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ISTITUTO DI RICOVERO E CURA
a CARATTERE SCIENTIFICO
Burlo Garofolo di Trieste
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IRCBG_21095

""L'alimentazione in gravidanza
Il sostegno dell'ospedale e del territorio"

1° edizione 25/10/2021
2°edizione 10/11/2021

Gravidanza e peso corporeo: quali rischi per la donna e per il nascituro.

Il fetal programming

Gianpaolo Maso
S.S.D. Gravidanza a Rischio- Dipartimento Materno-Neonatale
I.R.C.C.S Burlo Garofolo-Trieste

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E.C.M.

Salute → inizia prima di nascere

Mamma → bambino

La composizione della **dieta materna**, insieme alla **funzione placentare**, determina la composizione dei **nutrienti** nel sangue del cordone **ombelicale**

Barker hypothesis

Cetin, 2014

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Salute → inizia prima di nascere

Mamma → bambino

- Lo sviluppo si completa nei primi 1000 giorni dopo il concepimento.
- Ogni organo ha un periodo critico, spesso breve, durante il quale avviene il suo sviluppo
- La maggior parte dei periodi critici avviene in utero

Cetin, 2014

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Cetin, 2014

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ambiente – dieta materna – epigenetica

dieta materna → macro e micronutrienti regolano la stabilità del DNA e gli adattamenti del fenotipo, ***attraverso processi di metilazione del DNA***

modificazioni epigenetiche

espressione di geni fetali

espressione di geni placentari

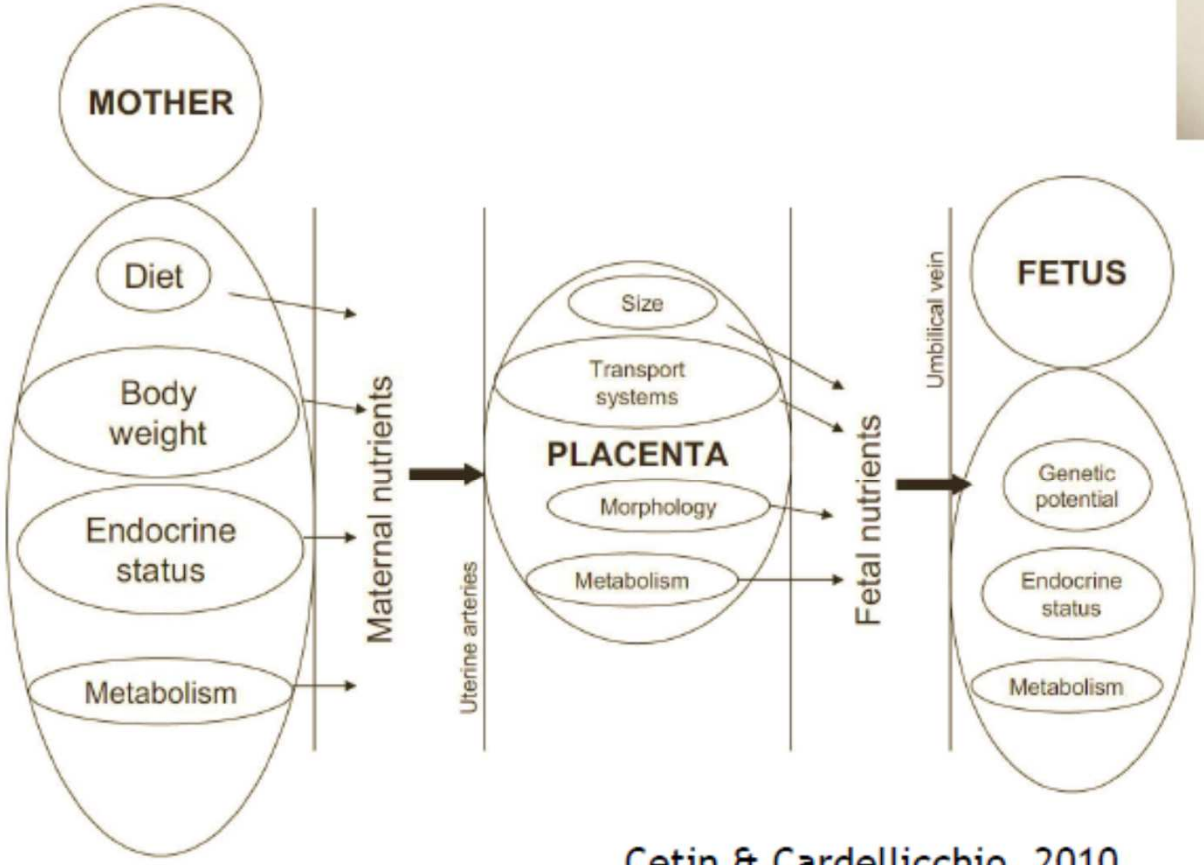
sviluppo fetale

PROGRAMMING NUTRIZIONALE

Cetin I et al. Curr Opin Clin Nutr Metab Care, 2013

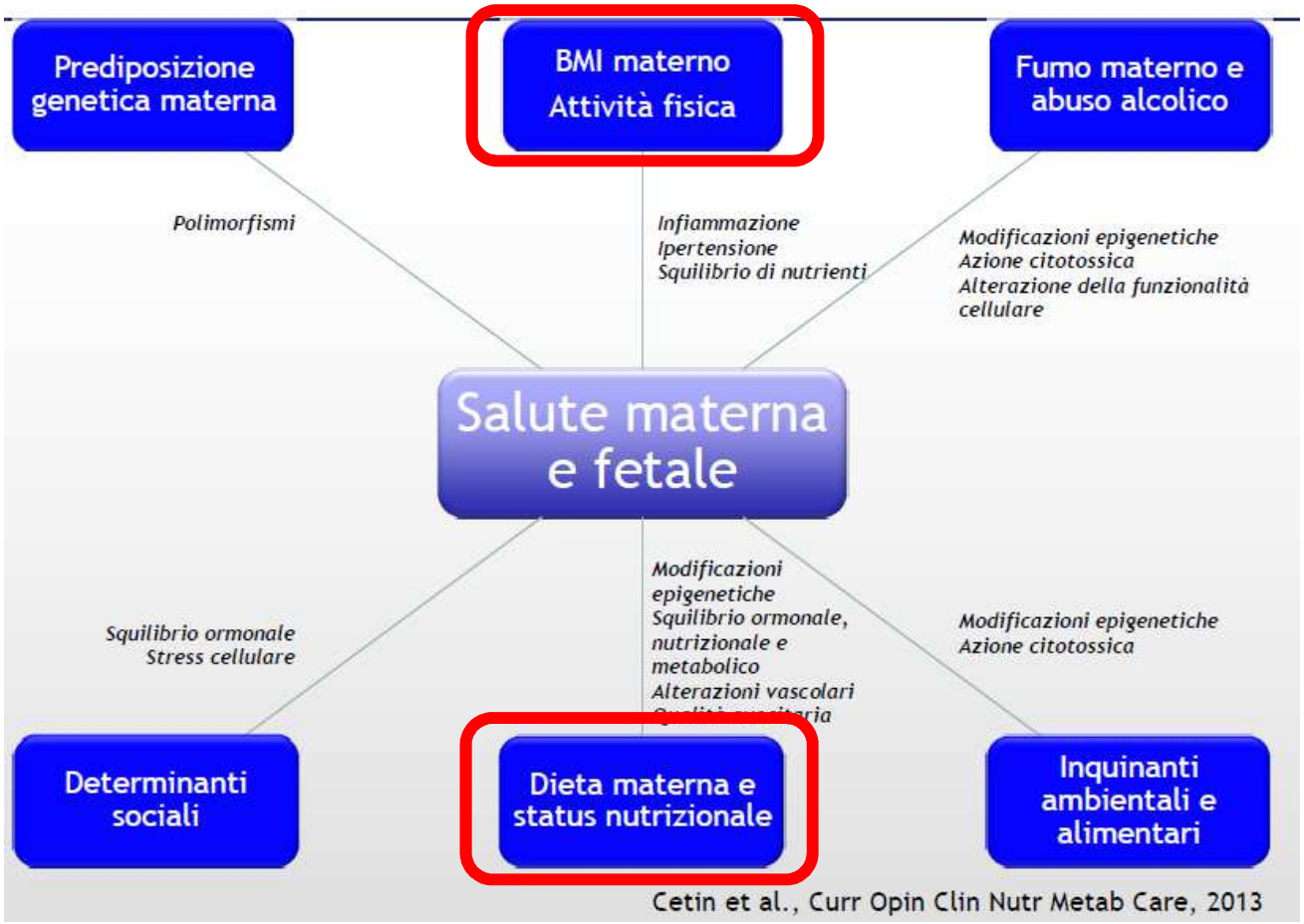
GRAVIDANZA =

3 compartimenti



Cetin & Cardellicchio, 2010

FATTORI DETERMINANTI LA SALUTE MATERNA E FETALE



Maternal obesity

Preconceptional and maternal obesity: epidemiology and health consequences

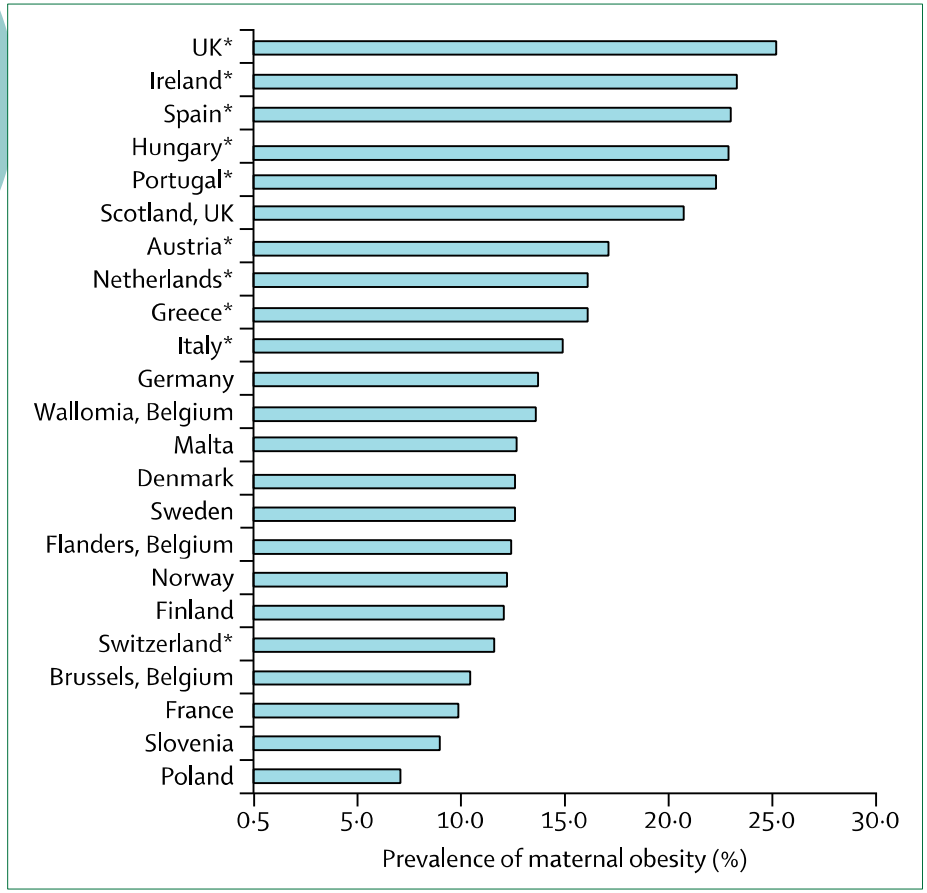
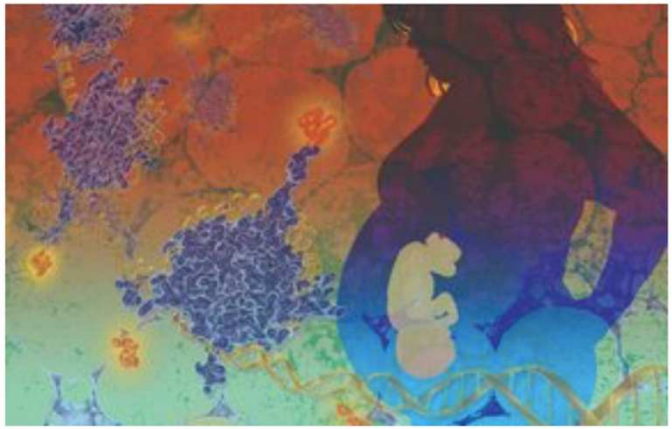


Figure 2: Distribution of maternal obesity from Euro-Peristat database and WHO



- Rates of obesity are increasing among pregnant women
- Obesity in pregnancy increase the risk of adverse outcomes for mother and child

Lancet Diabetes Endocrinol 2016

What changes occur during pregnancy?

Haematological

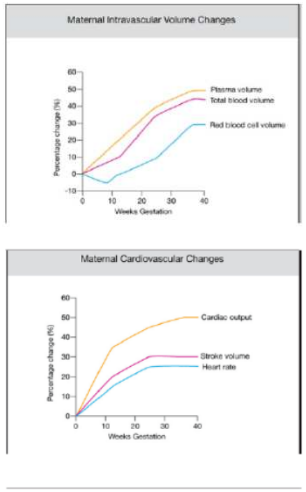
Cardiovascular

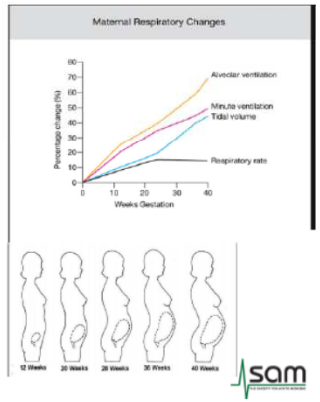
Renal

Metabolism

Respiratory

Neuromuscular





Pregnancy stresses a woman's health

- To unmask occult disease
- To predict health in a subsequent pregnancy
- To predict health many years remote from childbirth
- To predict health of child and future off-spring

Williams D. Current Op Obst Gyn 2003
Banjaree A, The Society for Acute Medicine.2013

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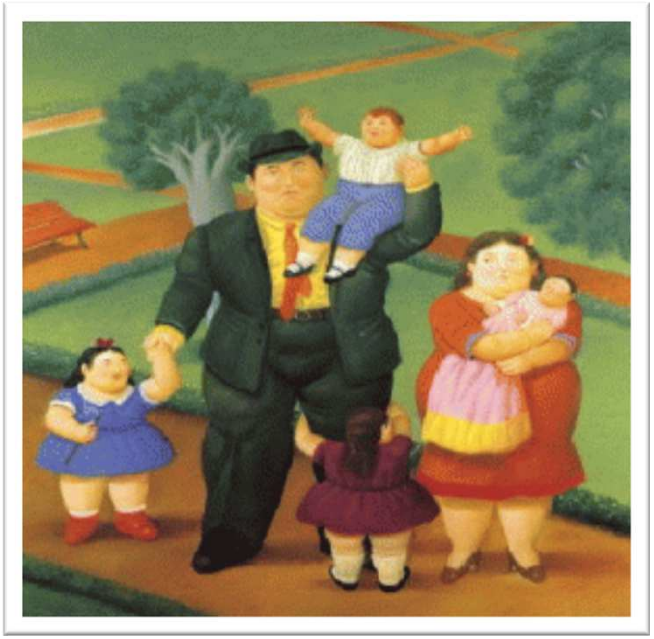
Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants

Lancet 2016; 387: 1377–96

From 1975 to 2014 prevalence of obesity increased:

- from 3.2% to 10.8% in men
- **from 6.4% to 14.9% in women**

- In the world were **severely obese** (BMI≥35 kg/m2):
  - 2.3% of men
  - **5.0% of women**
- Prevalence of **morbid obesity** was:
  - 0.64% in men
  - **1.6% in women**



Centre for Maternal and Child Enquiries
Improving the health of mothers, babies and children

CMACE

Management of Women with Obesity in Pregnancy

March 2010

Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

Maternal and fetal risks in women with a BMI ≥30 kg/m² compared to women with a healthy BMI

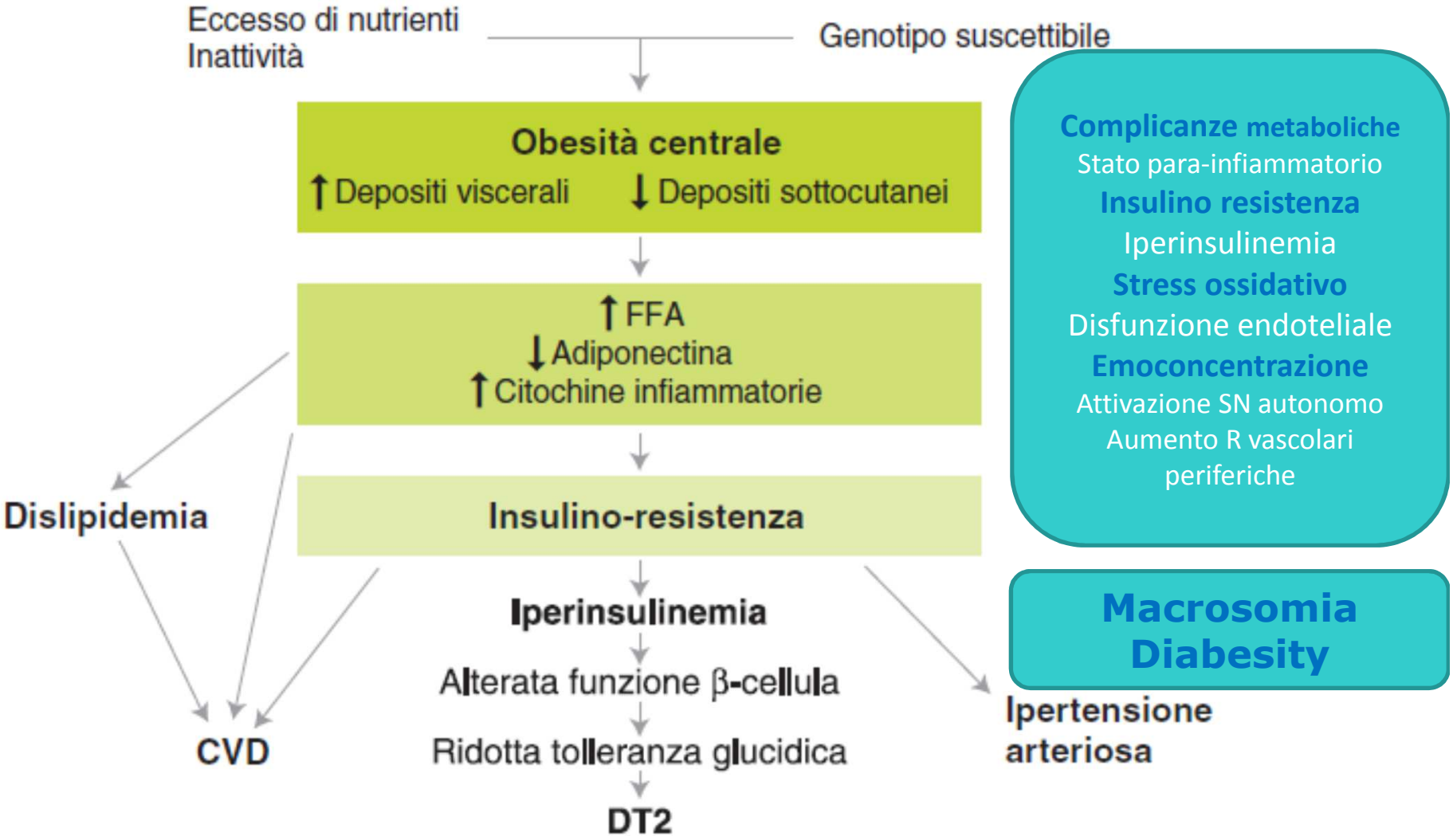
Risk	Odds ratio [95% Confidence interval]*
Gestational diabetes	3.6 [3.3-4.0] [a] 2.4 [2.2-2.7]
Hypertensive disorders	2.1[1.9-2.5] [a] 3.3 [2.7-3.9]
Venous thromboembolism	9.7 [3.1-30.8]
Slower labour progress 4 – 10cm	7 versus 5.4 hrs p<0.001
Caesarean	2.1 [1.9-2.3]
Emergency caesarean	1.8 [1.7-1.9] 2.0 [1.2-3.5]
Postpartum haemorrhage	1.4 [1.2-1.6] [a] 2.3 [2.1-2.6]

Risk	Odds ratio [95% Confidence interval]*
Wound infection	2.24 [1.91-2.64] [a]
Birth defects	1.6 [1.0-2.5]
Prematurity	1.2 [1.1-1.4] 1.2 [0.8-1.7]
Macrosomia	2.4 [2.2-2.5] [a] 3.1 [3.0-3.3] [b]
Shoulder dystocia	3.14 [1.86-5.31] [b] 2.9 [1.4-5.8]
Admission to NNU	1.3 [1.3-1.4] [a] 1.5 [1.1-2.3]
Stillbirth	2.1 [1.5-2.7]
Neonatal death	2.6 [1.2-5.8]

Sleep disorders

Marchi J et al. Maternal Obesity/Pediatric Health Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. Obesity reviews (2015) 16, 621–638

Meccanismi delle patologie correlate all'obesità



La Polla A et al. Obesità e gravidanza: Il diabete. Vol.18, 2006
Desoye G. The Feto-placental Dialogue and Diabesity. Best Pract Res Clin Obst Gynaecol 29 (2015) 15e23
Catalano PM. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child.BMJ 2017

Placenta 32 (2011) 247–254

Contents lists available at ScienceDirect

Placenta

journal homepage: www.elsevier.com/locate/placenta

Placental structure and inflammation in pregnancies associated with obesity

Results: Maternal obesity was associated with significantly greater IL-1β ($p < 0.05$), IL-8 ($p < 0.05$), MCP-1 ($p < 0.001$) and CXCR2 ($p < 0.05$) mRNA expression within the placenta and higher circulating maternal levels of IL-6 (3.30 ± 0.38 vs. 1.77 ± 0.15 pg/ml) ($p < 0.001$) compared with non-obese women. There were no differences in the number of $CD14^+$, $CD68^+$ cells or neutrophils within the placental villi of non-obese and obese women. However there were significantly higher numbers of neutrophils within the interstitial space ($p < 0.05$). Greater muscularity of placental vessel walls was associated with maternal obesity ($p = 0.03$), however no other associated structural changes were observed.

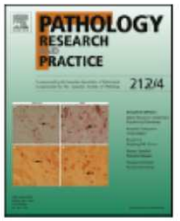
Conclusions: Our findings show that although pre-gravid obesity was associated with greater expression of placental pro-inflammatory cytokines and higher circulating IL-6 in pregnancy, there were no major differences in immune cell populations within the placental villi and only a greater degree of muscularity in the vessel walls.

Pathology – Research and Practice 212 (2016) 282–287

Contents lists available at ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.com/locate/prp



Original article

Placental findings associated with maternal obesity at early pregnancy

CrossMark

Placental pathology	Obese gravida ($n=47$)	Control ($n=45$)	p-Value
Histopathology related to impaired maternal circulatory disorders			
Decidual vasculopathy	13 (27.7%)	10 (22.2%)	0.6
Increased syncytial knots	13 (27.7%)	9 (20.0%)	0.5
Prominent septa with increased extravillous trophoblast	26 (55.3%)	23 (51.1%)	0.8
Parenchymal infarct	7 (14.9%)	14 (31.1%)	0.08
Abruption	1 (2.1%)	2 (4.4)	0.6
Distal villous hypoplasia	5 (10.6%)	5 (11.1%)	1.0
Trophoblastic giant cells at basal plate	1 (2.1%)	1 (2.2%)	1.0
Intervillous thrombi	13 (27.7%)	2 (4.4%)	0.004
Histopathology related to fetal circulation obstruction			
Villous edema	11 (23.4%)	19 (42.2%)	0.08
Villous capillary proliferative lesions such as chorangiosis, chorangioma, or chorangiomatosis	0 (0%)	2 (4.4%)	0.2
Fetal vascular obstruction (fetal thrombotic vasculopathy)	2 (4.3%)	3 (6.7%)	0.7
Histopathology related to infection/inflammation			
Chorioamnionitis only	9 (19.2%)	12 (26.7%)	0.5
Chorioamnionitis and fetal vessel vasculitis	13 (27.7%)	4 (8.9%)	0.03
Villitis of unknown etiology	2 (4.3%)	0 (0%)	0.5
Other			
Increased nucleated RBC in fetal circulation	4 (8.5%)	6 (13.3%)	0.5

Trieste, 25.10.2021

Dott Gianpaolo Maso

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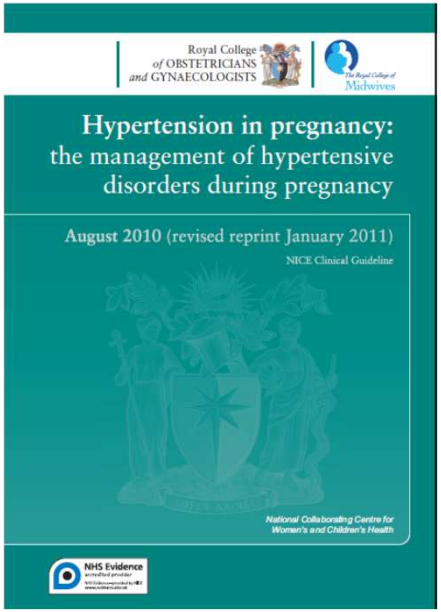
Preeclampsia

Rischio di preeclampsia raddoppia ogni
5-7 Kg/mq di BMI
3 X per BMI 30-39.9
7 X per BMI > 40

O'Brien et al.: Epidemiology 2009



Rasmussen KM, Yaktine AL, Institute of Medicine (U.S.). Weight Gain During Pregnancy: Reexamining the Guidelines. Washington, DC: National Academies Press; 2009. Committee to Reexamine IOM Pregnancy Weight Guidelines.

IOM guidelines for total and rate of weight gain during pregnancy, based on pre-pregnancy BMI.

Pre-pregnancy BMI	Total weight gain		Rates of weight gain during second and third trimesters	
	Range, kg	Range, lb	Mean (range), kg/wk	Mean (range), lb/wk
Underweight (<18.5)	12.5–18	28–40	0.51 (0.44–0.58)	1 (1–1.3)
Normal Weight (18.5–24.9)	11.5–16	25–35	0.42 (0.35–0.5)	1 (0.8–1)
Overweight (25–29.9)	7–11.5	15–25	0.28 (0.23–0.33)	0.6 (0.5–0.7)
Obese (≥30)	5–9	11–20	0.22 (0.17–0.27)	0.5 (0.4–0.6)

Advise women at high risk of pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Women at high risk are those with any of the following:

- hypertensive disease during a previous pregnancy
- chronic kidney disease
- autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome
- type 1 or type 2 diabetes
- chronic hypertension.

Advise women with more than one moderate risk factor for pre-eclampsia to take 75 mg of aspirin* daily from 12 weeks until the birth of the baby. Factors indicating moderate risk are:

- first pregnancy
- age 40 years or older
- pregnancy interval of more than 10 years
- body mass index (BMI) of 35 kg/m² or more at first visit
- family history of pre-eclampsia
- multiple pregnancy.

150mg

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E.C.M.

Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium

Royal College of Obstetricians & Gynaecologists

Green-top Guideline No. 37a
April 2015

Obesity

Sixty percent of women who died from PE in the UK between 2003 and 2008 were obese (body mass index [BMI] 30 or higher)[3,4] compared with the 20% prevalence of obesity in women aged 16–44 in the Health Survey for England 2010.[39,40] Obesity is a risk factor for VTE in pregnancy[7,12,31–33] and the risk is higher with increasing obesity.[41] It is associated with a higher risk of PE (adjusted OR [aOR] 14.9, 95% CI 3.0–74.8) than of DVT (aOR 4.4, 95% CI 1.6–11.9).[33] Being overweight (BMI 25–29.9), too, is a weak risk factor for pregnancy-related VTE and is extremely common, with a prevalence within the childbearing population of almost 50%.[39]

Evidence level 2+

MORTALITA' MATERNA

50% DELLE MORTI MATERNE COINVOLGE OBESE (15% obese di classe III che sono il 2%)

- 47% DELLE MORTI PER CAUSE DIRETTE SONO OVERWEIGHT O OBESE (obese 30%)

- 50% NELLE MORTI PER CAUSE INDIRETTE (obese 24%)

- 78% OVERWEIGHT O OBESE NELLE MORTI PER TEV

- 61% IN QUELLE PER CAUSE CARDIACHE

- PER LE ALTRE CAUSE SIAMO AL 40%, ECCETTO CHE PER SUICIDIO, EMORRAGIA E SEPSI DOVE SI E' AL 20-25% (come nella popolazione ostetrica generale)

TOP TEN RECOMENDATIONS

N.1 è RELATIVA A COUNSELING PREGRAVIDICO PER DONNE CON PATOLOGIA PREESISTENTE CHE PUO' PEGGIORARE O CONDIZIONARE LA GRAVIDANZA.

Obesity: a body mass index of 30 or more

Best Practice & Research Clinical Obstetrics and Gynaecology 29 (2015) 365–376

Contents lists available at ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

8

Deep venous thrombosis and pulmonary embolism in obese women

James Drife, MD, FRCOG, FRCPE, FRCSE, FFSRH, FCOG(SA), Emeritus Professor of Obstetrics and Gynaecology, University of Leeds

Thrombosis Research 151, Suppl. 1 (2017) S53–S55

Contents lists available at ScienceDirect

Thrombosis Research

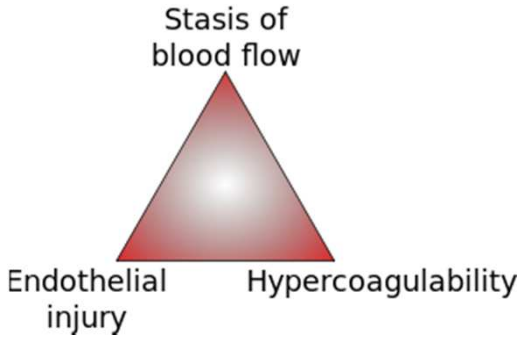
journal homepage: www.elsevier.com/locate/thromres

The effect of BMI on haemostasis: Implications for thrombosis in women's health

Beverley J. Hunt*

Hypothetical changes induced by obesity according to Virchow's triad.

Prothrombotic	⇑ Von Willebrand Factor ⇑ Fibrinogen ⇑ PAI-1 ⇑ TAT, PF1+2 ⇑ Platelet reactivity & ⇑ Procoagulant microparticles
Flow	⇓ Due to increased vein size? ⇓ Function of venous valves
Vessel wall	⇑ Tissue factor expression? Endothelial cell activation due to adipose cytokine production?
Other	Local pressure on veins?



- Physical effects of body fat may add to this physical limitation of venous return
- Fat produces hormones, cytokines and chemokines
- Adipose tissue remodeling involves angiogenesis, infiltration by inflammatory cells and the secretion of pro-angiogenic factors (VEGF) and transforming growth factor.
- Aberrant expression of adipose tissue-derived cytokines ('adipokines') modulates proinflammatory and prothrombotic pathways in obesity

  >leptin: increases platelet adhesion to fibrinogen and promote of thromboplastin (extrinsic coagulation cascade)

  <adiponectin: anti-inflammatory anti-thrombotic effects by modulating the function of endothelial cells

Risk factors for VTE

Pre-existing risk factors	Tick	Score
Previous VTE (except a single event related to major surgery)		4
Previous VTE provoked by major surgery		3
Known high-risk thrombophilia		3
Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		3
Family history of unprovoked or estrogen-related VTE in first-degree relative		1
Known low-risk thrombophilia (no VTE)		1[a]
Age (> 35 years)		1
Obesity		1 or 2[b]
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia in current pregnancy		1
ART/IVF (antenatal only)		1
Multiple pregnancy		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational operative delivery		1
Prolonged labour (> 24 hours)		1
PPH (> 1 litre or transfusion)		1
Preterm birth < 37[+0] weeks in current pregnancy		1
Stillbirth in current pregnancy		1
Transient risk factors		
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation		3
Hyperemesis		3
OHSS (first trimester only)		4
Current systemic infection		1
Immobility, dehydration		1
TOTAL		

Abbreviations: ART assisted reproductive technology; IVF in vitro fertilisation; OHSS ovarian hyperstimulation syndrome; VTE venous thromboembolism.

[a] If the known low-risk thrombophilia is in a woman with a family history of VTE in a first-degree relative postpartum thromboprophylaxis should be continued for 6 weeks.

[b] BMI ≥ 30 = 1; BMI ≥ 40 = 2

Royal College of Obstetricians & Gynaecologists

Appendix III: Risk assessment for venous thromboembolism (VTE)

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If admitted to hospital antenatally consider thromboprophylaxis.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium consider thromboprophylaxis.

For patients with an identified bleeding risk, the balance of risks of bleeding and thrombosis should be discussed in consultation with a haematologist with expertise in thrombosis and bleeding in pregnancy.

Table 3. Suggested thromboprophylactic doses for antenatal and postnatal LMWH

Weight	Enoxaparin	Dalteparin	Tinzaparin (75 u/kg/day)
< 50 kg	20 mg daily	2500 units daily	3500 units daily
50–90 kg	40 mg daily	5000 units daily	4500 units daily
91–130 kg	60 mg daily*	7500 units daily	7000 units daily*
131–170 kg	80 mg daily*	10 000 units daily	9000 units daily*
> 170 kg	0.6 mg/kg/day*	75 u/kg/day	75 u/kg/day*
High prophylactic dose for women weighing 50–90 kg	40 mg 12 hourly	5000 units 12 hourly	4500 units 12 hourly

*may be given in 2 divided doses

All women with BMI>40kg/m^2, should be considered for thromboprophylaxis LMWH for 10 days after delivery

4.2.a. La malattia tromboembolica

La malattia tromboembolica, sia pur rara in valore assoluto (13 casi per 10.000) (11), rappresenta una delle principali cause di mortalità materna diretta (15 casi mortali per milione di gravidanze) (1).

Il mancato riconoscimento dei fattori di rischio, di segni e sintomi della malattia tromboembolica ed i trattamenti non sufficientemente tempestivi o i dosaggi inappropriati in caso di tromboprofilassi sono gli aspetti di *substandard care* rilevati più frequentemente. Infatti, come riportato nel 2004 dal Report Anglosassone, una condizione di *substandard care* risulta presente in più della metà dei casi di malattia tromboembolica in donne gravide.

QUESITO 7 Tromboembolia	**RACCOMANDAZIONE 7** Le donne obese hanno un rischio maggiore di tromboembolismo venoso (TEV) durante la gravidanza e nelle 6 settimane successive al parto rispetto alle donne normopeso. Pertanto, nelle donne con BMI >30 kg/m2 è fondamentale la valutazione del rischio di TEV e l'eventuale inizio della tromboprofilassi.

FATTORI DI RISCHIO	**COSA FARE**	**QUANDO - DOVE**	**COMUNICAZIONE**
• assenza di protocollo / procedura per la donna obesa in gravidanza • precedente episodio, di TEV • trombofilia congenita, • patologie concomitanti, • età>35 anni, • parità>3, • fumo, • varici sintomatiche o sopra il ginocchio.	• per gravide con BMI>30, valutare opportunità di attivare profilassi eparinica, peso corretta, secondo le indicazioni della Linea Guida RCOG n.37a Aprile 2015 • aggiustamento della dose di eparina in relazione al peso corporeo • tromboprofilassi con eparina a basso peso molecolare in tutte le donne con BMI >30 kg/m2 sottoposte a cesareo in elezione o d'urgenza. • tutte le donne con BMI >40 kg/m2 dovrebbero ricevere la tromboprofilassi indipendentemente dalla modalità del parto. • compressione pneumatica automatica degli arti inferiori soprattutto in caso di eventi emorragici e TC complicato. **PERCORSO SPECIALISTICO PARALLELO** • Consulenza internistica o cardiologica **EMERGENZA URGENZA** • Pronto Soccorso Ostetrico	**QUANDO:** • per tutta la durata della gravidanza dove indicata e fino a 6 settimane dopo il parto **DOVE:** • Presso il medico ginecologo/ostetrico della struttura di riferimento	• relazione clinica e referti strumentali inseriti nella documentazione sanitaria che deve essere sempre fruibile da parte di tutti gli operatori sanitari del percorso. • cartelle computerizzate condivise, (auspicabile) • audit (vedi Racc. 1) • counseling sui rischi per tromboembolia

AGENZIA ITALIANA DEL FARMACO

DETERMINA 20 luglio 2016

Inserimento delle eparine a basso peso molecolare (EBPM) nell'elenco dei medicinali per uso umano erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648, per la profilassi del tromboembolismo in gravidanza e puerperio per le pazienti a rischio. (Determina n. 998/2016). (16A05805)

(GU n.183 del 6-8-2016)

Allegato 1

Denominazione: eparine a basso peso molecolare (EBPM).

Indicazione terapeutica: profilassi del tromboembolismo in gravidanza e puerperio per le pazienti a rischio.

Criteri di inclusione:

1. pregresso evento tromboembolico venoso idiopatico o in corso di trattamento con estro-progestinici indipendentemente dalla presenza di trombofilia (profilassi);

2. pregressi aborti ricorrenti altrimenti non spiegabili (definiti come un numero ≥ 3, o di 2 in presenza di almeno un cariotipo fetale normale) in presenza di documentata trombofilia congenita o acquisita (profilassi);

3. una o piu' morti endouterine del feto (MEF), definita come perdita fetale occorsa dalla 20a settimana di gestazione in poi di un feto morfologicamente normale (profilassi);

4. precedente pre-eclampsia severa, ritardo di crescita intrauterino e distacco di placenta normalmente inserita «sine causa» (profilassi);

5. valvole cardiache meccaniche: dalla positivizzazione del test di gravidanza fino alla fine del primo trimestre (10-14 settimane circa) e dalla 34 settimana fino al parto. Dalla 14 alla 34 settimana secondo il giudizio del clinico e dopo condivisione con la paziente (trattamento).

FATTORI DI RISCHIO CLINICI O COSITUZIONALI??????

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PRESCRIZIONE EPARINE A BASSO PESO MOLECOLARE IN PROFILASSI DEL TROMBOEMBOLISMO IN GRAVIDANZA E PUERPERIO PER LE PAZIENTI A RISCHIO

PERCORSO DIAGNOSTICO TERAPEUTICO ASSISTENZIALE

Codice identificazione file:
PDTA_OST_0004_00
F_DGNF_0003_03_PRO_DGN_0001

Bozza/in sperimentazione/definitivo

Data redazione:	23/10/2017
Struttura emittente:	S.S.DPT Gravidanza a Rischio
Process owner:	Dott. Gianpaolo Maso; Dott. Davide Zanon
Gruppo di redazione:	Dott. Gianpaolo Maso; Dott. Davide Zanon, Dott.ssa Alessandra Maestro, Dott.ssa Chiara Volpato, Dott. Stefano Loiacono, Dott. Paolo Bogatti; Direzione Sanitaria
Pareri tecnici:	Prof. Giuspe Ricci
Pareri favorevoli:	Direzione Sanitaria
Approvazione:	Prof. Giuseppe Ricci
Da rivedere entro:	*31/12/2017*
Modalità diffusione:	*intranet aziendale*
Parole chiave:	*eparine a basso peso molecolare, profilassi, tromboembolismo venoso, prescrizione*
Norme e standard applicabili:	*Legge 648/96, Legge 94/98, determinazione AIFA n° 1489/2016*

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

NUMBER 156, DECEMBER 2015 *(Replaces Committee Opinion Number 549, January 2013)*

Obesity in Pregnancy

OBSTRUCTIVE SLEEP DISORDER

- Preeclampsia adj OR, 2.5; 95% CI, 2.2–2.9
- Eclampsia adj OR, 5.4; 95% CI, 3.3–8.9
- Cardiomyopathy adj OR 9.0; 95% CI, 7.5–10.9
- Pulmonary embolism adj OR, 4.5; 95% CI, 2.3–8.9
- In-hospital mortality adj OR, 5.28; 95% CI, 2.45–11.53

Women with suspected OSA (snoring, excessive daytime sleepiness, witnessed apneas, or unexplained hypoxia) should be referred to a sleep medicine specialist for evaluation and possible treatment

CLINICAL OPINION ajog.org

OBSTETRICS

The multidisciplinary approach to the care of the obese parturient

Neda Ghaffari, MD; Sindhu K. Srinivas, MD, MSCE; Celeste P. Durnwald, MD

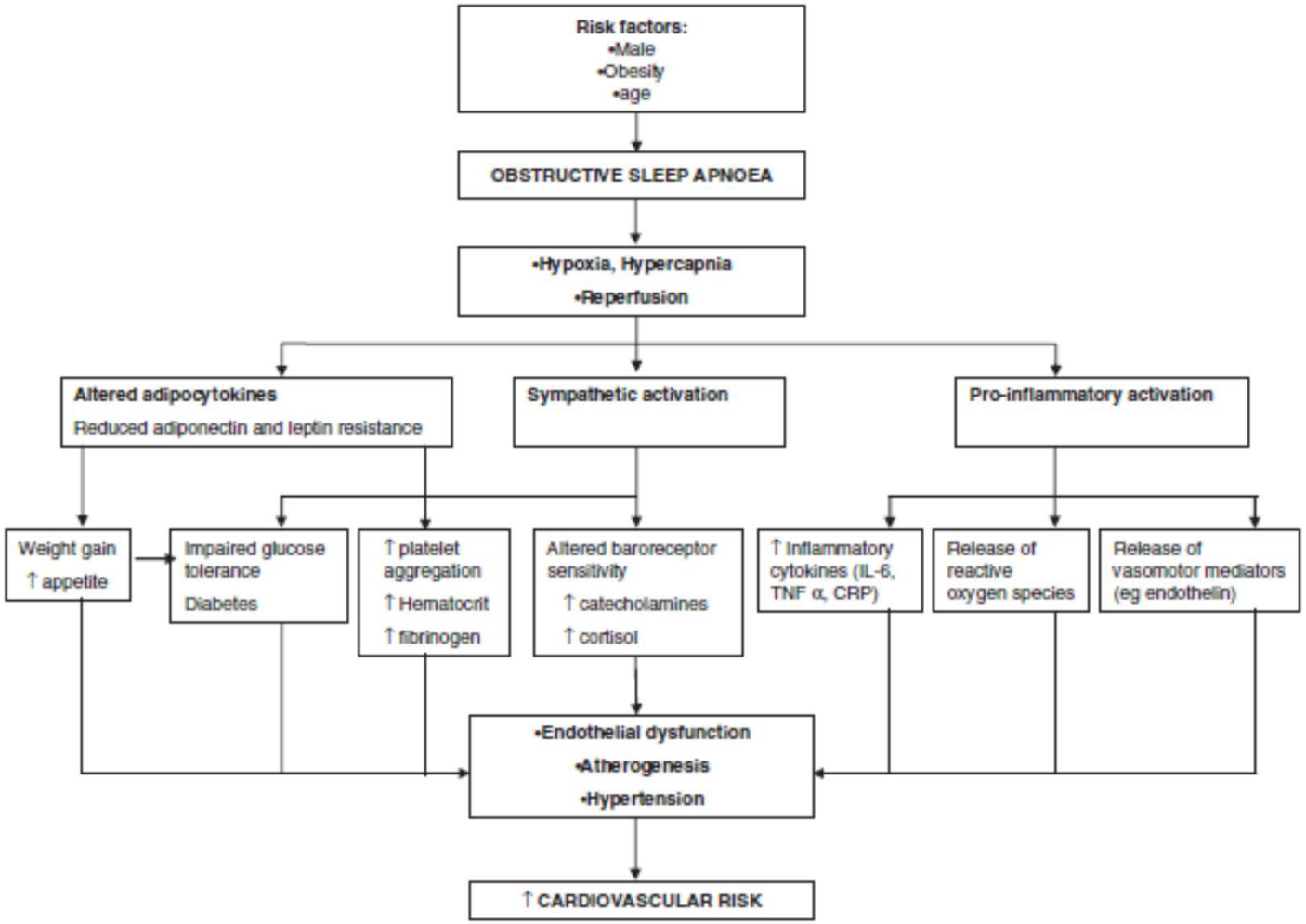
STOP questionnaire[a]

S	"Do you *snore* loudly (louder than talking or loud enough to be heard through closed doors)?"
T	"Do you often feel *tired*, fatigued, or sleepy during daytime?"
O	"Has anyone *observed* you stop breathing during your sleep?"
P	"Do you have or are you being treated for high blood *pressure*?"

[a] If answer is yes to 2 or more questions, refer to a sleep specialist.
Adapted from Chung et al.[44]

OBSTRUCTIVE SLEEP DISORDER IN PREGNANCY

PATOPHYSIOLOGY OF COMPLICATIONS (Fung Am, J Perinatol.2012)



OBSTRUCTIVE SLEEP DISORDER IN PREGNANCY

PATOPHYSIOLOGY OF COMPLICATIONS (Fung Am, J Perinatol.2012)

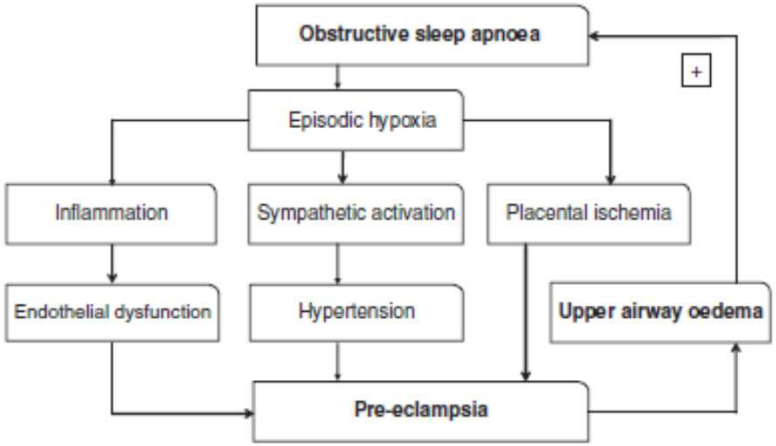


Figure 2 Potential interaction between obstructive sleep apnea and hypertensive disorders of pregnancy.

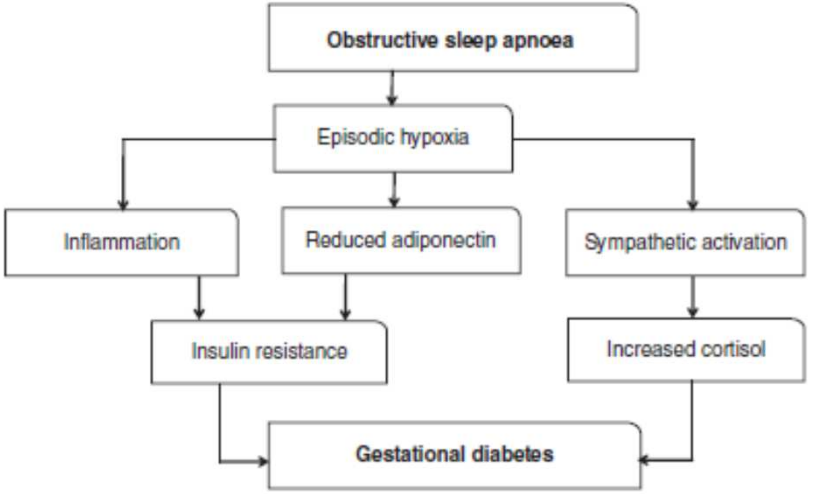


Figure 3 Potential interaction between obstructive sleep apnea and gestational diabetes.

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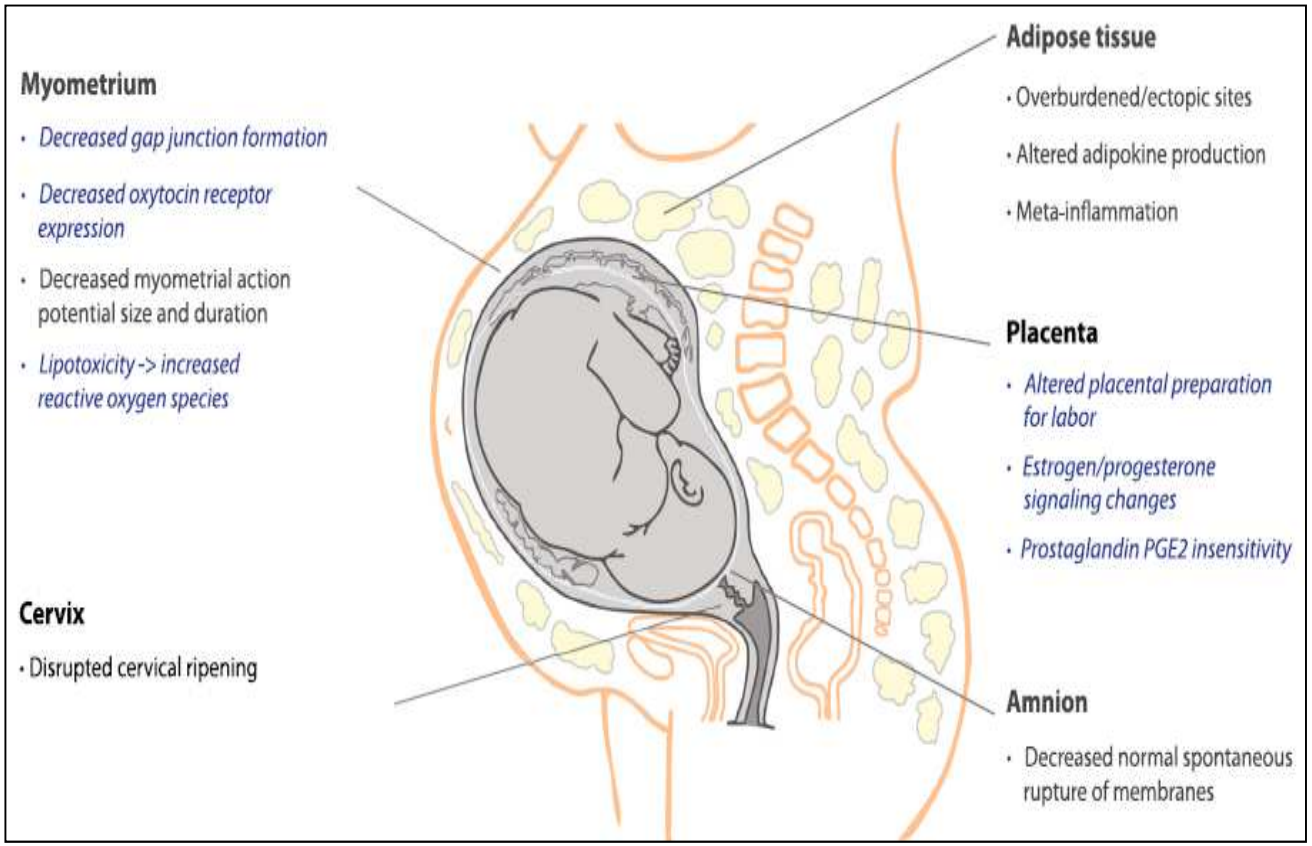
OBESITÀ E MODALITÀ DEL PARTO

N=118,978 Consortium of Safe Labor: incremento del rischio di taglio cesareo 5%/ 1 kg/m^2 BMI DA DISTOCIA

Kominiarek et al, 2010. The maternal body mass index: a strong association with delivery route. Am J Obstet Gynecol, 203(3), 264 e261-267.



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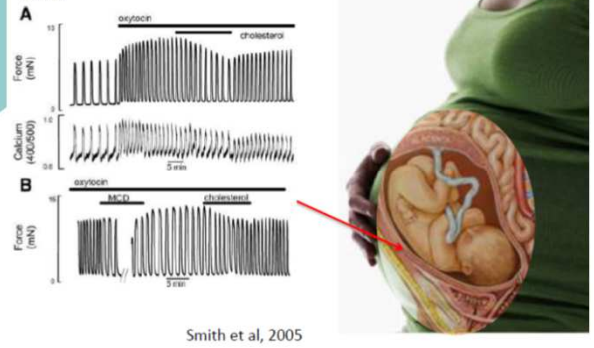
BIOLOGY OF OBESITY IN PREGNANCY (4 MODELS)

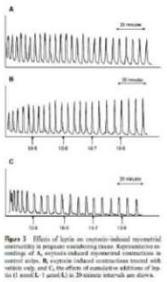
Cholesterol causes disrupted contractility in uterus



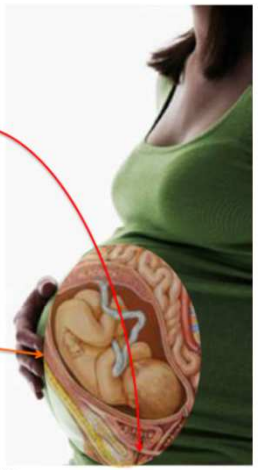
Smith et al, 2005

MODEL 1
Cholesterol causes disrupted uterine contractility

MODEL 2
Leptin disrupts contractility & cervical/uterine ripening.
Wendremaire et al, 2012



From Moynihan et al, 2006

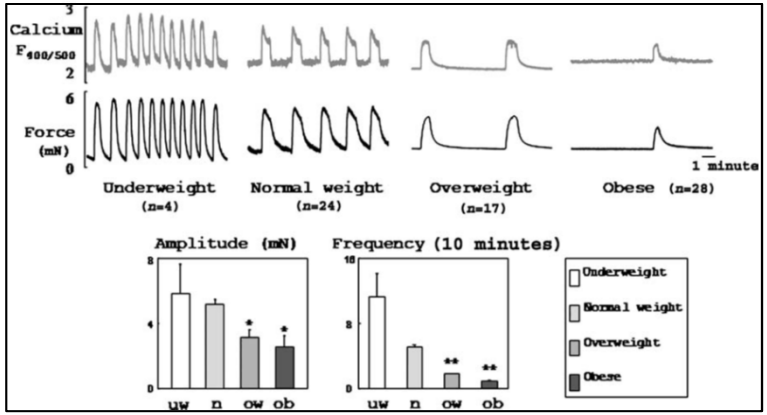


MODEL 1
Cholesterol disrupts uterine contractility.

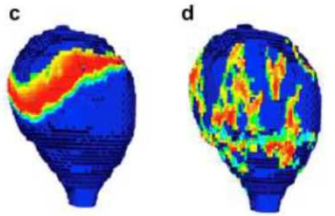
MODEL 2
Leptin disrupts contractility & cervical/uterine ripening.

MODEL 3
Decreased oxytocin receptors & Connexin-43 connections between myocytes.

Garabedian et al, 2011; Elmes et al, 2011



Electrophysiologic Model of Uterus with Irregular Propagation



Aslanidi, et al (2011). Towards a computational reconstruction of the electrodynamics of premature and full term human labour. *Prog Biophys Mol Biol, 107*(1), 183-192.

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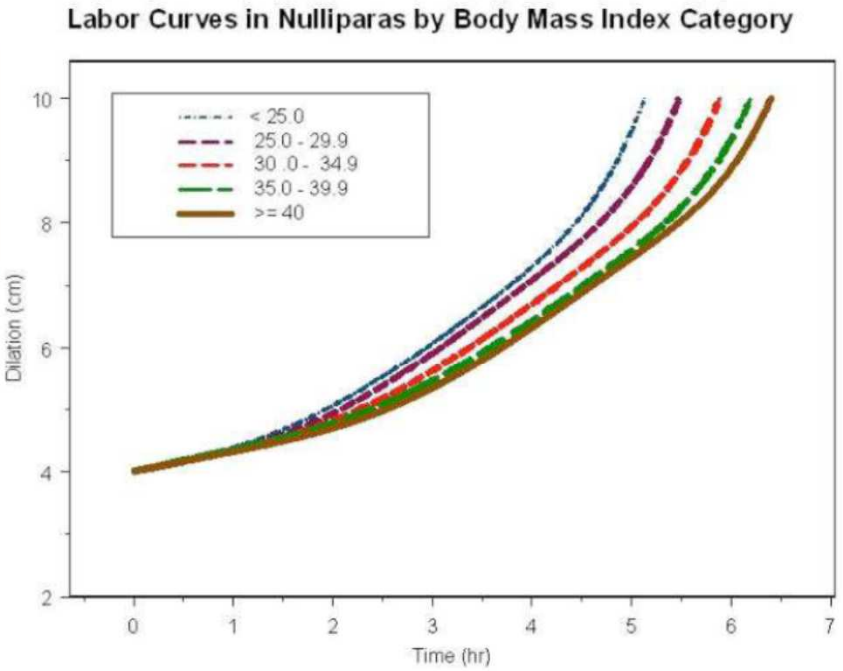

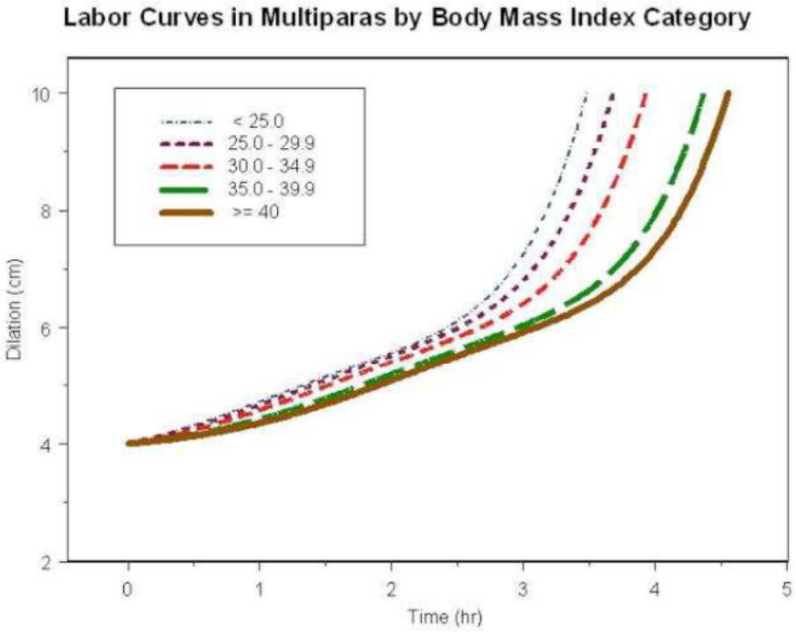

Kominiarek et al, 2011

Le obese sono «poor responders» all'infusione ossitocica

Il tasso di mancata induzione è significativamente maggiore rispetto alle donne con BMI normale

La durata del travaglio è inversamente correlata al BMI

I travagli nelle obese sono più «lenti»

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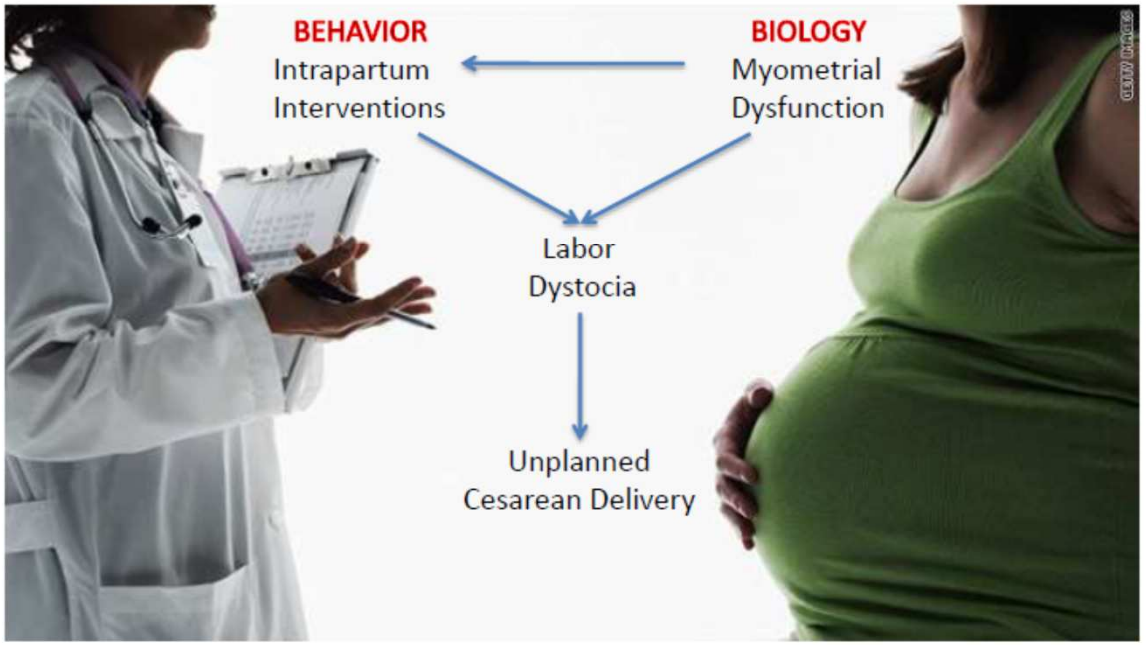
Interaction: Provider & Biology of Obesity



Carlson N, 2015
Bogaerts A.Obesity in pregnancy: Altered onset and progression-Midwifery 29, 2013

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Pre-pregnancy body mass index (BMI) and gestational weight gain are independent risk factors of operative vaginal and cesarean deliveries?

- A prospective study collected data on mode of delivery and maternal/neonatal outcomes
- 11 Hospitals in Friuli Venezia Giulia (Italy) – 18 months
- The sample included 14983 women with singleton pregnancies

Associations between exposure variables and mode of delivery were analyzed using Pearson's chi squared test

Multiple logistic regression models were built to assess the independent association between potential predictors and operative delivery (cesarean and vaginal)

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BMI

BMI Standards / National Institute of Health
(Body Mass Index)

Underweight	<18.5
Normal	18.5 - 24.9
Overweight	25 - 29.9
Obesity (Class I)	30 – 34.9
Obesity (Class II)	35 – 39.9
Extreme Obesity (Class III)	>40

IOM RECOMMENDATIONS FOR WEIGHT GAIN BY PRE-PREGNANCY BMI

Prepregnancy BMI	Total weight gain (kg)
Underweight (BMI < 18.5)	12.5 – 18
Normal weight (BMI 18.5 – 24.9)	11.5 – 16
Overweight (BMI 25 – 29.9)	7.0 – 11.5
Obese (BMI > 30)	5.0 – 9.0

Institute of Medicine, National Research Council
Implementing Guidelines on Weight Gain & Pregnancy

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Variables

- maternal age (20–24 years, <20 years, 25–29 years, 30–35 years, >35 years)
- gestational age at delivery (37–41 weeks, <30 weeks, 30–36 weeks, >41 weeks)
- classification of pregnancy at risk (no risk, low/intermediate risk, high risk)
- parity (multiparous, nulliparous)
- gestations (singleton, twin)
- presentation (cephalic, other)
- presence of previous CD (no past CD, one, more than one)
- newborn birth weight (2,500-4,000 grams, <1,000 grams, 1,000-1,499 grams, 1,500-2,499 grams, >4,000 grams)
- onset of labor (spontaneous vs. induced vs. no labour)
- Maternal height

CLUSTER VARIABLES

- number of deliveries per center (≥1000 deliveries/year, <1000 deliveries/year)
- presence of a Neonatal Intensive Care Unit (available, non-available)

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Results

	Number	Percentage
Weight Gain		
IOM reccommended	6847	45.7
< IOM reccommended	4953	33.1
> IOM reccommended	3183	21.2

Weight Gain

IOM reccommended	6847 (45.7)
< IOM reccommended	4953 (33.1)
> IOM reccommended	3183 (**21.2**)

25-29	3,281	21.9
30-35	6,626	44.2

BMI

18.5-25	11684 (78.0)
<18.5	1104 (7.4)
26-30	1590 (**10.6**)
>30	605 (**4.0**)

Yes	13626	90.9
No	1357	9.1
Fetal presentation		
Cephalic	14,344	95.7
Non cephalic	639	4.3

	Number	Percentage
Labor		
Spontaneous	10946	73.1
Induced	2078	13.8
No labour	1959	13.1
Gestational Age at birth (weeks)		
<30	62	0.4
1000-1499	64	0.4
1500-2499	591	3.9
2500-4000	13218	88.2
>4000	1071	7.2
Center		
>=1000	6791	45.3
<1000	8192	54.7
NICU		
Non available	9873	65.9
Available	5110	34.1

Mode of delivery

Spontaneous vaginal	10409 (69.4)	
Operative vaginal	1137 (7.6)	
Emergency CS	2076 (13.9)	} 23%
Elective CS	1361 (9.1)	

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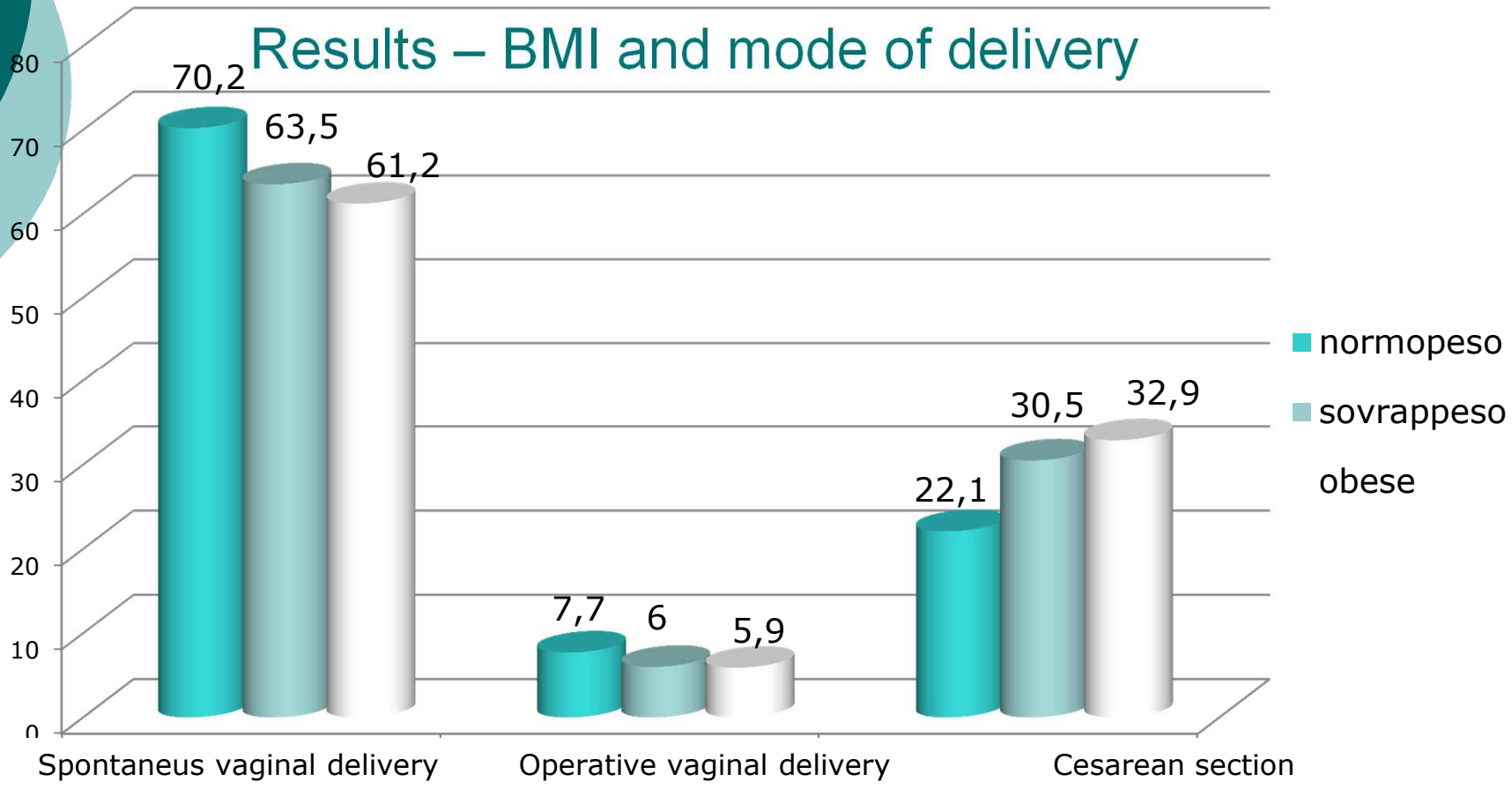
Results – BMI and mode of delivery



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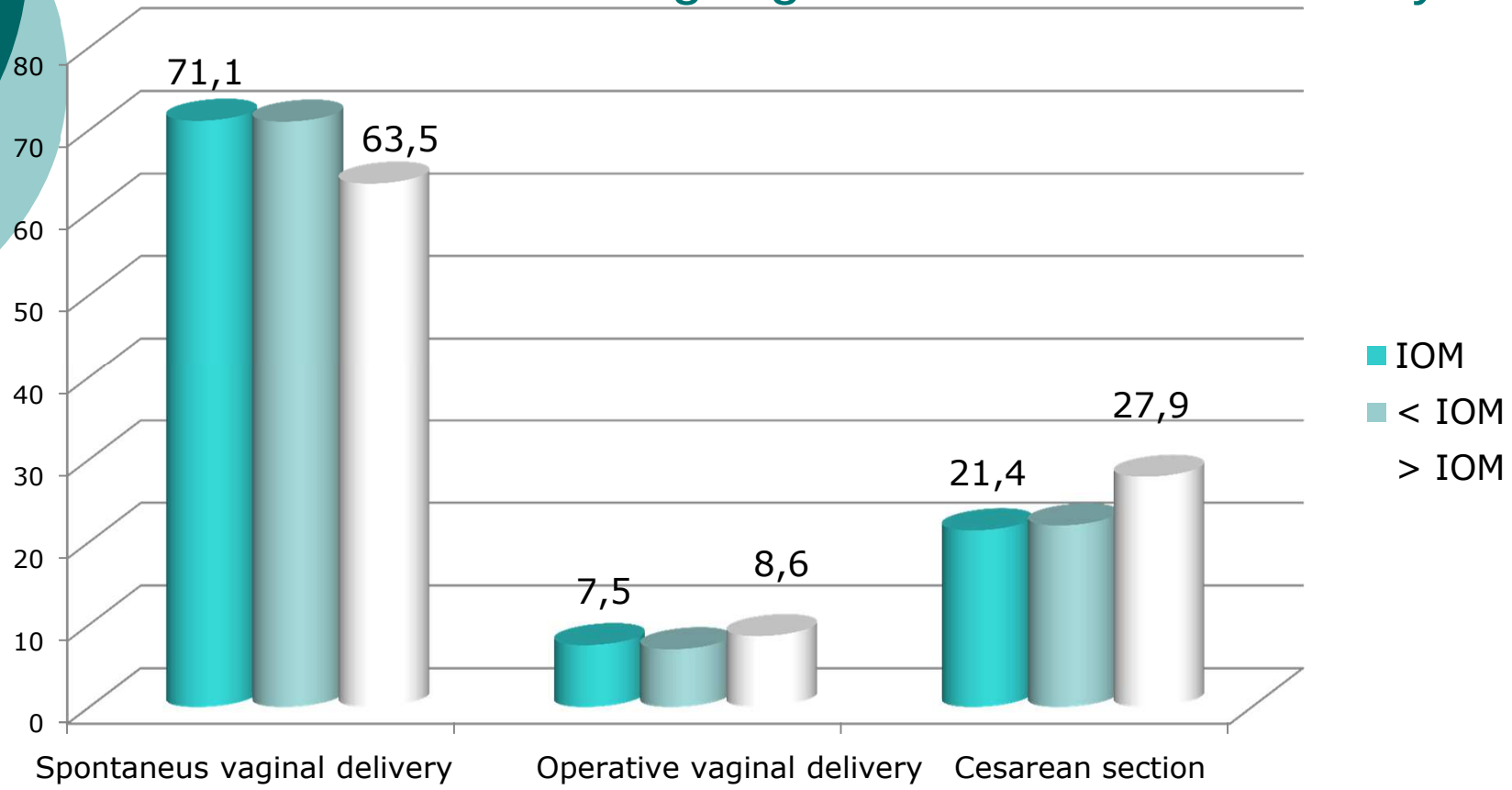
Results – Weight gain and mode of delivery



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Bivariate analysis on mode of delivery

	OVD		Emergency CS		Elective CS		Overall CS		Overall Operative	
	RR (CI 95%)	**p**	**RR (CI 95%)**	**p**	**RR (CI 95%)**	**p**	**RR (CI 95%)**	**p**	**RR (CI 95%)**	**p**
Weight Gain										
< IOM recc	0.94 (0.83-1.06)	0.327	1.11 (0.99-1.23)	0.052	0.91 (0.78-1.05	0.219	1.03 (0.93-1.14)	0.610	1.00 (0.93-1.09)	0.867
IOM recc	Reference		Reference		Reference		Reference		Reference	
> IOM recc	1.24 (1.10-1.39)	0.000	1.38 (1.29-1.48)	0.000	1.28 (1.19-1.38)	0.000	1.29 (1.24-1.35)	0.000	1.24 (1.19-1.30	0.000
BMI										
<18.5	1.15 (0.96-1.37)	0.118	0.89 (0.80-0.99)	0.040	0.85 (0.72-0.99)	0.042	0.89 (0.81-0.98)	0.000	0.96 (0.88-1.04)	0.323
18.5-25	Reference		Reference		Reference		Reference		Reference	
26-30	0.87 (0.68-1.11)	0.283	1.46 (1.22-1.76)	0.000	1.64 (1.45-1.84)	0.000	1.44 (1.26-1.65)	0.000	1.28 (1.12-1.47)	0.000
>30	0.90 (0.63-1.29)	0.578	1.78 (1.48-2.14)	0.000	1.92 (1.52-2.41)	0.000	1.69 (1.44-1.98)	0.000	1.46 (1.25-1.70)	0.000
37-41	Reference		Reference		Reference		Reference		Reference	
>41	1.32 (1.05-1.67)	0.019	1.67 (1.06-2.62)	0.025	0.91 (0.74-1.11)	0.378	1.13 (0.75-1.70)	0.551	1.15 (0.88-1.50)	0.288
Neonatal BW (g)										
<1000	Not evaluable		5.03 (3.88-6.52)	0.000			3.11 (2.45-3.94)	0.000	2.47 (1.99-3.06)	0.000
1000-1499	Not evaluable		6.02 (5.03-7.21)	0.000			3.72 (3.16-4.37)	0.000	2.96 (2.57-3.41)	0.000
1500-2499	0.47 (030-0.73)	0.001	3.29 (3.05-3.54)	0.000	0.71 (0.55-0.91)	0.007	2.14 (1.99-2.31)	0.000	1.75 (1.64-1.88)	0.000
2500-4000	Reference		Reference		Reference		Reference		Reference	
>4000	1.28 (1.00-1.63)	0.047	1.29 (1.13-1.46)	0.000	0.91 (0.74-1.11)	0.378	1.11 (1.01-1.25)	0.043	1.13 (1.02-1.25)	0.012
Center										
>=1000	Reference		Reference		Reference		Reference		Reference	
<1000	0.82 (0.53-1.27)	0.391	0.64 (0.48-0.85)	**0.002**	0.80 (0.48-1.34)	0.412	0.74 (0.54-1.01)	0.056	0.78 (0.59-1.02)	0.074
NICU										
Non available	1.34 (0.86.2.09)	0.189	1.37 (0.92-2.04)	0.117	1.23 (0.69-2.20)	0.474	1.27 (0.85-1.88)	0.233	1.25 (0.89-1.74)	0.197
Available	Reference		Reference		Reference		Reference		Reference	

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Multivariate analysis on mode of delivery

	Operativo vaginale		TC emergente		TC elettivo		TC totale		Operativo totale	
	RR (CI 95%)	P	RR (CI 95%)	P	RR (CI 95%)	P	RR (CI 95%)	P	RR (CI 95%)	P
Incremento ponderale										
< IOM	1.02 (0.89-1.17)	0.327	1.00 (0.87-1.16)	0.909	0.88 (0.73-1.05)	0.177	1.00 (0.96-1.04)	0.927	1.00 (0.96-1.05)	0.738
IOM	1		1		1		1		1	
> IOM	1.19 (1.05-1.35)	0.006	1.31 (1.18-1.45)	0.000	0.98 (0.87-1.11)	0.805	1.09 (1.04-1.15)	0.000	1.10 (1.04-1.15)	0.000
BMI										
< 18.5	1.20 (0.99-1.44)	0.059	0.90 (0.77-1.04)	0.171	0.85 (0.61-1.20)	0.379	0.95 (0.87-1.04)	0.346	1.01 (0.91-1.12)	0.739
18.5 – 24.9	1		1		1		1		1	
25 – 29.9	0.86 (0.69-1.08)	0.212	1.18 (0.96-1.45)	0.113	1.12 (0.94-1.33)	0.183	1.11 (1.00-1.24)	0.049	1.06 (0.94-1.18)	0.299
≥ 30	0.86 (0.60-1.22)	0.393	1.21 (0.93-1.59)	0.159	1.04 (0.81-1.34)	0.734	1.08 (0.98-1.19)	0.096	1.04 (0.95-1.11)	0.366

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Key points

- Obese BMI and GWG excess are risk factor for operative vaginal delivery and CS

- GWG should be considered as **independent risk factor** for operative vaginal delivery and CS

Bias:

- ✓ Obesity 4%

L'OBESITA' E L'ECCESSIVO AUMENTO PONDERALE SONO FATTORI DI RISCHIO INDIPENDENTI PER COMPLICANZE MATERNE E FETO-NEONATALI?

Obiettivi dello studio

- Le complicanze dell'obesità e dell'eccessivo aumento ponderale in gravidanza sono correlate alle patologie preesistenti associate (es. ipertensione pre-esistente, DMT2) e/o insorgenti in gravidanza (es preeclampsia, diabete gestazionale)?

- **BMI ↑ pregravidico ed eccessivo incremento ponderale sono fattori di rischio indipendenti per:**
  - complicanze materne durante e post gravidanza
  - complicanze feto-neonatali
- **Fattore di rischio indipendente = di per sé decisivo nel determinare una certa complicanza**

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Multivariate analysis on maternal and fetal complications during pregnancy (PET/HDP: preeclampsia/hypertensive disorder of pregnancy)

	PET/HDP		GDM		IUGR/oligohydramnios		Acceleration of fetal growth/Polihydramnios	
	RR (CI 95%)	p	RR (CI 95%)	p	RR (CI 95%)	p	RR (CI 95%)	p
Weight Gain								
< IOM recc	1.03 (0.77-1.37)	0.868	0.97 (0.74-1.27)	0.815	1.24 (1.03-1.50)	0.024	0.53 (0.26-1.09)	0.085
IOM recc	Reference		Reference		Reference		Reference	
> IOM recc	1.51 (1.14-2.00)	0.003	1.56 (1.23-1.97)	0.000	1.12 (0.90-1.40)	0.304	1.40 (0.80-2.45)	0.240
BMI								
<18.5	0.54 (0.27-1.05)	0.868	0.33 (0.16-0.67)	0.002	1.28 (0.96-1.71)	0.093	0.30 (0.04-2.22)	0.241
18.5-25	Reference		Reference		Reference		Reference	
26-30	2.07 (1.52-2.81)	0.000	2.78 (2.13-3.63)	0.000	1.21 (0.93-1.58)	0.157	1.79 (0.91-3.52)	0.089
>30	3.90 (2.78-5.52)	0.000	4.72 (3.78-6.42)	0.000	1.86 (1.34-2.59)	0.000	4.85 (2.48-9.49)	0.000

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Conclusioni (I)

	Preeclampsia	GDM	IUGR	Acc. crescita fetale	Peso nascita < 2500	Peso nascita > 4000	Parto < 37 sett	Parto < 34 sett	Distress neonatale
Eccessivo > ponderale	X	X				X			
BMI 26 -30	X	X				X		X	
BMI > 30	X	X	X	X	X	X	X	X	X

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Stato nutrizionale

"Assessment" pre-gravidico

- Chirurgia bariatrica, diabete, ipertensione, patologie gastointestinali
- Sovrappeso/obesità
- Storia ostetrica: pregresso difetto del tubo neurale
- Dieta restrittive/disordini alimentari
- Gravidanza multipla
- Utilizzo di sostanze (fumo, alcool, droghe)

Riferire a consulenza nutrizionale

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Key message

Strategies to reduce caesarean births, operative deliveries and pregnancy complications must include

- ✓ measures to prevent overweight and obese BMI prior to conception
- ✓ promote recommended weight gain throughout pregnancy
- ✓ Avoid inappropriate interventions and consider the obesity biology

- ❖ Inform obese women about weight reduction and bariatric surgery
- ❖ Prenatal multidisciplinary approach for obese women in pregnancy
- ❖ Women shoud be counselled about GWG within the first trimester

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