preconception risk factors.	
5.1.4	PP	Healthcare professionals are encouraged to seek permission and if given, to assess weight and body mass index and initiate a dialogue on the importance of weight and lifestyle on women's health before pregnancy. This requires caution to avoid weight stigma and needs to consider the cultural, social and environmental determinants of health (see 3.6).	
5.1.5	PP	Chronic conditions such as diabetes, high blood pressure, anxiety, depression and other mental health conditions, should be optimally managed and women should be counseled regarding the risk of adverse pregnancy outcomes.	

The combined impact of maternal age and body mass index on cumulative live birth following in vitro fertilization

Cumulative likelihood of live birth (%) based on maternal age and BMI among 51,959 first fresh IVF cycles started in 2014 + 16,067 frozen embryo cycles between 2014 and 2015, representing data from >90% of IVF cycles in the United States and Puerto Rico

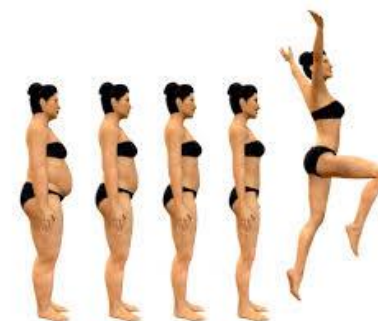
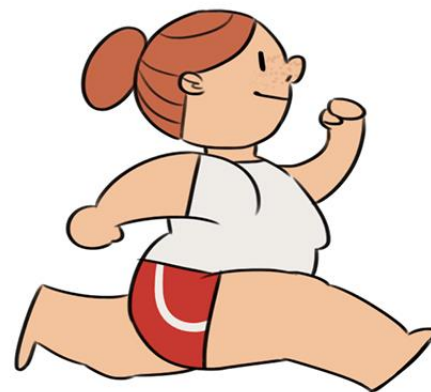



	BMI, kg/m ²							
Age, y	<18.5 Underweight	18.5–24.9 Normal weight	25.0–29.9 Overweight	30.0–34.9 Class I obesity	35.0–39.9 Class II obesity	40.0–44.9 Class III obesity	45.0–49.9 Morbid obesity	≥50 Super obesity
<30	129/199 (65%)	2299/3606 (64%)	980/1654 (59%)	491/823 (60%)	208/419 (50%)	61/128 (48%)	17/42 (40%)	3/12 (25%)
30	50/83 (60%)	979/1550 (63%)	355/619 (57%)	156/265 (59%)	91/168 (54%)	25/52 (48%)	5/25 (20%)	2/10 (20%)
31	63/104 (61%)	1040/1761 (59%)	436/766 (57%)	179/329 (54%)	78/163 (48%)	26/65 (40%)	6/20 (30%)	0/1 (0%)
32	61/100 (61%)	1122/1945 (58%)	477/872 (55%)	197/369 (53%)	77/179 (43%)	26/59 (44%)	8/23 (35%)	2/9 (22%)
33	55/122 (45%)	1144/2053 (56%)	472/914 (52%)	243/453 (54%)	89/203 (44%)	28/75 (37%)	9/21 (43%)	1/6 (17%)
34	48/109 (44%)	1126/2192 (51%)	470/983 (48%)	188/443 (42%)	101/229 (44%)	32/80 (40%)	9/21 (43%)	1/8 (13%)
35	60/127 (47%)	1056/2100 (50%)	414/931 (44%)	207/450 (46%)	102/241 (42%)	32/73 (44%)	9/24 (38%)	2/12 (17%)
36	34/83 (41%)	819/1927 (43%)	379/936 (40%)	197/472 (42%)	89/207 (43%)	32/82 (39%)	12/36 (33%)	2/7 (29%)
37	34/87 (39%)	669/1724 (39%)	333/875 (38%)	133/377 (35%)	73/192 (38%)	18/74 (24%)	11/33 (33%)	3/10 (30%)
38	21/69 (30%)	542/1711 (32%)	281/863 (33%)	118/393 (30%)	52/212 (25%)	11/56 (20%)	5/20 (25%)	3/14 (21%)
39	14/74 (19%)	389/1546 (25%)	216/814 (27%)	115/423 (27%)	61/215 (28%)	18/80 (23%)	2/19 (11%)	1/8 (13%)
40	11/59 (19%)	280/1387 (20%)	128/682 (19%)	73/349 (21%)	27/156 (17%)	7/57 (12%)	5/16 (31%)	0/6 (0%)
41	6/71 (8%)	167/1238 (13%)	94/613 (15%)	33/267 (12%)	24/125 (19%)	6/44 (14%)	1/15 (7%)	0/4 (0%)
42	1/33 (3%)	108/1020 (11%)	46/527 (9%)	29/266 (11%)	10/117 (9%)	5/45 (11%)	2/14 (14%)	0/3 (0%)
>42	0/59 (0%)	43/1544 (3%)	32/726 (4%)	17/351 (5%)	3/158 (2%)	3/57 (5%)	0/17 (0%)	0/4 (0%)

- Obesity decreased *responsiveness to fertility medications* and women with obesity had *fewer oocytes retrieved* and fewer zygotes than women with normal weight during IVF.
- The *implantation rate*, *clinical pregnancy rate*, and *LBR* decreased with increasing BMI.
- At older ages, age has a greater impact on the LBR than BMI.

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Helena J Teede,[§] Chau Thien Tay, Joop J E Laven, Anuja Dokras, Lisa J Moran, Terhi T Piltonen, Michael F Costello, Jacky Boivin, Leanne M Redman, Jacqueline A Boyle, Robert J Norman, Aya Mousa, and Anju E Joham, on behalf of the International PCOS Network



3.1.10

PP

Insulin resistance is a pathophysiological factor in PCOS, however, clinically available insulin assays are of limited clinical relevance and should not be used in routine care (refer to 1.9.12).

Treat the core of the disease!

Therapeutic strategies: lifestyle

- Lifestyle intervention should be recommended in all those with PCOS and excess weight, for reductions in weight, central obesity and insulin resistance.
- If the goal is to achieve weight loss, a tailored energy deficit could be prescribed for women, considering individual energy requirements, body weight and physical activity levels.
- A variety of balanced dietary approaches could be recommended [...] as per general population recommendations.
- To achieve weight loss in those with excess weight, an **energy deficit of 30% or 500-750 kcal/day (1,200 to 1,500 kcal/day)** could be prescribed for women.
- Advise for modest weight-loss and prevention of weight-regain, a minimum of **250 min/week of moderate intensity activities or 150 min/week of vigorous intensity** or an equivalent combination [...]

**What are the most effective
dietary interventions for
women with PCOS?**

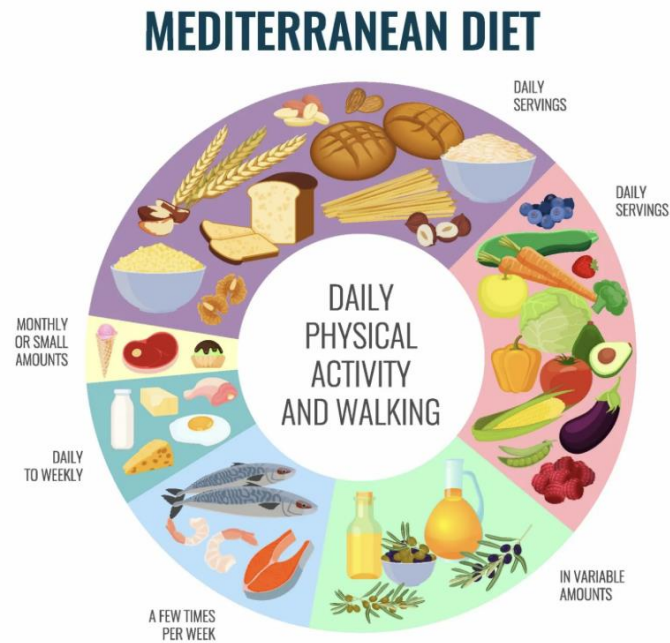


Mediterranean Diet and PCOS

Recognised as a health-promoting dietary pattern due to its peculiar features:

- regular consumption of unsaturated fats,
- low glycaemic index carbohydrates,
- fiber, vitamins and antioxidants,
- moderate amount of animal-derived proteins

Reported to have a well-established anti-inflammatory activity, mainly due to the microbiota-derived production of short chain fatty acids and the high intake of both polyunsaturated fatty acids omega 3 and antioxidants contained in fruits, vegetables, extra-virgin olive oil.



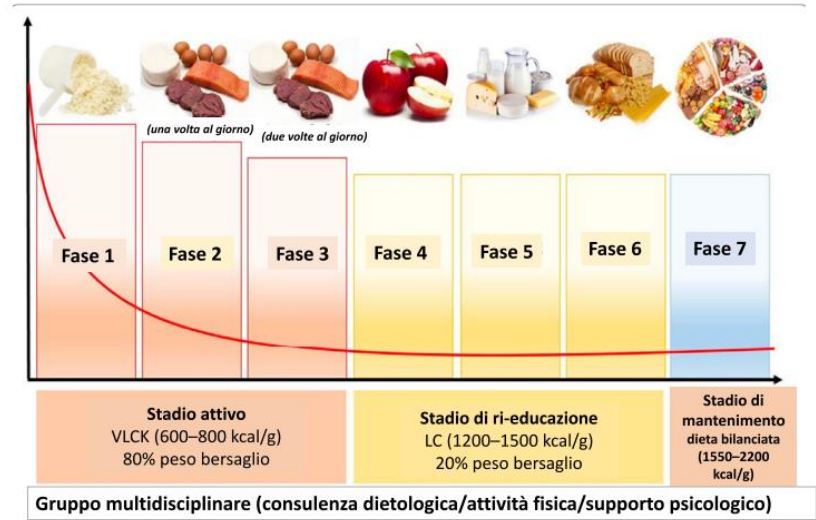
It is still debated what is the best effective nutritional pattern that should be followed to lose weight in PCOS.

CONSENSUS STATEMENT



Ketogenic nutritional therapy (KeNuT)—a multi-step dietary model with meal replacements for the management of obesity and its related metabolic disorders: a consensus statement from the working group of the Club of the Italian Society of Endocrinology (SIE)—diet therapies in endocrinology and metabolism

L. Barrea¹ · M. Caprio^{2,3} · E. Camajani^{2,3} · L. Verde⁴ · S. Perrini⁵ · A. Cignarelli⁵ · F. Prodam^{6,7} · A. Gambineri^{8,9} · A. M. Isidori¹⁰ · A. Colao^{11,12,13} · F. Giorgino⁵ · G. Aimaretti⁶ · G. Muscogiuri^{11,12,13}



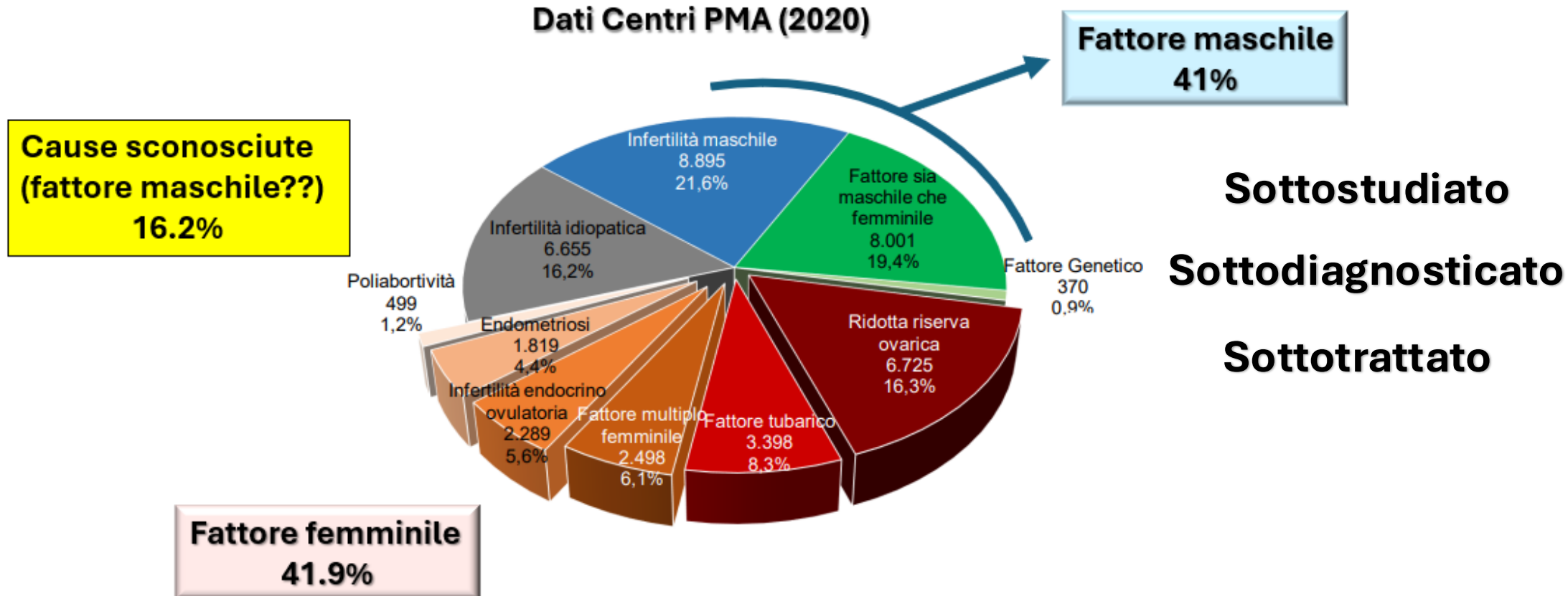
Strong recommendations	Strength of recommendations and quality of evidence according to GRADE system
Severe obesity	(1 ØØØØ)
Management of severe obesity before bariatric surgery	(1 ØØØØ)
Sarcopenic obesity	(1 ØØØØ)
Obesity associated with type 2 diabetes (preserved beta cell function)	(1 ØØØØ)
Obesity associated with hypertriglyceridemia	(1 ØØØØ)
Obesity associated with hypertension	(1 ØØØØ)
Pediatric obesity associated with epilepsy and/or with a high level of insulin resistance and/or comorbidities, not responsive to standardized diet	(1 ØØØØ)
Weak recommendations	
Obesity associated with dysbiosis of the gut microbiota	(2 ØØØØ)
Obesity associated with high levels of LDL-cholesterol and/or low levels of HDL-cholesterol	(2 ØØØØ)
Obesity associated with non-alcoholic fatty liver disease (NAFLD)	(2 ØØØØ)
Obesity associated with heart failure (NYHA I–II)	(2 ØØØØ)
Obesity associated with atherosclerosis	(2 ØØØØ)
Male obesity secondary hypogonadism	(2 ØØØØ)
Obesity associated with polycystic ovary syndrome (PCOS)	(2 ØØØØ)
Menopausal transition-related obesity	(2 ØØØØ)
Neurodegenerative disorders associated with sarcopenic obesity	(2 ØØØØ)



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Dati Centri PMA (2020)



Infertilità di coppia e fattore maschile: eziologia

➤ PATOLOGIE SISTEMICHE (METABOLICHE!)

- Alterazioni generali della salute possono influenzare sia la funzione sessuale che la fertilità maschile:
 - meccanismo della “regressione ontogenetica” (disfunzione ipofisaria), con deficit di testosterone
 - specifici meccanismi correlati alla singola patologia sistemica
- Farmaci utilizzati per la terapia di patologie sistemiche che possono alterare sia la funzione sessuale che la fertilità maschile

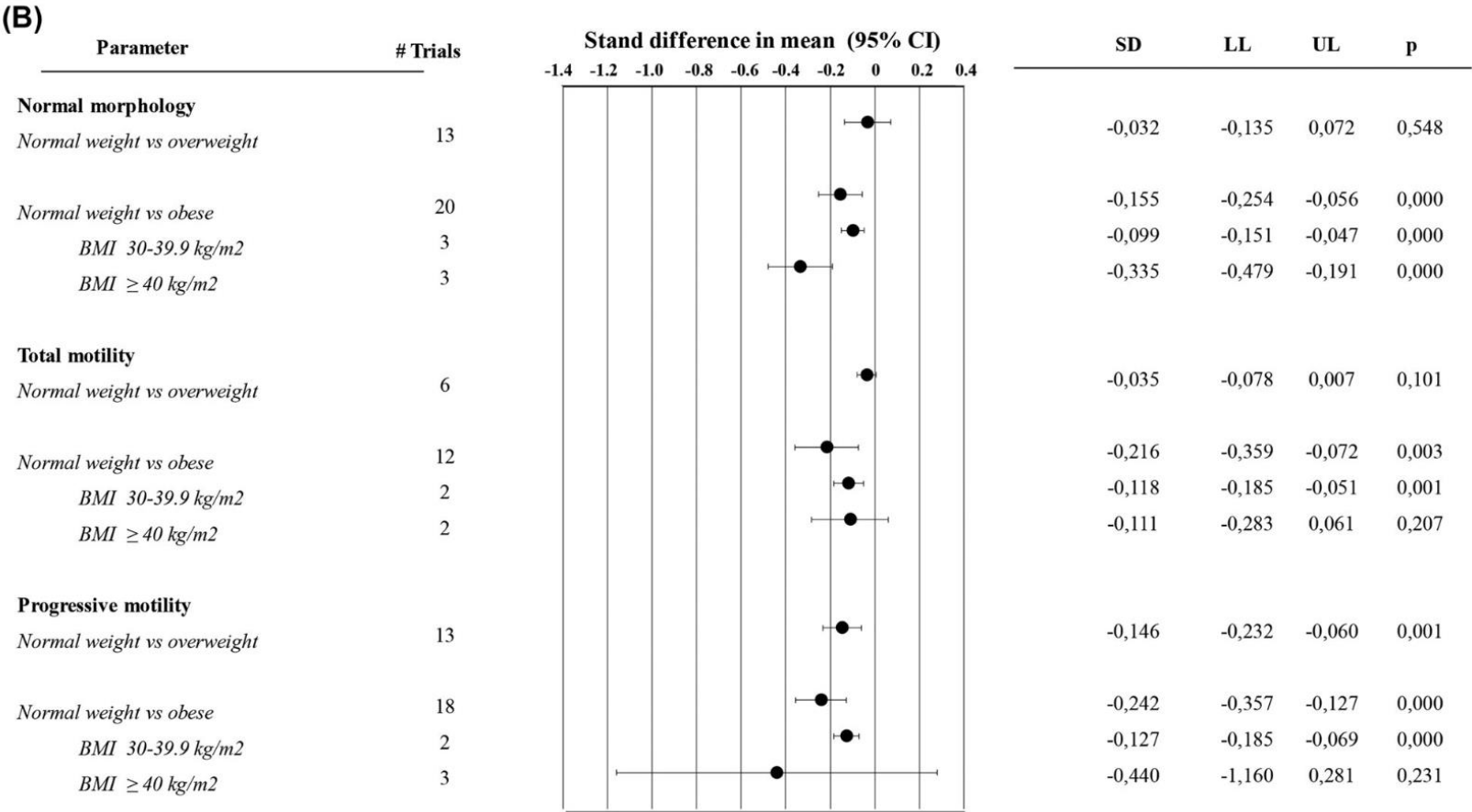
➤ STILE DI VITA (consumo di alcool, fumo)

➤ ENDOCRINE DISRUPTORS ambientali

Does an increase in adipose tissue ‘weight’ affect male fertility? A systematic review and meta-analysis based on semen analysis performed using the WHO 2010 criteria

Daniele Santi¹ | Francesco Lotti² | Clotilde Sparano³ | Giulia Rastrelli² |
Andrea M. Isidori⁴ | Rosario Pivonello^{5,6} | Arcangelo Barbonetti⁷ |
Andrea Salonia^{8,9} | Suks Minhas¹⁰ | Csilla Krausz² | Linda Vignozzi² |
Mario Maggi³ | Giovanni Corona¹¹

Obese men showed lower sperm concentration, total sperm number, progressive and total motilities, and normal morphology lower than normal weight subjects.



**What are the most effective dietary
interventions for male infertility?**



Association between adherence to the Mediterranean diet and semen quality parameters in male partners of couples attempting fertility

	MedDietScore tertile			P-value
	1st (≤30)	2nd (31–36)	3rd (≥37)	
Semen analysis				
Volume (ml) ^c	2.0 (1.7, 2.2)	2.2 (2.0–2.3)	2.1 (1.9–2.3)	0.403
Volume <1.5 ml, n (%)	15 (19.7)	11 (13.3)	8 (12.1)	
Concentration (×10 ⁶ /ml) ^c	30.5 (24.3–36.7)	37.1 (31.5–42.6)	37.9 (31.4–44.4)	<0.001
Concentration <15 × 10 ⁶ /ml, n (%)	36 (47.4) ^a	18 (21.7) ^b	11 (16.7) ^b	
Total sperm count (×10 ⁶ /ml) ^c	63.8 (47.2–80.4)	86.6 (71.8–101.4)	82.1 (64.7–99.5)	<0.001
Total sperm count <39 × 10 ⁶ /ml, n (%)	42 (55.3) ^a	27 (32.5) ^b	15 (22.7) ^b	
Motility (%) ^c	32.1 (27.4–36.8)	40.7 (36.5–44.9)	42.6 (37.6–47.5)	<0.001
Motility <40% motile, n (%)	50 (65.8) ^a	30 (36.1) ^b	21 (31.8) ^b	
Progressive motility (%) ^c	20.0 (16.2–23.8)	24.1 (20.7–27.5)	26.0 (22.0–30.0)	0.011
Progressive motility <32% motile, n (%)	64 (84.2) ^a	62 (74.7) ^a	41 (62.1) ^b	
Morphology (%) ^c	4.3 (3.7–4.9)	4.3 (3.8–4.8)	4.6 (4.0–5.1)	0.023
Morphology <4% normal, n (%)	38 (50.0) ^a	28 (33.7) ^b	19 (28.8) ^b	
Abnormal semen analysis, n (%) ^d	66 (86.8)	62 (74.7)	47 (71.2)	0.051

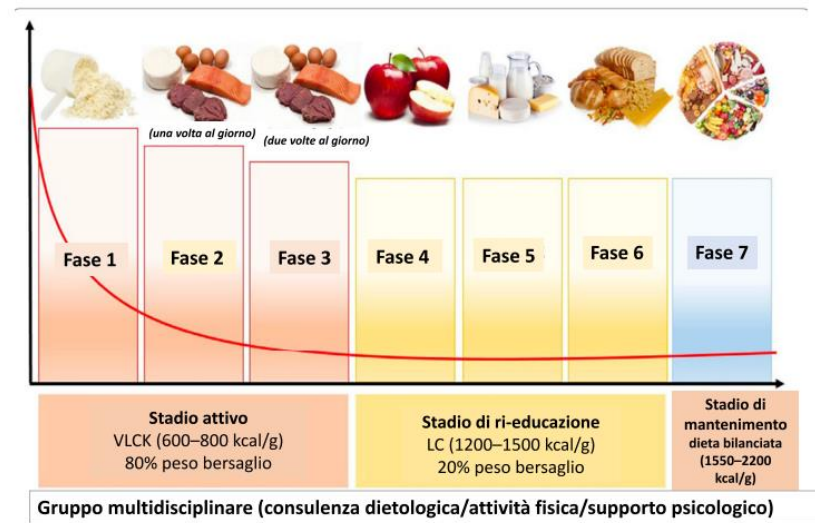
The results suggest that greater compliance to the **MedDiet** may help improve semen quality. Our findings are consistent with previous studies showing that dietary patterns with some of the characteristics of the MedDiet, i.e. rich in fruit, vegetables, legumes and whole grains, are associated with better measures of semen quality.

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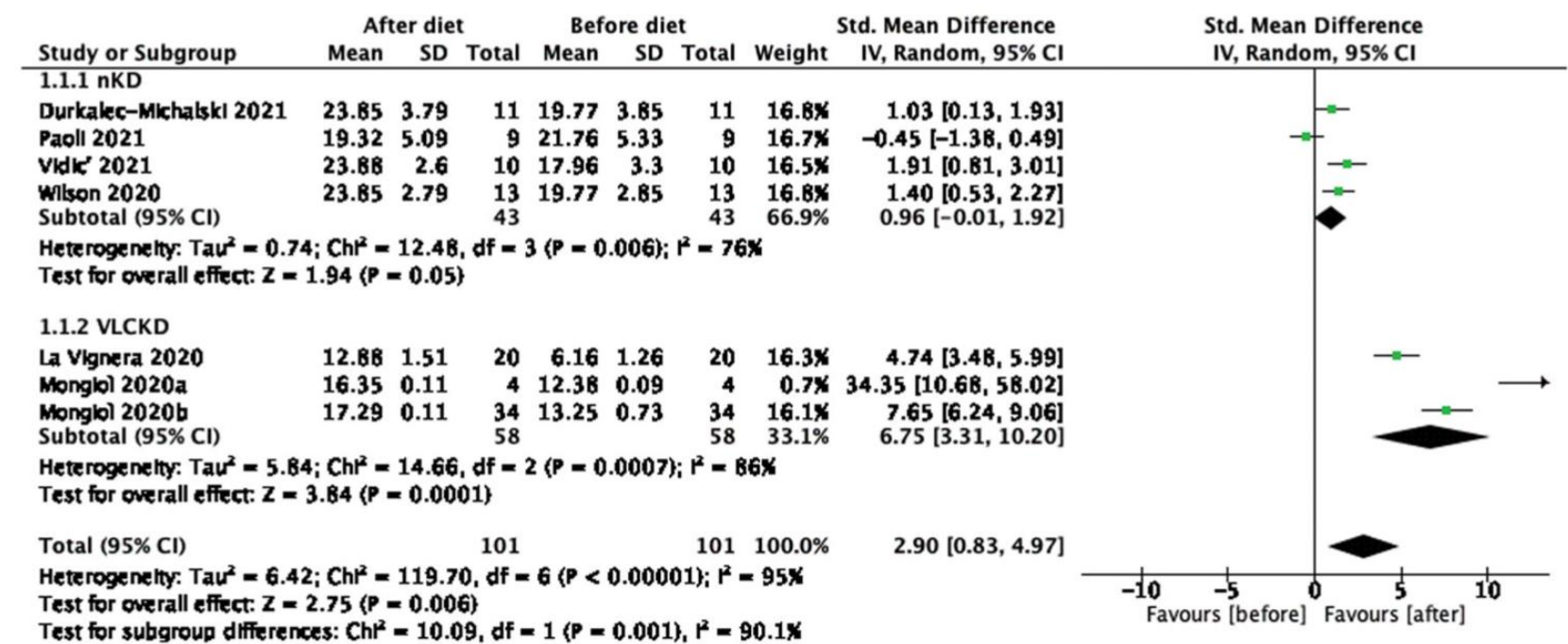
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Neurodegenerative disorders associated with sarcopenic obesity	(2 ØØØØ)

Ketogenic state improves testosterone serum levels—results from a systematic review and meta-analysis

7 studies (including 8 trials) were included in the analysis for a total of 230 patients (5 KD and 3 VLCKD)



Forest plot showing total testosterone serum levels change after ketogenic diet (KD), both normocaloric and very low calories KD.

Meta-regression analyses highlighted significant correlations between the post-KD testosterone raise with patients’ age ($p<0.001$) and weight loss ($p<0.001$).

Infertilità di coppia: risoluzione del *gap* di genere



Azienda
Ospedaliero
Universitaria
Careggi

Funzionigramma

CENTRO AZIEDALE PER LA PREVENZIONE, DIAGNOSI E CURA DELL'INFERTILITA'
Provvedimento del DG N°152 del 23/02/2022



DS123/01
ED. 1 Rev. 0
Emissio il
01/04/2021

DAI Materno infantile

Responsabile Centro
Prof.ssa Linda Vignozzi

SOD Andrologia, Endocrinologia
Femminile e Incongruenza di Genere
Direttore Prof.ssa Linda Vignozzi
(D/1353/04)

Ambulatorio Andrologia,
Endocrinologia Femminile
e Incongruenza di Genere

- Prevenzione e Cura dell'Infertilità
- Disturbi della Sessualità Maschile
- Endocrinologia della Sessualità Femminile
- Incongruenza di Genere
- Endocrinologia di Transizione Adolescenziiale
- Genetica e Oncologia Andrologica

ATTIVITA' di LABORATORIO
Resp. Prof.ssa Elisabetta Baldi

Laboratorio Andrologia
e C.R.R.
Crioconservazione
Liquido Seminale

- Valutazione Diagnostica Liquido Seminale
- Crioconservazione Liquido Seminale e TESE
- Screening e Bancaggio Donatori Seme Eterologa

Laboratorio
Procreazione
Medicalmente
Assistita

- Manipolazione Gameti ed Embrioni per PMA Omologa ed Eterologa
- Crioconservazione Gameti ed Embrioni

SOD Procreazione Medicalmente
Assistita
Direttore Prof.ssa Elisabetta Coccia
(D/1158/01)

Ambulatorio Procreazione
Medicalmente Assistita

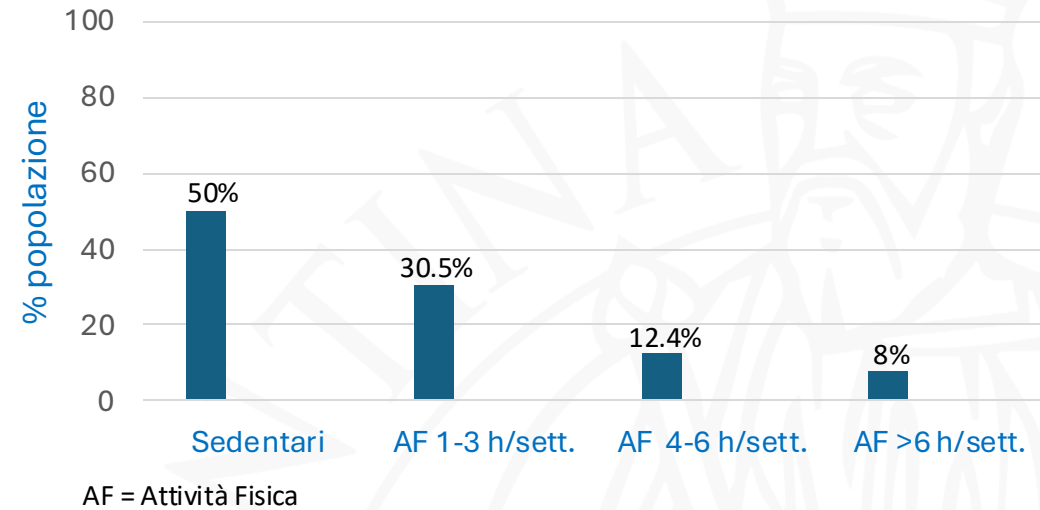
- Presso l'Azienda Ospedaliero-Universitaria (AOU) Careggi realizzato il **Centro aziendale per la prevenzione, diagnosi e cura dell'infertilità**
- Presa in carico della coppia infertile da parte di un **gruppo multidisciplinare**
- **Ginecologo e andrologo** procedono **congiuntamente** nella scelta dell'approccio clinico più **adeguato** per la coppia

239 partner maschili di coppie infertili

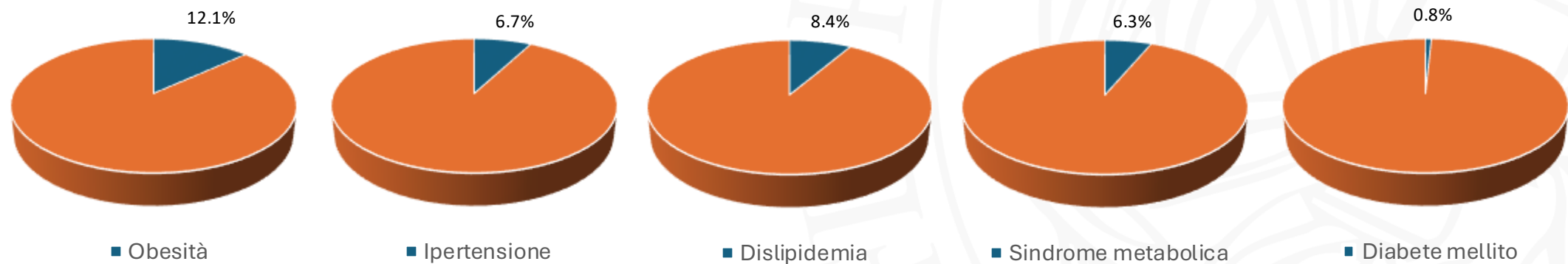
Età media della popolazione in studio:

- partner **maschili** 39.5 ± 6.1 anni
- partner **femminili** 35.5 ± 5.5 anni

Fattori di rischio comportamentali



Prevalenza di **disordini metabolici** nella popolazione in studio:



BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis

N. Sermondade^{1,2}, C. Faure^{1,2}, L. Fezeu², A.G. Shaye³, J.P. Bonde⁴, T.K. Jensen⁵, M. Van Wely⁶, J. Cao⁷, A.C. Martini⁸, M. Eskandar⁹, J.E. Chavarro^{10,11}, S. Koloszar¹², J.M. Twigt¹³, C.H. Ramlau-Hansen¹⁴, E. Borges Jr¹⁵, F. Lotti¹⁶, R.P.M. Steegers-Theunissen¹³, B. Zorn¹⁷, A.J. Polotsky¹⁸, S. La Vignera¹⁹, B. Eskenazi²⁰, K. Tremellen²¹, E.V. Magnusdottir²², I. Fejes²³, S. Hercberg^{2,24}, R. Lévy^{1,2†}, and S. Czernichow^{25,26,*†}

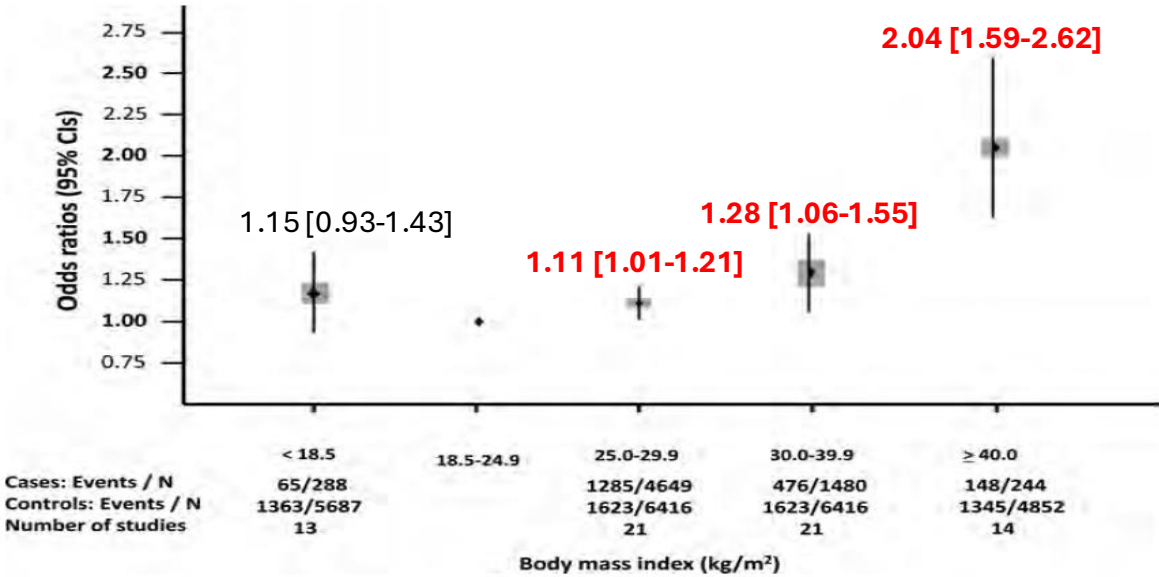
ORIGINAL ARTICLE: ENVIRONMENT AND EPIDEMIOLOGY

Men's body mass index in relation to embryo quality and clinical outcomes in couples undergoing in vitro fertilization

Daniela S. Colaci, M.D., M.Sc.,^a Myriam Afeiche, Ph.D., M.P.H.,^a Audrey J. Gaskins, B.S.E.,^a Diane L. Wright, Ph.D.,^b Thomas L. Toth, M.D.,^c Cigdem Tanrikut, M.D.,^c Russ Hauser, M.D., M.P.H., Sc.D.,^{b,d,e} and Jorge E. Chavarro, M.D., Sc.D.,^{a,d,f}

^a Department of Nutrition, Harvard School of Public Health, Harvard University; ^b Vincent Obstetrics and Gynecology, Massachusetts General Hospital and Harvard Medical School; ^c Department of Urology, Massachusetts General Hospital and Harvard Medical School; ^d Department of Epidemiology, Harvard School of Public Health; ^e Department of Environmental Health, Harvard School of Public Health; and ^f Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Harvard University, Boston, Massachusetts

Association between BMI and abnormal TCS (oligozoospermia or azoospermia) according to categories of BMI



Odds ratios (95% CI) for clinical outcomes in couples undergoing assisted reproduction according to fertilization method (conventional in vitro fertilization and intracytoplasmic sperm injection).

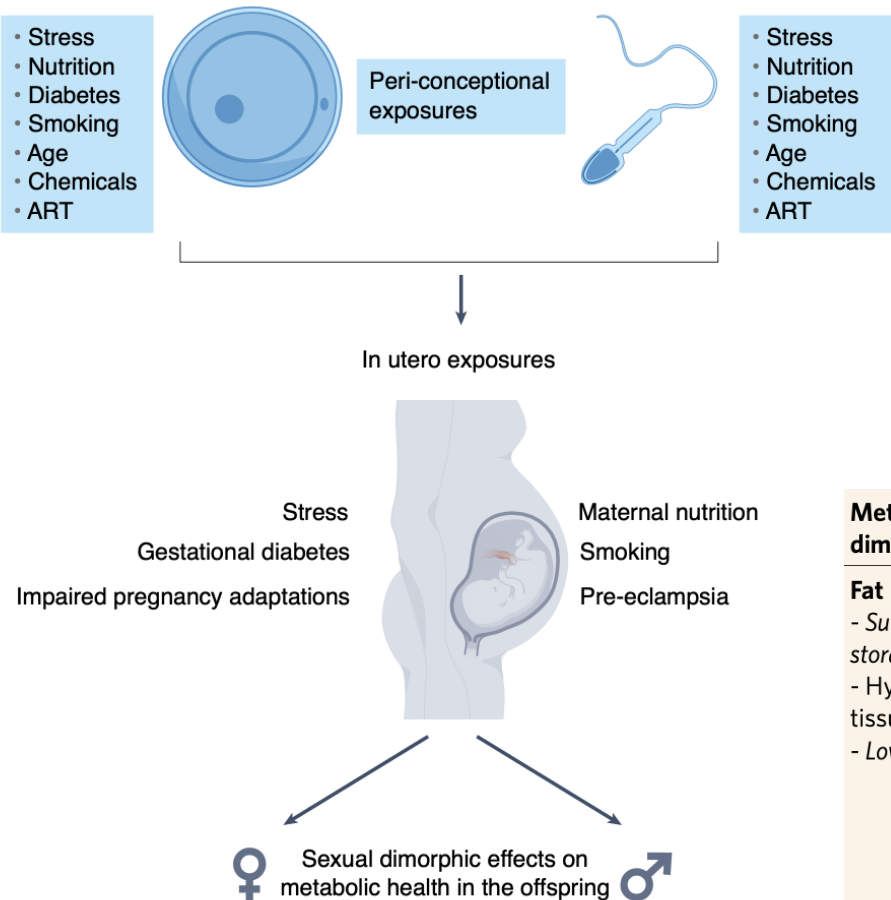
Clinical outcome	No. of cycles	18.5–24.99 kg/m ²	Male BMI		P trend
			25–29.99 kg/m ²	≥ 30 kg/m ²	
IVF cycles					
Clinical pregnancy per initiated cycle ^{a,b}	74	Ref	0.83 (0.34–2.06)	1.69 (0.52–5.46)	.38
Live birth per initiated cycle ^{a,b}	74	Ref	1.80 (0.58–5.65)	1.84 (0.48–7.06)	.35
Clinical pregnancy per embryo transfer ^{c,b}	72	Ref	0.92 (0.38–2.22)	1.54 (0.47–5.06)	.51
Live birth per embryo transfer ^{c,b}	72	Ref	1.81 (0.59–1.71)	1.63 (0.43–6.16)	.44
ICSI cycles					
Clinical pregnancy per initiated cycle ^{b,d}	91	Ref	0.57 (0.20–1.63)	0.62 (0.14–2.67)	.35
Live birth per initiated cycle ^{b,d}	91	Ref	0.40 (0.14–1.17)	0.20 (0.04–1.00)	.03 ^f
Clinical pregnancy per embryo transfer ^{b,e}	86	Ref	0.53 (0.16–1.68)	0.53 (0.11–2.55)	.29
Live birth per embryo transfer ^{b,e}	86	Ref	0.40 (0.12–1.37)	0.16 (0.03–0.90) ^f	.04 ^f

Note: BMI = body mass index; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; Ref = reference value.
^a 53 Couples initiate an IVF cycle and underwent 74 IVF cycles.
^b Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and women's BMI.
^c 52 couples underwent 72 embryo transfers among IVF cycles.
^d 55 couples initiated an ICSI cycle and underwent 91 ICSI cycles.
^e 52 couples underwent 86 embryo transfers among ICSI cycles.
^f P < .05 compared with the reference group (men's BMI 19–24.99 kg/m²).

Modifica stile di vita → fertilità e outcome di gravidanza?



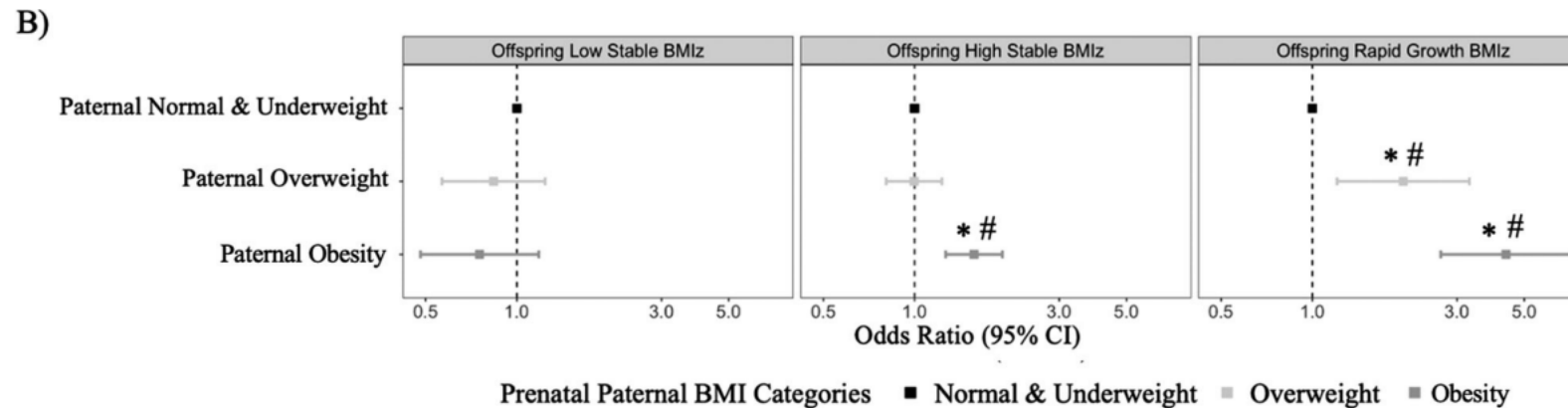
Sex differences in the intergenerational inheritance of metabolic traits



Parental germline exposures before pregnancy affect sperm and oocytes. In utero exposures experienced by the developing embryo during pregnancy due to adverse maternal environments may program sex-related dimorphic effects on the short-term and long-term health of the offspring.

Metabolic organs and sexual dimorphism (human observations)	Programming factor	Effect in the metabolic organ of the offspring	Disease in the offspring
Fat - Subcutaneous rather than visceral fat storage (hips and thighs) ⁶⁰ - Hypertrophic abdominal adipose tissue expansion ⁶⁰ - Lower adipose tissue inflammation ⁶⁰	Maternal undernutrition	- Indexes of fat mass distribution in adulthood (BMI, ratio of waist-to-mid-thigh circumferences) increased (human) ¹⁶	- Obesity (human) ¹⁶
	Maternal overnutrition	- Increased adipocyte size at P70 (mouse) ¹⁴⁵ - Increased gonadal fat pad weights (mouse) ¹⁷⁸ - Adipose inflammation (mouse) ¹⁷⁹	- Obesity (human) ¹⁷ - Increased adiposity (mouse) ³⁵
	Paternal overnutrition	- Increased gonadal and retroperitoneal fat pad weights in F1 (mouse) ¹⁴⁶ - Increased proportion of body fat and impaired insulin sensitivity in F2 (mouse) ¹⁴⁶	- Obesity in F1 and F2 (mouse) ¹⁴⁶

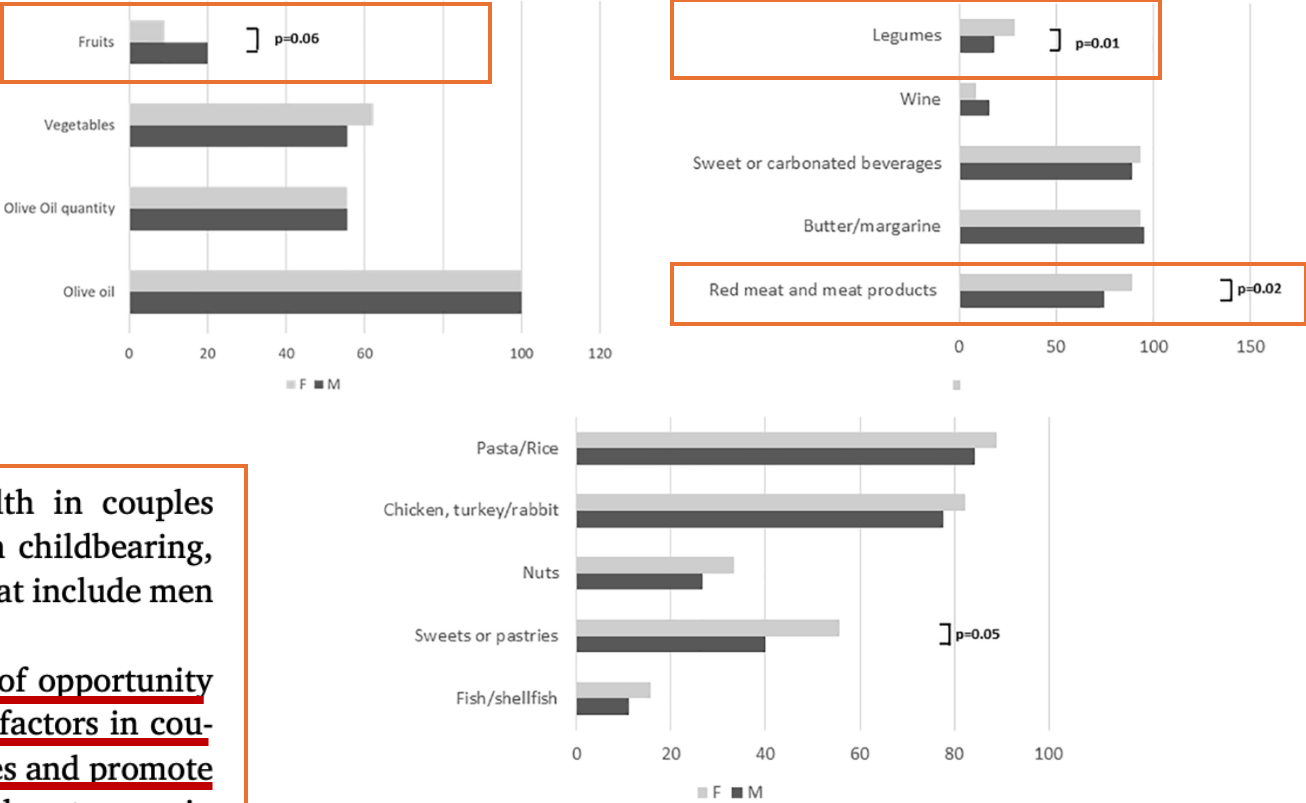
Determining the interplay of prenatal parental BMI in shaping child BMI trajectories: the CHILD Cohort Study



- **Maternal BMI in the normal/underweight range (n = 1,461):**
Elevated paternal BMI was significantly associated with a higher likelihood of the child following a high or rapid BMIz growth trajectory.
- **Maternal BMI in the overweight/obese range (n = 777):**
The effect of elevated paternal BMI was additive to that of maternal BMI, resulting in even greater cumulative risk for unfavorable trajectories (high or rapid BMIz growth) in offspring.

Preconception period in women and men undergoing Assisted Reproduction: A gender approach for reproductive health

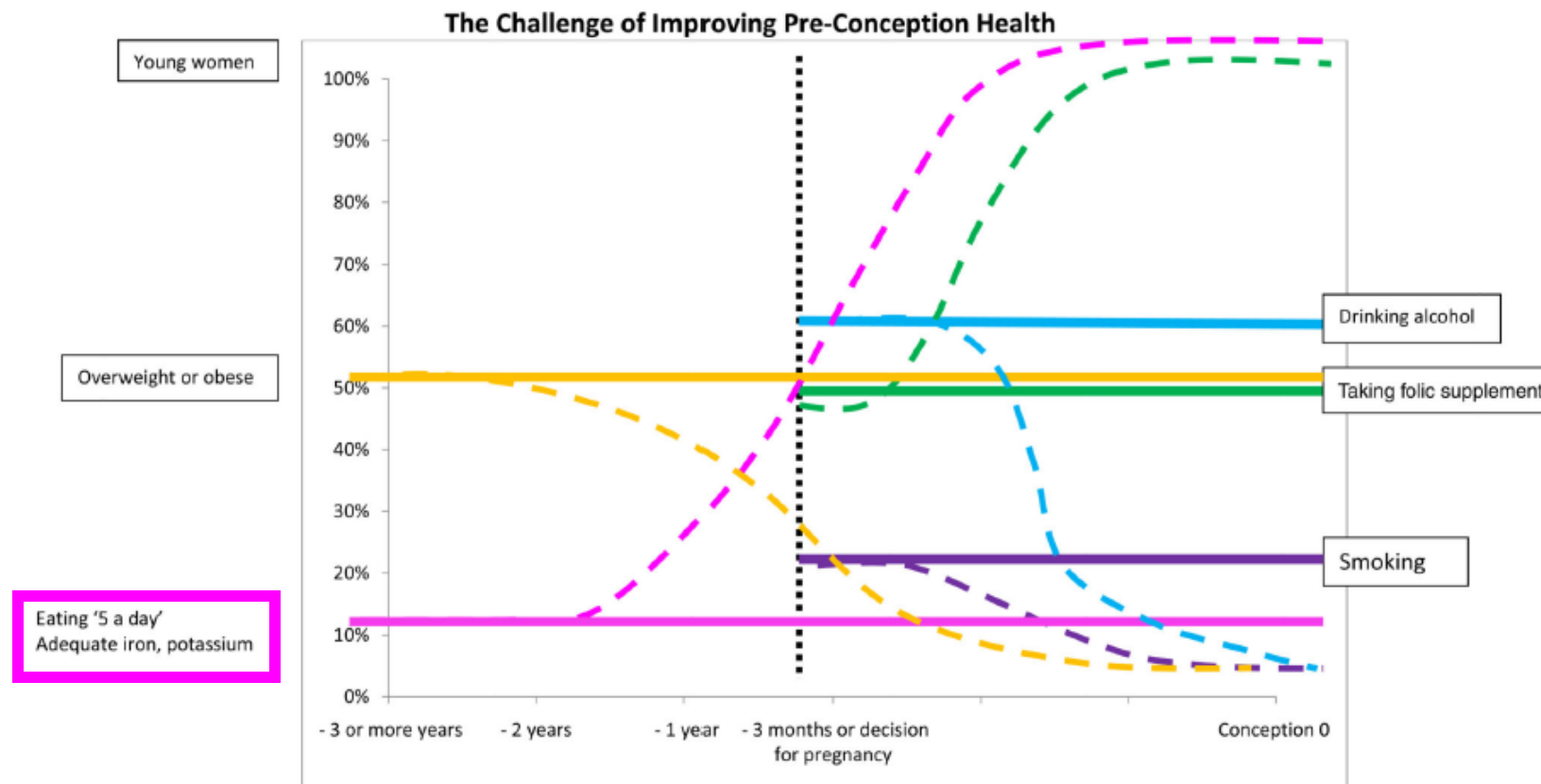
Michela Cirillo^{a,b}, Maria Elisabetta Coccia^{b,c}, Arianna Dimmito^d, Cinzia Fatini^{a,b,1,*}



This study paid attention on preconceptional health in couples planning ART. Women have a greater biological role in childbearing, whereas the role of men is underestimated and studies that include men are exceedingly rare.

The need to conceive through ART offers a window of opportunity not only to evaluate cardiovascular profile and lifestyle factors in couples prior to conception, but also to manage comorbidities and promote health behaviours in order to improve fertility and health outcomes in both women and men at short and long-term. Further and larger study are needed to confirm our results.

Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health



Eating '5 a day'

Overweight or obese

Drinking alcohol

Taking folic supplement

Smoking



Gender Differences in Food Choice and Dietary Intake in Modern Western Societies



- **Red meat, alcohol,** and hearty portion sizes are associated with **masculinity**.
- Men choose fewer high-fiber foods, eat fewer fruits and vegetables and low-fat foods than women.
- Men have ***fewer problems with their eating behavior***, and their *attitude to food is generally uncomplicated and enjoyable*, even though they are more frequently overweight and have higher risk of associated disease.

- **Vegetables, fruit, fish** and **sour dairy products** are associated with **femininity**.
- **Women** demonstrated superior knowledge regarding all the areas of nutrition.
- Women's greater concern about weight control and their higher frequency of dieting.

LA PIRAMIDE ALIMENTARE MEDITERRANEA



Consumo quotidiano di frutta e verdura

	Italia n = 70593		
	%	IC95% inf	IC95% sup
0 porzioni	3.0	2.8	3.2
1/2 porzioni	51.5	51.0	51.9
3/4 porzioni	38.1	37.7	38.6
5+ porzioni	7.4	7.2	7.7

- **Five a day (≥ 5 porzioni/die): 7%,** più frequente **nelle donne**, ma mai oltre il 9%.
- **Almeno 3 porzioni/die: 45%,** più diffuso **fra donne, persone adulte, con istruzione e risorse economiche maggiori.**
- Tendenza in calo nel tempo, per entrambi i sessi.
- Differenze geografiche: più alto nel Centro (50%), più basso al Sud (41%), con Sardegna e Sicilia in linea col Centro (~50%).

Consumo quotidiano di 5 porzioni frutta e verdura per regione di residenza

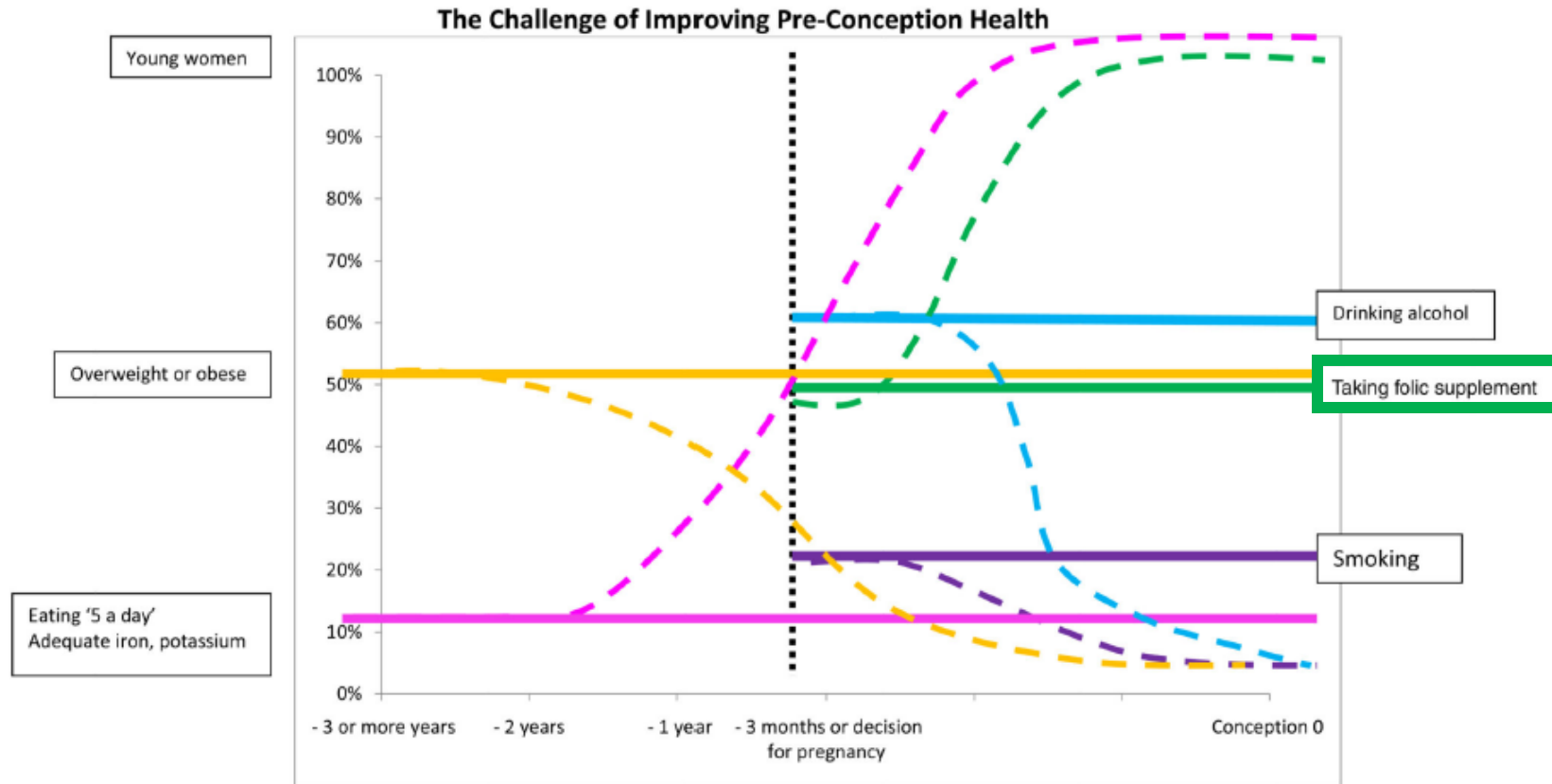
Passi 2023-2024



- peggiore del valore nazionale
- simile al valore nazionale
- migliore del valore nazionale

Sorveglianza Passi

Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health



Eating '5 a day'
Overweight or obese
Drinking alcohol
Taking folic supplement
Smoking



Linee guida

per una sana alimentazione



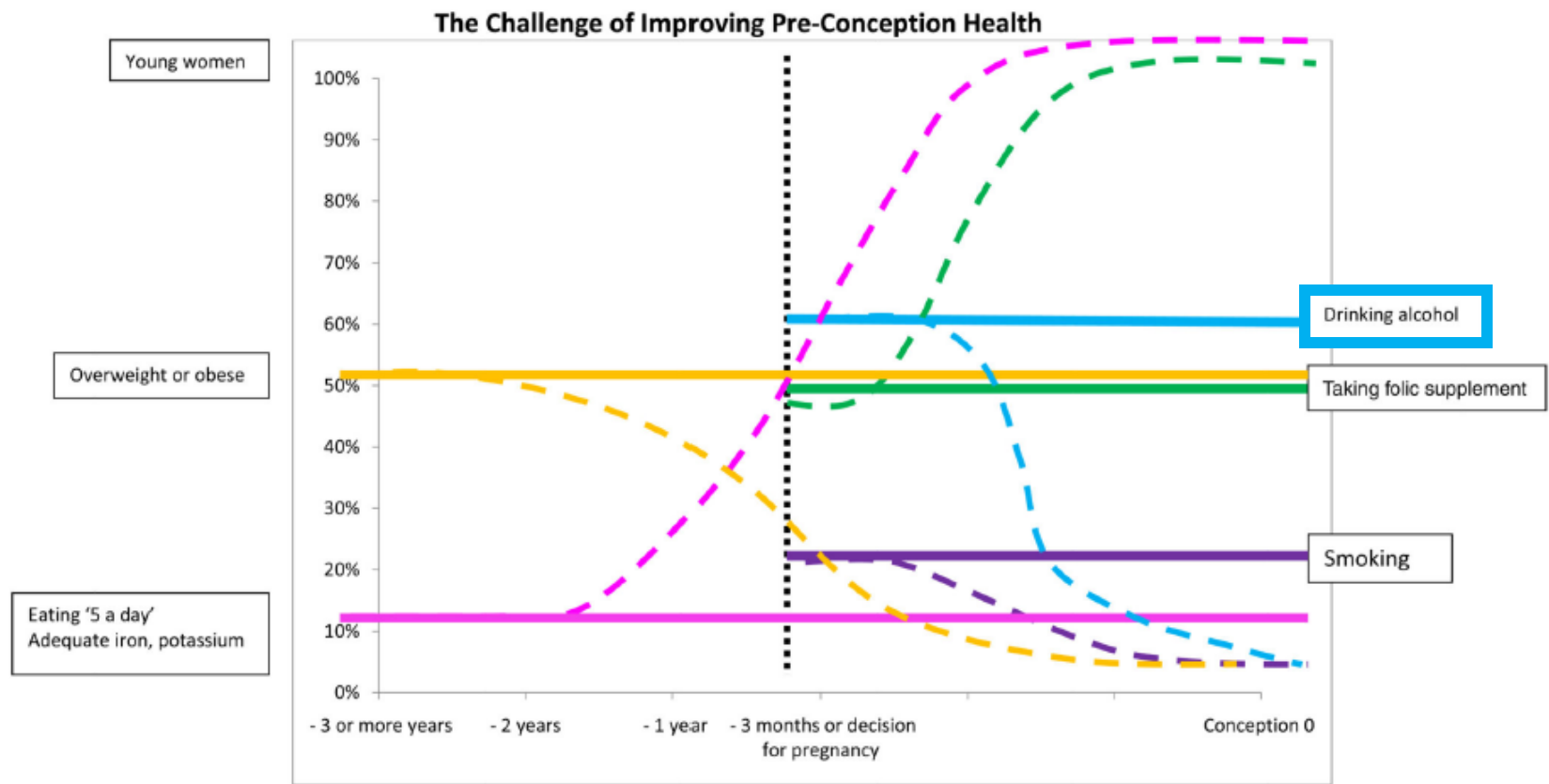
Acido folico, meglio pensarci prima

L'acido folico è una vitamina fondamentale per il corretto sviluppo degli organi, ma soprattutto del tubo neurale, dal quale poi durante lo sviluppo fetale si formeranno molte parti del nostro sistema nervoso. Il tubo neurale completa il suo sviluppo entro il 28° giorno dal concepimento, quando generalmente la donna non ha ancora accertato la sua gravidanza. Per queste ragioni la supplementazione giornaliera con 400 microgrammi (mcg) di acido folico (vitamina B₉), in aggiunta a quello assunto con un'alimentazione ricca di frutta e verdura, per tutte le donne in età fertile "che cominciano a pensare a una gravidanza o non ne escludono la possibilità" serve a ridurre molto il rischio di comparsa di malformazioni congenite, come i difetti del tubo neurale (spina bifida, anencefalia), ma anche altre gravi malformazioni congenite come le labiopalatoschisi e le labioschisi (es. labbro leporino) e alcune cardiopatie congenite. Per le donne che hanno avuto in precedenza un bambino affetto da difetto del tubo neurale, o che sono esse stesse affette da spina bifida, o da diabete, o che sono in trattamento con farmaci antiepilettici, il dosaggio di supplementazione con acido folico, da concordare con il proprio medico curante, raggiunge i 4000mcg al giorno. La pratica della supplementazione con acido folico prima del concepimento e per tutto il primo trimestre di gravidanza è una delle conquiste più rilevanti nel campo della salute infantile, insieme alle vaccinazioni e alla promozione dell'allattamento al seno, ed è a totale carico del Sistema Sanitario Nazionale.

I folati sono presenti in un'ampia varietà di alimenti, in quantità:

- elevata (100-300mcg per 100g) nelle verdure a foglia larga verde scuro come gli spinaci, negli asparagi, nei broccoli, nei carciofi, nei cavoli;
- intermedia (44-99mcg per 100g) in altre verdure (bietole, rape rosse), nei legumi (ceci, fagioli), nella frutta fresca (arance, kiwi, mandarini), nella frutta secca (mandorle, noci), in alcuni formaggi e nelle uova. Il pane ha un contenuto moderato (20-39mcg per 100g) di folati. Mentre la donna adulta, con una dieta ricca di frutta e verdura, riesce ad assumere tutti i folati di cui ha bisogno, le aumentate necessità della gravidanza potrebbero non essere coperte con la sola dieta. Per questo anche chi mangia tantissima frutta e verdura deve comunque ricorrere alla supplementazione per avere la sicurezza della copertura.

Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health



Eating '5 a day' —

Overweight or obese —

Drinking alcohol —

Taking folic supplement —

Smoking —



BEVANDE ALCOLICHE

COME COMPORTARSI

Se si è astemi è bene continuare a non assumere bevande alcoliche, perché non esiste un consumo di alcol esente da rischi per la salute; se invece sei consumatore di alcol e decidi di continuare a bere, è opportuno rispettare le condizioni che seguono per minimizzare i rischi per la salute:

La quantità di consumo di alcol compatibile con un “basso rischio” si riassume in un 2-1-0:

- fino a 2 unità alcoliche al giorno se sei un uomo adulto;
- fino a 1 unità alcolica al giorno se sei una donna o una persona con più di 65 anni;
- 0 alcol sotto i 18 anni.



7. LIMITA IL CONSUMO DI BEVANDE ALCOLICHE

Indipendentemente dal tipo di bevanda, il consumo eccessivo di alcol aumenta il rischio di sviluppare malattie oncologiche. L'etanolo, classificato come cancerogeno, viene metabolizzato nel fegato e trasformato in acetaldeide, molecola che gioca un ruolo importante nel processo neoplastico. Per di più, le ricerche mostrano che il consumo di alcol è associato spesso all'uso di tabacco, amplificando così l'effetto negativo per la salute.



ASSUNZIONE ALCOLICI: CONSUMO A RISCHIO

- 42% degli adulti non consuma alcol
- 18% consumo a rischio:**
 - 9% binge drinking
 - 10% consumo fuori pasto
 - 2% consumo abituale elevato
- Rischio più alto tra:
 - Giovani (18-24 anni): 36%
 - Uomini: 22% (vs. 14% donne)
 - Persone con alto livello socio-economico
 - Aree critiche: Nord Italia, Molise, Sardegna
- Da attenzione:
 - 48% dei malati di fegato beve
 - 10% donne in gravidanza**
 - 22% donne che allattano**
- Trend:



Stabile negli uomini
In aumento tra le donne (soprattutto binge drinking)
Differenze di genere in calo

Consumo a maggior rischio
per regione di residenza
Passi 2023-2024



- peggiore del valore nazionale
- simile al valore nazionale
- migliore del valore nazionale

Sorveglianza Passi



Mancanza di prevenzione

Solo il **7%** dei consumatori a rischio ha ricevuto **consigli** per ridurre il consumo

ASSUNZIONE DI ALCOL IN GRAVIDANZA

Smettere di bere in gravidanza è il comportamento più sicuro.

DOSI ALTE/FASE CRITICA SINDROME FETALE ALCOLICA (FAS):

- Ritardi della crescita intrauterina e postnatale
- Anomalie cranio-facciali e cardiache
- Disturbi dell'udito
- Anomalie neurologiche (microencefalia)
- Alterazioni dell'attenzione e dell'apprendimento (ADHD, autismo)



DOSI MODERATE/DEFICIT NEUROCOMPORTAMENTALI

- anche in assenza di alterazioni strutturali nella progenie



Caffeine, alcohol, smoking, and reproductive outcomes among couples undergoing assisted reproductive technology treatments

Findings suggest that *moderate alcohol intake in the year before ART* treatment does not seem to have an appreciable impact on the success of ART; however current alcohol intake *immediately before the start of (and during) treatment may be harmful*.

Minguez-Alarcón et al, Fertil Steril 2018.

Effects of maternal and paternal alcohol consumption on the success rates of in vitro fertilization and gamete intrafallopian transfer

Women who consumed one more drink per day *1 month before the attempt* had an adverse effect on attaining and maintaining pregnancy.

Klonoff-Cohen et al, Fertil Steril 2003.

Fathers' Role in Alcohol-Exposed Pregnancies

Systematic Review of Human Studies

41,062 men

Paternal preconception and prenatal alcohol use has various impacts on maternal prenatal health behaviors, fetal health outcomes, and infant health. It is therefore important to recognize that decisions about **alcohol use during preconception and pregnancy are not the sole responsibility of women** but occur within the context of the home and the broader social environment, and thus require more complex policy to assist in reducing alcohol-exposed pregnancies and increasing the potential for healthy fetal and infant outcomes.

	Strength	Consistency	Specificity	Temporality
Paternal social facilitation of maternal drinking, and relationship quality	High	High	High	Present
Effects of alcohol on sperm health	Moderate	Needs replication	High	Present
Impacts on fetal/infant health				
Spontaneous abortion	High	High	High	Present
Acute lymphoblastic leukemia	Moderate	Needs replication	Moderate	Present
Ventricle malformation	Moderate	Needs replication	Moderate	Present
Live birth	Moderate	Needs replication	Moderate	Present
Low birth weight	Low	Low	Low	Present

FIGO nutrition checklist for pre-pregnant/early pregnant women

Good nutrition in the mother, both before and during pregnancy, is important in ensuring healthy outcomes for her and her baby. This checklist is designed for women to complete in conjunction with her health care professional in order to assess whether nutritional intake is sufficient, and provide a basis for the health care professional to advise where changes need to be made (if applicable).

For the woman to complete in conjunction with her healthcare professional:

1). Do you have any special dietary requirements (e.g. vegetarian, vegan, allergies)? If yes, please list below:

.....
.....

2). What is your:

a. Weight kgs c. (Health care professional to complete): Divide weight in kg by height in metres then divide the answer by your height again to get your BMI.

b. Height m Your BMI is kg/m²

3). Quality of diet

i) Do you eat meat or chicken 2-3 times per week? Yes / No

ii) Do you regularly eat more than 2 – 3 portions of fruit or vegetables per day? Yes / No

iii) Do you eat fish at least 1-2 times per week? Yes / No

iv) Do you consume dairy products (such as milk, cheese, yogurt) every day? Yes / No

v) Do you eat whole grain carbohydrate foods (brown bread, brown pasta, brown rice or other) at least once a day? Yes / No

vi) Do you consume packaged snacks, cakes, pastries or sugar-sweetened drinks less than 5 times a week? Yes / No

4). What is your:

i) If you are pregnant, did/do you take folate/folic acid supplements in pre-pregnancy and in early pregnancy (first 12 weeks)? Yes / No

ii) Do you get regular exposure to the sun (face, arms and hands for at least 10-15 mins per day)? Yes / No

iii) Has the doctor/nurse tested your haemoglobin (level of iron in the blood)? Yes / No

(Health care professional to complete) If yes, is it more than 110 g/l? Yes / No Enter the value:

If you have answered No to any of the questions in section 3 or 4 your nutritional status may need to be assessed in more detail.



Additional details for health care provider:

The intention is that this document will be adapted to the context of the country in which it is being used.

1. A healthy BMI is usually considered to be between 18.5–25 Kg/m², although this depends on age and geographical region.

2. For women who are not pregnant, counsel on achieving a healthy weight before conceiving.

* For pregnant women provide indications for appropriate gestational weight gain according to pregravidic BMI (see right). This may vary according to local contexts.

3. Q 3. i. is to assess whether vitamin B12, iron and protein intake is sufficient.

4. Q 3. ii. is to assess whether intake of antioxidants, micronutrients and fibre is sufficient.

5. Q 3. iii. is to assess whether intake of omega 3 / omega 6 polyunsaturated fatty acids, vitamin D and iodine is sufficient.

6. Q 3. iv. if the patient answers No to this question, calcium supplementation should be considered.

7. Q 3. v. and vi. – if No, advice should be given to increase wholegrains and reduce processed sugar intake.

8. Q 4. i. if not taking a folate supplement suggest a folate supplement.

9. Q 4. ii. if the patient has little sun exposure or has dark skin, consider vitamin D supplementation.

10. Q 4. iii. if Hb < 110 g/l suggest an iron supplement. This cutoff may vary according to local contexts.

11. Health care professionals should consider any foods available in their country which are considered unsafe for pregnancy.

12. As well as the questions in the questionnaire, health care professionals should assess whether any other potential unsafe aspects of the woman's lifestyle should be counselled on, such as smoking, alcohol, recreational drug use, or lack of physical exercise

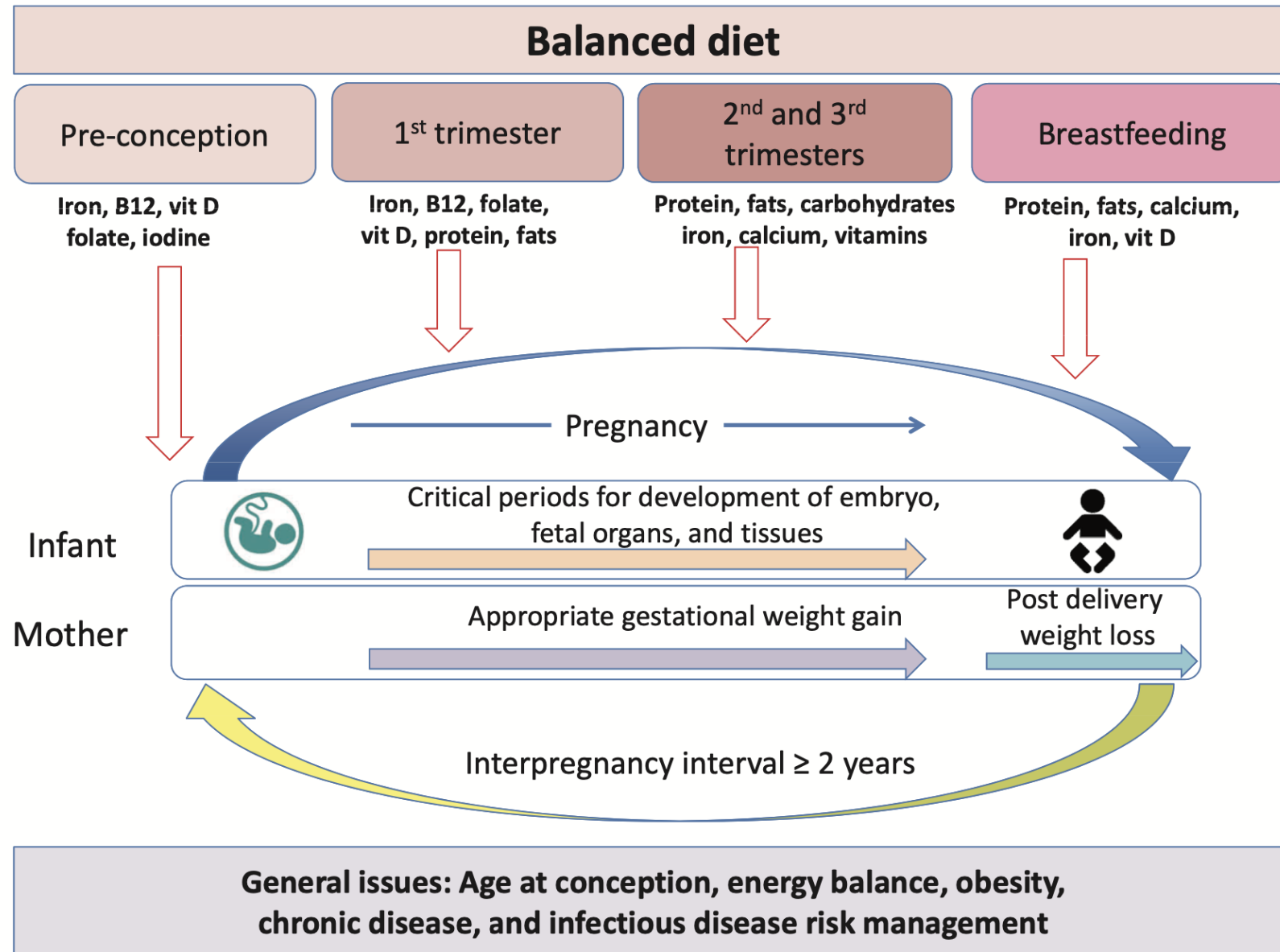
Pre-pregnancy BMI category	Total weight gain (kg)	Rate of weight gain 2 nd and 3 rd trimester (kg/wk)
Underweight <18.5 kg/m ²	12.5 - 18	0.51 (0.44 – 0.58)
Normal weight 18.5-24.9 kg/m ² weight	11.5 - 16	0.42 (0.35 – 0.50)
Overweight 25.0 – 29.9 kg/m ² weight	7-11.5	0.28 (0.23 – 0.33)
Obese >30 kg/m ²	5-9	0.22 (0.17 – 0.27)

From 2009 Institute of Medicine guidelines on gestational weight gain: <https://www.nationalacademies.org/hmd/~/media/Files/Reports/2009/WeightGainDuringPregnancy/ExaminingtheGuidelines/Report%20Brief%20-%20Weight%20Gain%20During%20Pregnancy.pdf>

Pre-pregnancy – when planning a pregnancy		
Involved professionals	Assessment considerations	Discussion points
- Community health workers - Nutritionists - Family doctors (GPs) - Ob-gyns - Midwives	- Diet composition - Physical activity history - Height, weight, BMI - Obesity risk - WC (+ other anthropometric measures) - Anemia - Risk of specific nutritional problems (low nutrient density) - Folate - Iron - Calcium - Vitamin B12 - Vitamin D - Iodine - Zinc - PUFAs	- Importance of a healthy diet and exercise - Problems of sedentary behaviour such as screen-time - Risky behaviors and exposures - Tobacco, alcohol - recreational drugs - Environmental toxins - Chronic disease screening and management - Supplementation - Folic acid supplementation 400 µ/day - Other nutrients (iron, iodine, vitamin B12)

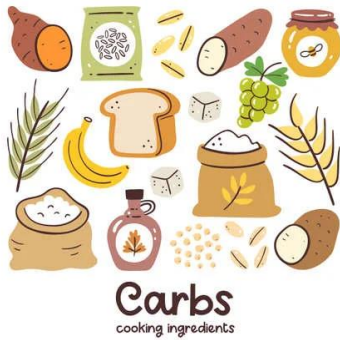
During pregnancy		
Involved professionals	Assessment considerations	Discussion points
- Community health workers - Nutritionists - Family doctors (GPs) - Ob-gyns - Midwives	- Diet composition - Physical activity history - Height, weight, BMI, WC (other anthropometric measures) - Gestational weight gain - Blood pressure - Risk of specific nutritional problems (low nutrient density), deficiencies during specific diets or under-nutrition) - First trimester - Folate - Vitamin B12 - Iodine - PUFAs - Second and third trimesters - Iron, iodine, zinc, copper, calcium - Folate, B vitamins, vitamin D - Energy (+450 kcal/day) - Iodine - PUFAs	- Dietary counselling - Safe levels of exercise - Sedentary time - Weight management and gestational weight gain - Risky behaviors and exposures - Tobacco, alcohol - recreational drugs - Sources of food borne infection - Pregnancy complication screening and management (GDM, blood pressure) - Supplementation - Folic acid supplementation 400 µ/day - Iron supplementation 30-60 mg/day - Other nutrients as required (iodine, vitamin B12, vitamin D)

The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: “Think Nutrition First”#



Nutrizione e differenze di genere

Uomini e donne si differenziano per il **metabolismo basale**, quello delle donne risulta più basso (5-15%). I **fabbisogni nutrizionali** sono diversi: le donne consumano meno energia, sebbene in alcune fasi o condizioni della loro vita i fabbisogni aumentino (**gravidanza, allattamento**).



Il **fabbisogno proteico** è lo stesso per donne e uomini, ma poiché viene calcolato in base al peso corporeo, la quantità in grammi di proteine da consumare giornalmente è inferiore nella donna rispetto all'uomo.

Stessa cosa per i **grassi** e per i **carboidrati**, i cui fabbisogni nutritivi vanno calcolati anche in base all'età, al tipo di attività fisica, al tipo di lavoro, allo stato ormonale, etc.





LIVELLI DI ASSUNZIONE DI RIFERIMENTO IN GRAVIDANZA

LIPIDI:

TOTALI 20-35% En

SFA <10%

PUFA 5-10% (**n-6** 4-8%, **n-3** 0,5-2%)

EPA-DHA 250mg/die+DHA 100-200mg/die

Acidi grassi trans il meno possibile

PROTEINE:

I trimestre +0,5g/die*

II trimestre +6g/die*

III trimestre +19,9 g/die*

ASSUNZIONE DI ACQUA:

+350 ml/die

MINERALI:

Calcio: 850 mg/die*

Ferro: 22 mg/die*

Zinco: 9 mg/die*

VITAMINE:

Riboflavina: 1,6 mg/die* Folati 600 mcg/die**

Niacina: 17 mg/die* Vit. B12 4,5 mcg/die**

Vit. B6: 1,6 mg/die*

Vit. D: 10 mcg/die*

Vit. A: 540 mcg/die*

*AR Fabbisogno medio

** AI Assunzione adeguata



LIVELLI DI ASSUNZIONE DI RIFERIMENTO IN ALLATTAMENTO

LIPIDI:

TOTALI 20-35% En

SFA <10%

PUFA 5-10% (**n-6** 4-8%, **n-3** 0,5-2%)

EPA-DHA 250mg/die+DHA 100-200mg/die

Acidi grassi trans il meno possibile

PROTEINE:

I semestre +16g/die*

II semestre +11g/die*

ASSUNZIONE DI ACQUA:

+700 ml/die

MINERALI:

Calcio: 850 mg/die*

Ferro: 8 mg/die*

Zinco: 10 mg/die*

VITAMINE:

Riboflavina: 1,6 mg/die* Folati 500 mcg/die**

Niacina: 17 mg/die* Vit. B12 5 mcg/die**

Vit. B6: 1,7 mg/die*

Vit. D: 10 mcg/die*

Vit. A: 1020 mcg/die*

*AR Fabbisogno medio

** AI Assunzione adeguata

Take home messages

- ✓ **La salute preconcezionale influisce significativamente sugli esiti di gravidanza e sulla salute a lungo termine della prole.**
- ✓ **Le donne in età fertile mostrano maggiore adesione ai controlli sanitari,** ma sono anche soggette a un maggiore carico psico-sociale e a pressioni legate alla fertilità e alla gestazione, fattori che influenzano anche la salute mentale.
- ✓ **La salute preconcezionale maschile è spesso trascurata,** nonostante evidenze crescenti indichino che obesità, fumo, esposizione a tossici ambientali e dieta influenzano la qualità del liquido seminale, la fertilità e la salute della prole attraverso meccanismi epigenetici.
- ✓ **Fattori di rischio modificabili preconcepimento** impattano diversamente uomini e donne a causa di differenze biologiche, ormonali e comportamentali, e richiedono quindi approcci preventivi e terapeutici sensibili al genere.
- ✓ **L'integrazione della prospettiva di genere nei percorsi di salute preconcezionale è essenziale per migliorare gli esiti clinici e promuovere equità** nella salute riproduttiva.





Dip. Scienze Biomediche, Sperimentali e Cliniche “Mario Serio” SOD Andrologia, Endocrinologia Femminile e Incongruenza di Genere

Direttore Prof. LINDA VIGNOZZI

EQUIPE CLINICA

Dr. Sarah Cipriani
Dr. Elisa Maseroli
Dr. Noemi Fralassi
Dr. Francesca Frizza
Prof. Csilla Krausz
Prof. Giulia Rastrelli
Prof. Francesco Lotti
Dr. Alessandra Fisher
Dr. Matteo Vannucci
Dr. Alessia Romani
Dr. Chiara Alfaroli

PSICOLOGIA

D. Francesca Mazzoli
Dr. Teresa Angotti
Prof. Giovanni
Castellini

NUTRIZIONE

Dr. Michela Cirillo

EQUIPE DI LABORATORIO

Dr. Sandra Filippi
Dr. Ilaria Cellai
Dr. Paolo Comeglio

LABORATORIO SEMINOLOGIA

Dr. Sara Marchiani
Dr. Lara Tamburrino
Dr. Selene Degl’Innocenti
Dr. Sara Dabizzi
Dr. Marisa Fino
Dr. Gabriella Torcia

LABORATORIO SPETTROMETRIA DI MASSA

Dr. Fabio Villanelli

