



La pianificazione della gravidanza nella donna con diabete

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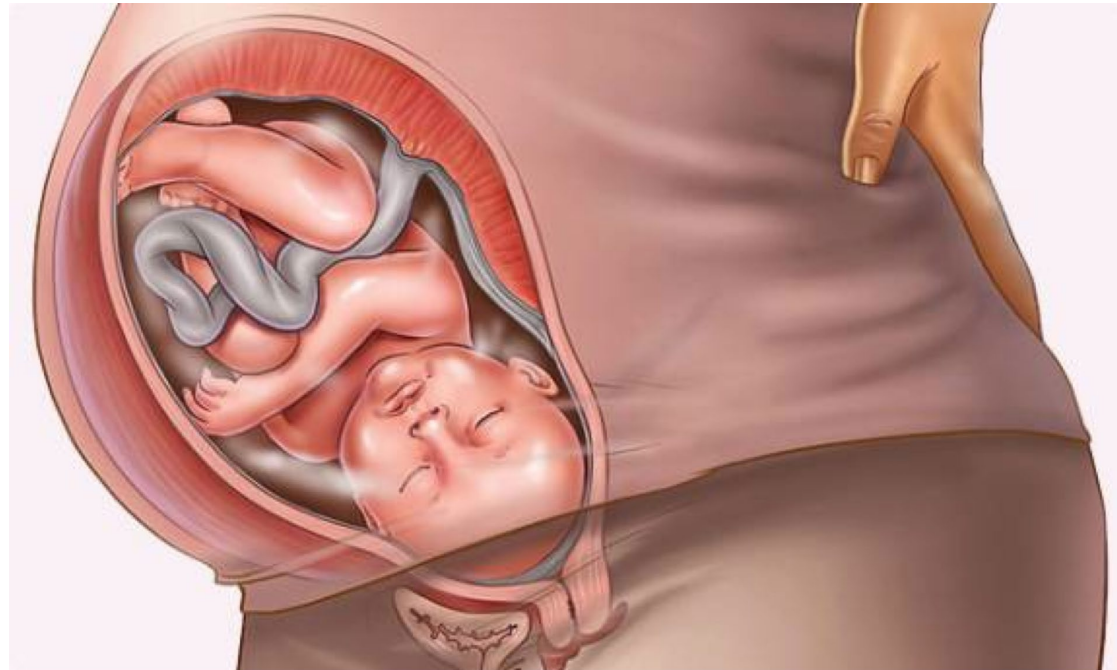
La Prof.ssa Elena Succurro dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Novo Nordisk, Abbott Srl (*per eventi e advisory board*)

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Diabete e Gravidanza

Il Diabete in gravidanza si associa ad un aumentato rischio di morbidità materna e feto/neonatale



Aumentato rischio di complicanze Materne nelle Gravidanze con Diabete tipo 1

Outcome variable	Proportions (%)		OR (95% CI) for group differences	
	Type 1 diabetes	Nondiabetes	Crude	Adjusted
PIH	1.6	0.87	1.93 (1.50–2.49)	1.53 (1.18–1.99)
Preeclampsia, mild	9.7	2.0	5.37 (4.81–6.00)	4.30 (3.83–4.83)
Preeclampsia, severe	4.3	0.8	5.58 (4.75–6.57)	4.47 (3.77–5.31)
Cesarean section	46	12	5.85 (5.49–6.25)	5.31 (4.97–5.69)
Vacuum extraction/forceps	9.6	6.6	1.48 (1.33–1.66)	1.41 (1.25–1.58)

Data are proportions or OR (95% CI). $n = 5,089$ for diabetic pregnancies; $n = 1,260,207$ for control pregnancies. Adjusted OR, OR adjusted for group differences in maternal age, BMI, parity, chronic hypertensive disorder, smoking habits, and ethnicity.

Aumentato rischio di complicanze neonatali nelle Gravidanze con Diabete tipo 1

Outcome variable	Proportions (% if not indicated otherwise)		OR (95% CI) for group differences	
	Type 1 diabetes	Control	Crude	Adjusted
Stillbirth	1.5	0.3	4.04 (3.02–5.40)	3.34 (2.46–4.55)
Fetal distress	14	6.2	2.45 (2.24–2.69)	2.34 (2.12–2.58)
Perinatal mortality (‰)	20	4.8	4.02 (3.11–5.20)	3.29 (2.50–4.33)
Neonatal mortality, 0–7 days (‰)	5.1	1.8	2.91 (1.97–4.28)	3.05 (1.68–5.55)
Neonatal mortality, 0–28 days (‰)	7.0	2.2	3.08 (2.02–4.70)	2.67 (1.72–4.16)
Birth <37 weeks gestational age	21	5.1	5.27 (4.88–5.71)	4.86 (4.47–5.28)
Birth <32 weeks gestational age	2.3	0.7	3.58 (2.89–4.44)	3.08 (2.45–3.87)
LGA	31	3.6	12.2 (11.4–13.1)	11.4 (10.6–12.4)
SGA	2.3	2.5	0.80 (0.63–1.02)	0.71 (0.55–0.91)
Major malformations	4.7	1.8	2.70 (2.37–3.08)	2.50 (2.13–2.94)
Apgar score <7 at 5 min	3.1	1.1	2.98 (2.54–3.50)	2.60 (2.14–3.17)
Apgar score <4 at 5 min	0.80	0.30	2.60 (1.79–3.78)	2.39 (1.64–3.51)
Erb palsy*	2.1	0.25	7.91 (5.77–10.8)	6.69 (4.81–9.31)
Respiratory distress syndrome	1.0	0.20	4.88 (3.51–6.81)	4.65 (2.20–9.84)
Respiratory disorders	9.5	2.6	4.02 (3.67–4.42)	3.42 (3.04–3.85)

Data are proportions or OR (95% CI). Adjusted OR, OR adjusted for group differences in maternal age, BMI, parity, chronic hypertensive disorder, smoking habits, and ethnicity. *Vaginal deliveries only.

Aumentato rischio di complicanze neonatali nelle Gravidanze con Diabete tipo 1 e 2

	Type 1 and 2 diabetes (n=2356 live and stillbirths)		National rate* (n=620 841)	Rate ratio (95% CI)
	Number	Rate (95% CI)		
Stillbirth†	63	26.8 (19.8 to 33.8)	5.7	4.7 (3.7 to 6.0)
Perinatal death†	75	31.8 (24.2 to 39.4)	8.5	3.8 (3.0 to 4.7)
Neonatal death‡	22	9.3 (5.2 to 13.3)	3.6	2.6 (1.7 to 3.9)

*Source for national data: CEMACH 2002.¹⁰

†Rate per 1000 live births plus stillbirths.

‡Rate per 1000 live births.

Aumentato rischio di complicanze neonatali nelle Gravidanze con Diabete tipo 1 e 2

Anomalies	Offspring of women with type 1 diabetes	Offspring of women with type 2 diabetes	Total	Standardised prevalence ratio (95% CI)
One or more major anomalies of any type	81 (37.0)	28 (12.8)	109 (49.8)	2.2 (1.8 to 2.6)
Anomaly system†				
Nervous system:	11 (4.1)	4 (1.5)	15 (5.6)	2.7 (1.5 to 4.4)
Neural tube defects	6 (2.4)	4 (0.9)	10 (2.4)	4.2 (2.0 to 7.8)
Remainder of CNS	5 (1.7)	0 (0.6)	5 (3.0)	1.5 (0.3 to 3.6)
Eye	1 (2.4)	0 (0.9)	1 (1.0)	1.0 (0.1 to 7.0)
Ear	0 (0.7)	0 (0.3)	0 (1.0)	–
Congenital heart disease	33 (8.9)	9 (3.4)	42 (12.3)	3.4 (2.5 to 4.6)
Cleft lip ± palate	0 (1.3)	0 (0.5)	0 (1.8)	–
Cleft palate	2 (0.9)	0 (0.3)	2 (1.2)	1.6 (0.2 to 5.9)
Digestive system	1 (2.6)	2 (1.0)	3 (3.5)	0.8 (0.2 to 2.5)
Internal urogenital system	9 (6.1)	1 (2.3)	10 (8.5)	1.2 (0.6 to 2.2)
External genital system	3 (2.5)	2 (0.9)	5 (3.4)	1.5 (0.5 to 3.4)
Limb, musculoskeletal, and connective tissue	15 (10.2)	4 (3.7)	19 (13.9)	1.4 (0.8 to 2.1)
Other non-chromosomal	6	4	10	–
Chromosomal:	4 (7.2)	2 (4.2)	6 (11.4)	0.5 (0.2 to 1.1)
Trisomy 21	2	0	2	–
Other chromosomal	2	2	4	–

CNS=central nervous system.

*Expected numbers in parentheses based on data from EUROCAT 2002, adjusted for maternal age.

†Multiple anomalies within groups counted only once; total anomalies thus do not add up to 141.

Macintosh MCM et al BMJ, 2006; 333(7560):177.

Diabete e Gravidanza

Lo scompenso glicemico è associato ad un aumento di outcome avversi materni e neonatali

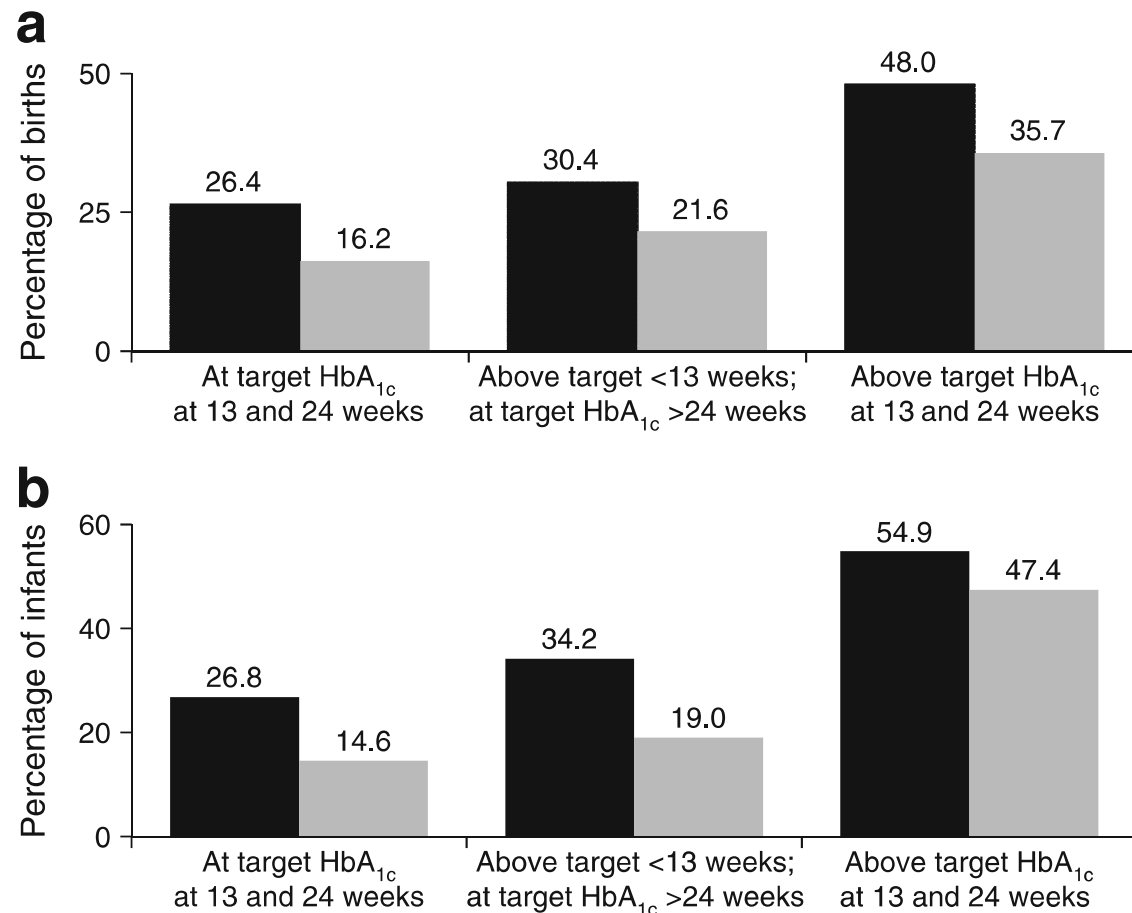


Fig. 2 Relationships for achievement of glycaemic control targets (HbA_{1c} < 6.5% [48 mmol/mol]) with (a) preterm delivery before 37 weeks' gestation and (b) rates of LGA in infants (customised birthweight >90th percentile). Black bars, type 1 diabetes; grey bars, type 2 diabetes

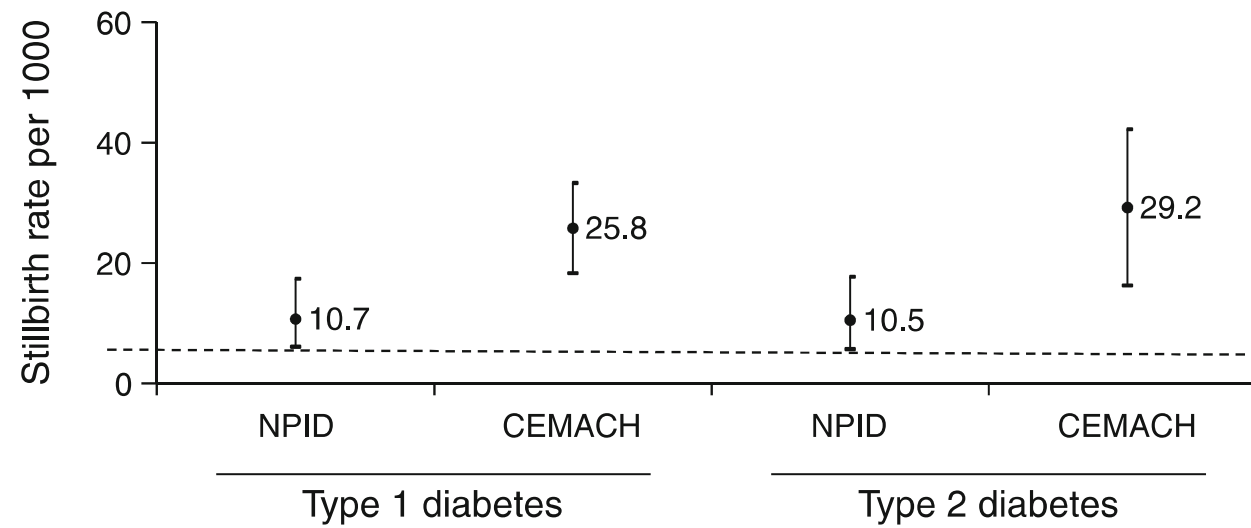
Diabete e Gravidanza

Il compenso glicemico riduce gli outcome avversi materni e neonatali

	NPID 2015	CEMACH 2002/2003
Number of women	3036	2359
Number of infants	2866	2400
Number of clinics ^a	155	231
Pregnancies per clinic	19.6	10.2
Type 1 diabetes ^b	1563 (51%)	1707 (72%)
Type 2 diabetes ^b	1386 (46%)	652 (28%)
Maternal duration of diabetes (years)		
Type 1 diabetes	14.9	13
Type 2 diabetes	4.8	3
Preconception folic acid (any dose) ^c		
Type 1 diabetes	51.7%	42.9%
Type 2 diabetes	33.7%	29.4%
Maternal glycaemic control		
Early pregnancy measurement <13 weeks	78%	67%
Type 1 diabetes		
HbA _{1c} %	7.6 (6.8–8.7)	7.5 (6.6–8.5)
HbA _{1c} mmol/mol	60 (51–72)	58 (48–69)
HbA _{1c} < 7% (53 mmol/mol)	29.4%	35.2%
Type 2 diabetes		
HbA _{1c} %	6.8 (6.2–8.0)	7.0 (6.1–8.1)
HbA _{1c} mmol/mol	51 (44–64)	53 (43–65)
HbA _{1c} < 7% (53 mmol/mol)	52.4%	49.0%
Late pregnancy >24 weeks		
Type 1 diabetes		
HbA _{1c} %	6.7 (6.1–7.5)	6.6 (6.0–7.3)
HbA _{1c} mmol/mol	50 (43–58)	49 (42–56)
HbA _{1c} < 7% (53 mmol/mol)	59.5%	65.0%
Type 2 diabetes		
HbA _{1c} %	5.9 (5.5–6.5)	6.3 (5.7–6.9)
HbA _{1c} mmol/mol	41 (37–47)	45 (39–52)
HbA _{1c} < 7% (53 mmol/mol) ^d	85.9%	75.4%
Severe adverse pregnancy outcomes		
Congenital anomaly ^e	117	109
Type 1 diabetes	69 (46.2/1000)	81 (48/1000)
Type 2 diabetes	46 (34.6/1000)	28 (43/1000)
Stillbirth	30	63
Type 1 diabetes	16 (10.7/1000)	44 (25.8/1000)
Type 2 diabetes	14 (10.5/1000)	19 (29.2/1000)
Neonatal death	27	22
Type 1 diabetes	12 (8.1/1000)	16 (9.6/1000)
Type 2 diabetes	15 (11.4/1000)	6 (9.5/1000)

Diabete e Gravidanza

Il compenso glicemico riduce gli outcome avversi materni e neonatali



Diabete e Gravidanza

Programmazione della gravidanza

Preconception Counseling

Recommendations

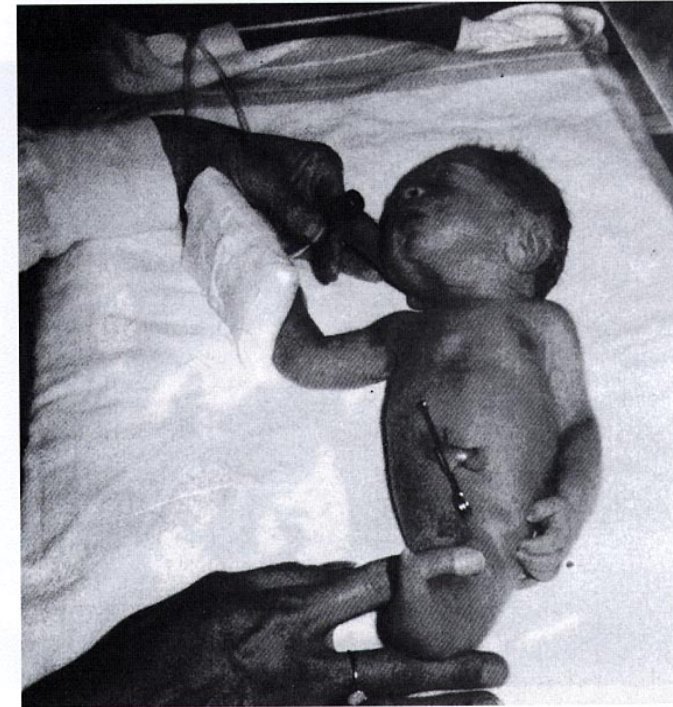
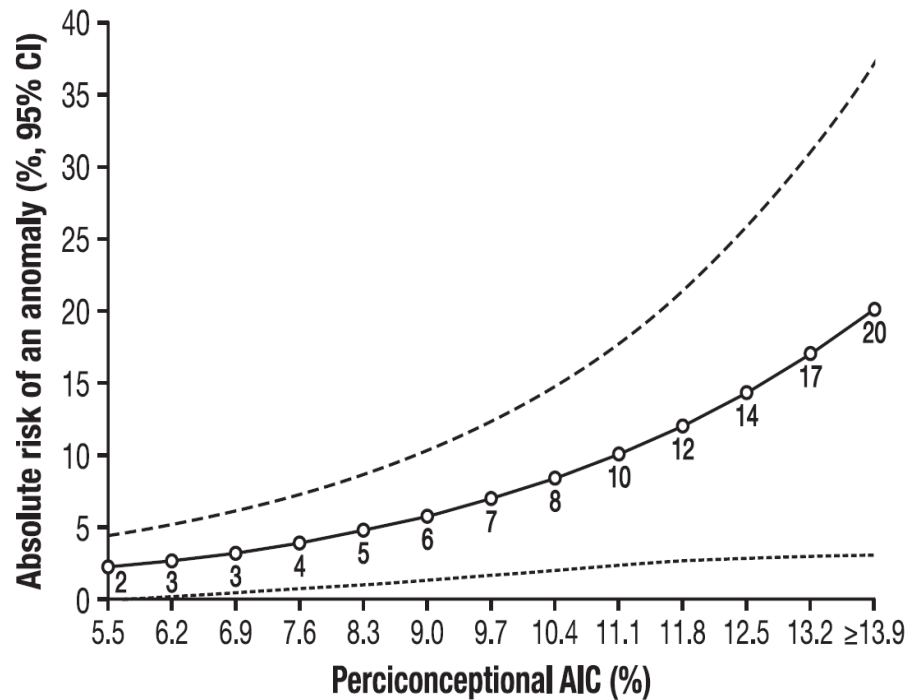
15.1 Starting at puberty and continuing in all people with diabetes and child-bearing potential, preconception counseling should be incorporated into routine diabetes care. **A**

15.2 Family planning should be discussed, and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until an individual's treatment plan and A1C are optimized for pregnancy. **A**

15.3 Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (<48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications. **A**

Diabete e Gravidanza

Controllo glicemico ottimale richiesto



15.3 Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (<48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications. **A**

(Livello della prova III, Forza della raccomandazione D)

Diabete e Gravidanza

Programmazione della gravidanza

Preconception Care

Table 15.1—Checklist for preconception care for people with diabetes

Preconception education should include:

- ☐ Comprehensive nutrition assessment and recommendations for:
 - Overweight/obesity or underweight
 - Meal planning
 - Correction of dietary nutritional deficiencies
 - Caffeine intake
 - Safe food preparation technique
- ☐ Lifestyle recommendations for:
 - Regular moderate exercise
 - Avoidance of hyperthermia (hot tubs)
 - Adequate sleep
- ☐ Comprehensive diabetes self-management education
- ☐ Counseling on diabetes in pregnancy per current standards, including: natural history of insulin resistance in pregnancy and postpartum; preconception glycemic goals; avoidance of DKA/severe hyperglycemia; avoidance of severe hypoglycemia; progression of retinopathy; PCOS (if applicable); fertility in people with diabetes; genetics of diabetes; risks to pregnancy including miscarriage, still birth, congenital malformations, macrosomia, preterm labor and delivery, hypertensive disorders in pregnancy, etc.
- ☐ Supplementation
 - Folic acid supplement (400 µg routine)
 - Appropriate use of over-the-counter medications and supplements

cations. **B**

15.6 Individuals with preexisting type 1 or type 2 diabetes who are planning a pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then pregnant individuals should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care health care professional. **B**

Diabete e Gravidanza

Programma di educazione della gravidanza

Recommendations

15.21 In pregnant individuals with diabetes and chronic hypertension, a blood pressure threshold of 140/90 mmHg for initiation or titration of therapy is associated with better pregnancy outcomes than reserving treatment for severe hypertension, with no increase in risk of small-for-gestational-age birth weight. **A** There are limited data on the optimal lower limit, but therapy should be deintensified for blood pressure <90/60 mmHg. **E** A blood pressure target of 110–135/85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension. **A**

15.22 Potentially harmful medications in pregnancy (i.e., ACE inhibitors, angiotensin receptor blockers, statins) should be stopped prior to conception and avoided in sexually active individuals of childbearing potential who are not using reliable contraception. **B**



Programma di educazione sui temi della riproduzione e della sessualità femminile deve far parte del corrente approccio educativo rivolto a tutte le donne diabetiche in età fertile nei centri diabetologici. Un counseling mirato deve portare a un'effettiva programmazione, sia prima del concepimento, coinvolgendo eventualmente anche il partner e tutte le persone professionali che sono a contatto con la paziente diabetica e prescrivendo una contraccezione che tenga conto del tipo di diabete, delle complicanze e di altri fattori di rischio (30). La programmazione della gravidanza deve comprendere diversi aspetti: la valutazione della capacità di eseguire la terapia insulinica e adattarla ai valori della glicemia, di riconoscere e trattare le ipoglicemie, di praticare correttamente il monitoraggio glicemico domiciliare.

La valutazione medica e laboratoristica dello stato di salute, screening della funzionalità renale, studio delle complicanze. Si considerano controindicazioni alla gravidanza: malattia cardiovascolare coronarica, retinopatia in fase attiva non trattata, ipertensione arteriosa grave, insufficienza renale (creatinina >3 mg/dl, filtrato glomerulare stimato 30 ml/min), gastroparesi, diabete gestazionale. Valutazione psicosociale.

La sospensione di farmaci potenzialmente tossici: ACE-inibitori, sartani, statine. E' stata dimostrata una tossicità degli ACE-inibitori già nelle prime settimane di gestazione (31); è raccomandata la loro sospensione in fase di programmazione della gravidanza.

La terapia insulinica nelle pazienti in trattamento con ipoglicemizzanti orali. Mancano, a tutt'oggi evidenze certe sulla innocuità o meno di molte di queste sostanze nella fase

della organogenesi.

Diabete e Gravidanza

Programmazione della gravidanza

Health assessment and plan should include:

- ☐ General evaluation of overall health
- ☐ Evaluation of diabetes and its comorbidities and complications, including DKA/severe hyperglycemia; severe hypoglycemia/hypoglycemia unawareness; barriers to care; comorbidities such as hyperlipidemia, hypertension, NAFLD, PCOS, and thyroid dysfunction; complications such as macrovascular disease, nephropathy, neuropathy (including autonomic bowel and bladder dysfunction), and retinopathy
- ☐ Evaluation of obstetric/gynecologic history, including a history of cesarean section, congenital malformations or fetal loss, current methods of contraception, hypertensive disorders of pregnancy, postpartum hemorrhage, preterm delivery, previous macrosomia, Rh incompatibility, and thrombotic events (DVT/PE)
- ☐ Review of current medications and appropriateness during pregnancy

Screening should include:

- ☐ Diabetes complications and comorbidities, including comprehensive foot exam; comprehensive ophthalmologic exam; ECG in individuals starting at age 35 years who have cardiac signs/symptoms or risk factors and, if abnormal, further evaluation; lipid panel; serum creatinine; TSH; and urine albumin-to-creatinine ratio
- ☐ Anemia
- ☐ Genetic carrier status (based on history):
 - Cystic fibrosis
 - Sickle cell anemia
 - Tay-Sachs disease
 - Thalassemia
 - Others if indicated
- ☐ Infectious disease
 - *Neisseria gonorrhoeae/Chlamydia trachomatis*
 - Hepatitis B and hepatitis C
 - HIV
 - Pap smear
 - Syphilis

Immunizations should include:

- ☐ Inactivated influenza
- ☐ Tdap (tetanus, diphtheria, and pertussis)
- ☐ COVID-19 (certain populations)
- ☐ Hepatitis A and hepatitis B (certain populations)
- ☐ Others if indicated

Preconception plan should include:

- ☐ Nutrition and medication plan to achieve glycemic goals prior to conception, including appropriate implementation of monitoring, continuous glucose monitoring, and pump technology
- ☐ Contraceptive plan to prevent pregnancy until glycemic goals are achieved
- ☐ Management plan for general health, gynecologic concerns, comorbid conditions, or complications, if present, including hypertension, nephropathy, retinopathy; Rh incompatibility; and thyroid dysfunction



Programmazione della Gravidanza in Italia 1998-2002 *(A.Lapolla)*

668 donne con Diabete Pregravidico
Programmazione della Gravidanza 46%

Contraception in Diabetic Women : an Italian Study

A.Napoli et al
Diab Res Cl Pr, 2004

Indagine condotta in 12 centri;
667 diabetiche (446 tipo 1, 202 tipo 2)
30.4% contraccezione ormonale
12% IUD
47% Metodi naturali
10.7% Nessun metodo



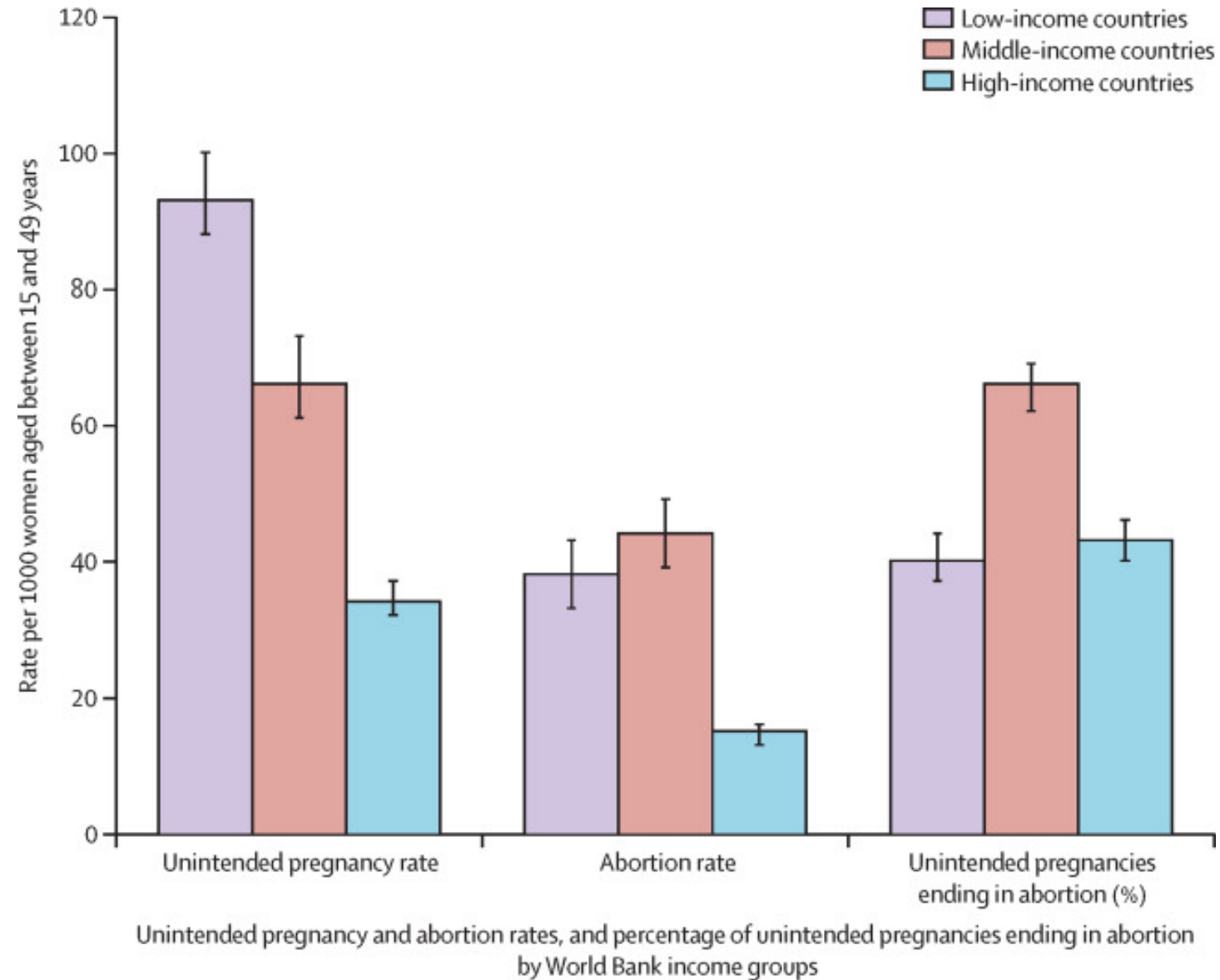
MANAGEMENT OF PREEXISTING TYPE 1 DIABETES AND TYPE 2 DIABETES IN PREGNANCY

Recommendations

15.18 Insulin should be used to manage type 1 diabetes in pregnancy. **A**
Insulin is the preferred agent for the management of type 2 diabetes in pregnancy. **B**

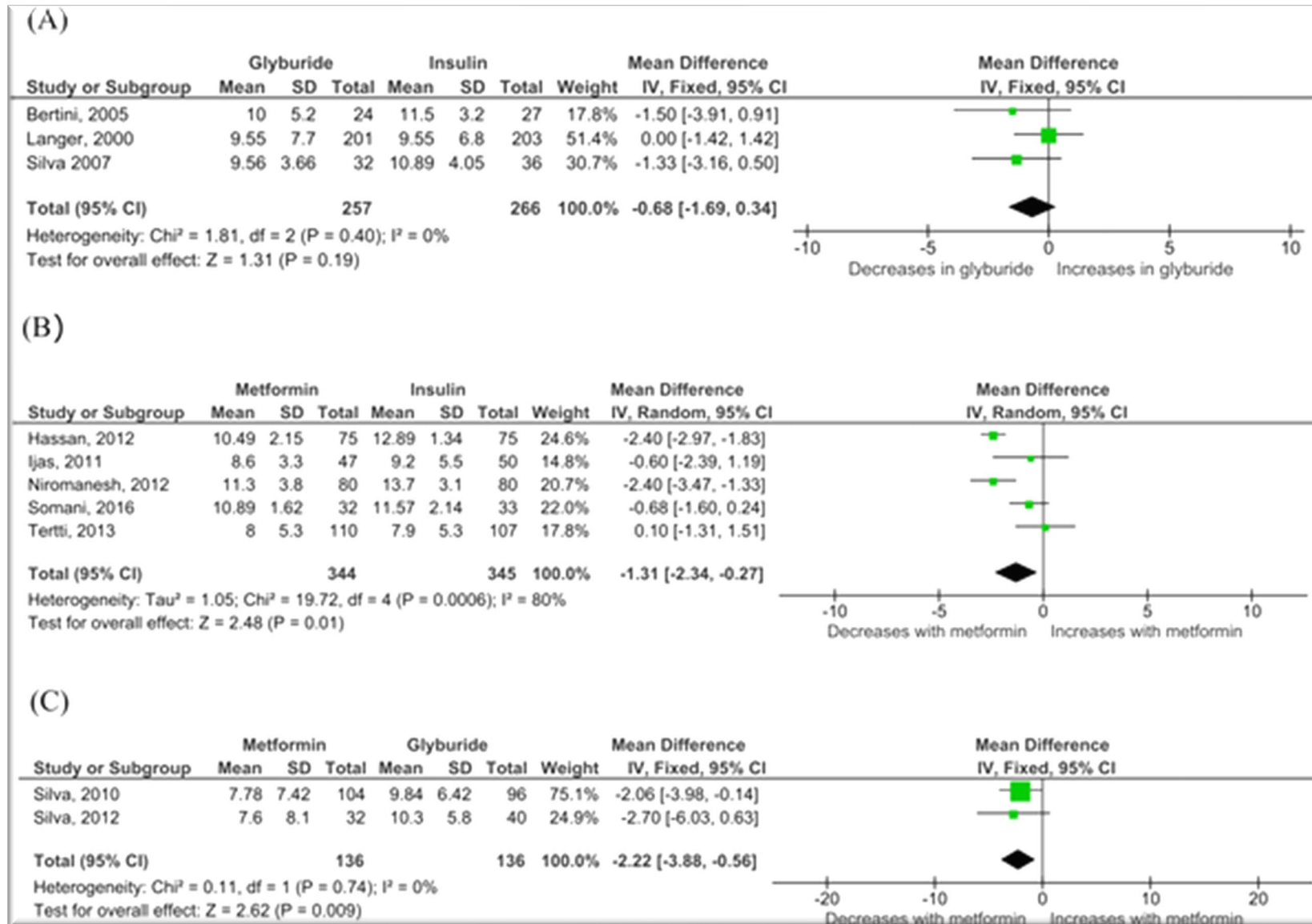
15.19 Either multiple daily injections or insulin pump technology can be used in pregnancy complicated by type 1 diabetes. **C**

Gravidanze non programmate

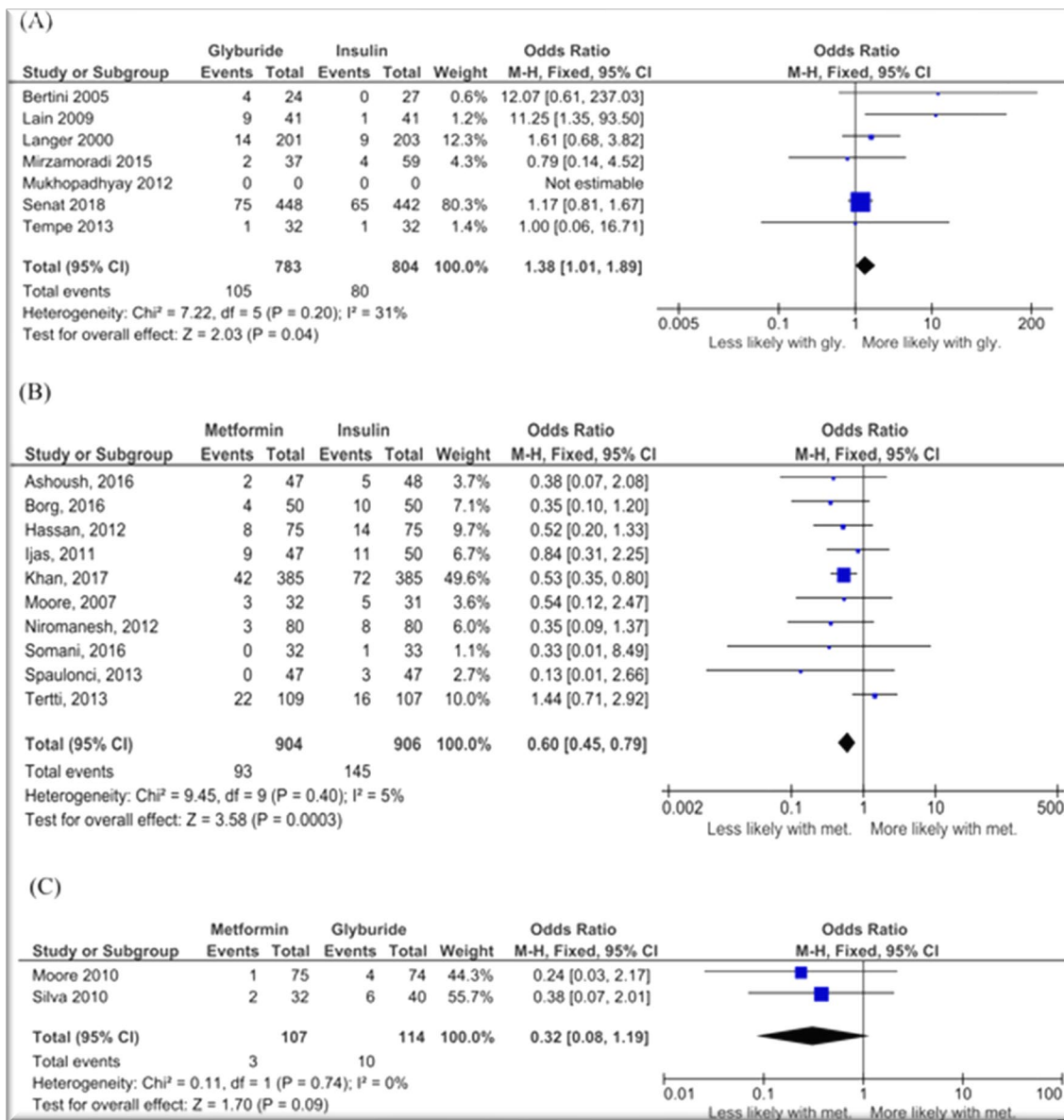




Diabete e Gravidanza



Diabete e Gravidanza



Diabete e Gravidanza

LGA

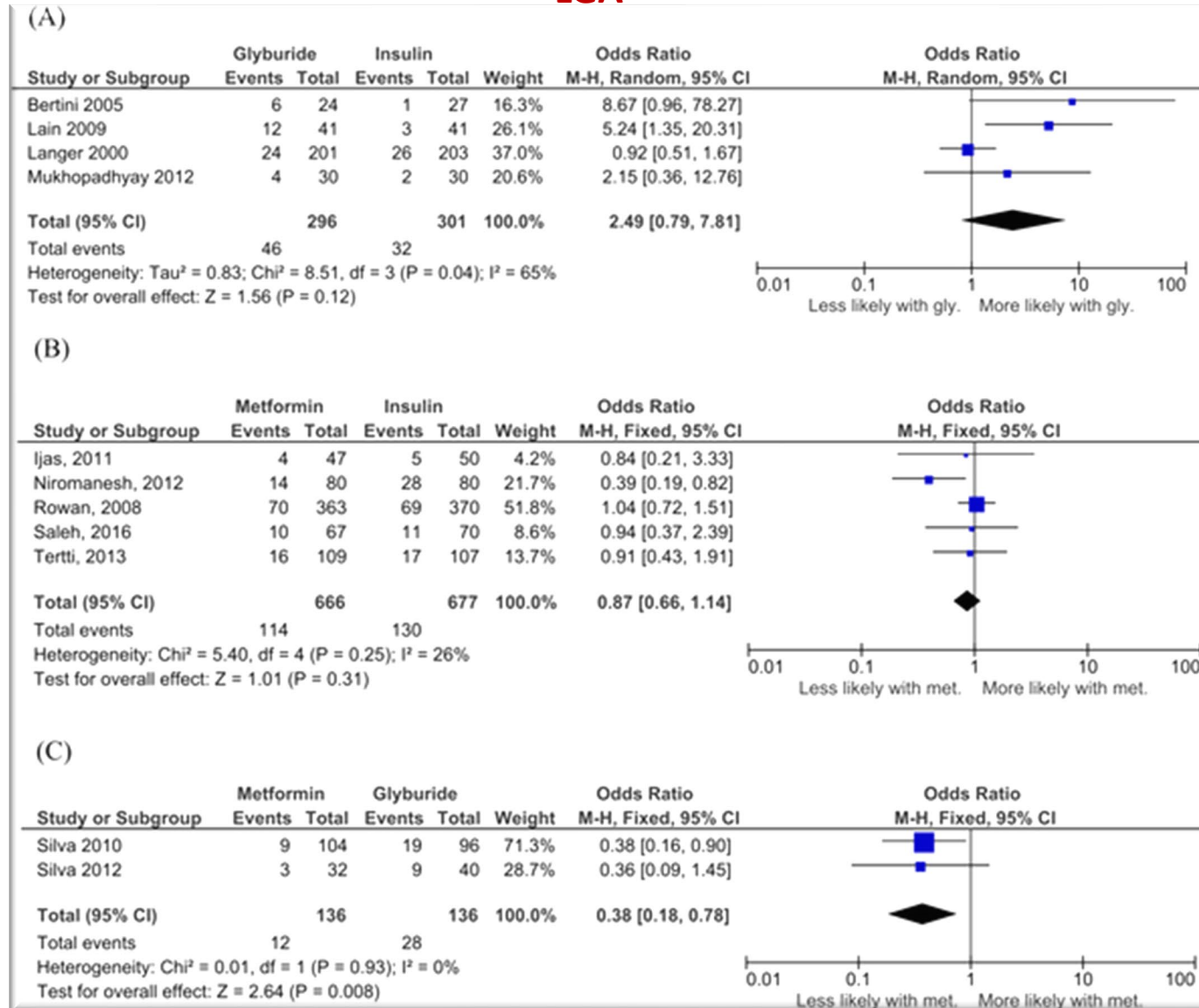
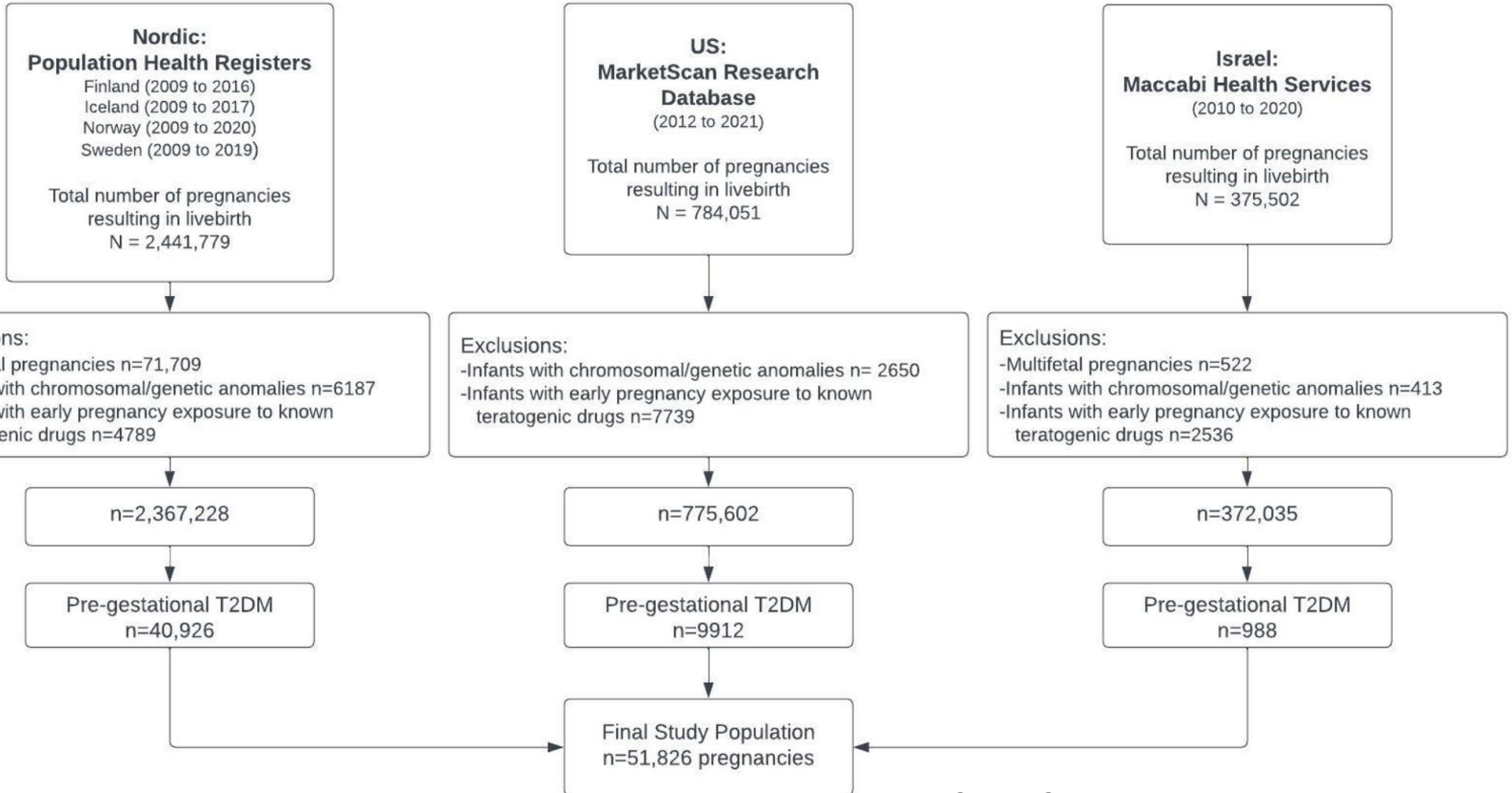


Table 11 Maternal outcomes in T2DM women treated with metformin during pregnancy		T2DM women	
	Glycemic control		Comparable or slightly improved as compared to insulin alone
	Hypoglycemia		Lower rate as compared to insulin alone
	Total insulin dose		Reduced
Table 13 Main maternal and infant outcomes in metformin treated women with T2DM			Reduced
Maternal outcomes	Gestational hypertension/reclampsia rate		No significant difference
	Cesarian section	Infant outcomes	Decreased
Type 2 diabetes	Reduced maternal weight gain		No significant difference
	Decreased risk of maternal hypoglycemia		Decreased risk of neonatal hypoglycemia
	Better metabolic control during the later stages of pregnancy		Decreased LGA and reduced body fat of neonates
			Increased risk for SGA in women with comorbidities as chronic hypertension or nephropathy in pregnancy
		T2DM women	2 years old children have similar BMI Z score and skinfolds thickness
Newborns			
	Birth weight		Lower
	LGA/Macrosomia		Decreased
	SGA		Increased
	Hypoglycemia		Decreased
	Neonatal intensive care unit admission		No significant difference
Infants			
	BMI		No significant difference
	Fasting glycemia		Increased

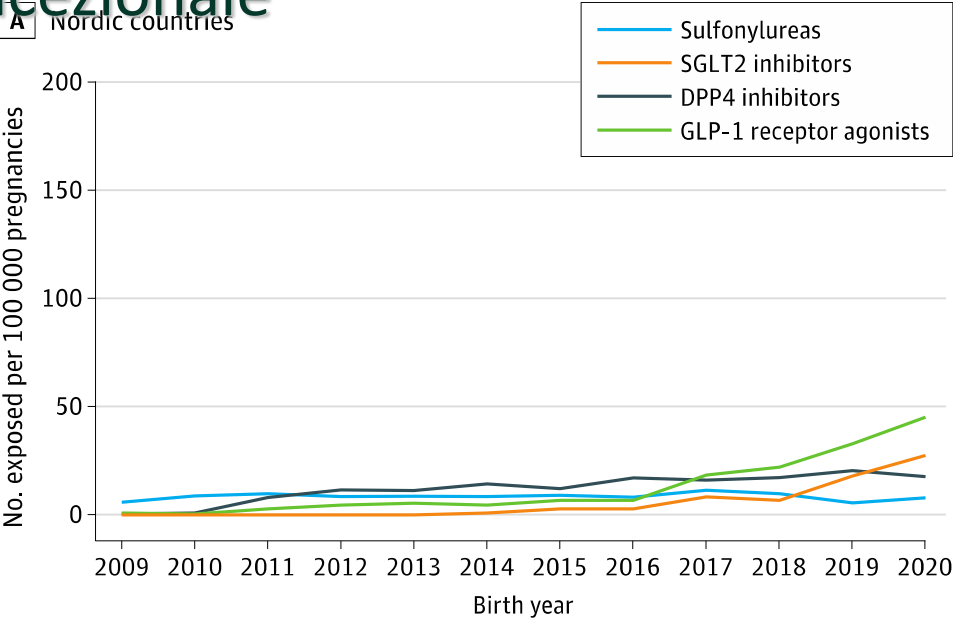
Safety of GLP-1 Receptor Agonists and Other Second-Line Antidiabetics in Early Pregnancy

Carolyn E. Cesta, PhD; Ran Rotem, ScD; Brian T. Bateman, MD, MSc; Gabriel Chodick, PhD;
 Jacqueline M. Cohen, PhD; Kari Furu, PhD; Mika Gissler, PhD; Krista F. Huybrechts, PhD; Lars J. Kjerpeseth, PhD;
 Maarit K. Leinonen, PhD; Laura Pazzagli, PhD; Helga Zoega, PhD; Ellen W. Seely, MD;
 Elisabetta Paterno, MD, DrPH; Sonia Hernández-Díaz, MD, DrPH

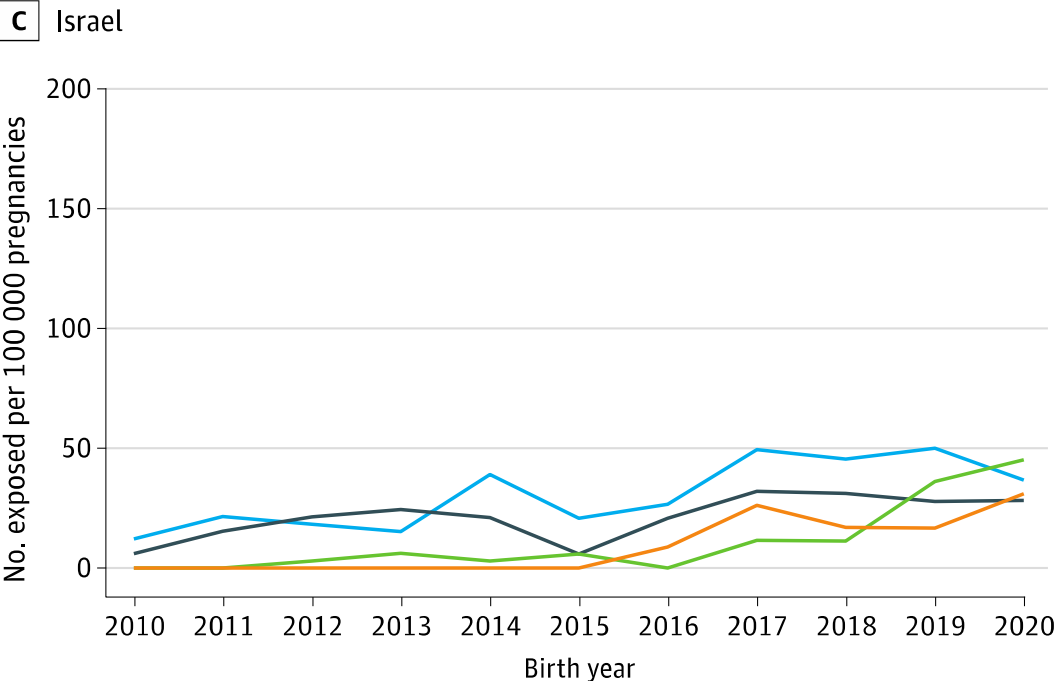
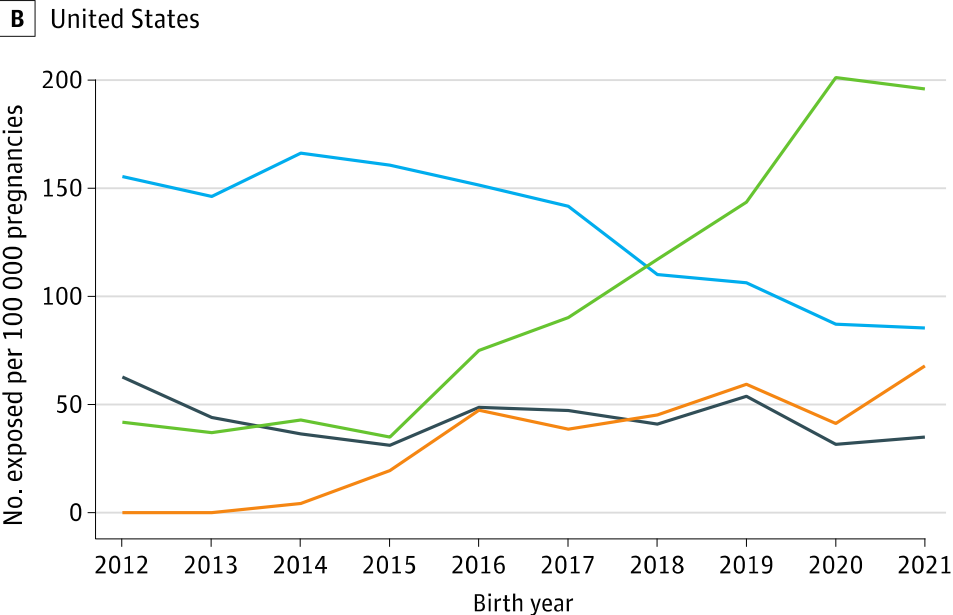
InPreSS consortium



Prevalenza dell'uso di farmaci antidiabetici di seconda linea nel periodo periconcezionale



Periconceptional exposure: from 90 days before the first day of the last menstrual period to the end of the first trimester



BMJ Open Use of GLP1 receptor agonists in early pregnancy and reproductive safety: a multicentre, observational, prospective cohort study based on the databases of six Teratology Information Services

Kim Dao,¹ Svetlana Shechtman,² Corinna Weber-Schoendorfer,³ Orna Diav-Citrin,^{2,4} Reem Hegla Murad,² Maya Berlin ,⁵ Ariela Hazan,⁵ Jonathan L Richardson,⁶ Georgios Eleftheriou,⁷ Valentin Rousson,⁸ Leonore Diezi,¹ David Haefliger,¹ Ana Paula Simões-Wüst ,⁹ Marie-Claude Addor,¹⁰ David Baud ,¹¹ Faiza Lamine,^{12,13} Alice Panchaud,^{14,15} Thierry Buclin,¹ François R Girardin,¹ Ursula Winterfeld ¹

MATERIAL AND METHODS

Study design and dataset description

This multicentre, prospective, observational cohort study was conducted involving six participating centres that are members of the European Network of Teratology Information Services (ENTIS) in five countries: Germany, Israel, Italy, Switzerland, and the UK. ENTIS is an organisation of specialised services providing expertise on potential risks associated with medication exposure during pregnancy and breastfeeding at an individual level.¹⁹ Standardised

Nessun incrementato rischio di outcome avversi in seguito a esposizione a GLP1-RA nel primo trimestre

	GLP1-RA group (n=168)	Reference group with diabetes (n=156)	Overweight/obese reference group (n=163)
Live-born infants, n	113	126	117
Elective termination of pregnancy for personal reasons, n	20	5	6
Medical termination of pregnancy, n	3*	1†	7‡§
Spontaneous abortion, n	31	23	29
Stillbirth, n	1	1	4
Preterm delivery, n (%) (n=113, 126, 127)	9 (8.0)	19 (15.1)	17 (14.5)
Gestational age at birth (week), median (IQR) (n=113, 125, 117)	39 (38–40)	38 (37–39)	39 (38–40)
Birth weight (g), median (IQR) (n=113, 124, 117)	3400 (3100–3660)	3370 (2890–3682)	3245 (2850–3560)
Large for gestational age, n (%) (n=113, 124, 117)	20 (17.7)	29 (23.4)	7 (6.0)
Small for gestational age, n (%) (n=113, 124, 117)	9 (8.0)	10 (8.1)	17 (14.5)
Delivery mode, n (%) (n=112, 135, 108)			
Spontaneous vaginal delivery	60 (53.6)	68 (50.4)	60 (55.6)
Assisted delivery and caesarean section	52 (46.4)	67 (49.6)	48 (44.4)

Nessun incrementato rischio di outcome avversi in seguito a esposizione a GLP1-RA nel primo trimestre

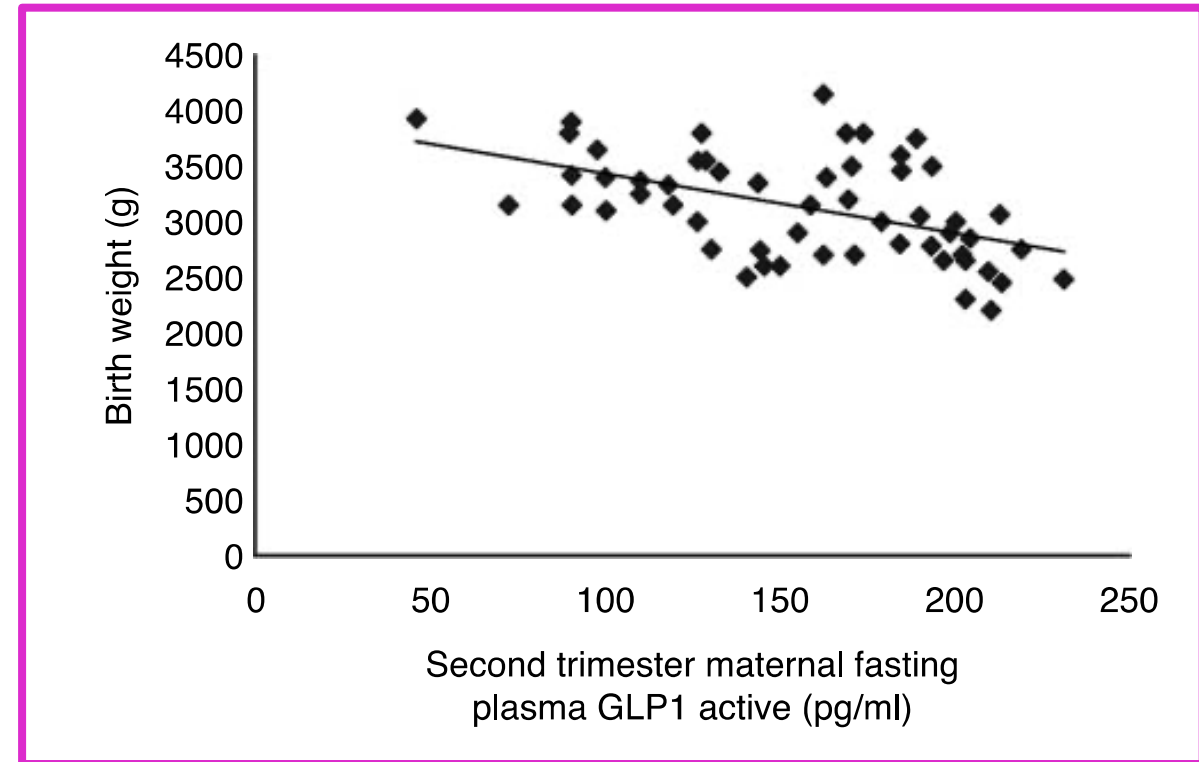
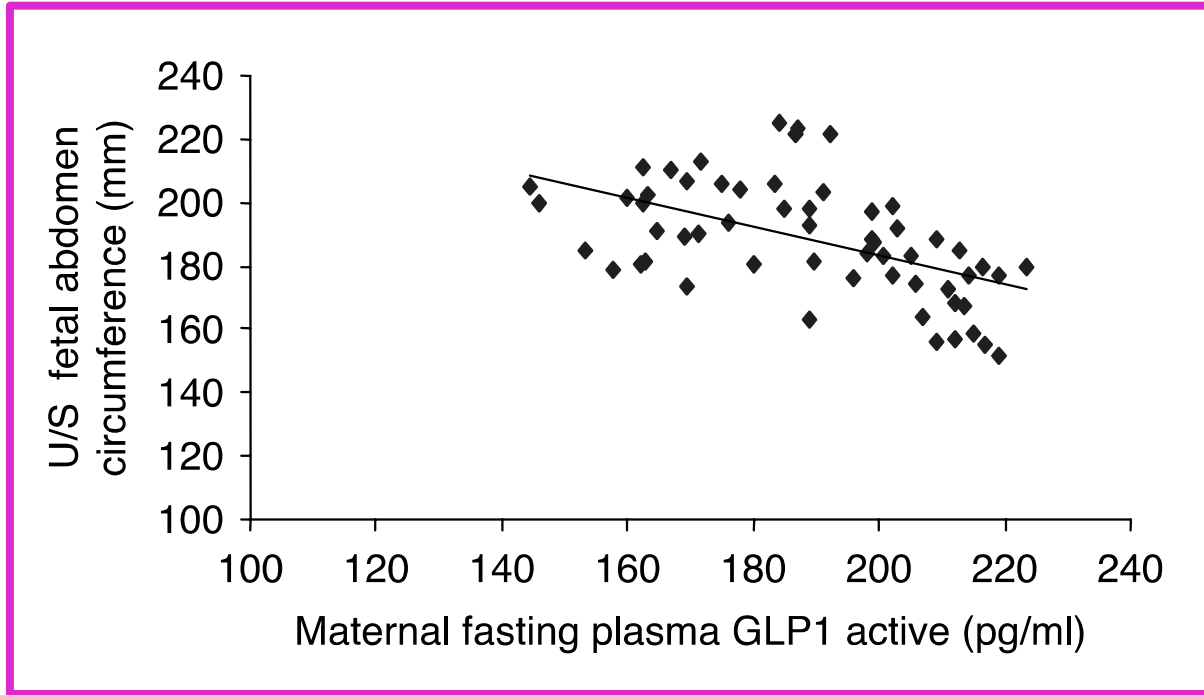
	GLP1-RA group vs diabetic reference group		GLP1-RA group vs overweight/obese reference group	
	HR (95% CI)	HR _{adj} (95% CI)*	HR (95% CI)	HR _{adj} (95% CI)*
Pregnancy loss†	1.10 (0.65 to 1.89)	1.67 (0.93 to 3.01)	0.92 (0.56 to 1.49)	0.80 (0.48 to 1.33)
Pregnancy termination‡	2.92 (1.18 to 7.20)	3.89 (1.48 to 10.2)	1.79 (0.89 to 3.62)	1.39 (0.66 to 2.93)
*Adjusted for maternal age, tobacco use, folate intake, past abortion or termination history. †Spontaneous abortions and stillbirths. ‡Elective or medical termination of pregnancy. GLP1-RA, glucagon-like peptide 1 receptor agonists; HR_{adj}, adjusted HR.				

I livelli di GLP-1 aumentano nel terzo trimestre nelle gravidanze fisiologiche

Prepregnancy			
BMI (kg/m ²)	24.7 (2.2)		
Pregnancy	First trimester	Second trimester	Third trimester
Maternal weight (kg)	68.5 (13.1)	73 (12.7) ^a	77.9 (14.5) ^{a,b}
Maternal fat (%)	31.1 (5.3)	32.1 (4.6) ^a	33 (5.9) ^{a,b}
U/S fetal abdomen circumference (mm)		189.1 (177–209.5)	298.3 (280.5–309.9) ^b
U/S fetal biparietal diameter (mm)		60.6 (54.5–64.6)	86 (81.8–95.5) ^b
U/S fetal head circumference (mm)		208.4 (193.1–228)	312.1 (300.6–319) ^b
U/S fetal femur length (mm)		42.6 (37.8–46)	69.5 (63.6–89.2) ^b
U/S fetal estimated weight (g)		607 (496–783)	2178.8 (1870–2443) ^b
Fasting active GLP1 (pg/ml)	159.7 (89.8–209)	169.6 (127.5–203)	200.3 (166–234.5) ^{a,b}
Fasting active ghrelin (pg/ml)	41.1 (29–58.3)	37.9 (29–50.9)	41.8 (36.7–44)
Fasting total PYY (pg/ml)	97.1 (69.4–129.6)	92.3 (73.8–137)	98 (89–113.9)
Fasting total GIP (pg/ml)	14 (9.5–22.4)	9.4 (6.2–14.8)	10.3 (8.6–14.7)
Fasting glucose (mmol/l)	4.3 (0.3)	4.4 (0.2)	4.5 (0.4)
Fasting insulin (pmol/l)	56.3 (42.5–73)	59 (49–119.3)	117 (88–147) ^{a,b}
ISI	0.1 (0.07–0.1)	0.08 (0.05–0.1) ^a	0.04 (0.004–0.06) ^{a,b}
HOMA-R	1.7 (1.3–2.4)	1.9 (1.6–3.9)	3.9 (2.8–4.9) ^{a,b}
First PHIS	969 (812–1254)	1117 (886–1381) ^a	1116.4 (673.5–1413) ^a
Second PHIS	283 (213–375)	328 (257–436) ^a	339.4 (223.2–446.5) ^a
Postpregnancy			
Birth weight (g)	3175 (2730–3512)		

Maternal GLP1 might be involved in mechanisms that compensate for the pregnancy-related increase in glycemia and insulin resistance

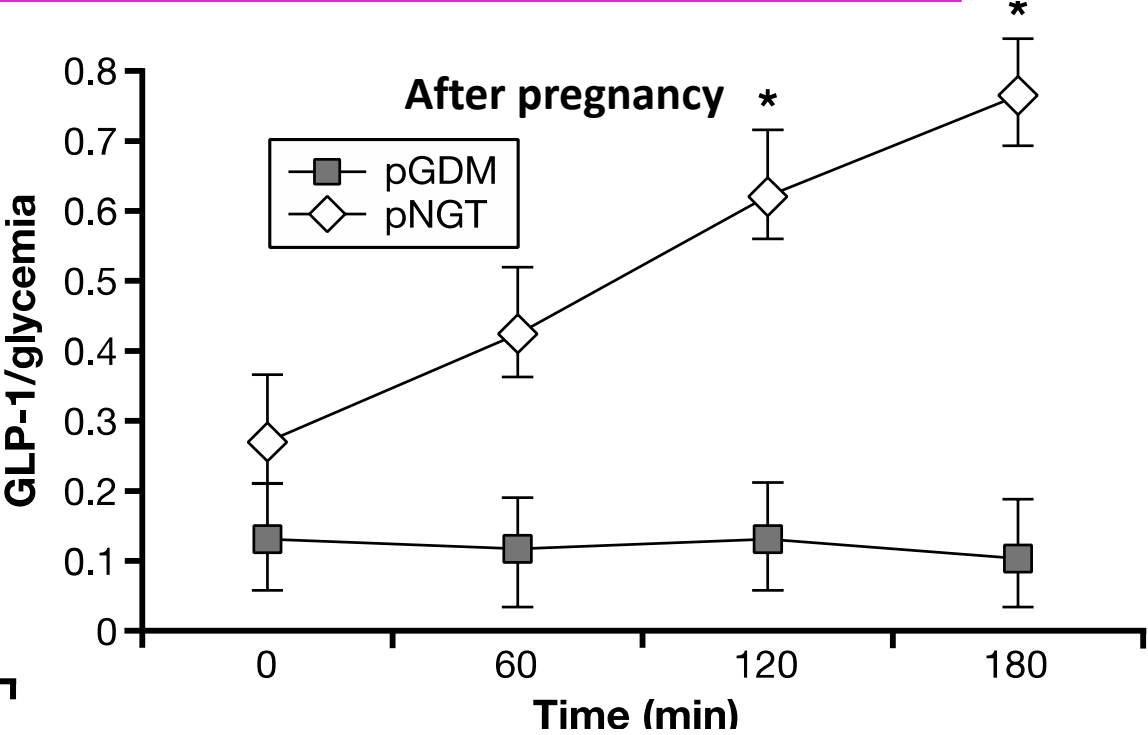
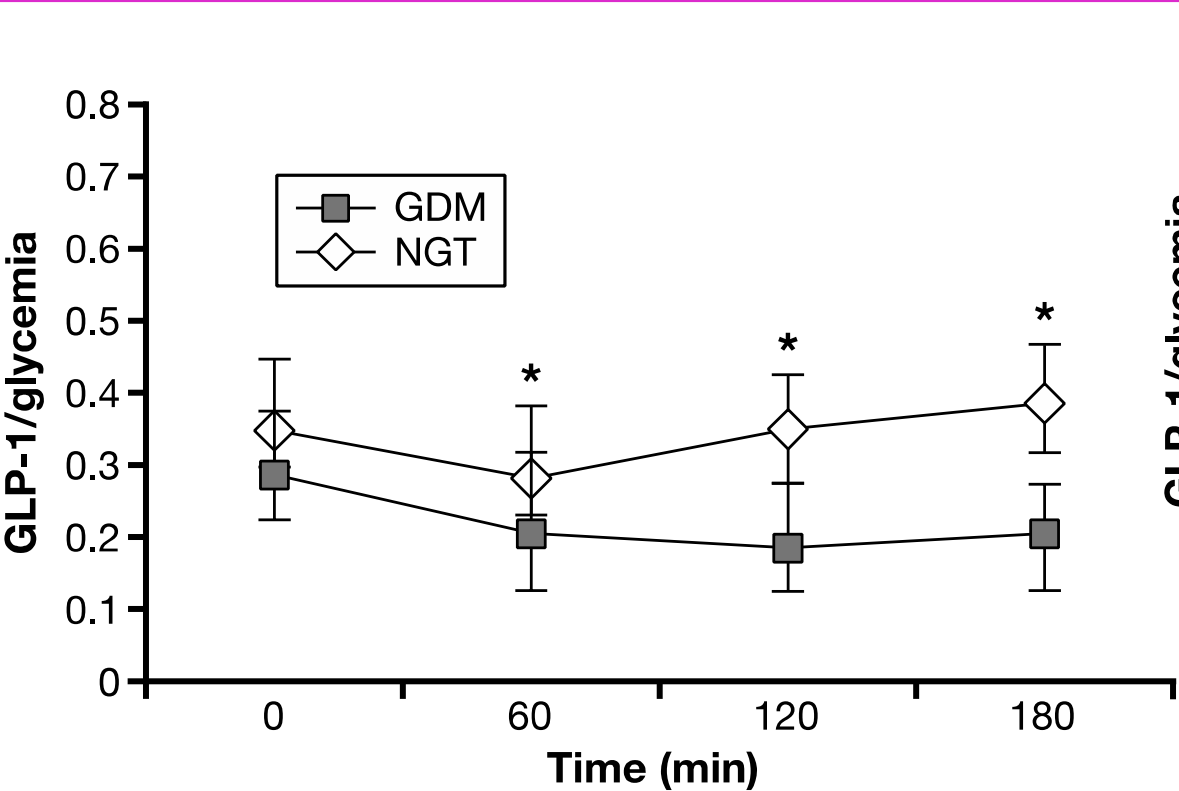
Correlazione inversa tra i livelli di GLP-1 e circonferenza fetale addominale e peso alla nascita



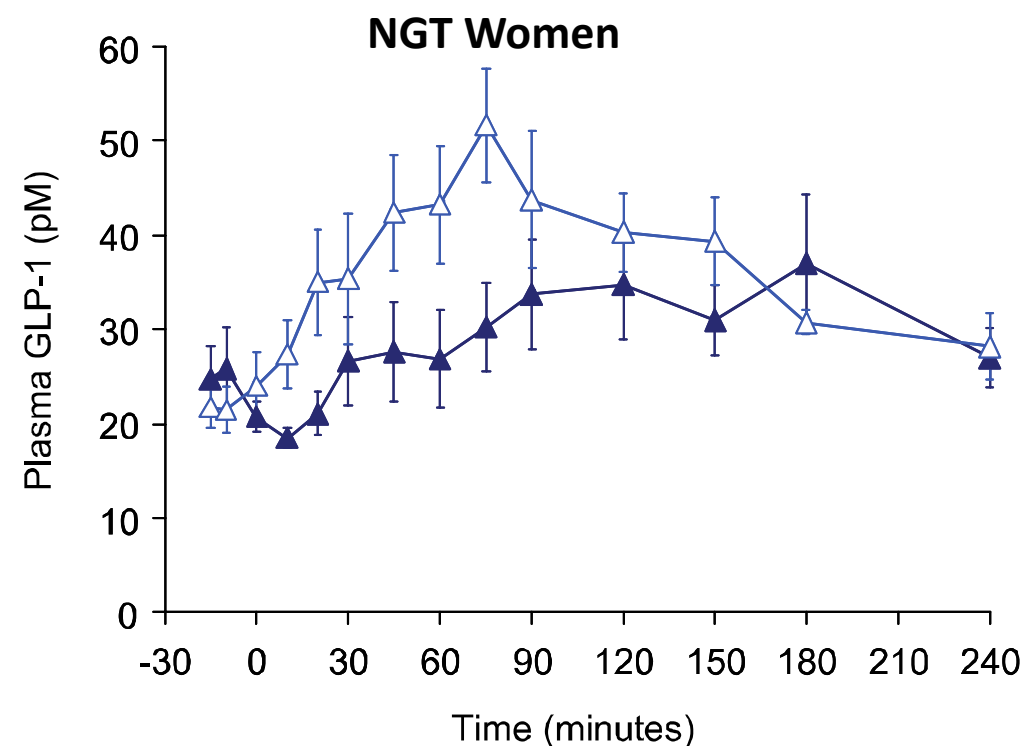
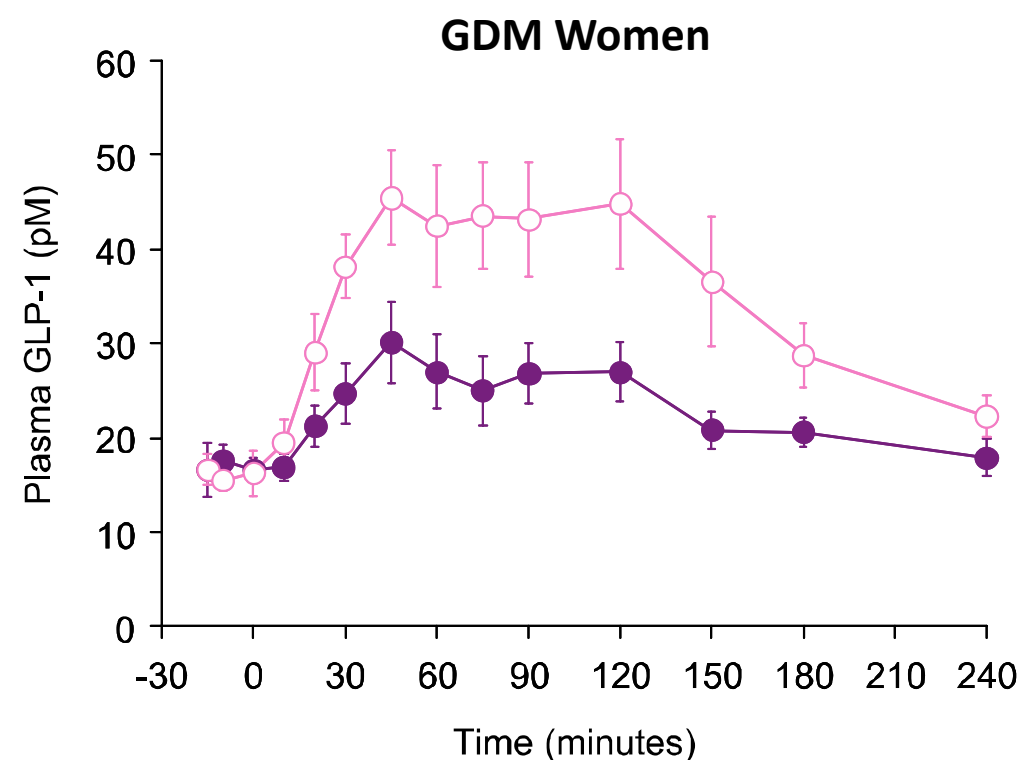
Maternal GLP1 might be involved in mechanisms that compensate for the pregnancy-related increase in glycemia and insulin resistance

Ridotti livelli di GLP-1 in donne con GDM

Time (min)	GDM (no.=12)				NGT (no.=16)			
	Glucose (mg/dl)	Insulin (μUI/ml)	C-peptide (ng/ml)	GLP-1 (pmol/l)	Glucose (mg/dl)	Insulin (μUI/ml)	C-peptide (ng/ml)	GLP-1 (pmol/l)
0	85.08±5.83	9.6±5.2	1.83±0.48	24.5±5.3	83.17±5.8	9.4±4.4	1.75±0.47	29.38±9.9
60	197.58±13.5*	99.74±30.8	10.40±2.47	40.7±17.1	139.47±24.5	96.47±42.2	10.63±3.42	38.12±12.3
120	172.58±22.89*	110.26±45.4	12.41±3.13	29.9±11.8	114±20.05	93.13±45.4	14.84±14.15	38.67±15.1
180	118.83±27.3**	68.79±31.8	8.61±4.49	21.6±9.57**	99.41±15.7	62.18±35.5	12.41±14.9	37.08±23.4



Ridotti livelli di GLP-1 in donne con GDM



GLP-1			
Fasting baseline _{TT} (pM)	16.9 ± 4.2	23.8 ± 8.2	0.030
Fasting baseline _{PP} (pM)	16.1 ± 5.1	22.4 ± 7.2	0.039
p (TT vs. PP)	0.67	0.75	
AUC _{TT} (nM × min)	5.5 ± 1.3	7.3 ± 2.8	0.076
AUC _{PP} (nM × min)	8.4 ± 3.2	8.8 ± 2.0	0.73
p (TT vs. PP)	0.005	0.066	



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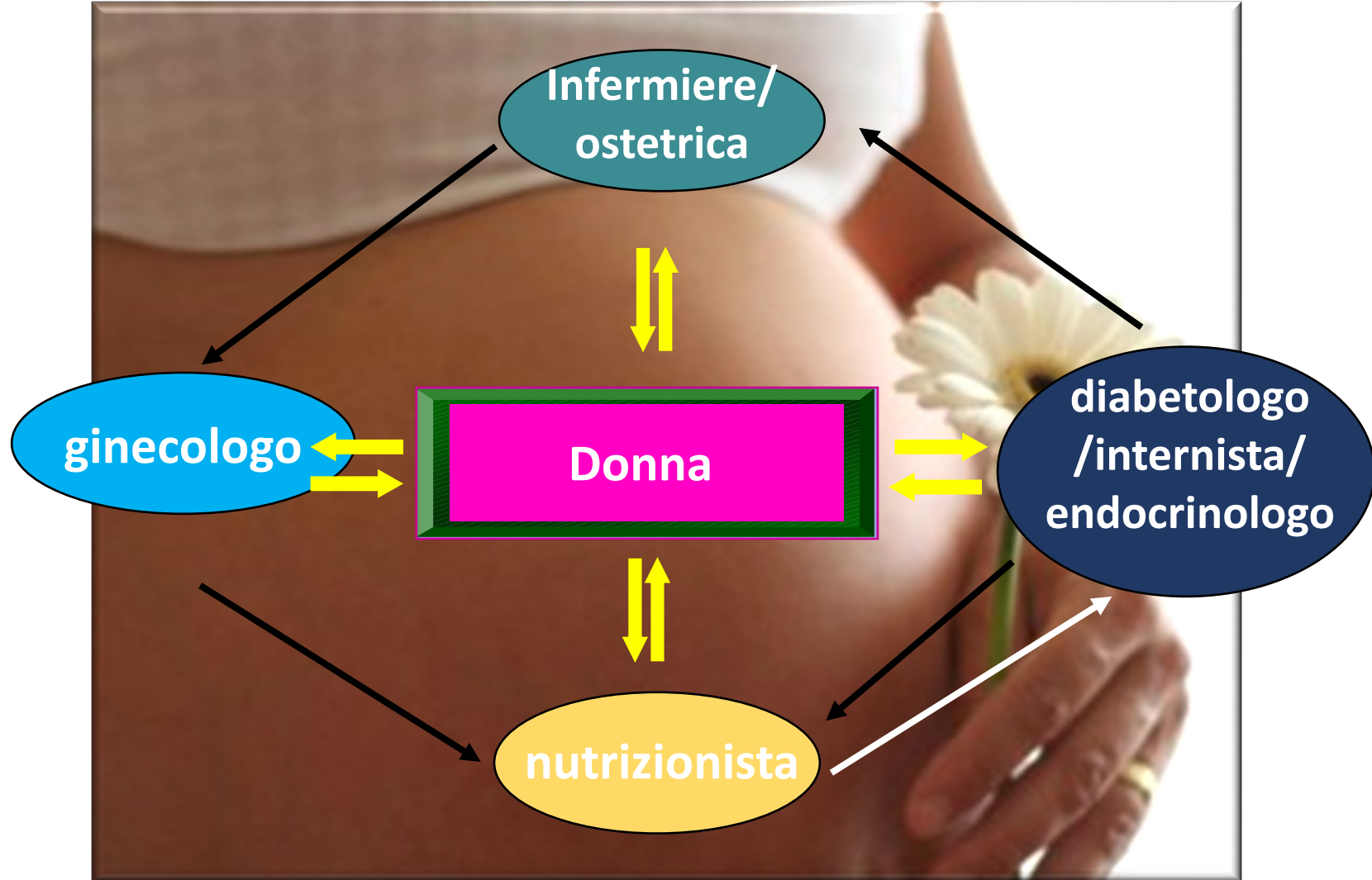
Safety of GLP-1 Receptor Agonists and Other Second-Line Antidiabetics in Early Pregnancy

Carolyn E. Cesta, PhD; Ran Rotem, ScD; Brian T. Bateman, MD, MSc; Gabriel Chodick, PhD; Jacqueline M. Cohen, PhD; Kari Furu, PhD; Mika Gissler, PhD; Krista F. Huybrechts, PhD; Lars J. Kjerpeseth, PhD; Maarit K. Leinonen, PhD; Laura Pazzagli, PhD; Helga Zoega, PhD; Ellen W. Seely, MD; Elisabetta Paterno, MD, DrPH; Sonia Hernández-Díaz, MD, DrPH

BMJ Open Use of GLP1 receptor agonists in early pregnancy and reproductive safety: a multicentre, observational, prospective cohort study based on the databases of six Teratology Information Services

inhibitors, 7.0% (n = 335); and insulin, 7.8% (n = 5078). Compared with insulin, adjusted RRs for MCMs were 1.18 (95% CI, 0.94-1.48), 0.83 (95% CI, 0.64-1.06), 0.95 (95% CI, 0.72-1.26), and 0.98 (95% CI, 0.65-1.46) for infants exposed to sulfonylureas, DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors, respectively.

CONCLUSIONS AND RELEVANCE Use of second-line noninsulin ADMs is rapidly increasing for treatment of T2D and other indications, resulting in an increasing number of exposed pregnancies. Although some estimates were imprecise, results did not indicate a large increased risk of MCMs above the risk conferred by maternal T2D requiring second-line treatment. Although reassuring, confirmation from other studies is needed, and continuous monitoring will provide more precise estimates as data accumulate.



Grazie per l'attenzione!

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