INOSITOLI e DIABETE in GRAVIDANZA

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Conflitti di interesse

- Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

Takeda

MSD

Bruno

LA GRAVIDANZA DIABETICA IN ITALIA

Il diabete complica dall'8 al 25% delle gravidanze a seconda degli studi e delle popolazioni, e rappresenta la più frequente complicanza non ostetrica.

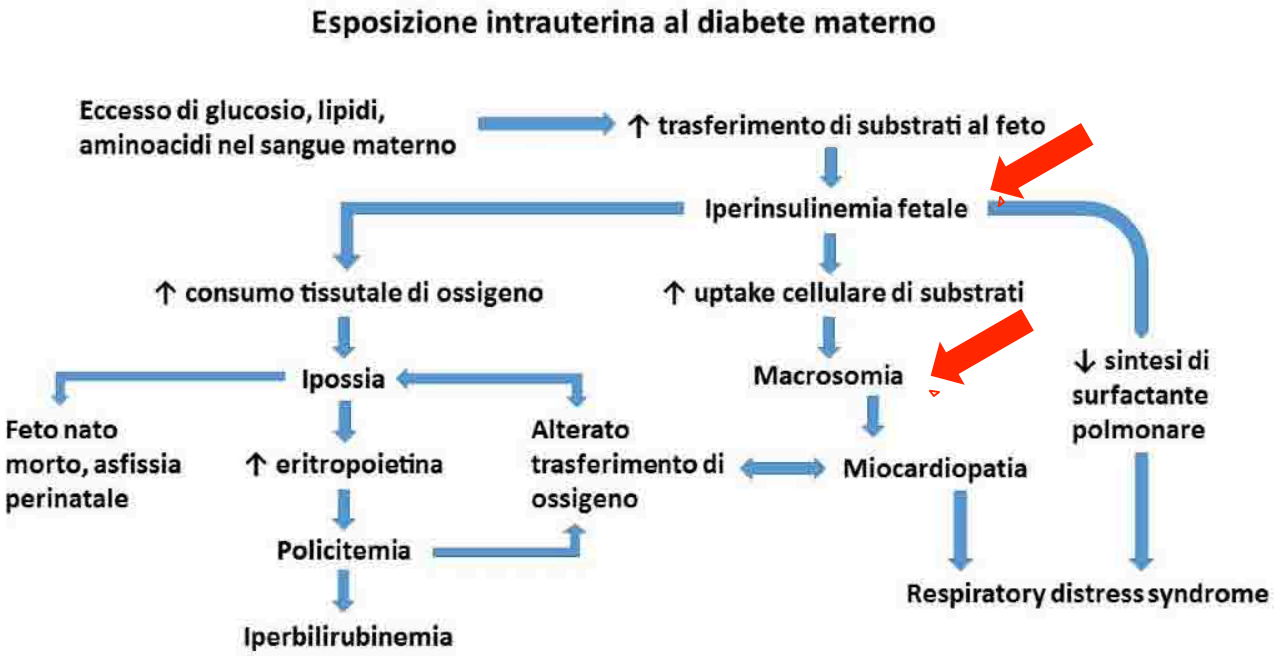
La maggior parte delle donne è affetta da diabete gestazionale e solo circa l'1% è affetta da diabete pregestazionale, sia tipo 1 che tipo 2; sia il diabete gestazionale che il diabete tipo 2 sono in progressivo aumento con l'incremento dell'obesità nel nostro paese soprattutto nella popolazione più giovane (1, 2).

Nonostante i notevoli progressi nel monitoraggio e cura del diabete in gravidanza, le gravidanze complicate da diabete presentano ancora un'elevata incidenza di outcome avversi (1-6).

	Pregnancy	Labor	Postpartum and beyond
Mother 	↑ Pre-eclampsia	↑ Induction of labor ↑ Cesarean section ↑ Operative deliveries ↑ Labor complications	↑ Recurrent GDM ↑ Type 2 diabetes
Offspring 	**Congenital** – CNS – Cardiac Fetal programming – ↑ LGA – ↑ Macrosomia – Increased fat mass	**Neonatal complications** Prematurity Perinatal asphyxia Respiratory distress Metabolic complications (hypoglycemia and hypocalcemia) Polycythemia and hyperviscosity Low iron stores Hyperbilirubinemia Cardiomyopathy	**Long-term outcome** ↑ Obesity ↑ Type 1 diabetes ↑ Type 2 diabetes ↑ Metabolic syndrome

Nonostante i notevoli progressi nel monitoraggio e cura del diabete in gravidanza, le gravidanze complicate da diabete presentano ancora un'elevata incidenza di outcome avversi (1-6).

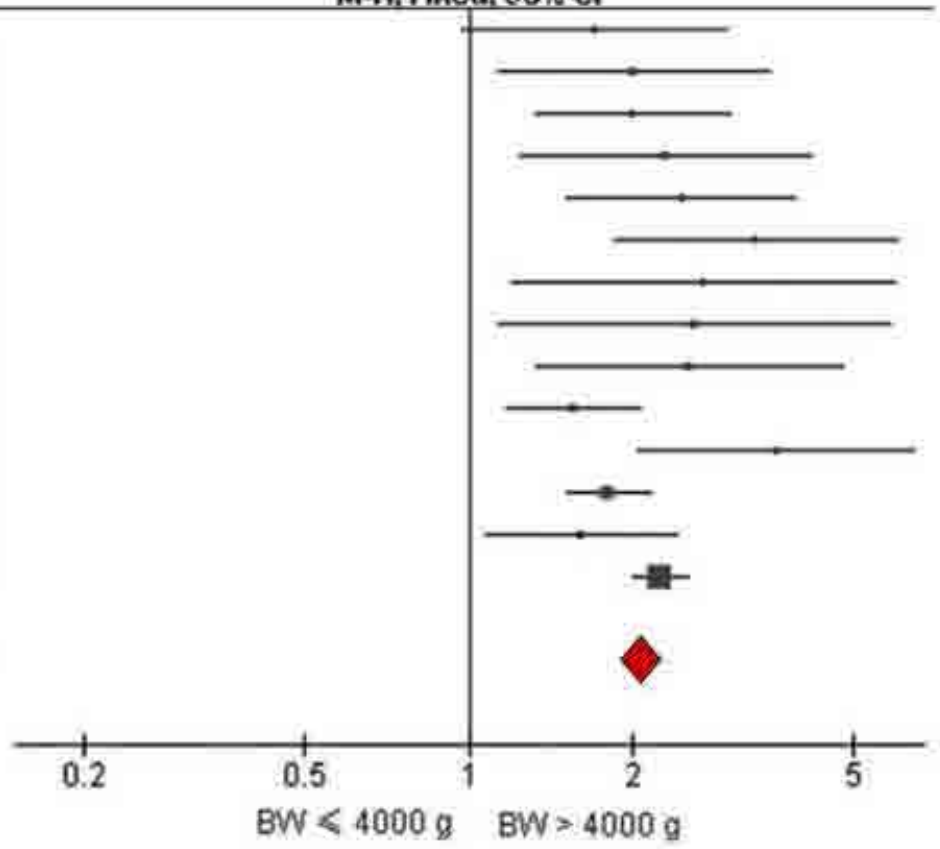
a breve termine



Study or Subgroup	BW > 4000 g Events	Total	BW ⩽ 4000 g Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Che 2010	16	142	106	1526	2.2%	1.70 [0.98, 2.97]
Gu 2003	16	163	69	1336	1.9%	2.00 [1.13, 3.53]
He (a) 2000	74	114	388	805	4.7%	1.99 [1.32, 2.99]
He (b) 2005	14	143	57	1256	1.5%	2.28 [1.24, 4.21]
Hirschler 2008	28	95	136	932	2.5%	2.45 [1.52, 3.94]
Li 2007	36	141	20	214	1.6%	3.33 [1.83, 6.04]
Lu 2008	8	52	52	819	0.7%	2.68 [1.20, 5.99]
Mao 2007	21	30	115	242	1.1%	2.58 [1.13, 5.85]
Monteiro 2003	13	81	70	992	1.2%	2.52 [1.33, 4.78]
Ruan 2009	82	260	488	2135	10.0%	1.55 [1.17, 2.06]
Shi 2007	54	75	80	193	1.7%	3.63 [2.03, 6.49]
Wang 2009	179	1537	640	9360	22.0%	1.80 [1.51, 2.14]
Yang 2009	72	120	290	601	5.3%	1.61 [1.08, 2.40]
Zhang 2009	456	1977	1642	13875	43.6%	2.23 [1.99, 2.51]
Total (95% CI)		**4930**		**34286**	**100.0%**	**2.07 [1.91, 2.24]**
Total events	1069		4153			

Heterogeneity: Chi² = 17.87, df = 13 (P = 0.16); I^2 = 27%

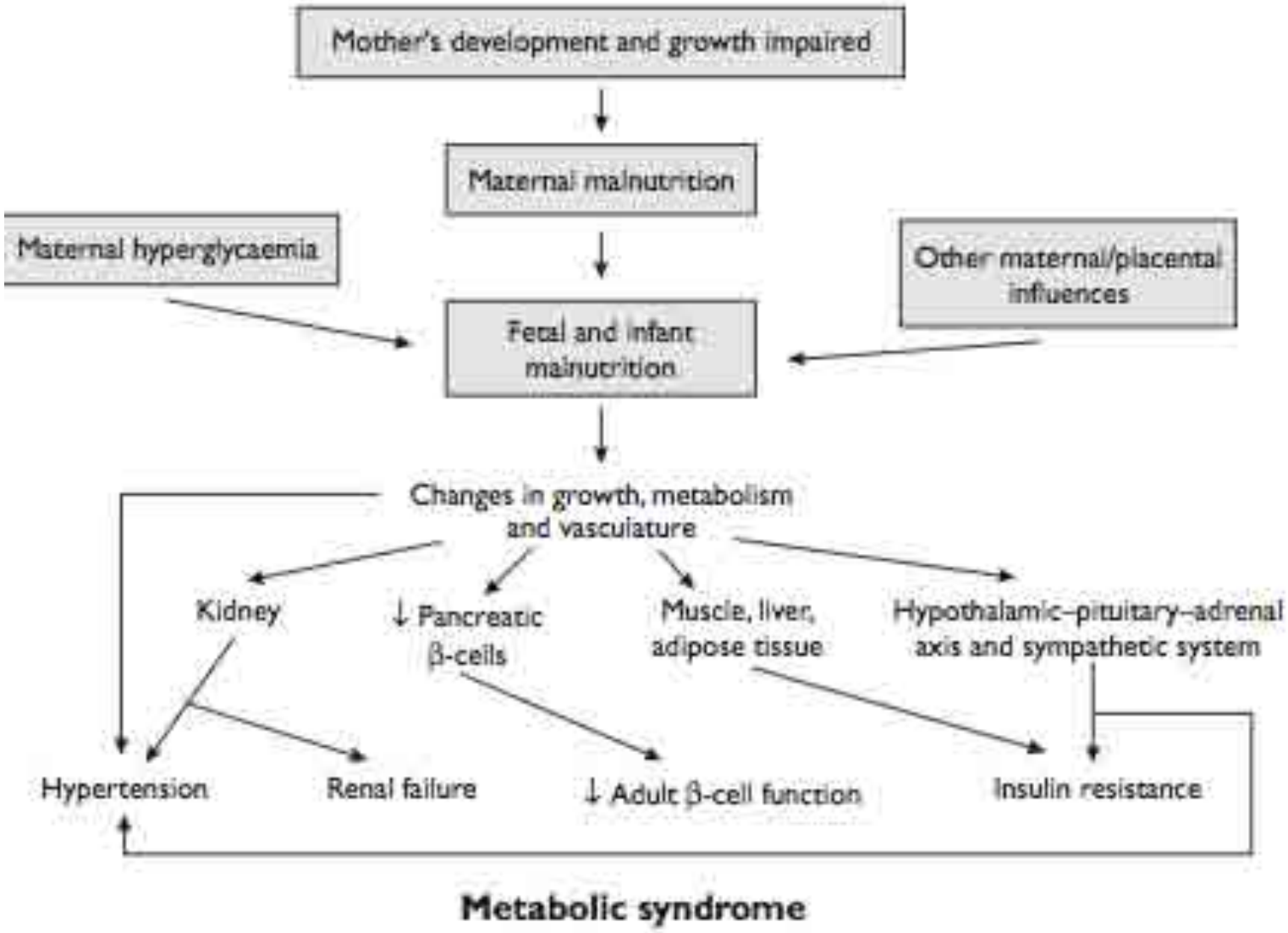
Test for overall effect: Z = 17.75 (P < 0.00001)



Birthweight >4 kg doubles: 2x adult obesity

Systematic review & meta-analysis

Yu et al. Obes Rev. 2011;12:525-42.



Yu et al. Obes Rev. 2011;12:525-42.

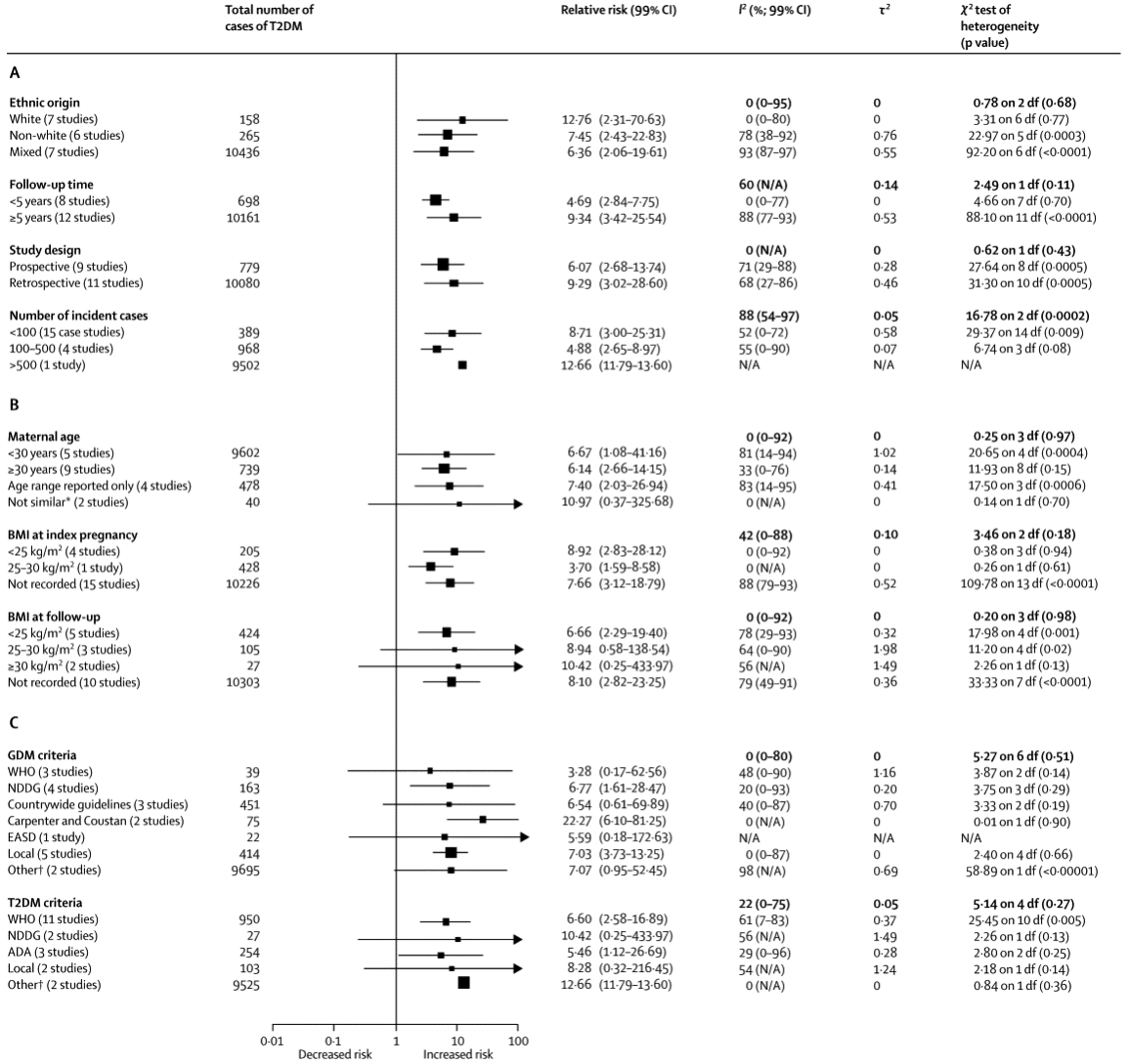

Environment Special:
The oceans—why 70%
of our planet is in danger
The Facebook Movie:
The secret history of
social networking
TIME
How the
first nine
months
shape
the rest
of your life
The new science
of fetal origins
BY ANNIE MURPHY PAUL

Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis

revisione sistematica (20 RCT, n=675.455)

31.867 pt GDM

rischio aumentato (RR: **7,43**; intervallo di confidenza al 95%, IC 95%: 4,79-11,51) di DMT2 almeno 6 settimane dopo la fine della gravidanza indice, rispetto alle 643.588 donne non affette da GDM



	Total number of cases of T2DM	Relative risk (99% CI)	I^2 (%; 99% CI)	τ^2	χ^2 test of heterogeneity (p value)
A					
Ethnic origin			**0 (0–95)**	**0**	**0·78 on 2 df (0·68)**
White (7 studies)	158	12·76 (2·31–70·63)	0 (0–80)	0	3·31 on 6 df (0·77)
Non-white (6 studies)	265	7·45 (2·43–22·83)	78 (38–92)	0·76	22·97 on 5 df (0·0003)
Mixed (7 studies)	10436	6·36 (2·06–19·61)	93 (87–97)	0·55	92·20 on 6 df (<0·0001)
Follow-up time			**60 (N/A)**	**0·14**	**2·49 on 1 df (0·11)**
<5 years (8 studies)	698	4·69 (2·84–7·75)	0 (0–77)	0	4·66 on 7 df (0·70)
≥5 years (12 studies)	10161	9·34 (3·42–25·54)	88 (77–93)	0·53	88·10 on 11 df (<0·0001)
Study design			**0 (N/A)**	**0**	**0·62 on 1 df (0·43)**
Prospective (9 studies)	779	6·07 (2·68–13·74)	71 (29–88)	0·28	27·64 on 8 df (0·0005)
Retrospective (11 studies)	10080	9·29 (3·02–28·60)	68 (27–86)	0·46	31·30 on 10 df (0·0005)
Number of incident cases			**88 (54–97)**	**0·05**	**16·78 on 2 df (0·0002)**
<100 (15 case studies)	389	8·71 (3·00–25·31)	52 (0–72)	0·58	29·37 on 14 df (0·009)
100–500 (4 studies)	968	4·88 (2·65–8·97)	55 (0–90)	0·07	6·74 on 3 df (0·08)
>500 (1 study)	9502	12·66 (11·79–13·60)	N/A	N/A	N/A
B					
Maternal age			**0 (0–92)**	**0**	**0·25 on 3 df (0·97)**
<30 years (5 studies)	9602	6·67 (1·08–41·16)	81 (14–94)	1·02	20·65 on 4 df (0·0004)
≥30 years (9 studies)	739	6·14 (2·66–14·15)	33 (0–76)	0·14	11·93 on 8 df (0·15)
Age range reported only (4 studies)	478	7·40 (2·03–26·94)	83 (14–95)	0·41	17·50 on 3 df (0·0006)
Not similar* (2 studies)	40	10·97 (0·37–325·68)	0 (N/A)	0	0·14 on 1 df (0·70)
BMI at index pregnancy			**42 (0–88)**	**0·10**	**3·46 on 2 df (0·18)**
<25 kg/m² (4 studies)	205	8·92 (2·83–28·12)	0 (0–92)	0	0·38 on 3 df (0·94)
25–30 kg/m² (1 study)	428	3·70 (1·59–8·58)	0 (N/A)	0	0·26 on 1 df (0·61)
Not recorded (15 studies)	10226	7·66 (3·12–18·79)	88 (79–93)	0·52	109·78 on 13 df (<0·0001)
BMI at follow-up			**0 (0–92)**	**0**	**0·20 on 3 df (0·98)**
<25 kg/m² (5 studies)	424	6·66 (2·29–19·40)	78 (29–93)	0·32	17·98 on 4 df (0·001)
25–30 kg/m² (3 studies)	105	8·94 (0·58–138·54)	64 (0–90)	1·98	11·20 on 4 df (0·02)
≥30 kg/m² (2 studies)	27	10·42 (0·25–433·97)	56 (N/A)	1·49	2·26 on 1 df (0·13)
Not recorded (10 studies)	10303	8·10 (2·82–23·25)	79 (49–91)	0·36	33·33 on 7 df (<0·0001)
C					
GDM criteria			**0 (0–80)**	**0**	**5·27 on 6 df (0·51)**
WHO (3 studies)	39	3·28 (0·17–62·56)	48 (0–90)	1·16	3·87 on 2 df (0·14)
NDDG (4 studies)	163	6·77 (1·61–28·47)	20 (0–93)	0·20	3·75 on 3 df (0·29)
Countrywide guidelines (3 studies)	451	6·54 (0·61–69·89)	40 (0–87)	0·70	3·33 on 2 df (0·19)
Carpenter and Coustan (2 studies)	75	22·27 (6·10–81·25)	0 (N/A)	0	0·01 on 1 df (0·90)
EASD (1 study)	22	5·59 (0·18–172·63)	N/A	N/A	N/A
Local (5 studies)	414	7·03 (3·73–13·25)	0 (0–87)	0	2·40 on 4 df (0·66)
Other† (2 studies)	9695	7·07 (0·95–52·45)	98 (N/A)	0·69	58·89 on 1 df (<0·00001)
T2DM criteria			**22 (0–75)**	**0·05**	**5·14 on 4 df (0·27)**
WHO (11 studies)	950	6·60 (2·58–16·89)	61 (7–83)	0·37	25·45 on 10 df (0·005)
NDDG (2 studies)	27	10·42 (0·25–433·97)	56 (N/A)	1·49	2·26 on 1 df (0·13)
ADA (3 studies)	254	5·46 (1·12–26·69)	29 (0–96)	0·28	2·80 on 2 df (0·25)
Local (2 studies)	103	8·28 (0·32–216·45)	54 (N/A)	1·24	2·18 on 1 df (0·14)
Other† (2 studies)	9525	12·66 (11·79–13·60)	0 (N/A)	0	0·84 on 1 df (0·36)

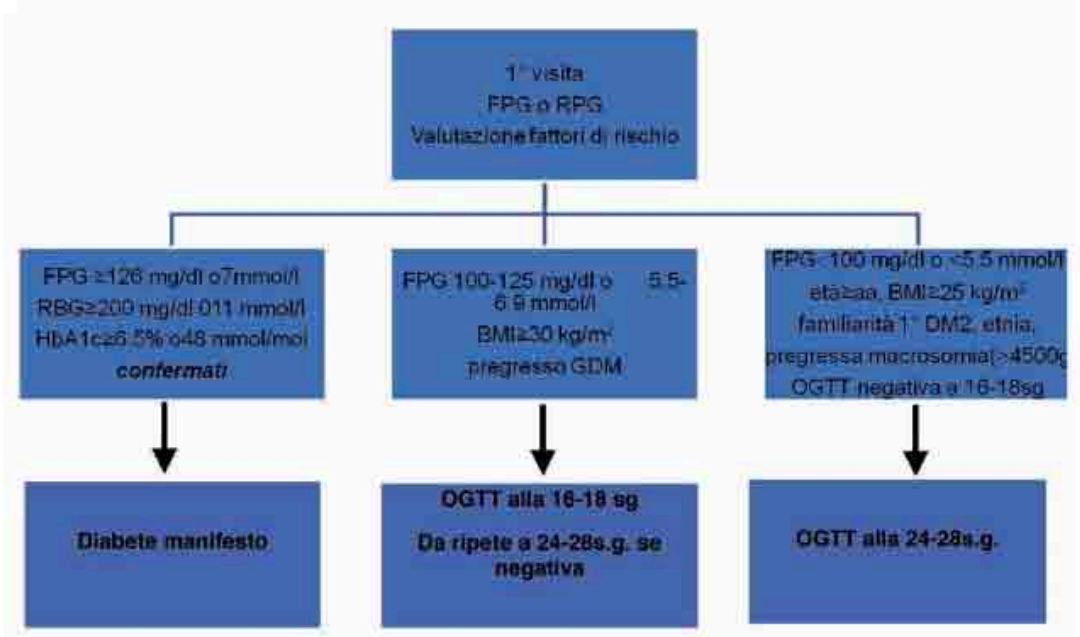
0·01 0·1 1 10 100
Decreased risk Increased risk

Leanne Bellamy, Volume 373, Issue 9677, 2009, 1773–1779

I fattori di rischio Anamnestici Maggiori sono:
il pregresso Diabete Gestazionale,
la familiarità di 1° grado per diabete,
l'appartenenza ad un gruppo etnico ad elevato rischio per lo sviluppo del diabete,
l'età > 35 anni, la presenza di obesità, la familiarità per diabete, la parità.
l' obesità, l' età >35 anni,
la pregressa macrosomia fetale (>4 Kg) o LGA (>90° C) e
la mortalità perinatale da causa ignota.

I fattori di rischio Anamnestici Minori sono:
il sovrappeso,
l'ipertensione arteriosa,
la presenza di 2 o più aborti spontanei,
il polidramnios,
la gestosi,
l'elevata parità o anche la presenza di parti pre-termine.

Figura 1 ◆ lo screening del diabete gestazionale secondo le Linee Guida per la Gravidanza Fisiologica del Ministero della Salute (2011).



FPG = fasting plasma glucose; RBC = Random plasma glucose; DM2 = diabete tipo 2; OGTT = curva da carrico di glucosio, s.g. settimana gestazionale.

Effetti della gravidanza sul metabolismo

La gravidanza è una condizione diabetogena.

•Fasi precoci della gestazione: insulino-sensibilità anabolismo e lipogenesi

•Terzo trimestre di gestazione: insulino-resistenza tendenza all'iperglicemia per mantenere un adegua livello di glucosio per le necessità fetali e lipolisi per soddisfare le necessità energetiche materne. A term della gravidanza il profilo lipidico presenterà un aum della concentrazione di colesterolo, trigliceridi, LDL

Le pazienti soggette a fattori di rischio per lo svilupp Diabete raggiungeranno più facilmente il valore sog condurrà all'intolleranza ai carboidrati.

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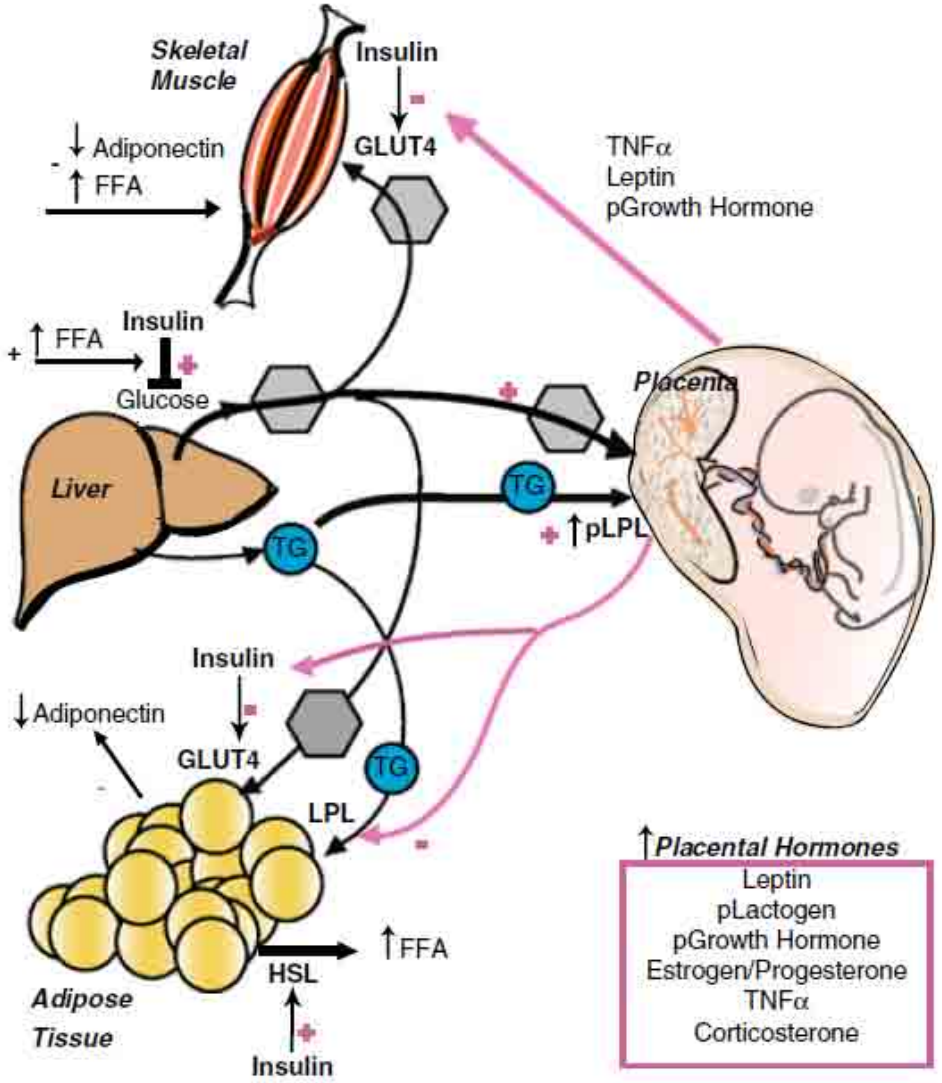


Effetti della gravidanza sul Metabolismo glucidico e insulinico

Glicemia	↓ Nello stato di digiuno ↑ In condizioni postprandiali	
Secrezione insulinica		
- A Digiuno	↑ Gravidanza normale	↑ Diabete Gestazionale
- Dopo Carico Glucidico		
1ª fase	↑↑ Gravidanza Normale	↑ Diabete Gestazionale
2ª fase	↑ Gravidanza Normale	↑ Diabete Gestazionale
Insulino-Resistenza	↑ Gravidanza Normale	↑↑ Diabete Gestazionale
Organo Bersaglio	Tessuto Muscolare	

L'insulino resistenza, che compare soprattutto nella seconda metà della gestazione, fa della gravidanza una condizione diabetogena ed il Diabete Gestazionale (GDM) compare solo in concomitanza di fattori predisponenti di natura genetica e/o ambientale.

G.Di Cianni et all.:Il Diabete 2001

Metformin *Versus* Placebo from First Trimester to Delivery in Polycystic Ovary Syndrome: A Randomized, Controlled Multicenter Study

TABLE 2. Primary endpoints

	Metformin [n (%)]	Placebo [n (%)]	Risk difference (%)	95% CI	*P* value
Preeclampsia	10/135 (7.4)	5/135 (3.7)	3.7	−1.7–9.2	0.18
Preterm delivery[a]	5/135 (3.7)	11/135 (8.2)	−4.4	−10.1–1.2	0.12
New GDM	22/125 (17.6)	21/124 (16.9)	0.8	−8.6–10.2	0.87
Composite primary endpoints	35/135 (25.9)	33/135 (24.4)	1.5	−8.9–11.3	0.78

New GDM was diagnosed after inclusion in the study. Composite endpoints were calculated as follows: if one patient had two complications, it was counted as one composite outcome.

Primary outcomes

There were no differences between the groups in the prevalence of preeclampsia, preterm delivery, GDM, or the composite of these three pregnancy complications (Table 2).

J Clin Endocrinol Metab, December 2010, 95(12):E448–E455

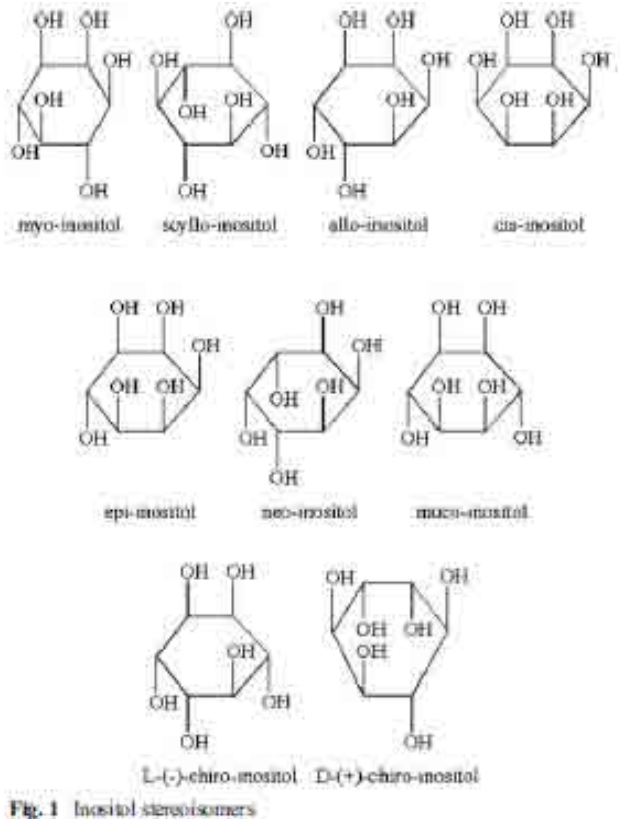


Fig. 1 Inositol stereoisomers

Significant Sources of Myo-Inositol (MI)

Endogenous synthesis: 2-4g MI/day may be produced from glucose in humans.

MI occurs in foods as:
1. Phytic acid (also called myo-inositol hexaphosphate or IP6) is often a component of the insoluble fiber of the bran found in seeds. Significant amounts of IP6 are found in grains, legumes, nuts or certain citrus fruits.
2. Phosphatidyl-myo-inositol is found in plant- and animal-derived foods.
Estimated average MI intake is 900 mg/day

Supplements: MI and IP6

Significant sources of D-*Chiro*-Inositol (DCI)

Foods: buckwheat, soy, lentils, beans, wheat germ

Supplements: DCI (derived from demethylating pinitol found in carob)

Significant sources of D-Pinitol (methylated DCI)

Foods: carob, soy

Supplements: pinitol

Inositol Phosphates IP1 to IP6

IP6 is converted to MI or IP1 to IP5 by intestinal flora and in human metabolism

(MI) Myo-Inositol

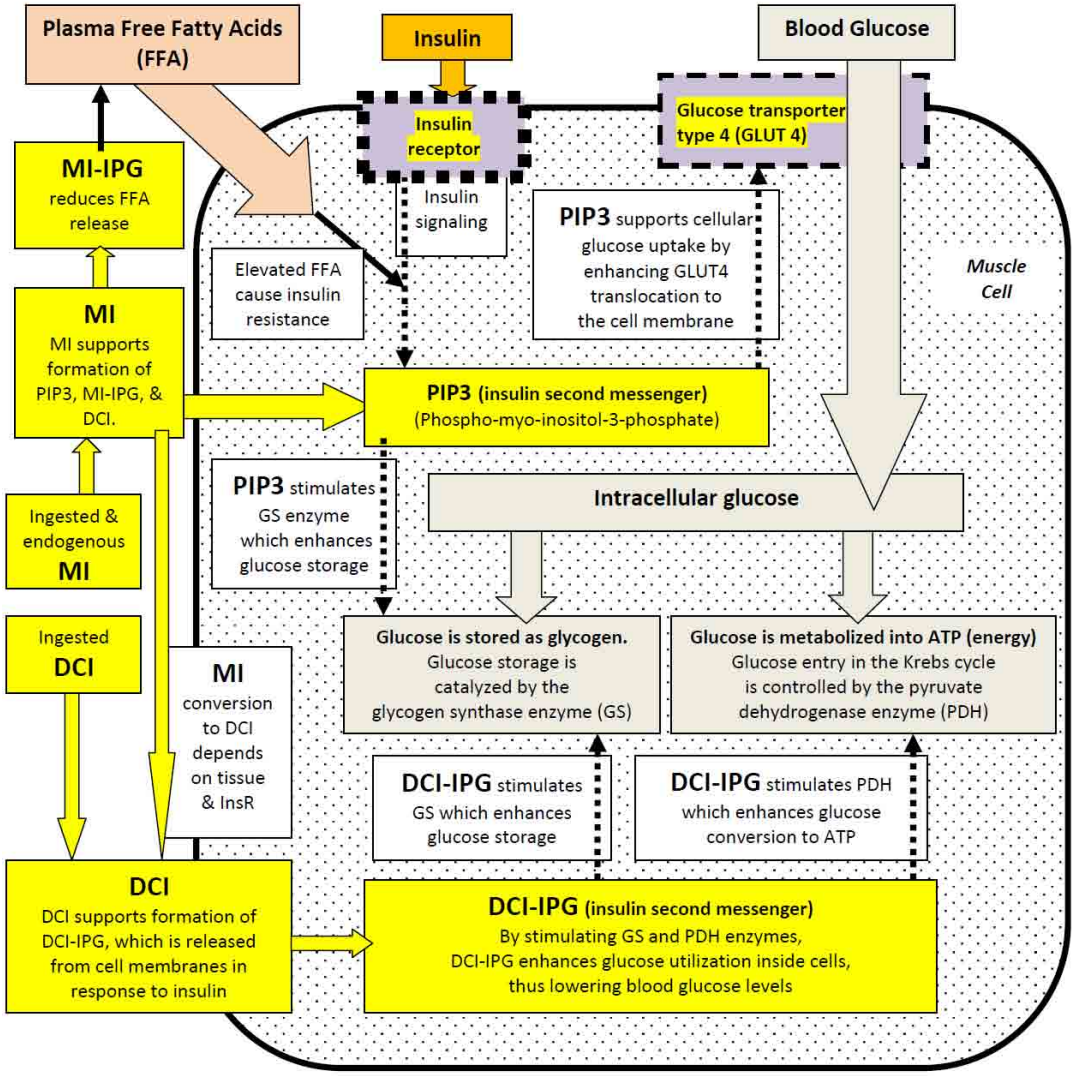
Phosphatidylinositols (PI) & Phosphatidylinositol-Phosphates (PIP)

MI to DCI conversion (about 8%) is catalyzed by an epimerase enzyme. Its activity may be reduced in the state of insulin resistance to as low as 1%, for example.

D-*Chiro*-Inositol (DCI)

Approx. 33% of pinitol may be converted to DCI in humans. It is not clear if pinitol can be utilized in human physiology without first being converted to DCI

D-Pinitol (Methylated DCI)



Function	Benefits
Cell survival and growth	Essential for the growth an survival of cells [5•]
Central nervous system	MI is essential for the development and function of peripheral nerves [8]
Osteogenesis	Increase calcium in bone
	Increase the bone structure strength
	MI is essential to bone formation, osteogenesis and bone mineral density [9]
Mood	MI is proposed as selective serotonin reuptake inhibitor-like role [10]
Reproduction	Restore normal ovulatory activity [11]
	Increase oocyte and egg quality [12, 13]
	Increase fertilization rate
	Increase sperm motility and mitochondrial membrane potential in vitro [14, 15]
Metabolism	Increase insulin sensitivity (reduce HOMA-IR, reduce glycemia, reduce insulinemia)
	Reduce total and LDL cholesterol
	Increase HDL cholesterol
	Reduce serum triglycerides [11, 16–19]

HDL high-density lipoprotein, *HOMA-IR* homeostatic model assessment and insulin resistance, *LDL* low-density lipoprotein, *MI* myo-inositol

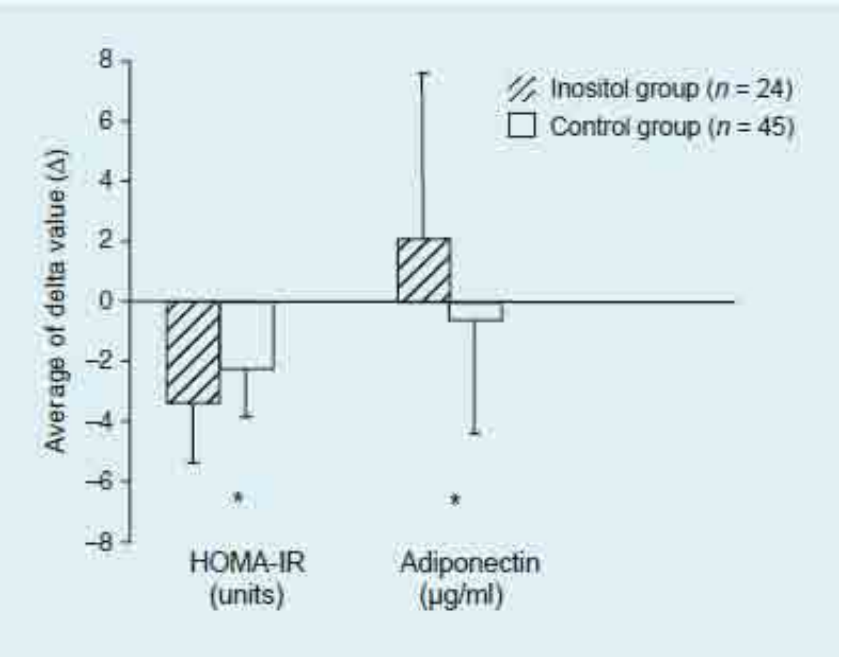
Da Curr Diab Rep (2016) 16: 30

The effect of myoinositol supplementation on insulin resistance in patients with gestational diabetes

F. Corrado, R. D'Anna, G. Di Vieste*, D. Giordano, B. Pintaudi*, A. Santamaria and A. Di Benedetto*

	Inositol group (n = 24)		Control group (n = 45)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Age (years)	28.7 ± 3.5		28.4 ± 3.7	
Pre-pregnancy BMI (kg/m^2)	25.1 ± 4.7		24.2 ± 4.1	
Parity ≥ 1 (N)	10		15	
Gestational age at OGTT (weeks)	26.0 ± 0.6		26.3 ± 0.8	
Weight increase in pregnancy (kg)	7.5 ± 3.6	10.2 ± 5.1	8.4 ± 4.4	10.7 ± 6.3
Fasting glucose (mmol/l)	5.5 ± 0.3	4.6 ± 0.3*	5.4 ± 0.2	5.1 ± 0.3*
Fasting insulin (μIU/ml)	31.2 ± 7.1	19.0 ± 5.8*	33.9 ± 5.3	26.0 ± 6.8*
HOMA-IR (units)	6.9 ± 1.7	3.5 ± 1.1*	7.4 ± 1.1	5.3 ± 1.4*
Adiponectin (μg/ml)	12.8 ± 5.1	16.1 ± 6.6	12.2 ± 4.6	11.3 ± 4.8

All continuous variables are expressed as mean ± SD.
*Statistical significance ($P < 0.05$), obtained from paired Student's t-test, of the post-treatment with respect to the pre-treatment value.
HOMA-IR, homestasis model assessment of insulin resistance.



Results There were 69 evaluable patients, 24 in the study group and 45 in the control group. Fasting glucose and insulin, and consequently homeostasis model assessment of insulin resistance, decreased in both groups (50% in the study group vs. 29% in the control group), but the decline in the study group was significantly greater than that in the control group (P = 0.0001). Adiponectin increased in the myoinositol group while it decreased in the control group (P = 0.009).

Conclusion Myoinositol improves insulin resistance in patients with gestational diabetes.

Diabet. Med. 28, 972–975 (2011)

Clinical Care/Education/Nutrition/Psychosocial Research

ORIGINAL ARTICLE

myo-Inositol Supplementation and Onset of Gestational Diabetes Mellitus in Pregnant Women With a Family History of Type 2 Diabetes

A prospective, randomized, placebo-controlled study

Table 2—*OGTT evaluation in both groups*

	myo-Inositol	Placebo	*P*
N	99	98	
Weight increase at OGTT (kg)	7.2 ± 2.6	7.0 ± 3.0	0.29
Gestational age at OGTT (days)	182 ± 9.8	184 ± 10	0.27
Fasting glucose OGTT (mg/dL)	77.0 ± 6.7	80.5 ± 8.1	0.001
1-h glucose OGTT (mg/dL)	123.0 ± 30.6	133.0 ± 30.5	0.02
2-h glucose OGTT (mg/dL)	105.6 ± 22.0	110.1 ± 26.5	0.2

Data are means ± SD.

Outcomes	*myo*-Inositol	Placebo	*P*
N	99	98	
Gestational age at delivery (days)	274 ± 11.5	275 ± 12.3	ns
Birth weight (g)	3,111 ± 447	3,273 ± 504	0.018
Macrosomia (>4,000 g)	0	7	0.007
Caesarean section (%)	42.4	43.8	ns
Gestational hypertension	3	2	ns
Preterm delivery	3	4	ns
Shoulder dystocia	1	2	ns
Neonatal hypoglycemia	0	0	ns
Distress respiratory syndrome	1	1	ns

Data are means ± SD, percent (%), or *n* unless otherwise indicated. ns, not significant.

RESULTS—Incidence of GDM was significantly reduced in the *myo*-inositol group compared with the placebo group: 6 vs. 15.3%, respectively ($P = 0.04$). In the *myo*-inositol group, a reduction of GDM risk occurrence was highlighted (odds ratio 0.35). A statistically significant reduction of fetal macrosomia in the *myo*-inositol group was also highlighted together with a significant reduction in mean fetal weight at delivery. In the other secondary outcome measures, there were no differences between groups.

CONCLUSIONS— *myo*-Inositol supplementation in pregnant women with a family history of type 2 diabetes may reduce GDM incidence and the delivery of macrosomia fetuses.

Diabetes Care 36:854–857, 2013

Effect of dietary myo-inositol supplementation in pregnancy on the incidence of maternal gestational diabetes mellitus and fetal outcomes: a randomized controlled trial

Table 2. Intention-to-treat analysis: Primary and non-parametric secondary outcomes in women with gestational diabetes randomized to receive control treatment (folic acid: $n = 38$) or myo-inositol treatment (myo-inositol and folic acid: $n = 35$).

Outcome	Control group (n (%))	Myo-inositol group (n (%))	RR (95% CI)	p
Primary outcome				
Abnormal maternal OGTT	27/38 (71)	2/35 (6)	0.127 (0.032–0.502)	0.001
Secondary outcomes				
Insulin therapy	8/38 (21)	1/35 (3)	0.136 (0.018–1.031)	0.053
Polyhydramnios	7/38 (18)	1/35 (3)	0.072 (0.004–1.219)	0.068
Neonatal hypoglycemia	10/38 (26)	0/35 (0)	0.052 (0.003–0.849)	0.038

Outcome	Control group mean (SD)	Myo-inositol group mean (SD)	p	95% CI
Secondary outcomes				
Gestational age at OGTT	26.8 (1.8)	26.9 (1.2)	0.656	−0.898–0.569
OGTT				
0 min	5.1 (0.5)	4.7 (0.4)	0.001	3.300–11.157
60 min	8.5 (2.1)	7.6 (1.5)	0.040	0.780–32.171
120 min	7.1 (1.9)	6.4		
BMI increase	3.8 (2.4)	2.3		
Time diagnosis-OGTT (weeks)	13.1 (4.8)	14.8		
Fetal biparietal diameter percentiles	61.2 (20.0)	71.6		
Fetal head circumference percentiles	62.2 (14.2)	60.9		
Fetal femur length percentiles	58.7 (15.2)	63.4		
Fetal abdominal circumference percentiles	65.6 (22.1)	41.7		
Gestational age at delivery	37.2 (2.04)	39.3		
Birth weight (grams)	3251 (617)	3267		
Birth weight (percentiles)	56.6 (25.9)	42.8		

 DOI: 10.3109/14767058.2013.766691

Results: Thirty-six women were allocated to receive myo-inositol and 39 placebo. The incidence of GDM in mid-pregnancy was significantly reduced ($p = 0.001$) in women randomized to receive myo-inositol compared to placebo (relative risk 0.127). Women randomized to receive myo-inositol also required less insulin therapy, delivered at a later gestational age, had significantly smaller babies with fewer episodes of neonatal hypoglycemia.

Conclusions: Myo-inositol supplementation in pregnancy reduced the incidence of GDM in women at high risk of this disorder. The reduction in incidence of GDM in the treatment arm was accompanied by improved outcomes.

European Review for Medical and Pharmacological Sciences 2014; 18: 270-274

Myo-inositol, D-chiro-inositol, folic acid and manganese in second trimester of pregnancy: a preliminary investigation

A. MALVASI[1], F. CASCIARO[2], M.M. MINERVINI[2], I. KOSMAS[3], O.A. MYNBAEV[4], E. PACELLA[5], V. MONTI CONDESNITT[6], A. CREANZA[1], G.C. DI RENZO[7], A. TINELLI[8]

Table I. Baseline clinical characteristics and hematochemical parameters of two groups. Data are mean ± SD.

Variables	Control group (n = 24)	MDFM group (n = 24)	p*
Age	31.58 ± 5.66	32.2 ± 5.46	0.4854
Parity	1.04 ± 0.9	1.08 ± 0.97	0.8780
BMI	26.8 ± 0.22	26.98 ± 0.22	0.4042
Total Chol	225.54 ± 2.01	230.08 ± 2.01	0.0819
LDL	150.7 ± 11.39	163.16 ± 10.8	0.0003
HDL	74.83 ± 8.79	66.91 ± 7.64	0.0017
TG	176.29 ± 9.11	178.54 ± 7.54	0.2472
Glucose (blood)	79.70 ± 7.72	81.04 ± 5.63	0.3458
Mean pressure (systolic)	125.62 ± 6.30	122.5 ± 6.42	0.095
Mean pressure (diastolic)	83.75 ± 4.23	77.5 ± 8.34	0.002

*Statistical analysis was obtained with Student's t-test between the two group.

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Table II. Comparison of clinical characteristics and hematochemical parameters of two groups at time 30 and 60 days. Data are mean ± SD.

Variables	Time = 30			Time = 60		
	Control group (n = 24)	MDFM group (n = 24)	p*	Control group (n = 24)	MDFM group (n = 24)	p*
Total Chol	225.79 ± 10.67	209.54 ± 6.6	0.0001	232.66 ± 8.82	185.37 ± 10.8	0.0001
LDL	154.16 ± 12.04	141.95 ± 12.57	0.0013	158.33 ± 11.96	124.83 ± 9.90	0.0001
HDL	71.66 ± 7.22	67.58 ± 10.80	0.0903	74.33 ± 7.68	60.54 ± 10.25	0.0001
TG	170.20 ± 10.32	154.91 ± 7.44	0.0001	175.70 ± 8.85	136.37 ± 7.63	0.0001
Glucose (blood)	82.20 ± 6.16	77.29 ± 4.05	0.0021	82.25 ± 7.15	77.41 ± 4.19	0.0064
Mean pressure (systolic)	121.04 ± 6.91	119.16 ± 6.53	0.033	119.16 ± 6.86	115.83. ± 7.89	0.125
Mean pressure (diastolic)	78.75 ± 8.10	75.20 ± 5.98	0.091	77.5 ± 10.10	75.41 ± 7.50	0.421

*Statistical analysis was obtained with Student's *t*-test between the two group.

Myo-inositol may prevent gestational diabetes in PCOS women

R. D'Anna, V. Di Benedetto, P. Rizzo, E. Raffone, M. L. Interdonato, F. Corrado, and A. Di Benedetto

Gynecological Endocrinology Vol. 28 , Iss. 6,2012

98 pazienti 54 in terapia con mio-inositolo

44 in terapia con metformina fino all'inizio della gravidanza

Outcome primario prevalenza di GDM 17.4% vs 54%

Outcomes secondari ipertensione arteriosa, parto pre termine, macrosomia: nessuna differenza

Relationship Between Myo-Inositol Supplementary and Gestational Diabetes Mellitus

A Meta-Analysis

Xiangqin Zheng, MD, Zhaozhen Liu, MD, Yulong Zhang, MD, Yuan Lin, MD, Jianrong Song, MD, Lianghui Zheng, MD, and Sheng Lin, MD

TABLE 1. Baseline characteristic of patients in the included trials

Study	Design	Case (n)	Age (years)	BMI (kg/m2)	Nulliparous	Intervention	Time	Population
D'Anna et al[10]	pRCT	110	31.0±5.3	22.8±3.1	54.5%	2 g myo-inositol+0.2 g folic acid, twice a day	At 12–13 weeks of pregnancy	Normal, while parents were diabetes
		110	31.6±5.6	23.6±3.1	50%	0.2 g folic acid, twice a day		
Corrado et al[11]	pRCT	24	28.7±3.5	25.1±4.7	Unclear	4g myo-inositol+0.4 g folic acid, daily	Since GDM diagnosed	Diabetes
		45	28.4±3.7	24.2±4. 1	Unclear	0.4 g folic acid, daily		
Matarrelli et al[12]	pRCT	36	33.8±4.7	24.7±4.2	71.1%	4 g myo-inositol+0.4 g folic acid, daily	Throughout pregnancy	High-risk diabetes
		39	33.0±4.9	24.2±4. 1	62.9 %	0.4 g folic acid, daily		
Facchinetti et al[13]	pRCT	31	Unclear	Unclear	Unclear	2 g myo-inositol+0.2 g folic acid, twice a day	Throughout pregnancy	pCOS
		60	Unclear	Unclear	Unclear	0.2 g folic acid, twice a day		
D'Anna et al[14]	Case control	24	29.2±3.8	24.7±3.9	89.2%	4 g myo-inositol+0.4 g folic acid, daily	Throughout pregnancy	pCOS
		45	30.6±4.2	26.2±5.8	91.3%	1.5 g metformin_0.4 g folic acid, daily		

pCOS, polycystic ovary syndrome; pRCT, prospective randomized controlled trial.

Medicine, vol 94, N 42, 2015

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CONCLUSIONS

On the basis of current evidence, myo-inositol supplementation reduces the development of GDM, although this conclusion requires further evaluation in large-scale, multicenter, blinded, randomized controlled trials.

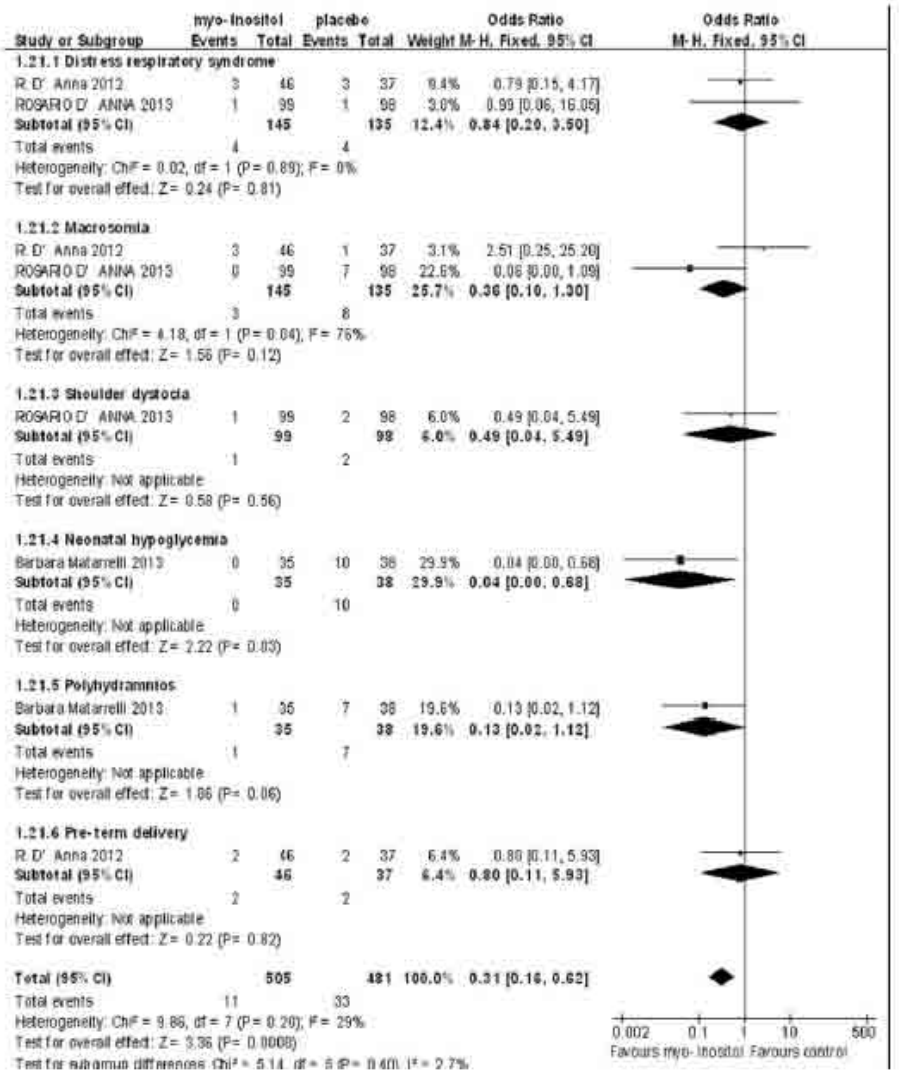

FIGURE 7. Meta-analysis result of the incidence of gestational diabetes mellitus related complications.

COMMENTARY (SEE D'ANNA ET AL., P. 854)

Can a Dietary Supplement Prevent Gestational Diabetes Mellitus?

This study by D'Anna et al. (7), along with earlier investigations of the effect of inositol supplementation on insulin resistance in GDM subjects and in preventing GDM in women with PCOS, lays the groundwork for more and larger studies to test the hypothesis that inositol supplementation can prevent GDM in the general pregnant population, including overweight and obese gravidas. *myo*-Inositol is inexpensive, particularly compared with most prescribed medications. If this intervention turns out to be safe and effective it could have a profound impact on improving pregnancy outcomes and lowering health care costs. If GDM diagnosed by the new ADA recommended criteria (2) is preventable by an intervention such as this, the anticipated onslaught of new cases may be dampened considerably!

Standard italiani per la cura del diabete mellito 2014

Sembrano poi promettenti i dati che riguardano la supplementazione di alcuni alimenti, utili nel migliorare l'azione insulinica, come la vitamina D e l'inositolo. Un tral clinico randomizzato europeo, al quale partecipano anche due centri italiani (98), si pone l'obiettivo di verificare l'efficacia dell'intervento sullo stile di vita e della supplementazione con la vitamina D nella prevenzione del diabete gestazionale. Anche la supplementazione con inositolo, da tempo utilizzata nelle donne con policistosi ovarica (PCOS), sembrerebbe efficace e sicura nel migliorare l'insulinoresistenza nel GDM. Due recenti tral clinici randomizzati italiani (99,100) hanno mostrato che l'inositolo può essere utile nella prevenzione del GDM, in donne a rischio per la malattia. Questi dati preliminari, se confermati su ampie casistiche, potrebbero prevedere l'utilizzo di questi supplementi insieme alle terapie tradizionali, soprattutto nelle forme con alterazioni più lievi del metabolismo glucidico (101-103).