

9⁰ CONGRESSO CONGIUNTO **SID-AMD** **Sicilia**

»» Il diabete oggi tra prevenzione,
nuovi farmaci e tecnologia:
un ponte verso il futuro

OBESITÀ IN GRAVIDANZA, NON SOLO RISCHIO DI DIABETE GESTAZIONALE

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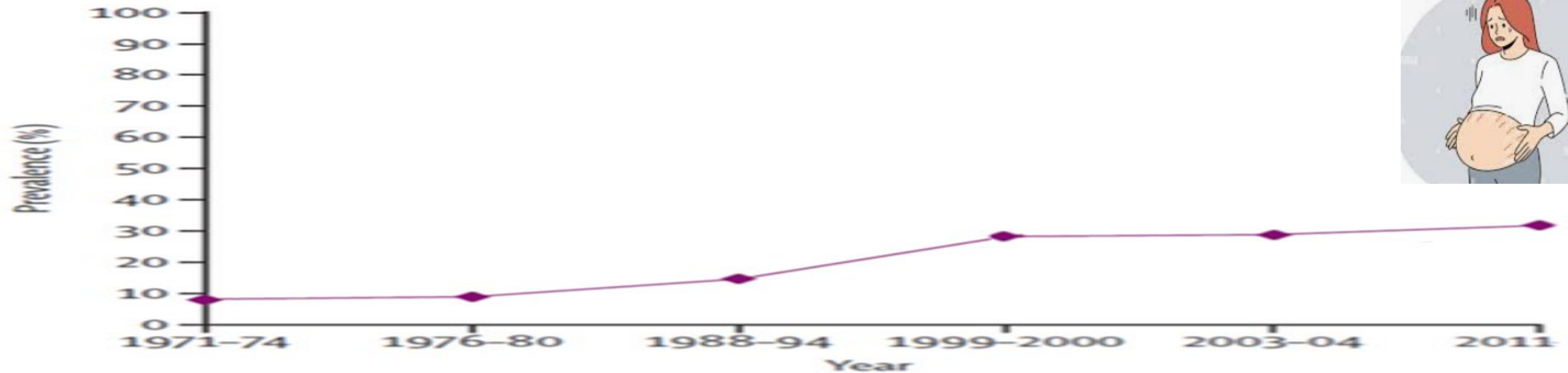
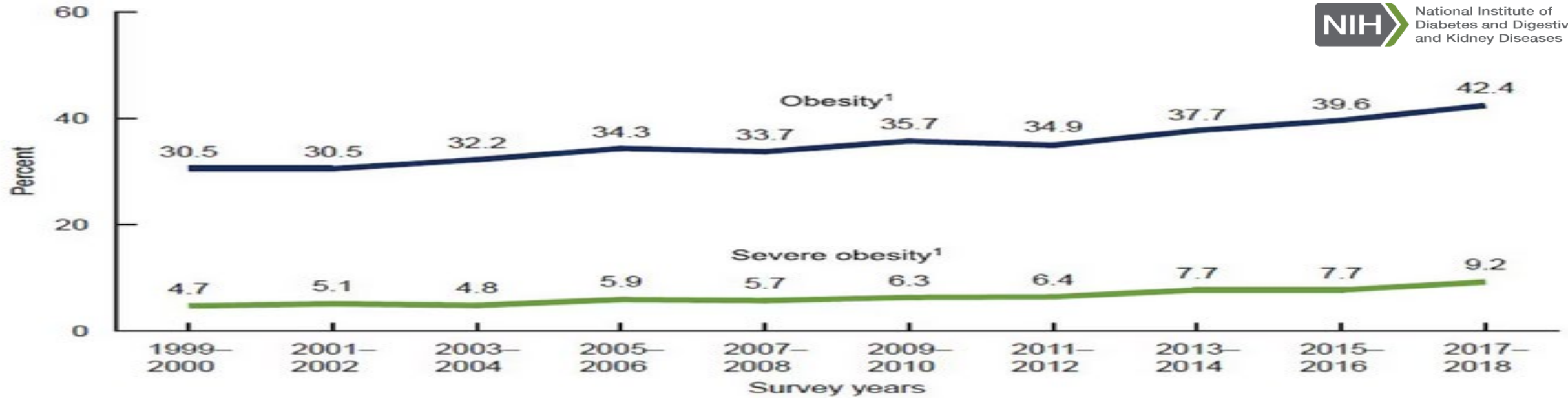
15 Novembre 2024

Il dr. Agostino Milluzzo dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- Eli Lilly
- Novo Nordisk
- Astrazeneca

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.).

PREVALENZA OBESITA'



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Obesity in Pregnancy

Andreea A. Creanga, M.D., Patrick M. Catalano, M.D.,
and Brian T. Bateman, M.D.

N ENGL J MED 387;3 NEJM.ORG JULY 21, 2022

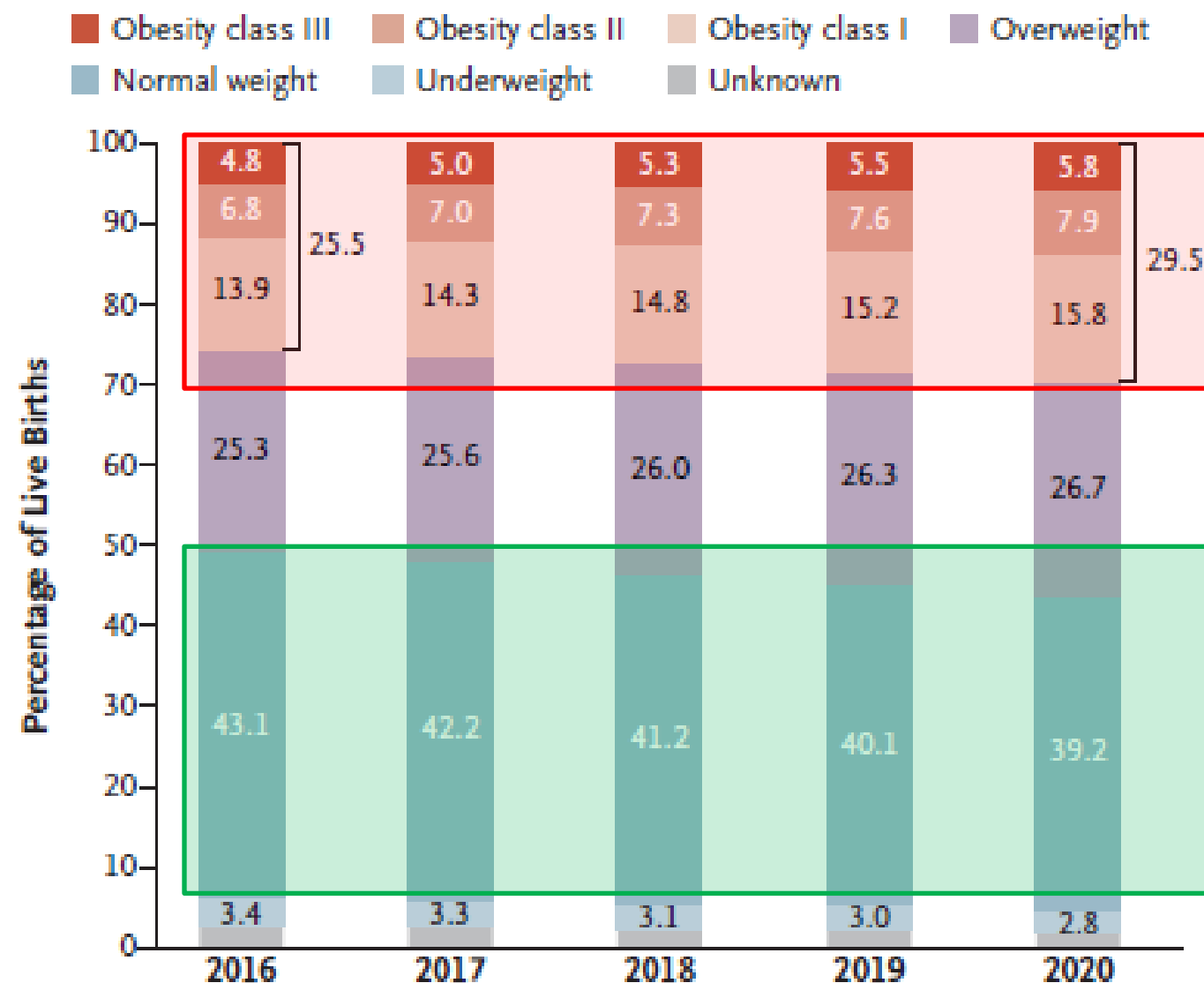


Figure 1. Trends in the Distribution of Live Births in the United States According to Maternal Prepregnancy Body-Mass Index (BMI), 2016 through 2020.

REVIEW ARTICLE

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Obesity in Pregnancy

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OBESITY IS THE MOST COMMON HEALTH PROBLEM IN WOMEN OF REPRODUCTIVE AGE.¹ Not only does obesity pose clinically significant health risks to women during pregnancy and after delivery, but it also has long-term health implications that require recognition and treatment.^{1,2} Maternal obesity can adversely affect fetal, neonatal, and infant outcomes, with lifelong consequences for the offspring. Evidence-based options for nutritional, behavioral, and surgical management of maternal obesity are available. Ideally, such management approaches should be instituted before pregnancy and should be continued after delivery and as part of long-term care, to ensure the best possible maternal and fetal outcomes and to prevent severe complications.³ This review provides an overview of conditions and factors associated with obesity in pregnancy, as well as key management considerations for obese persons who are pregnant or have given birth. This information is relevant not only to obstetricians but to all clinicians caring for women of reproductive age, since prevention of long-term complications associated with obesity in pregnancy requires a life-course approach.

Short-term complications

Maternal

- Pre-eclampsia/eclampsia

Neonatal

- Macrosomia
- Large for gestational age
- Shoulder dystocia
- Higher body fat

Delivery

- Prolonged labor
- Caesarean birth
- Surgical complications
- Longer hospital stay
- Maternal hemorrhage
- Infection

Long-term complications

Maternal and Child

- Type 2 diabetes mellitus
- Cardiovascular disease
- Metabolic syndrome
- Obesity

during pregnancy

after delivery

long-term health implications

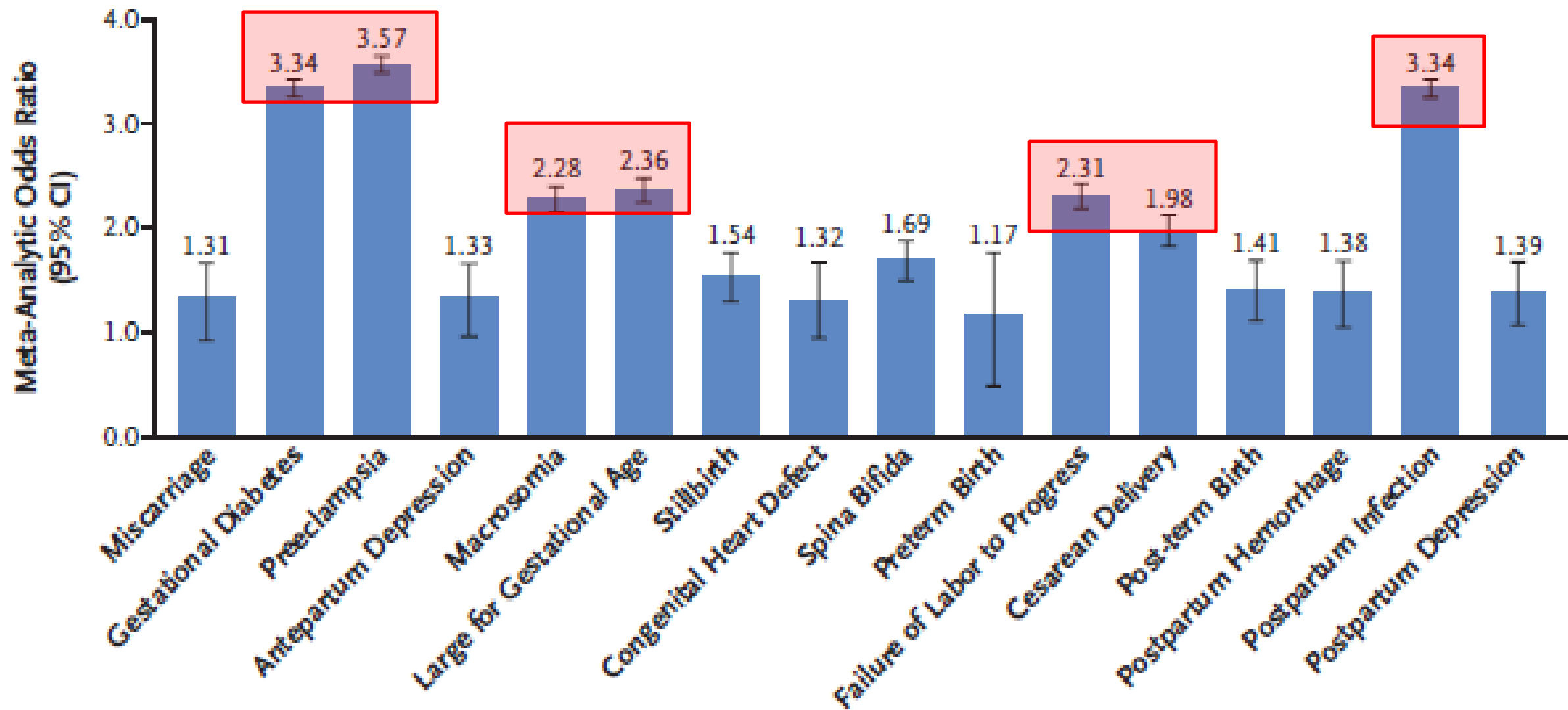


Figure 4. Risk of Adverse Outcomes Associated with Obesity.

Table 3. Adjusted odds ratios for maternal, delivery, and neonatal complications in the study population

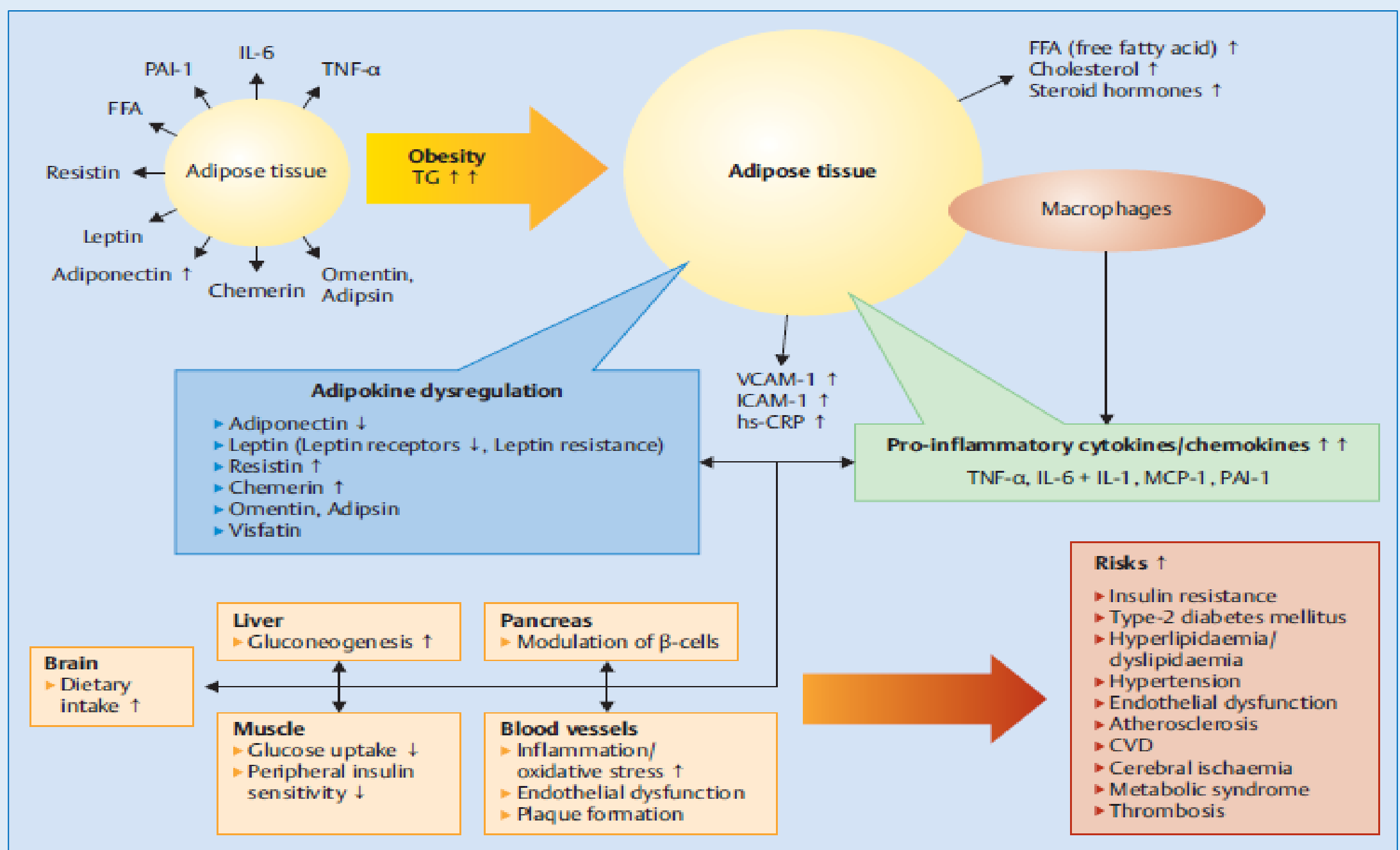
	Maternal BMI group (kg/m ²)				
	≤ 18.49 OR (95% CI)	18.50–24.99 OR (95% CI)	25.00–29.99 OR (95% CI)	30.00–39.99 OR (95% CI)	≥40.00 OR (95% CI)
Maternal complication					
Essential hypertension	0.60 (0.10–3.82)	1.00	1.87 (1.18–2.96)	11.90 (7.18–19.72)	36.10 (18.33–71.10)
Pregnancy-induced hypertension	0.63 (0.46–0.86)	1.00	1.76 (1.60–1.95)	2.98 (2.65–3.36)	4.48 (3.57–5.63)
Eclampsia	1.49 (0.35–6.34)	1.00	1.38 (0.76–2.49)	0.67 (0.28–1.64)	3.50 (1.21–10.11)
Placenta praevia	1.70 (0.82–3.52)	1.00	1.08 (0.80–1.48)	1.38 (0.98–1.94)	0.85 (0.31–2.31)
Abruption	0.89 (0.60–1.30)	1.00	0.86 (0.74–1.01)	0.89 (0.74–1.06)	0.95 (0.61–1.46)
Antepartum haemorrhage	0.88 (0.57–1.35)	1.00	0.87 (0.73–1.03)	0.83 (0.68–1.02)	0.82 (0.49–1.37)
Pre-existing diabetes	0.33 (0.07–1.53)	1.00	2.54 (1.79–3.61)	3.76 (2.59–5.47)	7.71 (4.04–14.71)
Gestational diabetes	0.22 (0.02–2.02)	1.00	3.39 (2.30–4.99)	11.90 (7.54–18.79)	67.40 (37.84–120.03)
Other maternal diseases	1.31 (1.12–1.53)	1.00	1.13 (1.06–1.21)	1.86 (1.73–2.00)	3.60 (3.07–4.22)
Delivery complication					
Induction of labour	0.85 (0.77–0.94)	1.00	1.30 (1.25–1.35)	1.64 (1.57–1.72)	1.97 (1.78–2.18)
Mode of delivery (normal = ref.)					
Ventouse/forceps	1.04 (0.93–1.16)	1.00	0.93 (0.89–0.98)	0.73 (0.68–0.77)	0.72 (0.61–0.85)
Elective caesarean section	1.08 (0.78–1.50)	1.00	2.06 (1.84–2.30)	4.61 (4.06–5.24)	17.92 (13.20–24.34)
Emergency caesarean section	0.52 (0.36–0.74)	1.00	1.94 (1.71–2.21)	3.40 (2.91–3.96)	14.34 (9.38–21.94)
Tears (none = ref.)					
1st–4th-degree or vaginal or cervical laceration	0.82 (0.74–0.90)	1.00	1.12 (1.07–1.16)	1.16 (1.10–1.21)	1.09 (0.96–1.24)
Neonatal complications					
Apgar ≤ 5 (>5 = ref.)	0.94 (0.65–1.38)	1.00	0.96 (0.83–1.11)	0.99 (0.83–1.17)	1.22 (0.82–1.81)
Stillbirth	0.92 (0.53–1.60)	1.00	1.07 (0.87–1.32)	1.43 (1.14–1.79)	1.91 (1.19–3.07)
Neonatal death	2.14 (0.74–6.20)	1.00	1.14 (0.62–2.11)	1.26 (0.64–2.51)	1.65 (0.39–6.97)
Admission to neonatal unit (no admission = ref.)					
≤48 hours	1.10 (0.91–1.33)	1.00	1.07 (0.99–1.15)	1.25 (1.15–1.36)	1.58 (1.31–1.90)
>48 hours	1.66 (1.39–1.97)	1.00	1.04 (0.96–1.12)	1.28 (1.17–1.40)	1.87 (1.53–2.28)
Preterm birth					
Spontaneous	1.56 (1.31–1.87)	1.00	0.85 (0.79–0.93)	1.03 (0.94–1.14)	1.25 (1.00–1.55)
Iatrogenic	1.74 (1.31–2.31)	1.00	1.25 (1.10–1.42)	1.45 (1.26–1.68)	2.12 (1.57–2.86)

Adjusted for maternal age, deprivation, and smoking. Odds ratios significant at *P* < 0.05 (highlighted in bold).

METHODS:
POPULATION-BASED
RETROSPECTIVE COHORT
STUDY OF SINGLETON
DELIVERIES

POPULATION:
A TOTAL OF **124,280** SINGLETON
DELIVERIES IN 109,592 WOMEN

SETTING:
OBSTETRIC UNITS IN SCOTLAND



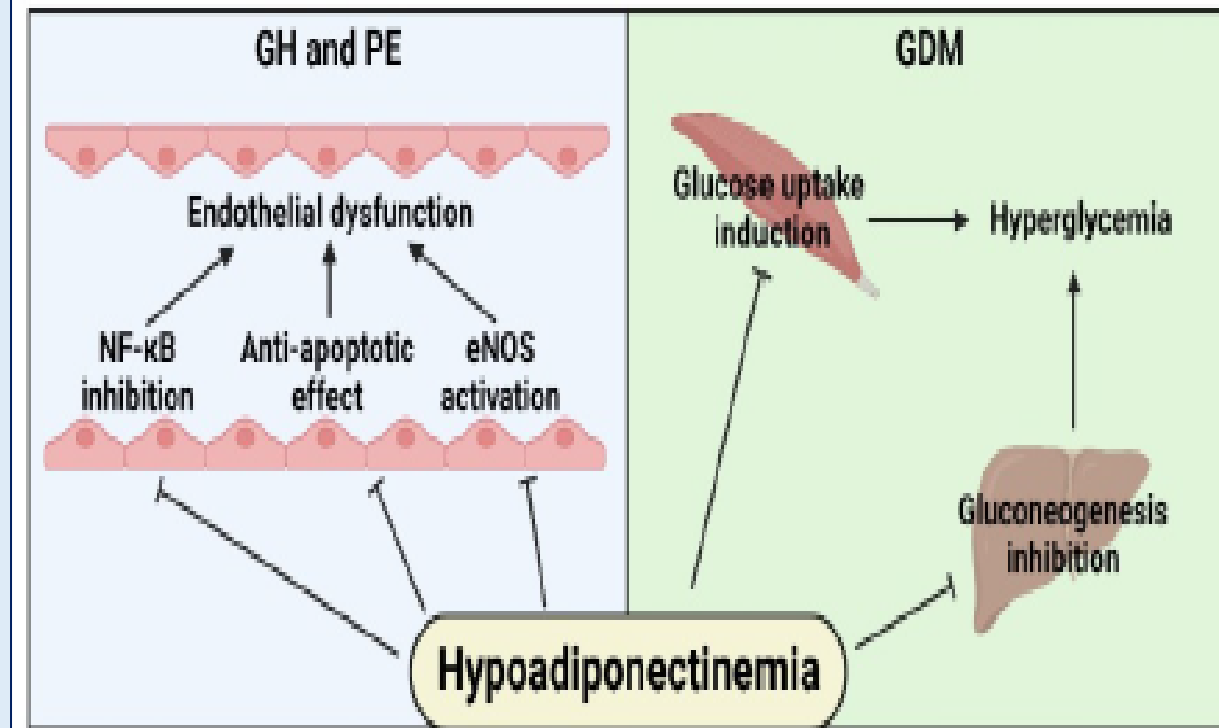
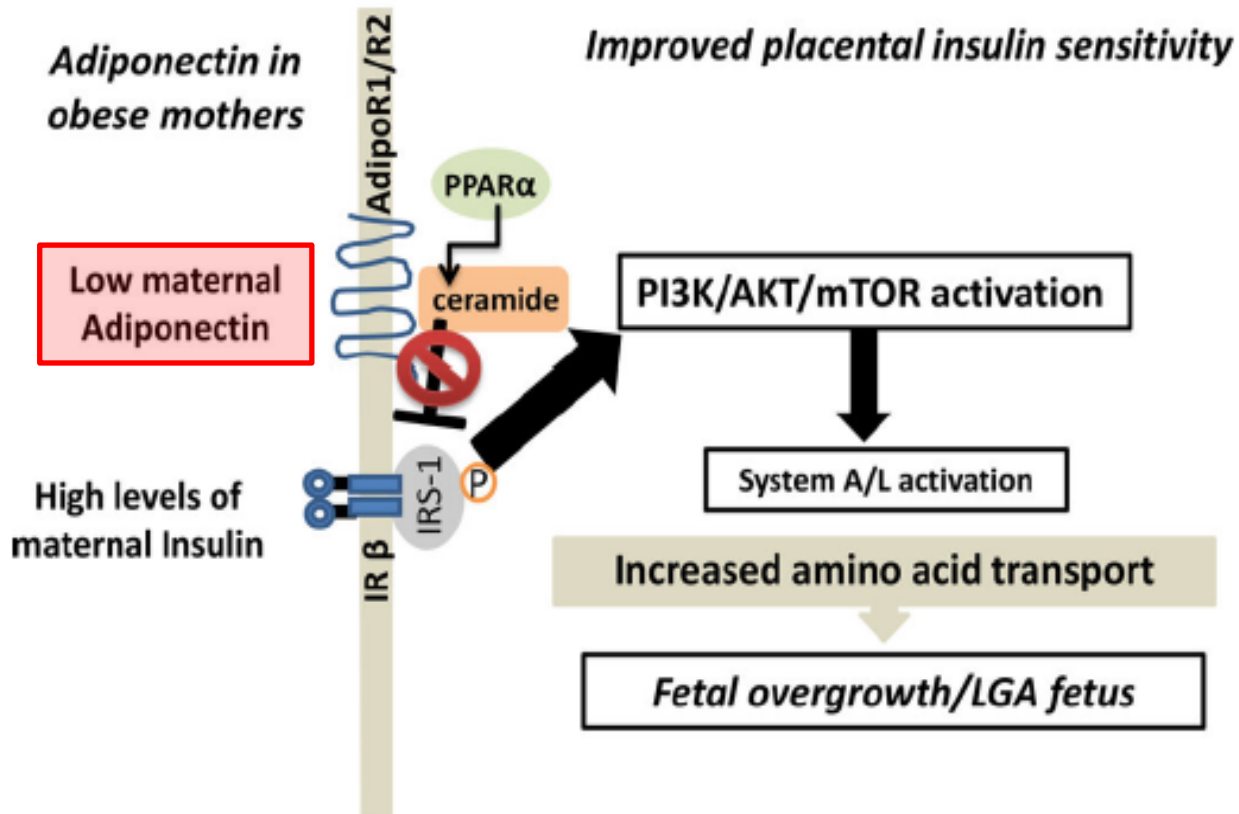
Effects of maternal obesity on placental function and fetal development

Kristy R. Howell, PhD and Theresa L. Powell, PhD¹

Departments of Psychiatry, Obstetrics/Gynecology and Pediatrics, University of Colorado,

Reproduction. 2017 March ; 153(3): R97–R108. doi:10.1530/REP-16-0495.

ADIPONECTINA



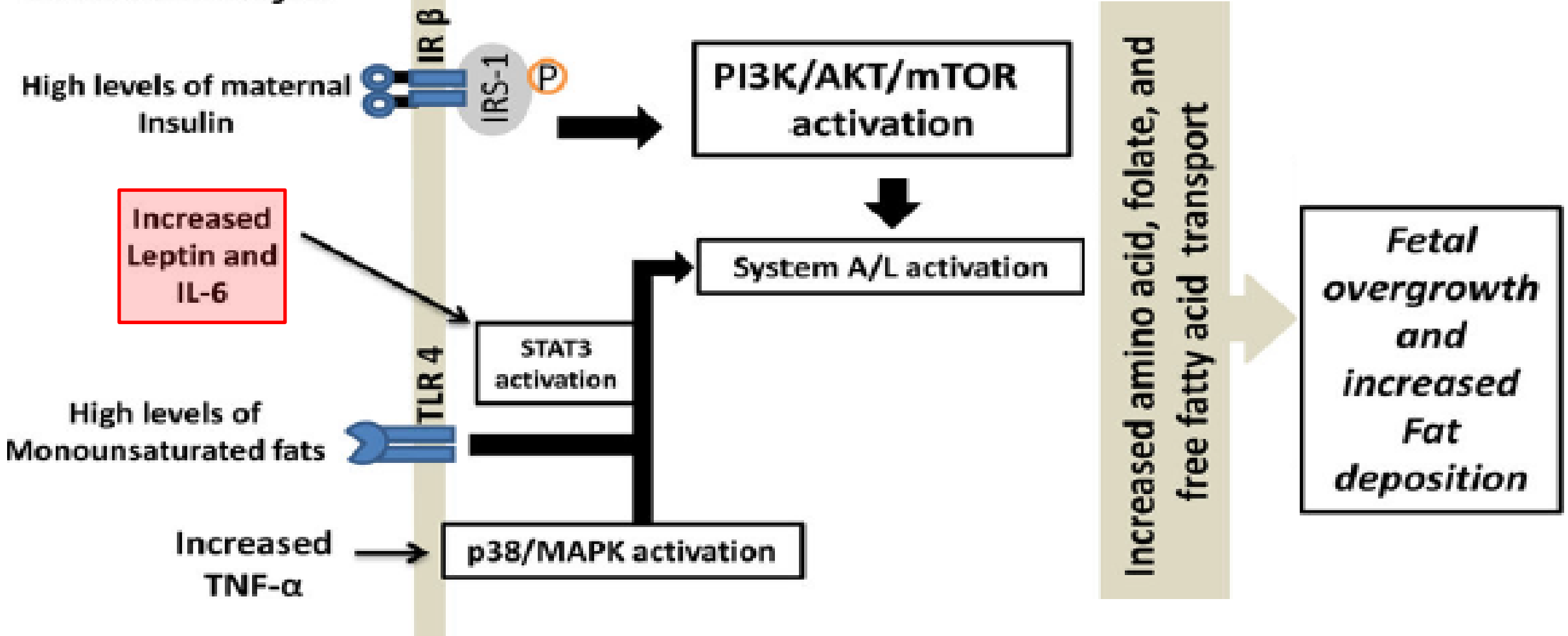
GH: gestational hypertension; PE: pre-eclampsia

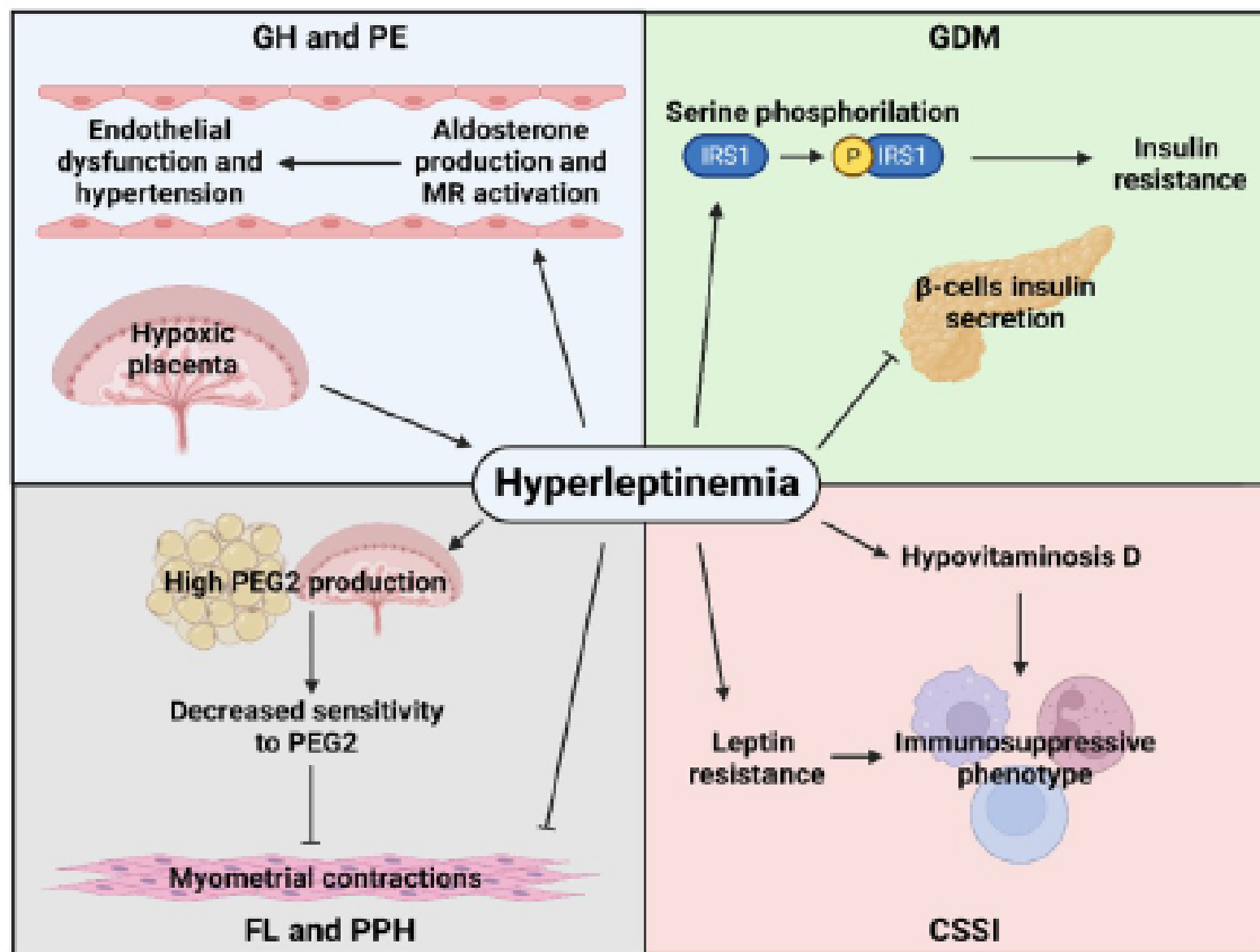
LEPTINA

Maternal Obesity Metabolic Profile

Placental function

Fetal impact

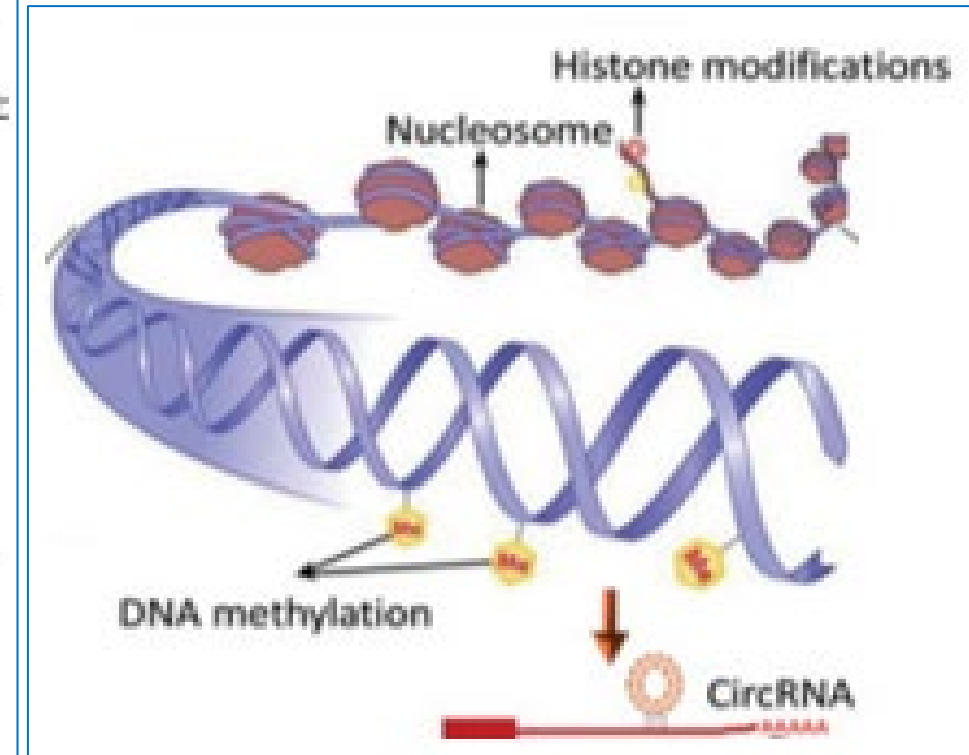
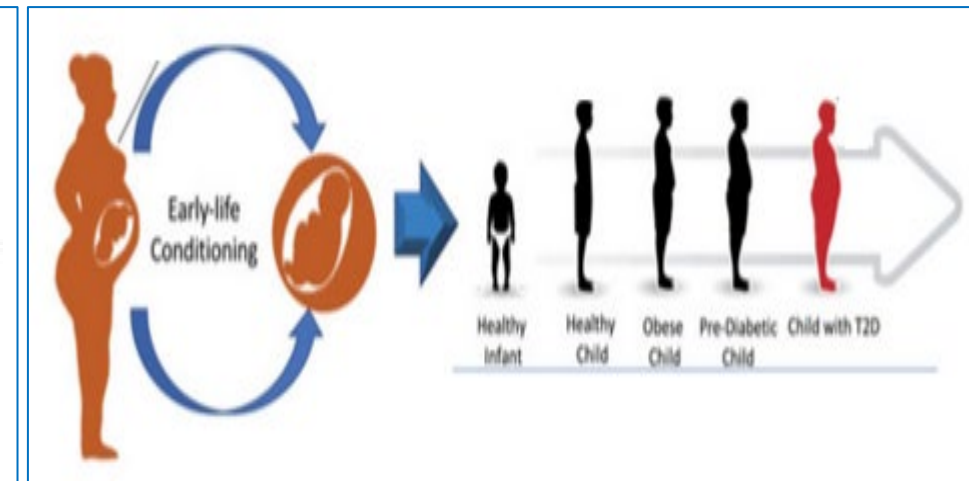
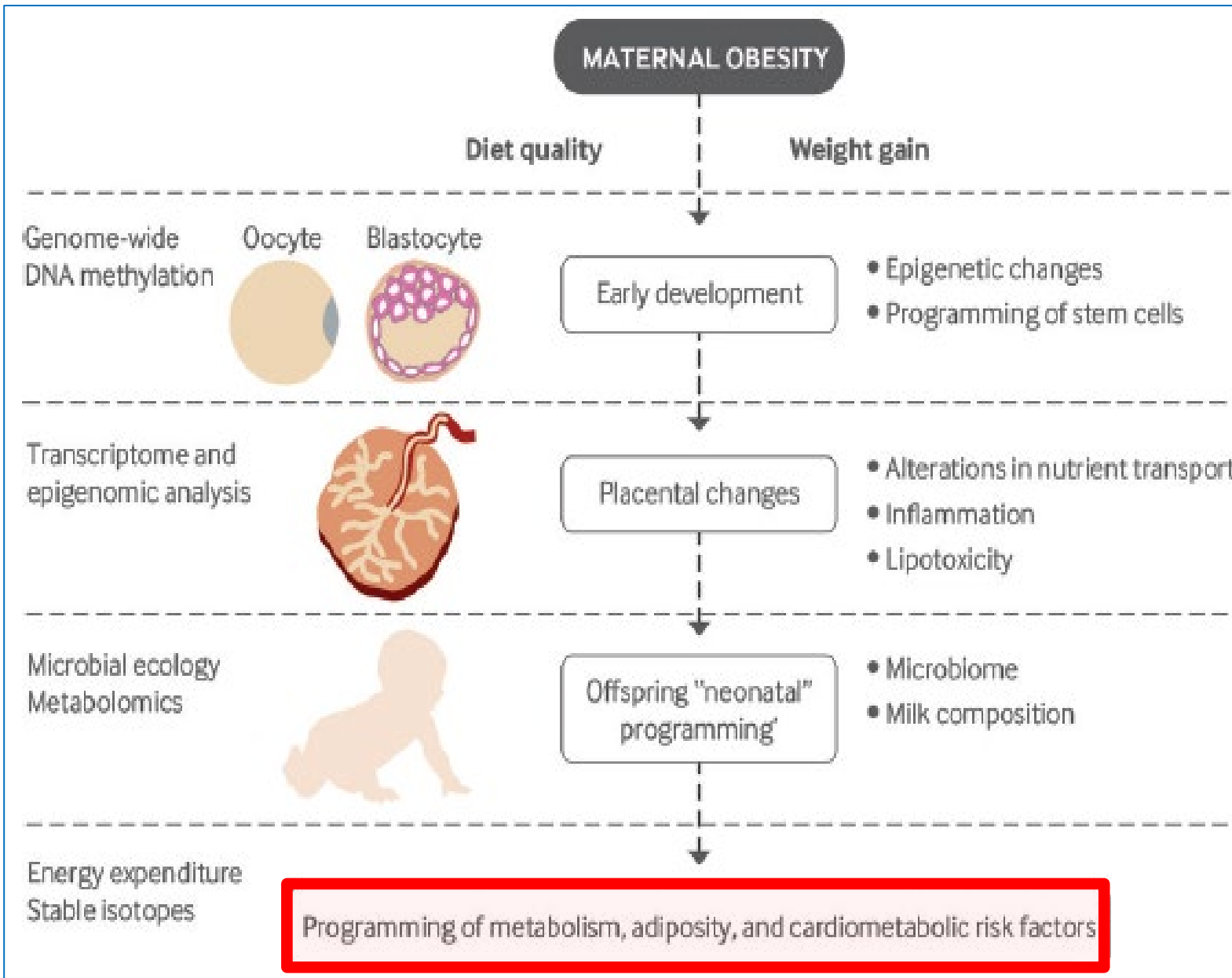




GH: gestational hypertension; PE: pre-eclampsia;

FL: failed labor; PPH: postpartum hemorrhage; CSSI: C-section surgical

AMBIENTE UTERINO SFAVOREVOLE



INCREMENTO PONDERALE IN GRAVIDANZA

IOM 2009 Recommendations

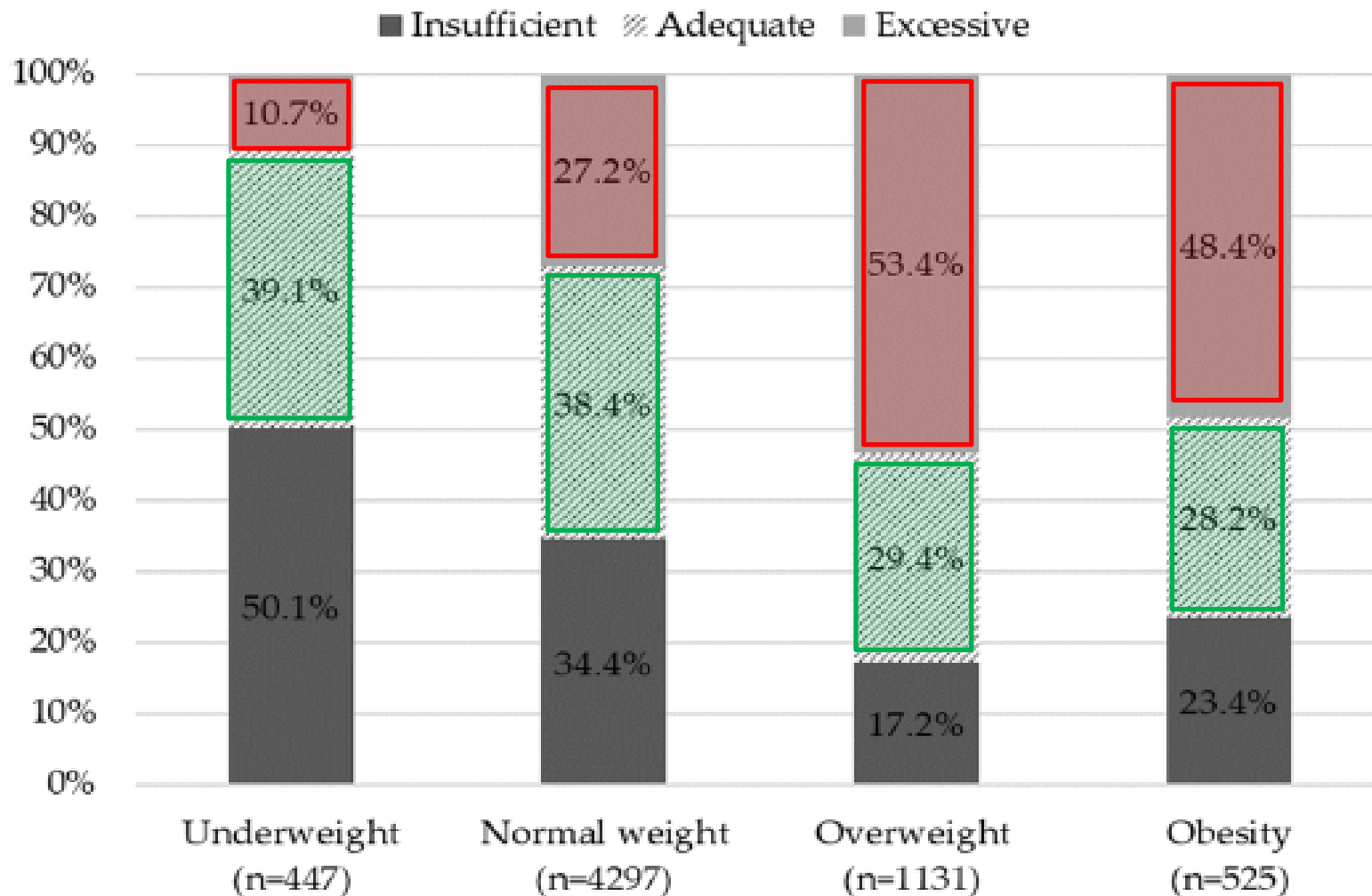




Monitoring gestational weight gain: setting up a regional surveillance system in Italy

Paola Pani¹, Claudia Carletti¹, Manuela Giangreco¹, Alessandra Knowles^{1*}, Elena Clagnan², Michele Gobbato², Stefania Del Zotto², Adriano Cattaneo³, Luca Ronfani¹ and on behalf of the Gestational Weight Survey Group (GWS group)

BMC Public Health (2023) 23:132



**6.400 DONNE
IN GRAVIDANZA**

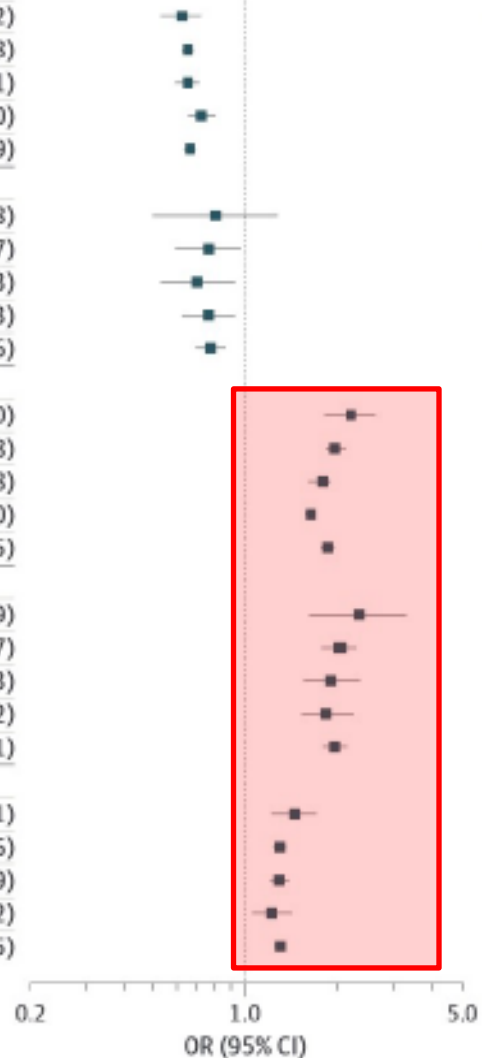
Association of Gestational Weight Gain With Maternal and Infant Outcomes A Systematic Review and Meta-analysis

Above recommended gestational weight gain

Outcomes by BMI category	Women, No.	OR (95% CI)
SGA	1019805	
<18.5	13711	0.62 (0.53-0.72)
18.5-24.9	88780	0.65 (0.62-0.68)
25-29.9	110665	0.65 (0.59-0.71)
≥30	103820	0.72 (0.65-0.80)
Overall		0.66 (0.63-0.69)
Preterm birth	360833	
<18.5	4063	0.80 (0.50-1.28)
18.5-24.9	60324	0.76 (0.59-0.97)
25-29.9	11162	0.70 (0.53-0.93)
≥30	30809	0.76 (0.62-0.93)
Overall		0.77 (0.69-0.86)
LGA	1041399	
<18.5	13978	2.17 (1.81-2.60)
18.5-24.9	215994	1.95 (1.83-2.08)
25-29.9	142236	1.79 (1.61-1.98)
≥30	104459	1.63 (1.56-1.70)
Overall		1.85 (1.76-1.95)
Macrosomia	241665	
<18.5	2214	2.31 (1.62-3.29)
18.5-24.9	35928	2.01 (1.77-2.27)
25-29.9	17627	1.90 (1.54-2.33)
≥30	1035	1.83 (1.52-2.22)
Overall		1.95 (1.79-2.11)
Cesarean delivery	218207	
<18.5	2227	1.45 (1.22-1.71)
18.5-24.9	35416	1.30 (1.24-1.36)
25-29.9	17419	1.29 (1.21-1.39)
≥30	9012	1.22 (1.05-1.42)
Overall		1.30 (1.25-1.35)

Decreased Odds of Outcome

Increased Odds of Outcome

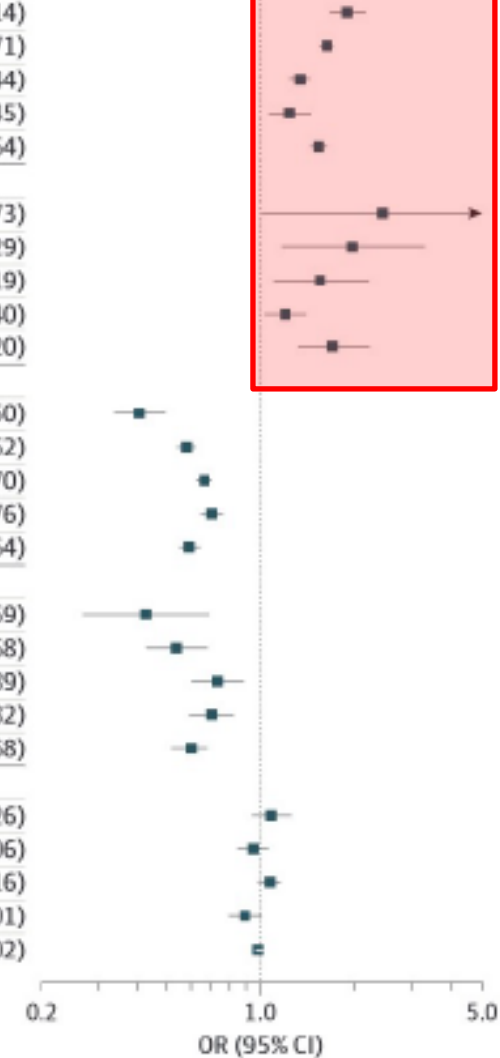


Below recommended gestational weight gain

Outcomes by BMI category	Women, No.	OR (95% CI)
SGA	1019805	
<18.5	28551	1.89 (1.67-2.14)
18.5-24.9	162331	1.63 (1.54-1.71)
25-29.9	27634	1.34 (1.24-1.44)
≥30	31526	1.24 (1.06-1.45)
Overall		1.53 (1.44-1.64)
Preterm birth	360833	
<18.5	19941	2.41 (1.01-5.73)
18.5-24.9	79537	1.96 (1.17-3.29)
25-29.9	6681	1.55 (1.10-2.19)
≥30	8598	1.20 (1.03-1.40)
Overall		1.70 (1.32-2.20)
LGA	1041399	
<18.5	29596	0.41 (0.34-0.50)
18.5-24.9	166212	0.58 (0.54-0.62)
25-29.9	27899	0.66 (0.62-0.70)
≥30	31675	0.70 (0.64-0.76)
Overall		0.59 (0.55-0.64)
Macrosomia	241665	
<18.5	15617	0.43 (0.27-0.69)
18.5-24.9	59503	0.54 (0.43-0.68)
25-29.9	4935	0.73 (0.60-0.89)
≥30	4740	0.70 (0.59-0.82)
Overall		0.60 (0.52-0.68)
Cesarean delivery	218207	
<18.5	15645	1.08 (0.94-1.26)
18.5-24.9	59100	0.95 (0.84-1.06)
25-29.9	2186	1.07 (0.98-1.16)
≥30	4336	0.89 (0.79-1.01)
Overall		0.98 (0.96-1.02)

Decreased Odds of Outcome

Increased Odds of Outcome



53 STUDIES

1,309,136 WOMEN

Association of Gestational Weight Gain With Maternal and Infant Outcomes A Systematic Review and Meta-analysis

BMI ≥ 30 Kg/m²

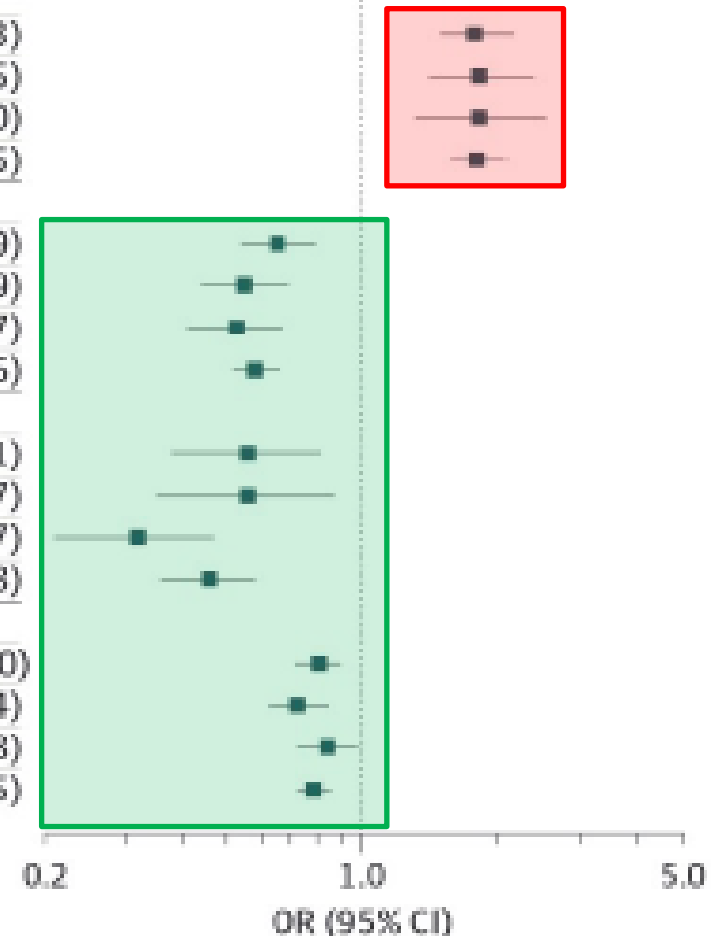
GESTATIONAL WEIGHT LOSS

Gestational weight loss

Outcomes by obesity class	Women, No.	OR (95% CI)
SGA	85 668	
Class 1	2167	1.77 (1.48-2.13)
Class 2	1415	1.81 (1.40-2.35)
Class 3	1174	1.81 (1.31-2.50)
Overall		1.79 (1.56-2.05)
LGA	85 668	
Class 1	2167	0.65 (0.54-0.79)
Class 2	1415	0.55 (0.44-0.69)
Class 3	1174	0.53 (0.41-0.67)
Overall		0.58 (0.52-0.66)
Macroomia	40 107	
Class 1	826	0.56 (0.38-0.81)
Class 2	617	0.56 (0.35-0.87)
Class 3	827	0.32 (0.21-0.47)
Overall		0.46 (0.36-0.58)
Cesarean delivery	86 702	
Class 1	2167	0.80 (0.71-0.90)
Class 2	1415	0.72 (0.62-0.84)
Class 3	1344	0.84 (0.72-0.98)
Overall		0.78 (0.72-0.85)

Decreased Odds of Outcome

Increased Odds of Outcome



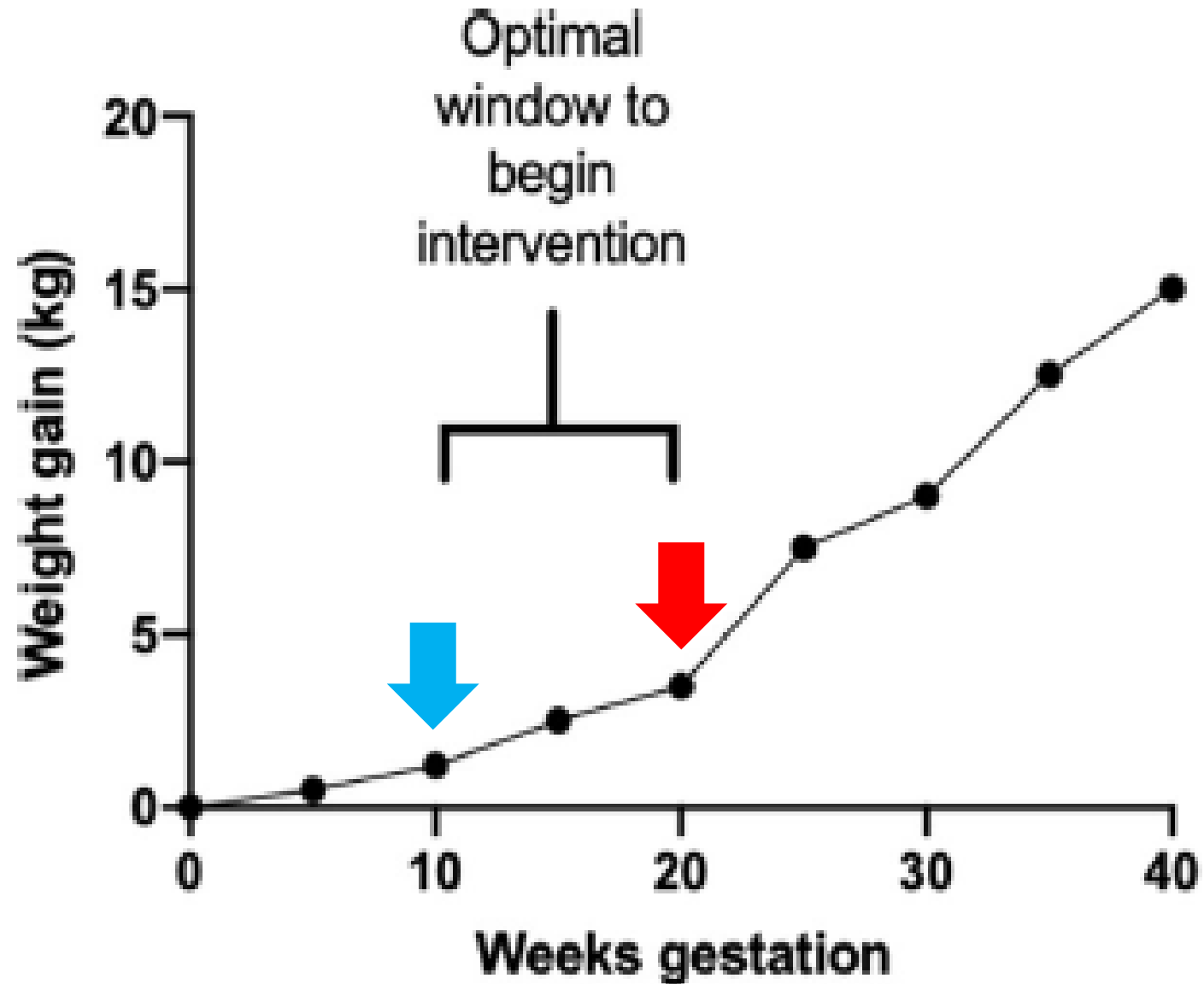
Does prepregnancy weight change have an effect on subsequent pregnancy health outcomes? A systematic review and meta-analysis

Obesity Reviews. 2022;23:e13324.

61 STUDY

Outcome	Weight gain			Weight loss		
	Overall	BMI < 25	BMI ≥ 25	Overall	BMI < 25	BMI ≥ 25
GDM	1.88 [1.66, 2.14]	2.01 [1.54, 2.64]	1.79 [1.33, 2.40]	0.75 [0.62, 0.92]	0.89 [0.83, 0.95]	0.68 [0.45, 1.03]
Hypertensive disorders of pregnancy	1.46 [1.12, 1.91]	1.94 [1.42, 2.64]	1.07 [0.58, 1.97]	0.95 [0.82, 1.10]	0.89 [0.76, 1.04]	0.85 [0.79, 0.93]
Preeclampsia	1.92 [1.55, 2.37]	-	-	1.23 [0.81, 1.85]	-	-
LGA	1.36 [1.25, 1.49]	1.31 [1.21, 1.41]	1.14 [1.02, 1.29]	0.91 [0.81, 1.03]	0.78 [0.76, 0.81]	0.81 [0.79, 0.84]
SGA	1.00 [0.87, 1.14]	1.08 [0.76, 1.55]	0.85 [0.35, 2.05]	1.29 [1.11, 1.50]	1.49 [1.15, 1.92]	0.97 [0.80, 1.18]
Cesarean delivery	1.32 [1.21, 1.45]	1.14 [1.02, 1.28]	2.04 [1.41, 2.95]	1.10 [0.92, 1.31]	0.96 [0.82, 1.13]	0.88 [0.82, 0.96]
VBAC	0.81 [0.71, 0.92]	-	-	0.98 [0.88, 1.12]	-	-
Stillbirth	1.49 [1.29, 1.72]	1.25 [1.11, 1.41]	1.28 [1.04, 1.58]	1.22 [1.05, 1.42]	1.10 [0.88, 1.37]	0.98 [0.75, 1.29]
Preterm delivery	0.95 [0.89, 1.02]	1.02 [0.92, 1.12]	1.11 [1.03, 1.20]	1.06 [1.00, 1.13]	1.21 [1.11, 1.32]	0.96 [0.85, 1.07]
Apgar score	1.24 [1.13, 1.36]	-	-	0.89 [0.78, 1.01]	-	-
Hemorrhage	1.12 [0.93, 1.34]	-	-	1.18 [0.89, 1.56]	-	-

The WINDOW of OPPORTUNITY



Lifestyle Interventions to Improve Pregnancy Outcomes: a Systematic Review and Specified Meta-Analyses

Behnam S et al. Lifestyle Interventions to ... Geburtsh Frauenheilk 2022; 82: 1249–1264

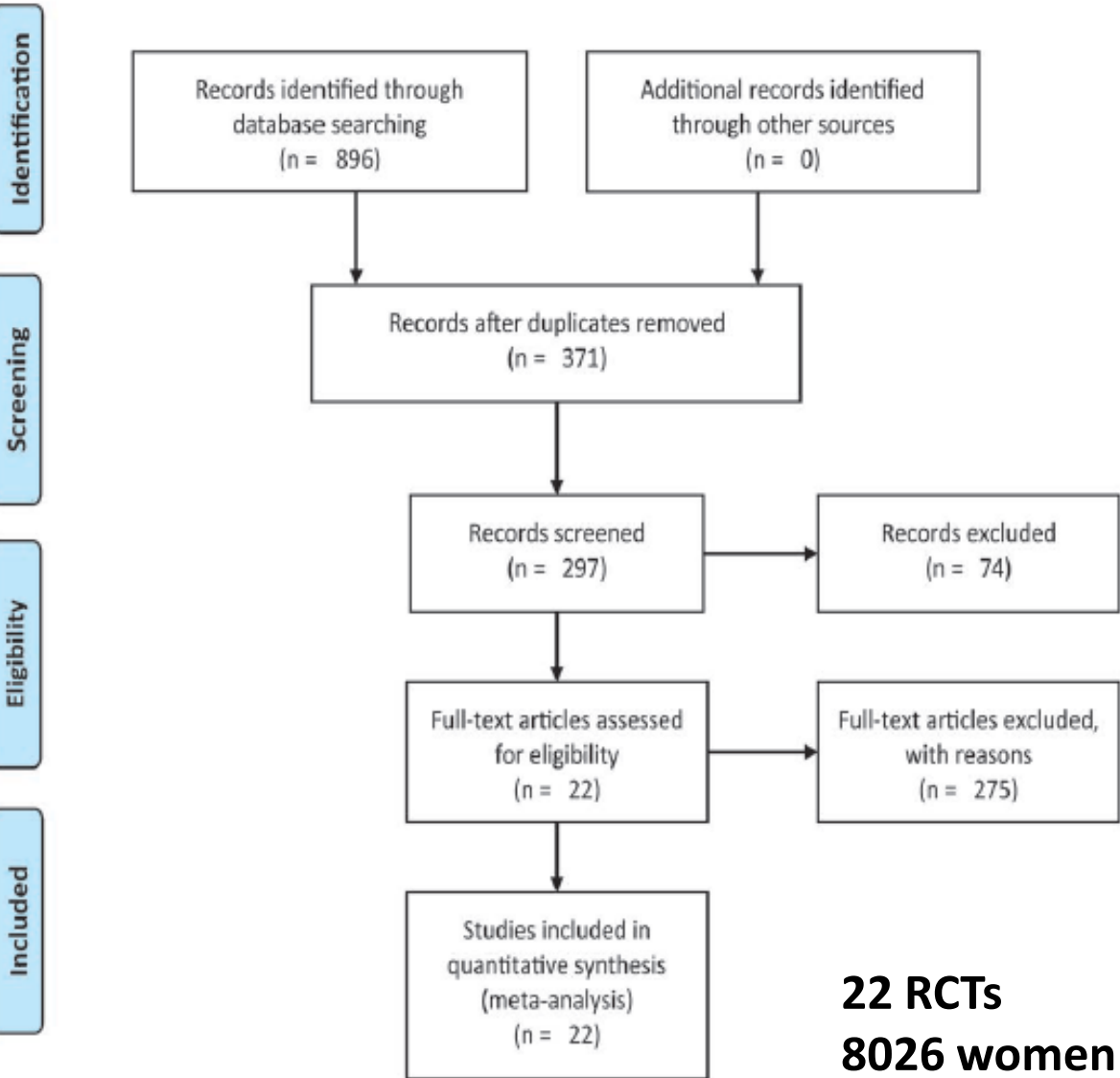
		All trials						All trials			
Outcome	Inter- vention	OR	95 % CI	n	I ² (%)	Outcome	Inter- vention	OR	95 % CI	n	I ² (%)
GDM	Exercise	0.83	0.51–1.36	9	59	NICU Ad- mission	Exercise	0.56	0.19–1.64	2	0
	Diet	0.87	0.55–1.39	6	69		Diet	NA	NA	1	NA
	Diet and Exercise	0.83	0.66–1.03	15	41		Diet and Exercise	1.04	0.89–1.22	5	0
	Subgroup: Behavioral therapy	0.91	0.75–1.11	5	0		Subgroup: Behavioral therapy	0.82	0.22–3.09	2	62
HDP	Exercise	0.52	0.28–0.96	4	49	Perinatal mortality	Exercise	NA	NA	1	NA
	Diet	1.23	0.79–1.92	4	34		Diet	NA	NA	0	NA
	Diet and Exercise	0.80	0.53–1.20	11	66		Diet and Exercise	1.00	0.54–1.86	5	0
	Subgroup: Behavioral therapy	1.08	0.75–1.57	4	0		Subgroup: Behavioral therapy	1.11	0.23–5.13	2	31

28 RCTs
11.416 women

		All trials			
Outcome	Inter- vention	OR/ SMD	95% CI	n	I ² (%)
Maternal					
Caesarean delivery	Exercise	0.96	0.75–1.22	5	0
	Diet	0.82	0.40–1.68	3	77
	Diet and Exercise	0.93	0.78–1.11	12	44
	Subgroup: Behavioral therapy	0.97	0.81–1.15	4	0
Gestational weight gain	Exercise	−0.18	−0.33–−0.02	8	59
	Diet	−0.55	−1.16–0.06	3	92
	Diet and Exercise	−0.38	−0.57–−0.20	12	89
	Subgroup: Behavioral therapy	−0.40	−0.62–−0.18	5	79
Excessive gestational weight gain (IOM recommendations)	Exercise	0.67	0.48–0.94	5	42
	Diet	NA	NA	0	NA
	Diet and Exercise	0.48	0.30–0.74	7	86
	Subgroup: Behavioral therapy	0.42	0.21–0.85	3	75
		All trials			
Outcome	Inter- vention	OR/ SMD	95% CI	n	I ² (%)
Fetal					
Large for gestational age (LGA)	Exercise	0.83	0.45–1.55	4	39
	Diet	NA	NA	1	NA
	Diet and Exercise	0.76	0.55–1.05	9	56
	Subgroup: Behavioral therapy	0.58	0.24–1.43	3	81
Small for gestational age (SGA)	Exercise	1.62	0.61–4.26	3	0
	Diet	0.97	0.36–2.64	2	66
	Diet and Exercise	1.21	0.92–1.59	7	0
	Subgroup: Behavioral therapy	1.26	0.90–1.75	3	0
		All trials			
Outcome	Inter- vention	OR/ SMD	95% CI	n	I ² (%)
Birthweight	Exercise	−0.04	−0.17–0.09	7	48
	Diet	0.28	−0.27–0.82	4	91
	Diet and Exercise	−0.05	−0.14–0.03	11	42
	Subgroup: Behavioral therapy	−0.16	−0.28–−0.04	4	0
Preterm birth below 37 completed weeks	Exercise	0.83	0.53–1.28	4	0
	Diet	0.77	0.41–1.45	2	0
	Diet and Exercise	0.70	0.48–1.02	7	7
	Subgroup: Behavioral therapy	3.92	0.63–24.36	2	0

The effects of exercise intervention on complications and pregnancy outcomes in pregnant women with overweight or obesity

A systematic review and meta-analysis Jun Kuang, MD^a, Suwen Sun, MD^a, Fengmei Ke, MD^{a,*}  *Medicine* 2023;102:40(e34804).



EXERCISE EFFECT vs. CONTROLS

OUTCOMES	OR
GDM	0.85
PREGNANCY-INDUCED HYPERTENSION	0.55
MACROSOMIA	0.78
PRE-ECLAMPSIA	1.01
CESAREAN SECTION	0.92
PREMATURE BIRTH	0.89
POST-PARTUM HEMORRHAGE	1.05
NEONATAL ASPHYXIA	0.68

LOWER WEIGHT GAIN

APPROCCIO NUTRIZIONALE

Fabbisogno energetico e incremento ponderale raccomandato in base al BMI pregravidico.

L'aumento ponderale raccomandato presuppone un incremento di 0,5-2 kg nel primo trimestre della gravidanza.

Struttura	BMI (kg/m ²)	Fabbisogno energetico kcal/kg/die	Aumento ponderale totale (kg)	Aumento ponderale kg/ sett. nel 2°-3° trimestre
Sottopeso	<18.5	40	12.5-18	0.51 (0.44-0.58)
Normopeso	18.5-24.9	30	11.5-16	0.42 (0.35-0.50)
Sovrappeso	25-29.9	24	7-11.5	0.28 (0.23-0.33)
Obese	≥30	12-24	5-7 (9)	0.22 (0.17-0.27)

Da: IOM (Institute of Medicine) and NRC (National Research Council). *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: The National Academies Press; 2009.

II trimestre: + 340 kcal/die
III trimestre: + 450 kcal/die

Fabbisogno energetico mai inferiore a 1500 kcal/die

Tabella 1. Controindicazioni relative ed assolute all'attività fisica in gravidanza

Relative	Absolute
Precedenti aborti spontanei	Sanguinamenti vaginali
Precedenti parti pre-termine	Rottura delle membrane
Malattie cardio-respiratorie lievi-moderate (Ipertensione, asma)	Attività contrattile prematura
Disordini alimentari o malnutrizione	Placenta previa
Gravidanza gemellare dalla 28ª settimana	Incontinenza della cervice, cerchiaggio
Obesità >40 Kg/m ²	Ritardo di crescita intra-uterino
Anemia con Hb>10g/dl	Pre-eclampsia
Altre condizioni clinicamente significative di grado lieve-moderato: (Tireopatie, diabete pre-gravidico, ...)	Gravidanza multipla (>2)
	Malattie cardio-respiratorie di grado severo
	Anemia con Hb<10g/dl
	Altre condizioni clinicamente significative di grado severo: (Tireopatie, diabete pre-gravidico, ...)

Examples of Exercises That Have Been Extensively Studied in Pregnancy and Found to Be Safe and Beneficial

Walking

Stationary cycling

Aerobic exercises

Dancing

Resistance exercises (eq. using weights, elastic bands)

Stretching exercises

Hydrotherapy, water aerobics



Attività Fisica nella Gravidanza
di Donne con Diabete



ACOG COMMITTEE

Physical Activity and Exercise During Pregnancy and the Postpartum Period

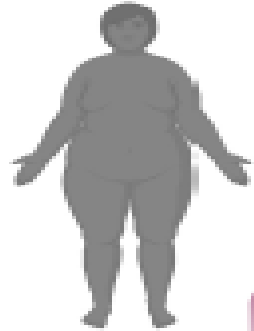
(Replaces Committee Opinion Number 650, December 2015)

Table 3. Characteristics of a Safe and Effective Exercise Regimen in Pregnancy

When to Start	First Trimester, More Than 12 Weeks of gestation
Duration of a session	30–60 minutes
Times per week	At least 3–4 (up to daily)
Intensity of exercise	Less than 60–80% of age-predicted maximum maternal heart rate*
Environment	Thermoneutral or controlled conditions (air conditioning; avoiding prolonged exposure to heat)
Self-reported intensity of exercise (Borg scale)	Moderate intensity (12–14 on Borg scale)
Supervision of exercise	Preferred, if available
When to end	Until delivery (as tolerated)

*Usually not exceeding 140 beats per minute.

Prepregnancy



*Excess
Nutrient
Availability*

In Utero



*Excess
Nutrient
Transfer*

Postnatal



*Hyperinsulinemia
& Abnormal
Leptin Surge*

Childhood



Lifestyle Modifications

Decrease caloric intake
Physical activity

Pharmaceutical Interventions

GLP-1R agonists
Naltrexone/Bupropion
Phentermine/Topiramate
Setmelanotide
Orlistat
Epigenetic modifiers*

Surgical Interventions

Gastric bypass
Sleeve gastrectomy
Biliopancreatic diversion

Lifestyle Modifications

Consume balanced diet
Physical activity
Slow and moderate
weight gain (11-20 lbs)

Pathways to Target

Placental glucose and
FFA transport
Placental mTOR, IGF
and insulin signaling
Maternal adiponectin

Lifestyle Modifications

Decrease caloric intake
Physical activity
Breastfeed (at least 6
months)
Avoid over-
supplementation with
formula

Pathways to Target

Leptin and IGF signaling
Central insulin and
leptin resistance

Lifestyle Modifications

Decrease caloric intake
Physical activity

Pharmaceutical Interventions

GLP-1R agonists**
Epigenetic modifiers*

Pathways to Target

Selective modulation
of RXRA, PPARA and
PPARG
Systemic insulin and
leptin resistance



Grazie per l'attenzione