REGIONE DEL VENETO
ULSS8 BERICA

PDTA DIABETE GESTAZIONALE ULSS8 BERICA: LA PRESA IN CARICO DELLA GESTANTE DALLA DIAGNOSI AL POST PARTO

Gestione metabolica e terapia nel GDM: controversie in tema di uso della metformina

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ULSS8 BERICA

STANDARD ITALIANI PER LA CURA DEL DIABETE MELLITO

2018

Gestione durante la gravidanza

Gli obiettivi glicemici da raggiungere durante la gravidanza in donne con diabete gestazionale sono i seguenti se compatibili con un adeguato accrescimento fetale ed un rischio non aumentato di ipoglicemia:

- **≤ 90 mg/dl a digiuno;**
- **≤ 130 mg/dl un'ora dopo i pasti;**

La terapia nutrizionale in gravidanza deve essere personalizzata, tenendo conto sia delle abitudini alimentari, culturali, etniche e dello stato economico della donna con diabete, sia del BMI pregravidico. Gli obiettivi sono: adeguata nutrizione materna e fetale, adeguato apporto calorico, vitaminico e minerale e controllo glicemico ottimale in assenza di chetonuria/chetonemia. ***VI B***

In tutte le donne con GDM o diabete tipo 2 nelle quali l'obiettivo glicemico non è raggiungibile con la sola dieta deve essere prontamente instaurata la terapia insulinica. Gli antidiabetici orali e la terapia iniettiva non-insulinica non sono attualmente raccomandati in gravidanza, una eventuale introduzione della metformina nella terapia del GDM rimane sospesa in attesa di dati certi sulla sua sicurezza nel lungo termine sul feto e sulla prole. ***VI B***

Durante la gravidanza possono essere mantenuti o introdotti in terapia gli analoghi rapidi dell'insulina aspart (I A) e lispro (I A), potenzialmente più efficaci dell'insulina umana regolare nel controllare l'iperglicemia postprandiale, con minor rischio di ipoglicemia (VI B). Non vi sono al momento dati sufficienti sull'uso in gravidanza dell'analogo rapido glulisina.

Il trattamento con gli analoghi ad azione ritardata può essere preso in considerazione per la terapia della donna in gravidanza sia per quanto riguarda detemir (II B), che glargine (IV B); per quanto concerne degludec non ci sono dati disponibili in termini di sicurezza.

15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2023*

Diabetes Care 2023;46(Suppl. 1):S254–S266 | https://doi.org/10.2337/dc23-S015

MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

Recommendations

15.14 Lifestyle behavior change is an essential component of management of gestational diabetes mellitus and may suffice as treatment for many individuals. Insulin should be added if needed to achieve glycemic targets. **A**

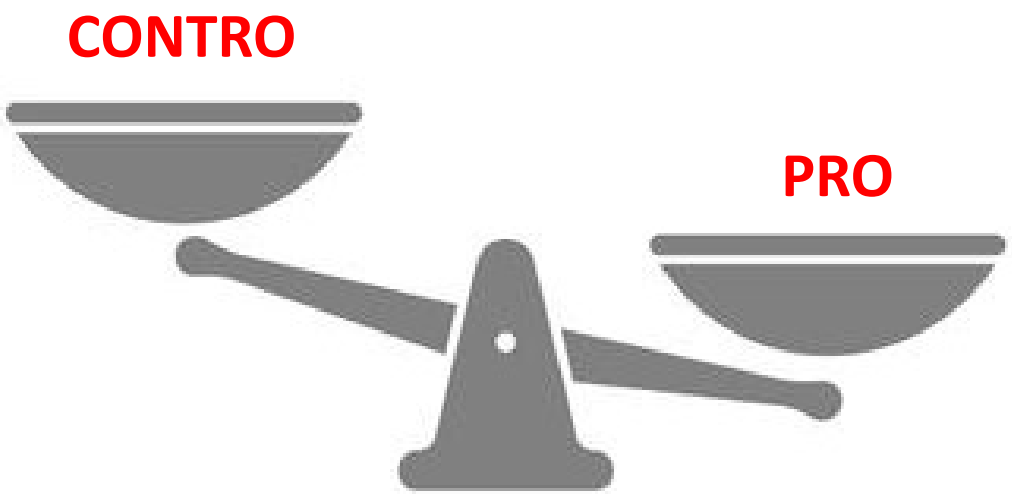
15.15 Insulin is the preferred medication for treating hyperglycemia in gestational diabetes mellitus. Metformin and glyburide should not be used as first-line agents, as both cross the placenta to the fetus. **A** Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data.

15.16 Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester. **A**

15.17 Telehealth visits for pregnant people with gestational diabetes mellitus improve outcomes compared with standard in-person care. **A**

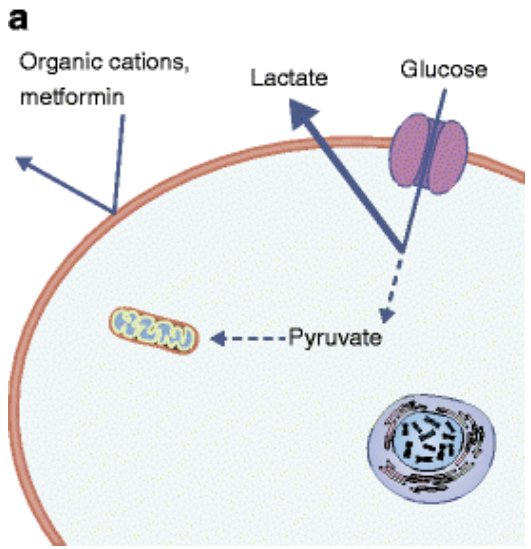
Controversie in tema di uso della metformina nella terapia del diabete gestazionale

EFFETTI A BREVE TERMINE



Passaggio transplacentare della metformina

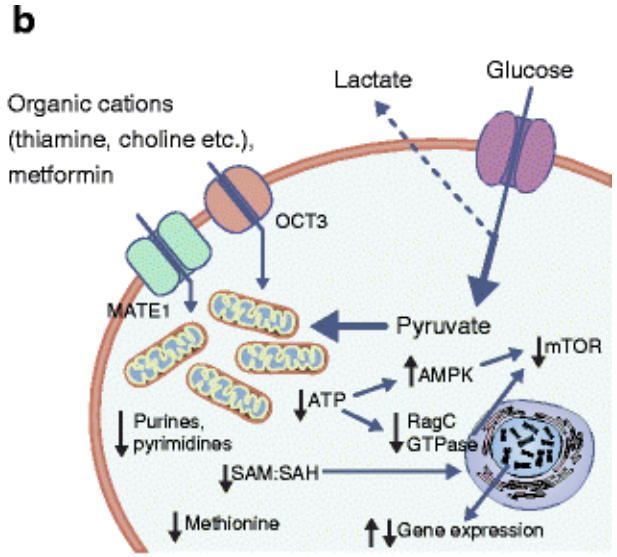
I trimestre di gravidanza



La suscettibilità alla metformina dipende dalla presenza di trasportatori della metformina e dalla maturità della funzione mitocondriale

Nel I trimestre le cellule fetali progenitrici sono resistenti alla metformina: l'espressione dei trasportatori è trascurabile.

Dal II trimestre di gravidanza



Vi è espressione dei trasportatori per la metformina a livello placentare.

Il passaggio transplacentare della metformina è diretto.

Il feto è esposto a concentrazioni di metformina paragonabili a quelle terapeutiche della madre.

Linsday (2017) Diabetologia; 60(9): 1612–1619.
Vanky E, Zahlsen K, Spigset O, CarlsenSM Fertil Steril. 2005 May;83(5):1575-8.

Metformin exposure in first trimester of pregnancy and risk of all or specific congenital anomalies: exploratory case-control study

Joanne E Given,[1] Maria Loane,[2] Ester Garne,[3] Marie-Claude Addor,[4] Marian Bakker,[5] Bénédicte Bertaut-Nativel,[6] Miriam Gatt,[7] Kari Klungsoyr,[8,9] Nathalie Lelong,[10] Margery Morgan,[11] Amanda J Neville,[12] Anna Pierini,[13] Anke Rissmann,[14] Helen Dolk[15]

- **11 European congenital anomaly registries**
- **2006 - 2013**
- **1 892 482 births in Europe**

No risk of congenital anomalies !

WHAT THIS STUDY ADDS

In a large international, population based database, no evidence was found of an overall increased risk of congenital anomalies after first trimester metformin exposure

A raised risk of one specific cardiac defect may be a chance finding

Further surveillance is needed to increase sample size and follow up the cardiac signal, but these results are reassuring given the increasing use of metformin in pregnancy

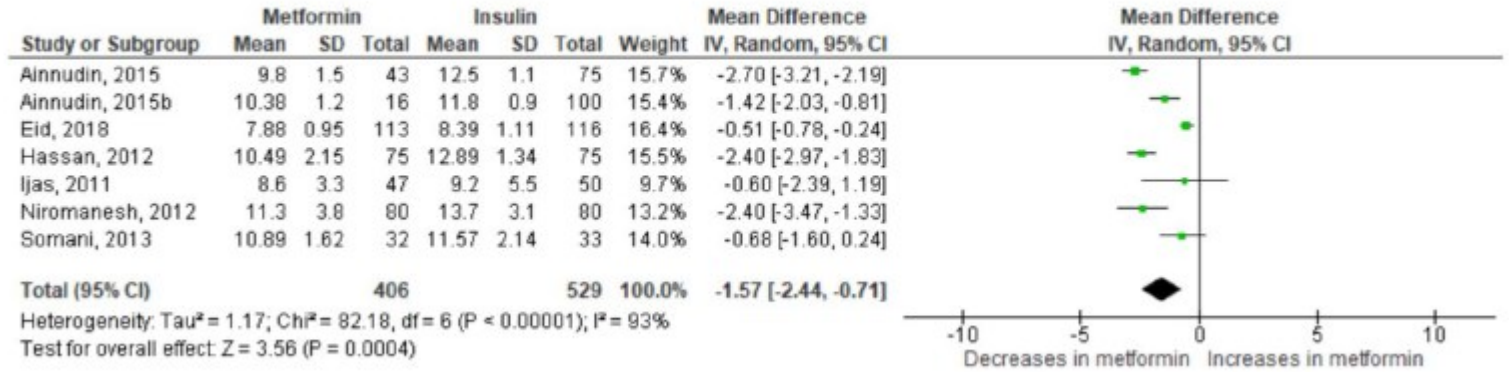
Impact of metformin treatment during pregnancy on maternal outcomes: a systematic review/ meta-analysis

Scientific Reports | (2021) 11:9240

The risk of gastrointestinal side-effects was greater in metformin-exposed versus other treatment groups (OR 2.43, 95% CI 1.53–3.84; I2 = 76%, p = 0.0002).

"… our meta-analysis highlights largely neutral or positive maternal outcomes …. Metformin may not be adequate pharmacological treatment of GDM in up to 46% of women"

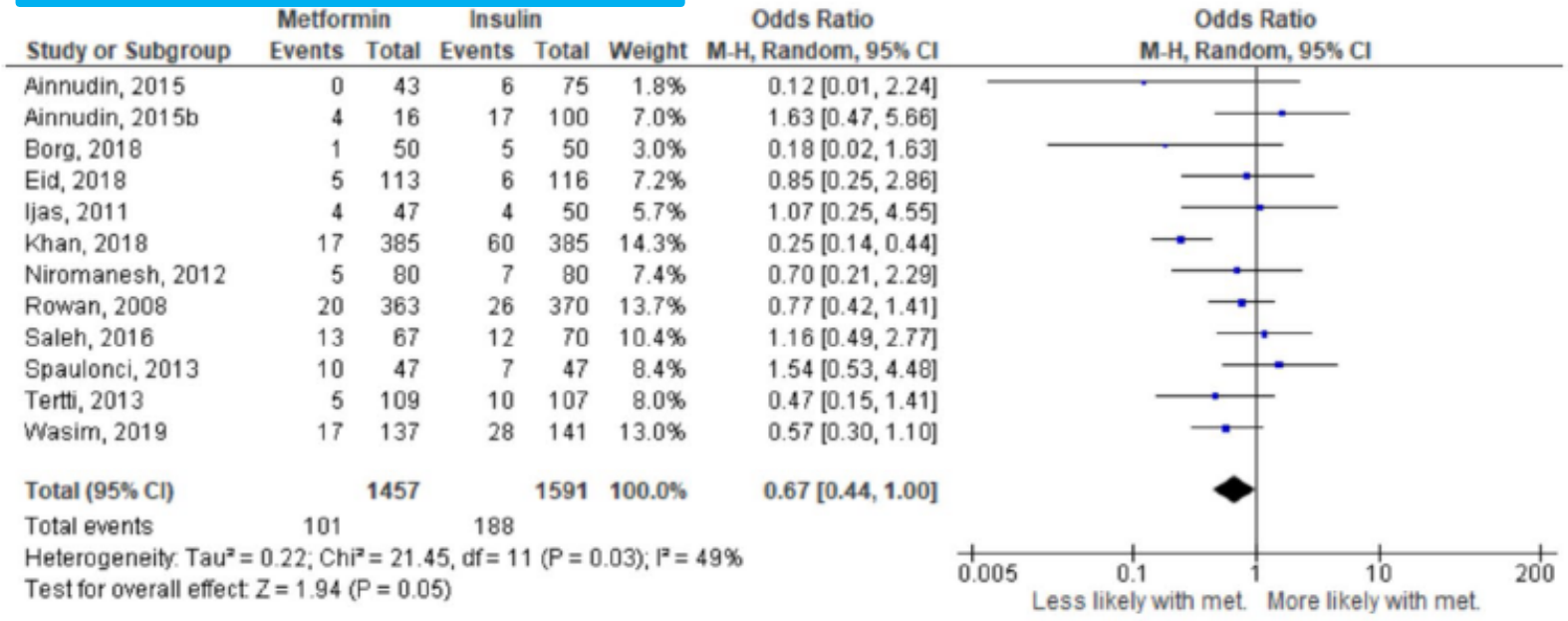
Incremento ponderale gravidico



Study or Subgroup	Metformin Mean	SD	Total	Insulin Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ainnudin, 2015	9.8	1.5	43	12.5	1.1	75	15.7%	-2.70 [-3.21, -2.19]
Ainnudin, 2015b	10.38	1.2	16	11.8	0.9	100	15.4%	-1.42 [-2.03, -0.81]
Eid, 2018	7.88	0.95	113	8.39	1.11	116	16.4%	-0.51 [-0.78, -0.24]
Hassan, 2012	10.49	2.15	75	12.89	1.34	75	15.5%	-2.40 [-2.97, -1.83]
Ijas, 2011	8.6	3.3	47	9.2	5.5	50	9.7%	-0.60 [-2.39, 1.19]
Niromanesh, 2012	11.3	3.8	80	13.7	3.1	80	13.2%	-2.40 [-3.47, -1.33]
Somani, 2013	10.89	1.62	32	11.57	2.14	33	14.0%	-0.68 [-1.60, 0.24]
Total (95% CI)			**406**			**529**	**100.0%**	**-1.57 [-2.44, -0.71]**

Heterogeneity: Tau² = 1.17; Chi² = 82.18, df = 6 (P < 0.00001); I² = 93%
Test for overall effect: Z = 3.56 (P = 0.0004)

Preeclampsia



Study or Subgroup	Metformin Events	Total	Insulin Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Ainnudin, 2015	0	43	6	75	1.8%	0.12 [0.01, 2.24]
Ainnudin, 2015b	4	16	17	100	7.0%	1.63 [0.47, 5.66]
Borg, 2018	1	50	5	50	3.0%	0.18 [0.02, 1.63]
Eid, 2018	5	113	6	116	7.2%	0.85 [0.25, 2.86]
Ijas, 2011	4	47	4	50	5.7%	1.07 [0.25, 4.55]
Khan, 2018	17	385	60	385	14.3%	0.25 [0.14, 0.44]
Niromanesh, 2012	5	80	7	80	7.4%	0.70 [0.21, 2.29]
Rowan, 2008	20	363	26	370	13.7%	0.77 [0.42, 1.41]
Saleh, 2016	13	67	12	70	10.4%	1.16 [0.49, 2.77]
Spaulonci, 2013	10	47	7	47	8.4%	1.54 [0.53, 4.48]
Tertti, 2013	5	109	10	107	8.0%	0.47 [0.15, 1.41]
Wasim, 2019	17	137	28	141	13.0%	0.57 [0.30, 1.10]
Total (95% CI)		**1457**		**1591**	**100.0%**	**0.67 [0.44, 1.00]**
Total events	101		188			

Heterogeneity: Tau² = 0.22; Chi² = 21.45, df = 11 (P = 0.03); I² = 49%
Test for overall effect: Z = 1.94 (P = 0.05)

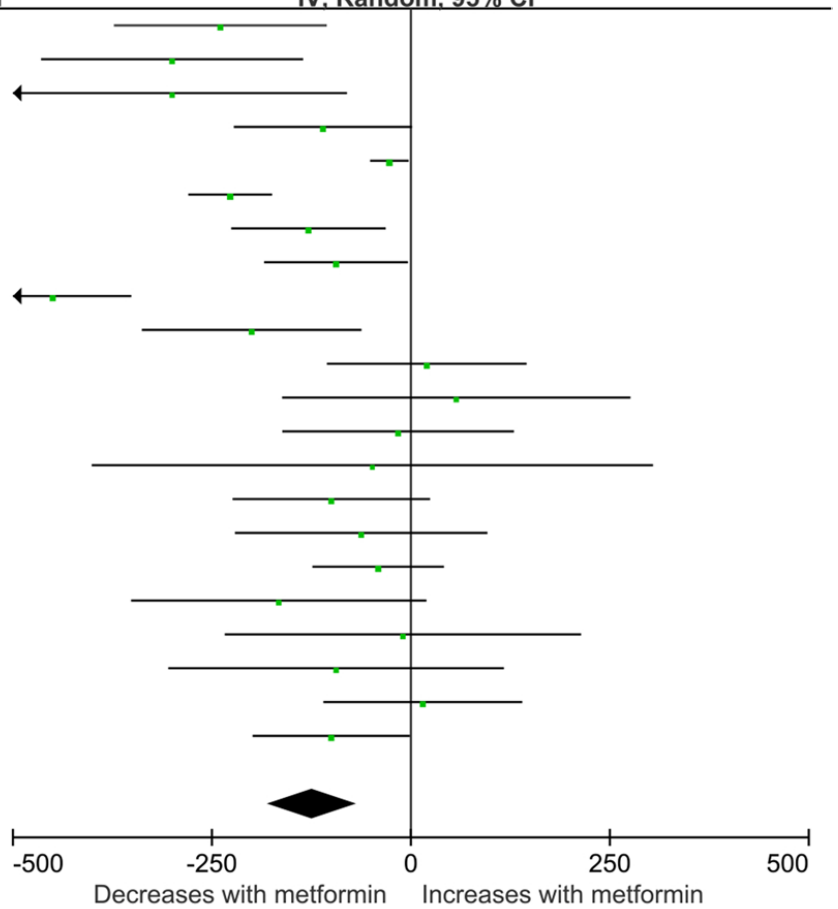
Short-term neonatal outcomes in women with gestational diabetes treated using metformin versus insulin: a systematic review and meta-analysis of randomized controlled trials

A

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Insulin Mean	Insulin SD	Insulin Total	Weight	Mean Difference IV, Random, 95% CI
Abdullah2021	3,410.2	480.08	94	3,649.6	468.87	100	4.7%	-239.40 [-373.06, -105.74]
Ainuddin2014	3,400	400	43	3,700	500	75	4.1%	-300.00 [-464.62, -135.38]
Arshad 2017	3,140	320	25	3,440	460	25	3.2%	-300.00 [-519.66, -80.34]
Ashoush2016	3,431.3	285.9	47	3,541.7	270.9	48	5.1%	-110.40 [-222.44, 1.64]
Barrett2013	3,401	137	236	3,428	133	242	6.4%	-27.00 [-51.21, -2.79]
Eid2018	3,037	204	113	3,264	202	116	6.1%	-227.00 [-279.59, -174.41]
Gamal2018	3,556.3	260.7	58	3,685	272.5	58	5.4%	-128.70 [-225.75, -31.65]
Ghomian2018	3,450	548	143	3,544	57	143	5.5%	-94.00 [-184.30, -3.70]
Hamadani2017	3,220	200	30	3,670	190	30	5.4%	-450.00 [-548.71, -351.29]
Hassan2012	3,400	400	75	3,600	460	75	4.6%	-200.00 [-337.96, -62.04]
Huhtala2020	3,610	490	109	3,590	450	107	4.9%	20.00 [-105.43, 145.43]
Ijas2010	3,615	417	32	3,558	593	50	3.2%	57.00 [-161.84, 275.84]
Mesdaghinia2013	3,512	484	100	3,528	563	100	4.5%	-16.00 [-161.52, 129.52]
Moore2007	3,451.8	727.5	32	3,500.2	700.5	31	1.8%	-48.40 [-401.02, 304.22]
Niromanesh2012	3,300	400	80	3,400	400	80	4.9%	-100.00 [-223.96, 23.96]
Picón-César2021	3,171.2	599.39	94	3,233.6	514.26	97	4.2%	-62.40 [-221.00, 96.20]
Roman2008	3,372	572	363	3,413	569	370	5.6%	-41.00 [-123.61, 41.61]
Ruholamin2014	3,176	438	50	3,342	506	50	3.8%	-166.00 [-351.50, 19.50]
Somani2016	2,840	320	32	2,850	570	33	3.1%	-10.00 [-233.86, 213.86]
Spaulonci2013	3,143.7	446.6	47	3,237.6	586.8	47	3.3%	-93.90 [-304.72, 116.92]
Tertti2013	3,604	488	109	3,589	448	107	4.9%	15.00 [-109.89, 139.89]
Wasim2019	3,000	400	137	3,100	440	141	5.4%	-100.00 [-198.80, -1.20]
Total (95% CI)			**2049**			**2125**	**100.0%**	**-122.76 [-178.31, -67.21]**

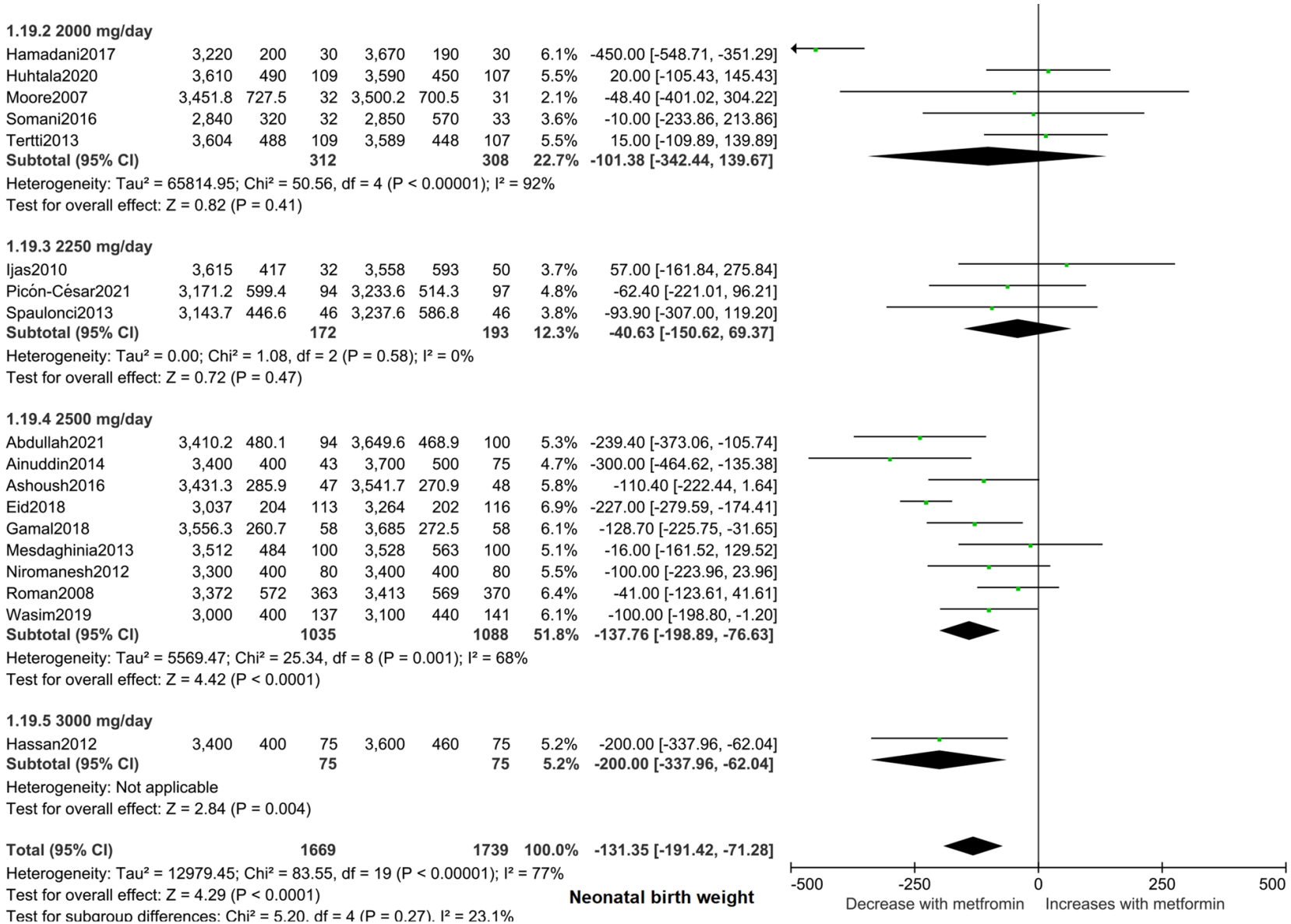
Heterogeneity: Tau² = 12460.96; Chi² = 131.77, df = 21 (P < 0.00001); I² = 84%

Test for overall effect: Z = 4.33 (P < 0.0001)



Neonatal birth weight

Short-term neonatal outcomes in women with gestational diabetes treated using metformin versus insulin: a systematic review and meta-analysis of randomized controlled trials

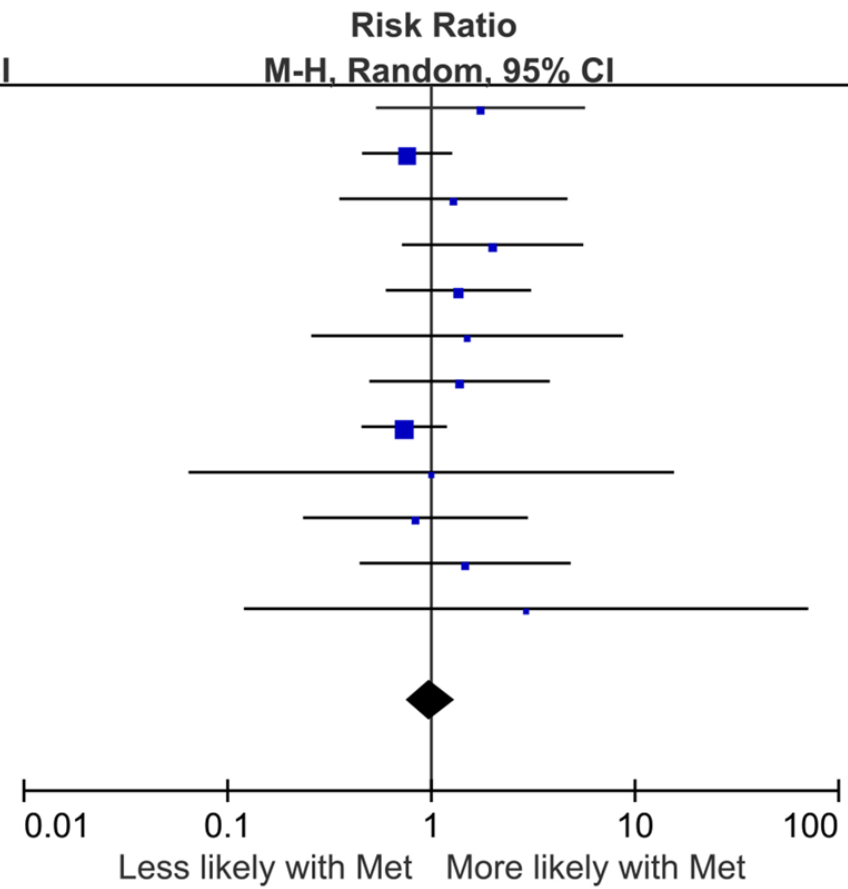


B

Study or Subgroup	Metformin Events	Metformin Total	Insulin Events	Insulin Total	Weight	Risk Ratio M-H, Random, 95% CI
Ainuddin2014	5	43	5	75	4.9%	1.74 [0.54, 5.68]
Barrett2013	23	236	31	242	26.2%	0.76 [0.46, 1.27]
Eid2018	5	113	4	116	4.1%	1.28 [0.35, 4.66]
Hassan2012	10	75	5	75	6.5%	2.00 [0.72, 5.57]
Huhtala2020	12	105	9	107	10.1%	1.36 [0.60, 3.09]
Niromanesh2012	3	80	2	80	2.2%	1.50 [0.26, 8.74]
Picón-César2021	8	94	6	97	6.5%	1.38 [0.50, 3.81]
Roman2008	26	363	36	370	29.1%	0.74 [0.45, 1.19]
Ruholamin2014	1	50	1	50	0.9%	1.00 [0.06, 15.55]
Saleh2016	4	67	5	70	4.2%	0.84 [0.23, 2.98]
Spaulonci2013	6	44	4	43	4.8%	1.47 [0.44, 4.83]
Tertti2013	1	110	0	107	0.7%	2.92 [0.12, 70.87]
Total (95% CI)		**1380**		**1432**	**100.0%**	**1.00 [0.77, 1.30]**
Total events	104		108			

Heterogeneity: Tau² = 0.00; Chi² = 7.43, df = 11 (P = 0.76); I² = 0%

Test for overall effect: Z = 0.00 (P = 1.00)



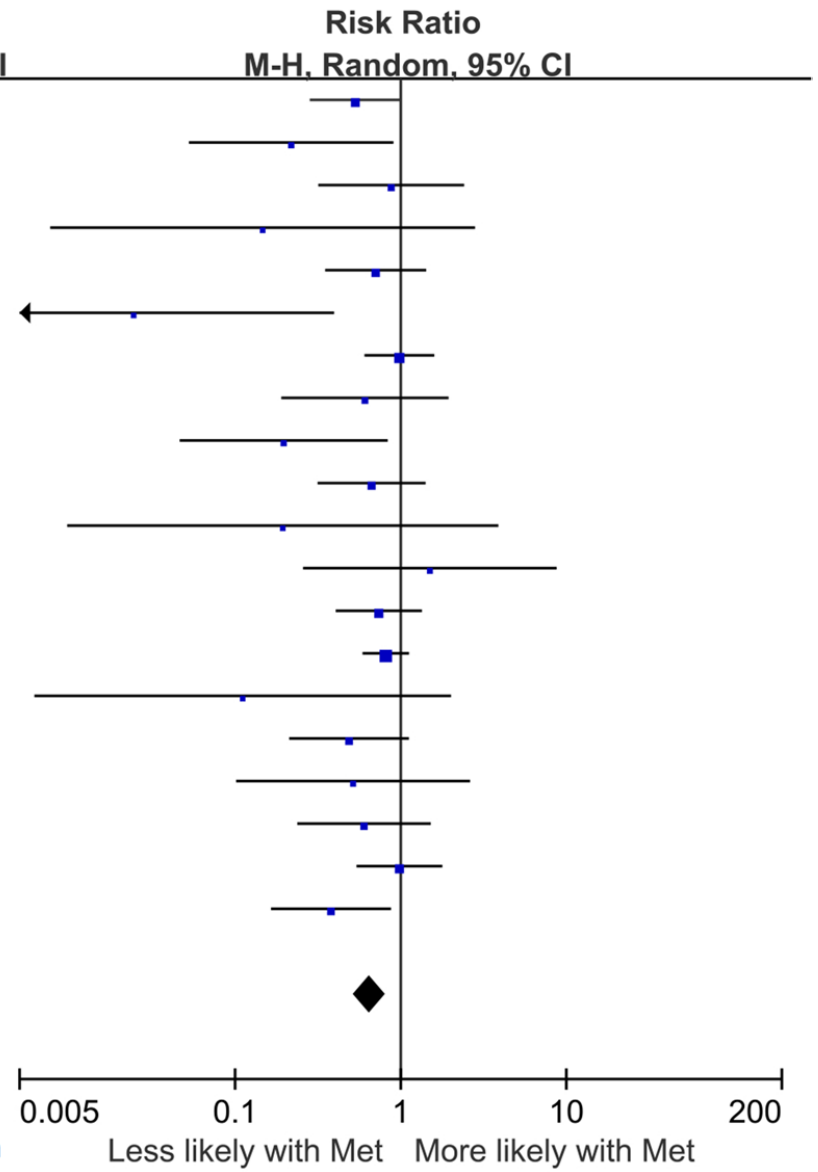
Small for gestational age

B

Study or Subgroup	Metformin Events	Metformin Total	Insulin Events	Insulin Total	Weight	Risk Ratio M-H, Random, 95% CI
Abdullah2021	12	94	24	100	8.2%	0.53 [0.28, 1.00]
Ainuddin2014	2	43	16	75	2.2%	0.22 [0.05, 0.90]
Ashoush2016	6	47	7	48	4.0%	0.88 [0.32, 2.41]
Eid2018	0	113	3	116	0.5%	0.15 [0.01, 2.81]
Ghomian2018	12	143	17	143	7.1%	0.71 [0.35, 1.42]
Hassan2012	0	75	20	75	0.6%	0.02 [0.00, 0.40]
Huhtala2020	25	108	25	106	11.4%	0.98 [0.60, 1.59]
Ijas2010	4	47	7	50	3.1%	0.61 [0.19, 1.94]
Jahanshahi2020	2	28	8	22	2.1%	0.20 [0.05, 0.83]
Mesdaghinia2013	10	100	15	100	6.4%	0.67 [0.31, 1.41]
Moore2007	0	32	2	31	0.5%	0.19 [0.01, 3.88]
Niromanesh2012	3	80	2	80	1.5%	1.50 [0.26, 8.74]
Picón-César2021	15	94	21	97	8.9%	0.74 [0.41, 1.34]
Roman2008	55	363	69	370	16.6%	0.81 [0.59, 1.12]
Ruholamin2014	0	50	4	50	0.6%	0.11 [0.01, 2.01]
Saleh2016	7	67	15	70	5.5%	0.49 [0.21, 1.12]
Somani2016	2	32	4	33	1.7%	0.52 [0.10, 2.62]
Spaulonci2013	6	47	10	47	4.6%	0.60 [0.24, 1.52]
Tertti2013	18	109	18	107	8.9%	0.98 [0.54, 1.78]
Wasim2019	7	137	19	141	5.5%	0.38 [0.16, 0.87]
Total (95% CI)		**1809**		**1861**	**100.0%**	**0.65 [0.52, 0.81]**
Total events	186		306			

Heterogeneity: Tau² = 0.05; Chi² = 24.47, df = 19 (P = 0.18); I² = 22%

Test for overall effect: Z = 3.85 (P = 0.0001)



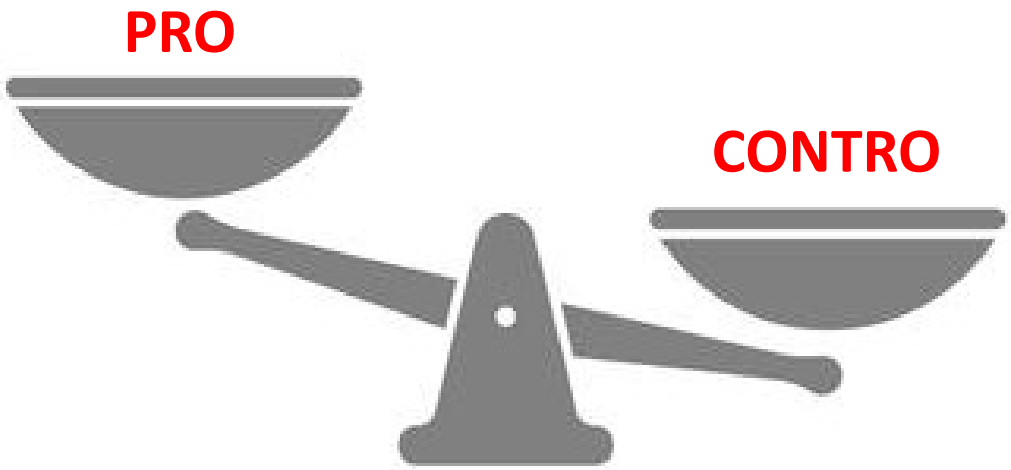
Neonatal hypoglycemia

EFFETTI A BREVE TERMINE

- **Minore incremento ponderale (GWG)**
- **Migliore outcome materno**
- **Trattamento più gradito rispetto a insulina**

- **Nessun evento avverso neonatale**
- **Riduzione ipoglicemia neonatale**
- **Neonati mediamente più piccoli ma non aumentano gli SGA**

EFFETTI A LUNGO TERMINE



Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7–9 years of age

- A longitudinal follow-up study of the offspring of women with GDM recruited into a prospective randomized trial comparing metformin with insulin treatment (MiG trial)

- Objective: to compare body composition and metabolic outcomes at 7–9 years in offspring of women with gestational diabetes (GDM) randomized to metformin (±insulin) or insulin treatment during pregnancy

- Children were assessed at 7 years in Adelaide (n=109/181) and 9 years in Auckland (n=99/396) by anthropometry, bioimpedance analysis (BIA), dual-energy X-ray absorptiometry (DXA), magnetic resonance imaging (MRI) (n=92/99) and fasting bloods (n=82/99)

BMJ Open Diab Res Care 2018;6:e000456

Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7–9 years of age

	Subgroup seen at 7years (Adelaide) n=109		
	Metformin n=58	Insulin n=51	P values
Age (years)	7.0±1.0	7.4±1.1	0.02
Male/female (n)	35/23	23/28	0.16
Weight (kg)	26.9±5.2	26.3±4.9	0.59
Height (cm)	124.5±5.2	124.5±5.0	0.99
BMI (kg/m²)	17.2±2.5	16.9±2.5	0.48
Leg length (cm)	55.8±7.7	57.5±3.1	0.13
Head circumference (cm)	52.2±1.2	51.9±1.5	0.24
Chest circumference (cm)	63.5±6.0	63.1±5.0	0.66
Mid-upper arm circumference (cm)	19.7±2.4	19.5±2.3	0.54
Waist circumference (cm)	60.2±6.7	59.5±6.1	0.57
Hip circumference (cm)	67.6±6.4	67.7±5.7	0.90
Waist:height ratio	0.48±0.05	0.48±0.04	0.54
Triceps skinfold thickness (mm)	11.4±4.3	11.4±4.0	0.997
Subscapular skinfold thickness (mm)	8.0±5.6	7.5±5.3	0.65
Biceps skinfold thickness (mm)	6.9±3.8	6.7±2.8	0.72
DXA	n=32	n=29	
Fat-free mass (g)	19702±2564	19271±2532	0.51
Total fat (g)	7651±3906	7987±3339	0.72
Abdominal fat (g)	423±384	430±315	0.93
Thigh fat (g)	1252±618	1323±618	0.63
Arm fat (g)	1079±492	1103±422	0.84
Abdominal fat:thigh fat ratio	0.30±0.11	0.30±0.10	0.99
Total fat %	26.8±7.6	28.5±6.8	0.37
Abdominal fat % of abdominal mass	21.3±11.8	22.4±10.5	0.71
Bioimpedance	n=56	n=51	
Fat-free mass (kg)	21.5±2.8	20.7±3.0	0.34
Total fat %	18.8±7.9	20.8±5.4	0.13
MRI – abdomen	n=7 Age:10.0±0.14 years	n=5 Age:10.0±0.08 years	
Abdominal fat volume (cm³)	2720±1786	1843±724	0.27
Abdominal fat % of abdominal volume	27.6±11.2	23.5±9.5	0.50
Abdominal subcutaneous fat volume (cm³)	1807±1468	1092±618	0.28
Abdominal subcutaneous fat %	17.5±9.6	14.1±8.6	0.54
Abdominal visceral fat volume (cm³)	913±610	752±221	0.54
Abdominal visceral fat %	10.1±4.8	9.3±1.2	0.69

Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7–9 years of age

	Subgroup seen at 9 years (Auckland) n=99		
	Metformin n=45	Insulin n=54	P values
Age (years)	8.9±0.5	8.9±0.4	0.23
Male/female (n)	28/17	28/26	0.32
Weight (kg)	37.0±12.6	32.7±7.7	0.049
Height (cm)	137.5±7.4	135.4±6.6	0.13
BMI (kg/m²)	19.3±4.6	17.7±3.0	0.051
Leg length (cm)	63.6±4.2	63.9±4.1	0.70
Head circumference (cm)	53.6±2.2	53.1±1.8	0.23
Chest circumference (cm)	70.4±10.2	67.7±8.0	0.16
Mid-upper arm circumference (cm)	23.0±4.3	21.2±2.9	0.02
Waist circumference (cm)	69.1±12.2	64.2±8.4	0.04
Hip circumference (cm)	77.6±11.1	74.7±7.1	0.16
Waist:height ratio	0.51±0.08	0.47±0.05	0.02
Triceps skinfold thickness (mm)	19.5±9.0	16.2±6.7	0.05
Subscapular skinfold thickness (mm)	13.1±9.6	10.5±6.8	0.14
Biceps skinfold thickness (mm)	13.9±7.5	11.8±5.9	0.14
DXA	n=45	n=53	
Fat-free mass (g)	24385±5894	22511±3689	0.07
Total fat (g)	12550±7214	10281±4550	0.07
Abdominal fat (g)	774±681	548±413	0.056
Thigh fat (g)	1983±1122	1655±710	0.10
Arm fat (g)	1568±801	1285±534	0.047
Abdominal fat:thigh fat ratio	0.34±0.13	0.30±0.09	0.15
Total fat %	32.0±8.5	30.3±6.6	0.28
Abdominal fat % of abdominal mass	29.7±14.4	26.6±10.5	0.24
Bioimpedance			
Fat-free mass (kg)	27.7±7.7	25.1±5.2	0.065
Total fat %	23.6±8.1	22.3±8.9	0.43
MRI – abdomen	n=42	n=50	
Abdominal fat volume (cm³)	4172±2964	3120±1898	0.051
Abdominal fat % of abdominal volume	36.0±14.4	32.2±10.9	0.16
Abdominal subcutaneous fat volume (cm³)	3231±2412	2398±1566	0.059
Abdominal subcutaneous fat %	27.6±12.3	24.4±9.7	0.18
Abdominal visceral fat volume (cm³)	941±629	722±365	0.051
Abdominal visceral fat %	8.5±3.1	7.7±1.9	0.19

BMJ Open Diab Res Care 2018;6:e000456

ADELAIDE COHORT (7 years)

- similar baseline characteristics at the time they were randomized to metformin or insulin treatment during pregnancy
- women treated with metformin had higher glycemia during treatment than women randomized to insulin
- metformin children larger at birth

Exposition to a higher nutrient load in utero (as measured by higher maternal glucose) were 'protected' by metformin, so that they were not more obese or glucose intolerant as they grew

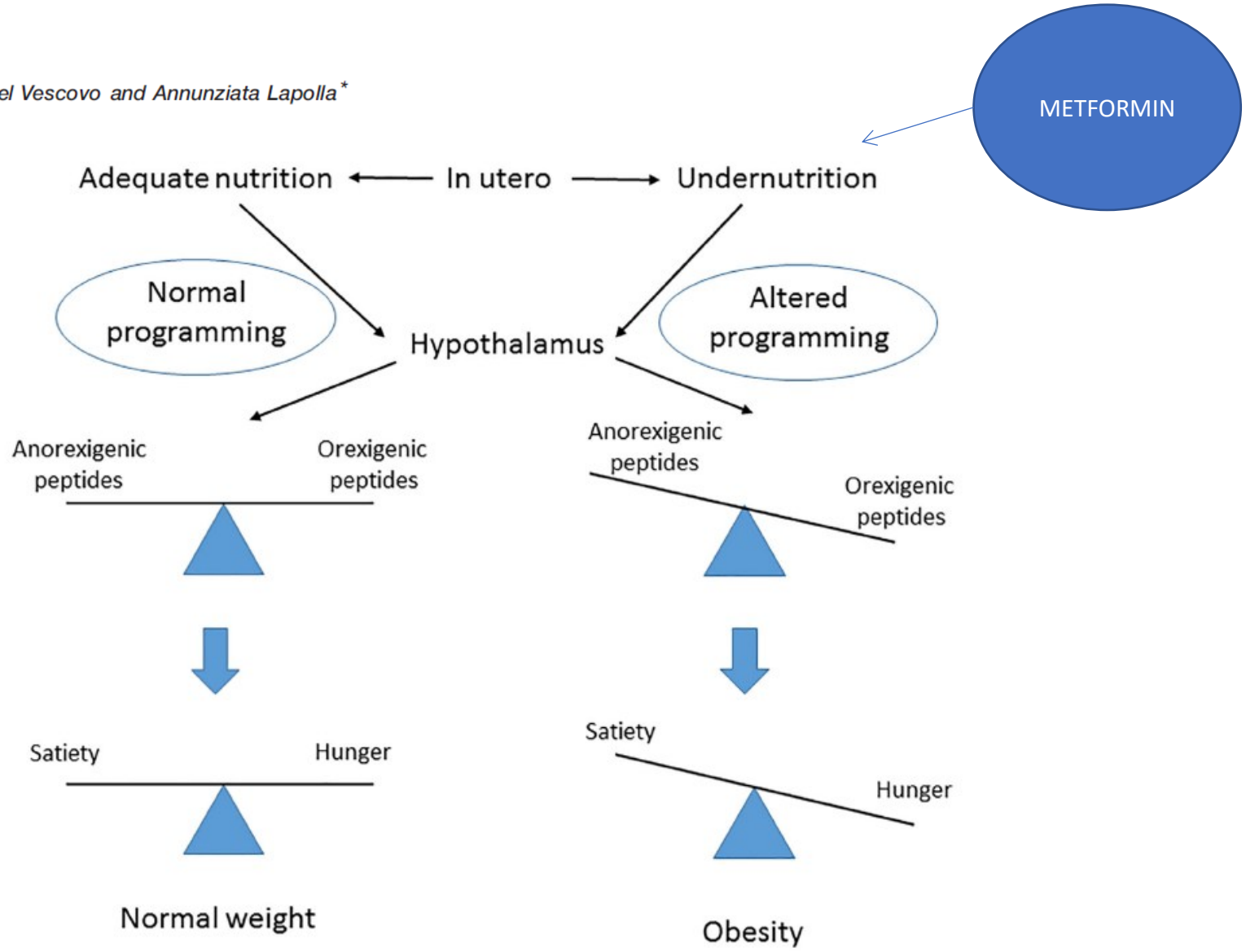
AUCKLAND COHORT (9 years)

- the population was more heterogeneous
- women randomized to metformin tended to be larger than those randomized to insulin
- maternal glycemia was similar
- metformin group had a trend to less weight gain
- pregnancy outcomes were similar

This may have led to relative 'undernutrition' for the fetus and a lower birth weight than expected. This could mask a beneficial effect of metformin in others

Genetics and Epigenetics: New Insight on Gestational Diabetes Mellitus

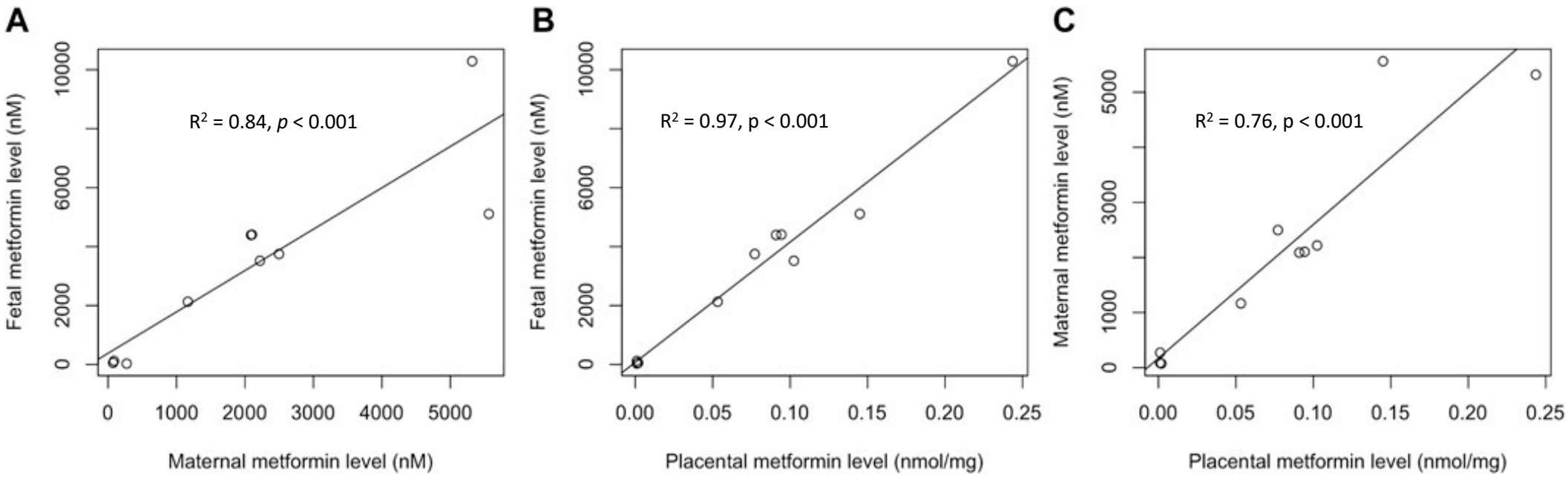
*Maria Grazia Dalfrà, Silvia Burlina, Gloria Giovanna Del Vescovo and Annunziata Lapolla**



Genetics and Epigenetics: New Insight on Gestational Diabetes Mellitus. Front. Endocrinol 11:602477

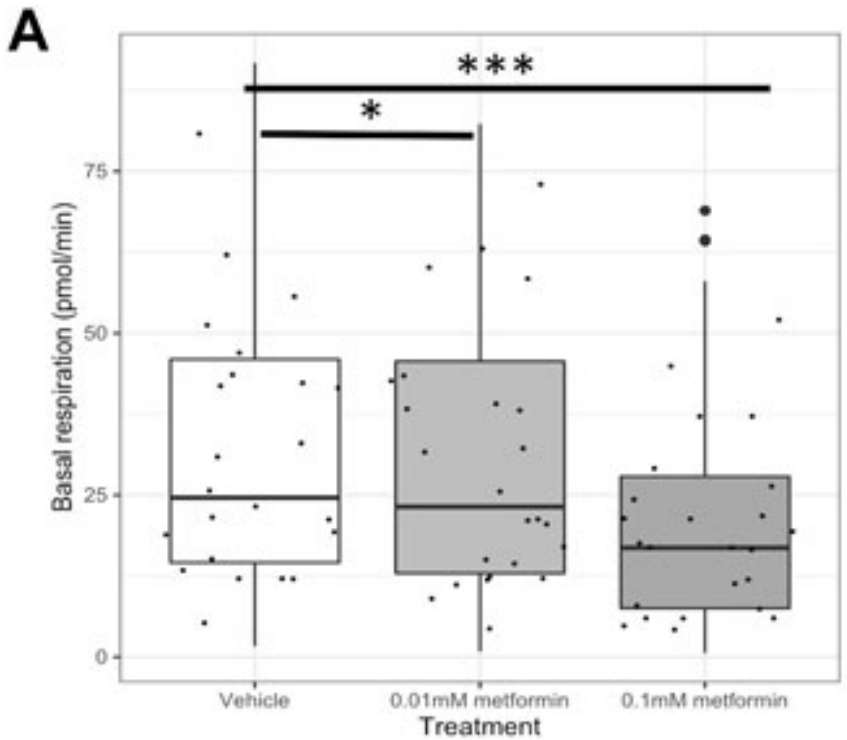
Impact of Metformin Treatment on Human Placental Energy Production and Oxidative Stress

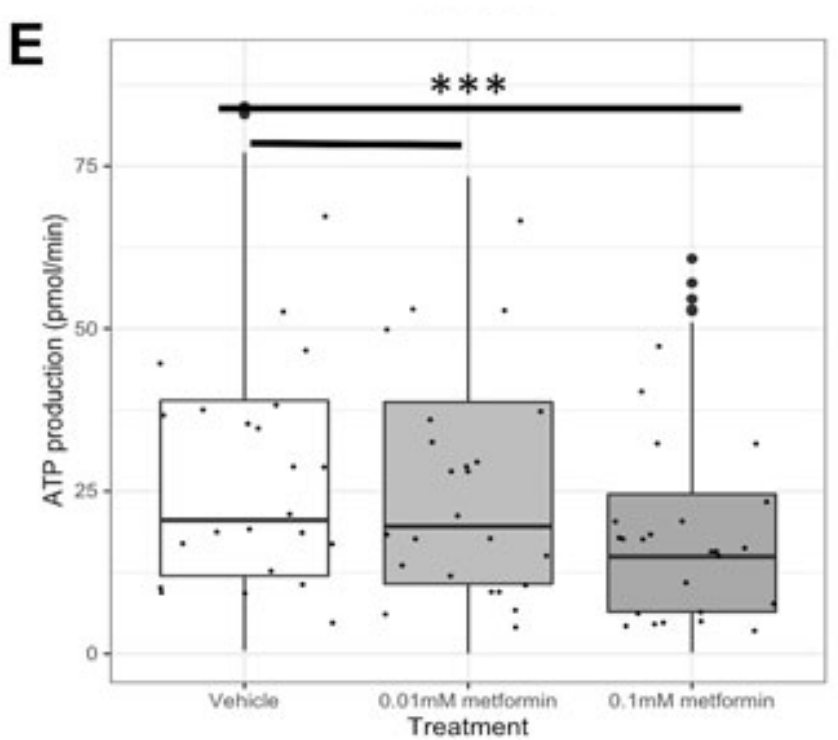
In vivo experiments utilised samples from pregnancies where women were prescribed metformin during pregnancy for gestational diabetes [500–2000 mg/day]. Matched maternal plasma, umbilical cord plasma, and placenta samples from 10 pregnancies were obtained.



Front. Cell Dev. Biol. 10:935403.
doi: 10.3389/fcell.2022.935403

Impact of Metformin Treatment on Human Placental Energy Production and Oxidative Stress





"…we conclude that primary human trophoblasts exposed to metformin in culture at clinically-relevant concentrations have reduced levels of mitochondrial respiration, cellular ATP production. Given the crucial role of placental energy production in supporting fetal growth and well-being during pregnancy, these results are of key importance in refining assessment of the risk versus benefit ratio of clinical application of metformin in pregnancy"

Front. Cell Dev. Biol. 10:935403.
doi: 10.3389/fcell.2022.935403

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https://doi.org/10.1007/s00592-023-02137-5

POSITION STATEMENT

Position paper of the Italian Association of Medical Diabetologists (AMD), Italian Society of Diabetology (SID), and the Italian Study Group of Diabetes in pregnancy: Metformin use in pregnancy

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Table 8 Maternal outcomes in GDM women treated with metformin during pregnancy

	GDM women
Glycemic control	Comparable to insulin
Total insulin dose	Reduced as compared to insulin alone
Total GWG	Reduced
Gestational hypertension/Preeclampsia rate	No significant difference
Caesarian section	No significant difference
Preterm delivery (< 37 weeks)	No significant difference

GWG, Gestational weight gain

Table 9 Neonatal and infant outcomes in GDM women treated with metformin during pregnancy

	GDM women
Newborns	
Birth weight	Lower
LGA/Macrosomia	Decreased
SGA	No significant difference
Hypoglycemia	Decreased
Neonatal intensive care unit admission	No significant difference
Infants	
BMI	Increased
Waist circumference	Increased

LGA, Large for gestational age; SGA, Small for gestational age; BMI, Body mass index

Pregnancy complicated by GDM	Metformin use could be a valid therapeutic option in obese GDM women to reduce GWG. In women with severe obesity metformin may reduce the insulin dose and the GWG

GRAZIE PER L’ATTENZIONE!