COGI 2017

DIABETES & PREGNANCY:

PREDICTION & PREVENTION

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Definition


11. DEFINITION.—A
thing which induces a
It is the substa
parties

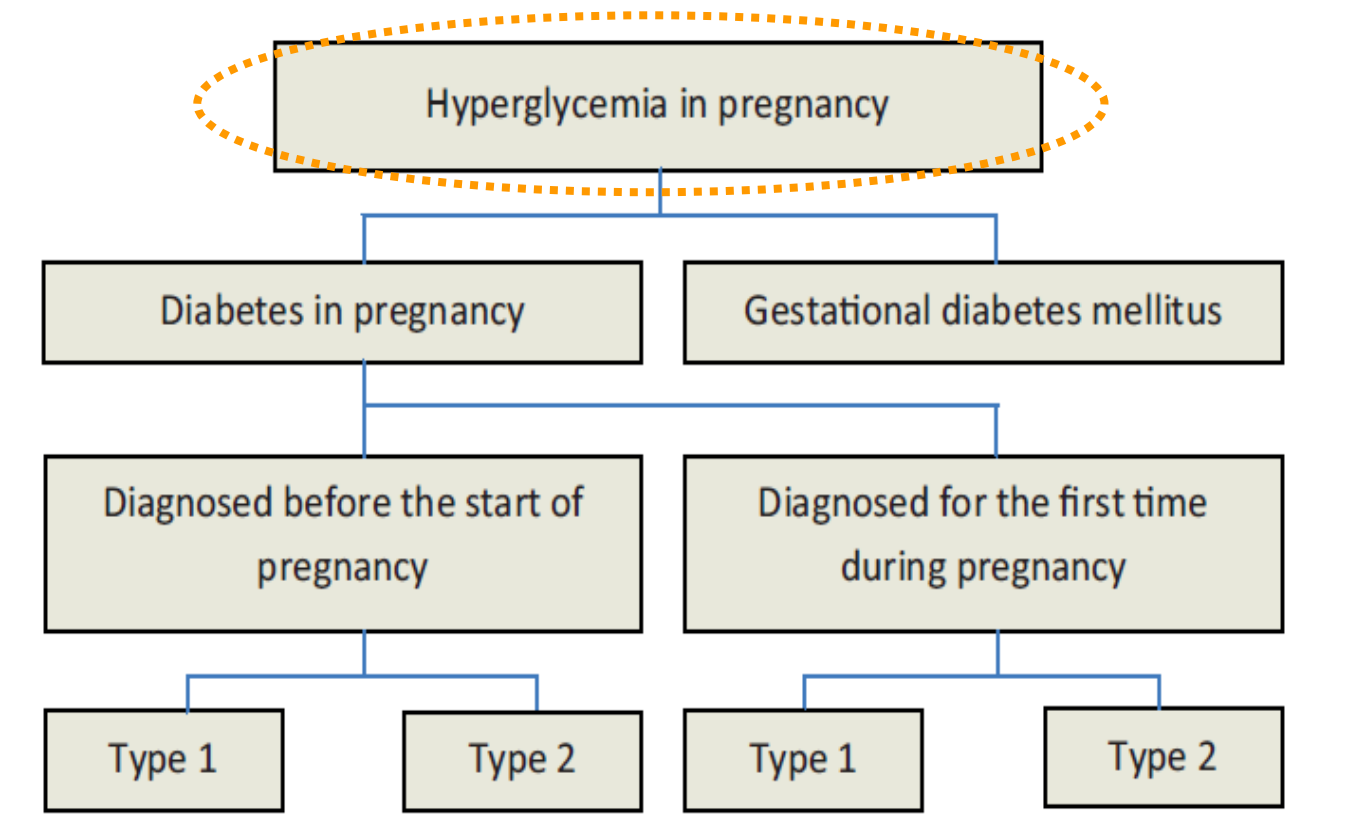
Gestational Diabetes (GDM)

- Definition:

  Insulin resistance/ glucose intolerance first diagnosed during pregnancy
- Prevalence: 5-15% of all pregnancies
- Indicates predisposition to later development of Type 2 Diabetes
- Chance of recurrence in future pregnancies:

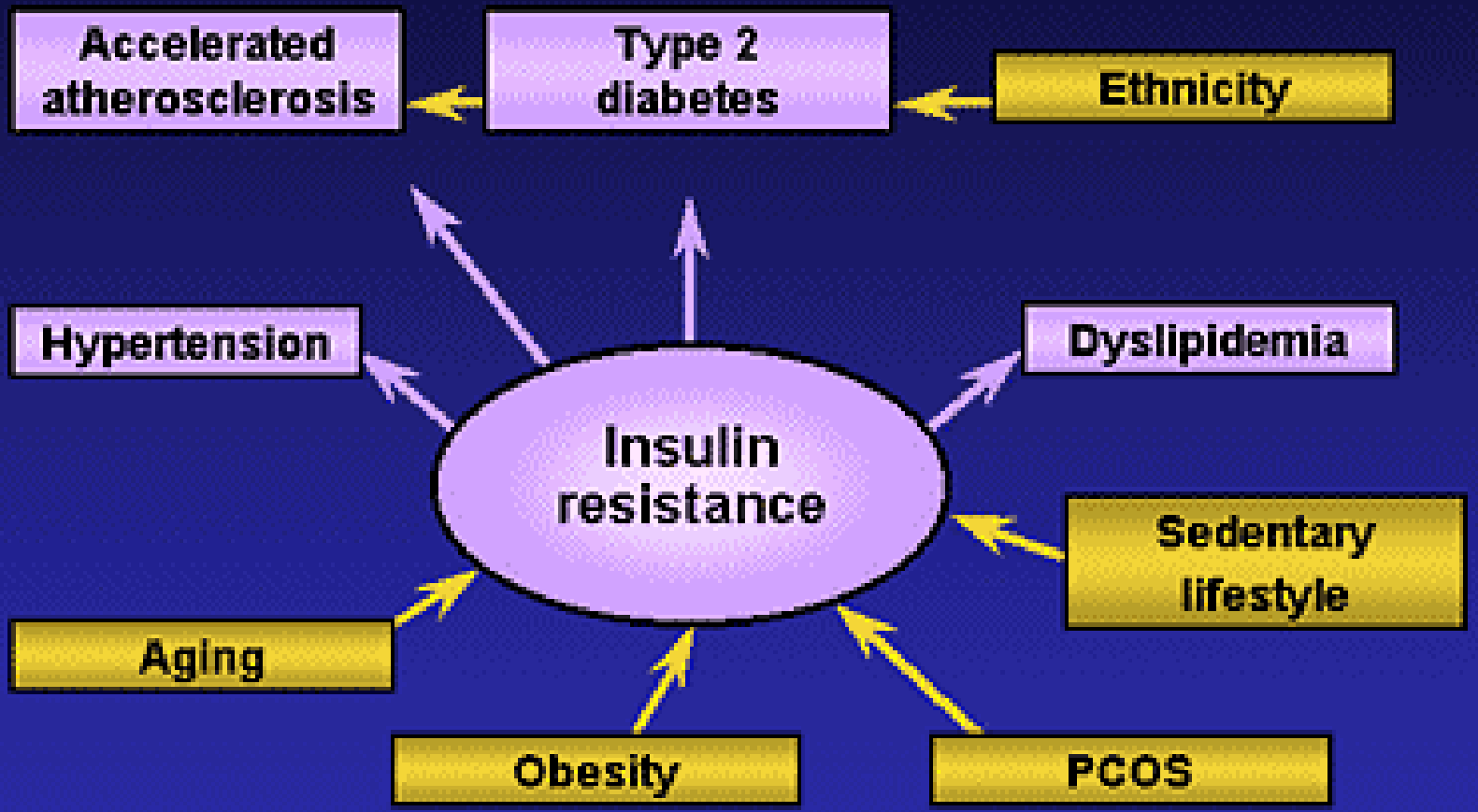
  30-84%

A new concept…



(FIGO 2015)

Insulin Resistance Syndrome



Olefsky JM. In: *Endocrinology*. 2nd ed. 1989:1369-1388.
Reaven GM. *Clinical Diabetes*. March/April 1994:32-36.

The Vicious Cycle - NCD Epidemic

The Great Obstetrical Syndromes

Obesity ,Diabetes, Metabolic Syndrome & Pregnancy

Pedersen & Freinkel Hypothesis

Diagnosis & Management

Abnormal Intrauterine Metabolic Environment

Programming & Imprinting Fetal - Neonatal

Insulin resistance Obesity

Pregnancy complicated with diabesity & Great Obstetrical Synd

Pre-Pregnancy Management

Childhood Obesity

Early T2DM Cardiovascular

Post-Pregnancy Management

Adult Obesity

PCOS

Early Metabolic syndrome

SHOULD WE EXPECT AN INCREASE IN DIABETIC PREGNANTS?

INCREASE OF BMI & OBESITY

INCREASE IN CHILDREN OBESITY

INCREASED MEAN AGE AT 1° PREGNANCY

YES

International Federation of Gynecology and Obstetrics
Working Group on Good Practice in Maternal-Fetal Medicine

Chair: G C Di Renzo

Expert members:
E Fonseca, Brasil
E Gratacos, Spain
S Hassan, USA
M Kurtser, Russia
F Malone, Ireland
S Nambiar, Malaysia
M Sierra, Mexico
K Nicolaides, UK
H Yang, China

Expert members ex officio:
C Fuchtner, FIGO
M Hod, EAPM
GH Visser, SM Committee
L Cabero, CBET Committee
V Berghella, SMFM
Y Ville, ISUOG
M Hanson, DOHaD
PP Mastroiacovo, Clearinghouse
JL Simpson, March of Dimes
D Bloomer, GLOWM

International Federation of Gynecology and Obstetrics

GDM initiative

Chair: M Hod

Expert members:
Mukesh Agarwal
Hector Bolatti
Blami Dao
Gian Carlo Di Renzo
Hema Divakar
Eran Hadar
Anil Kapur

Expert members ex officio:
C N Purandare , FIGO
G Visser , SM Committee
D Ayres do Campo, SM Comm
L Cabero, CBET Committee
D Bloomer, GLOWM
R Fabienke, Novo Nordisk

International Federation of Gynecology and Obstetrics
Working Group on Best Practice on Maternal-Fetal Medicine

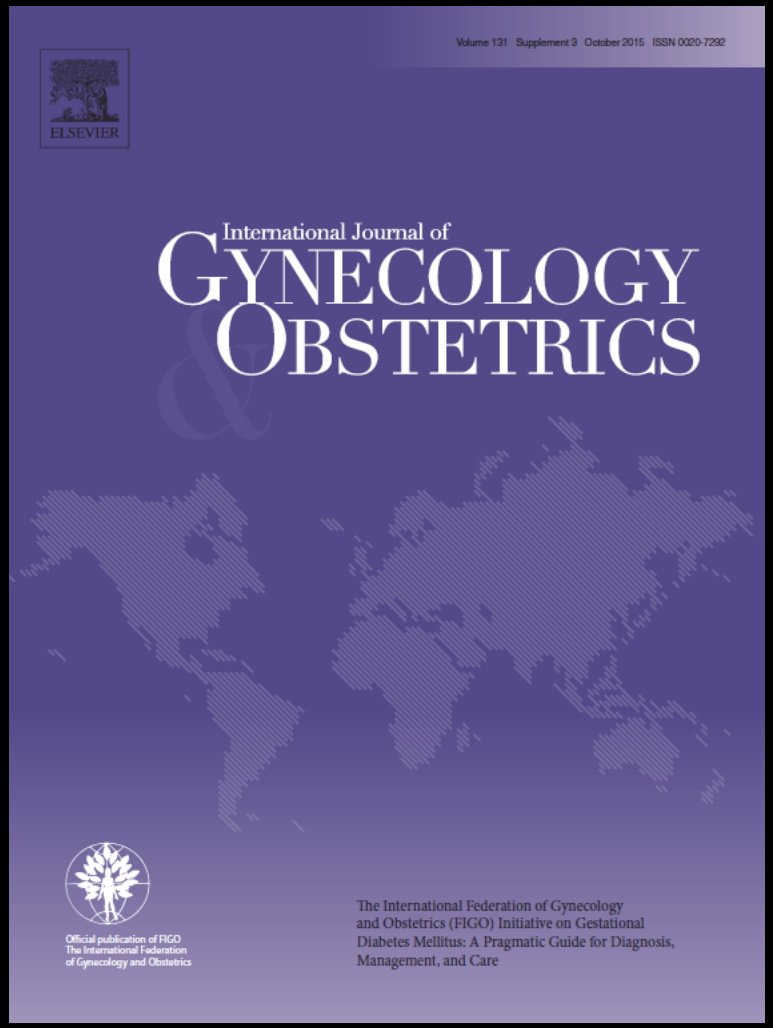
Best Practice Advice
Hyperglycemia in pregnancy

- **All pregnant women should be tested for hyperglycemia. Universal testing by all member associations**
- **WHO(2013) and IADPSG(2010) criteria for diagnosis of gestational diabetes must be used**
- **Diagnosis of HDP should be on properly collected venous plasma samples. In developing countries a plasma calibrated hand held gluocometer is acceptable**
- **Management of HDP should be in accordance with available national resources and infrastructure**

FIGO

International Federation of Gynecology and Obstetrics
Working Group on Best Practice on Maternal-Fetal Medicine

Best Practice Advice
Hyperglycemia in pregnancy



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www.figo.org

The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care*

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Conflict of interest

The authors have no conflicts of interest to declare.

Women queue for gestational diabetes services in Barranquilla, Colombia. Photograph by Jesper Wessley for the World Diabetes Foundation.

* This document was endorsed by the FIGO Executive Board at its annual meeting held on May 30–31, 2015, in Melbourne, Australia

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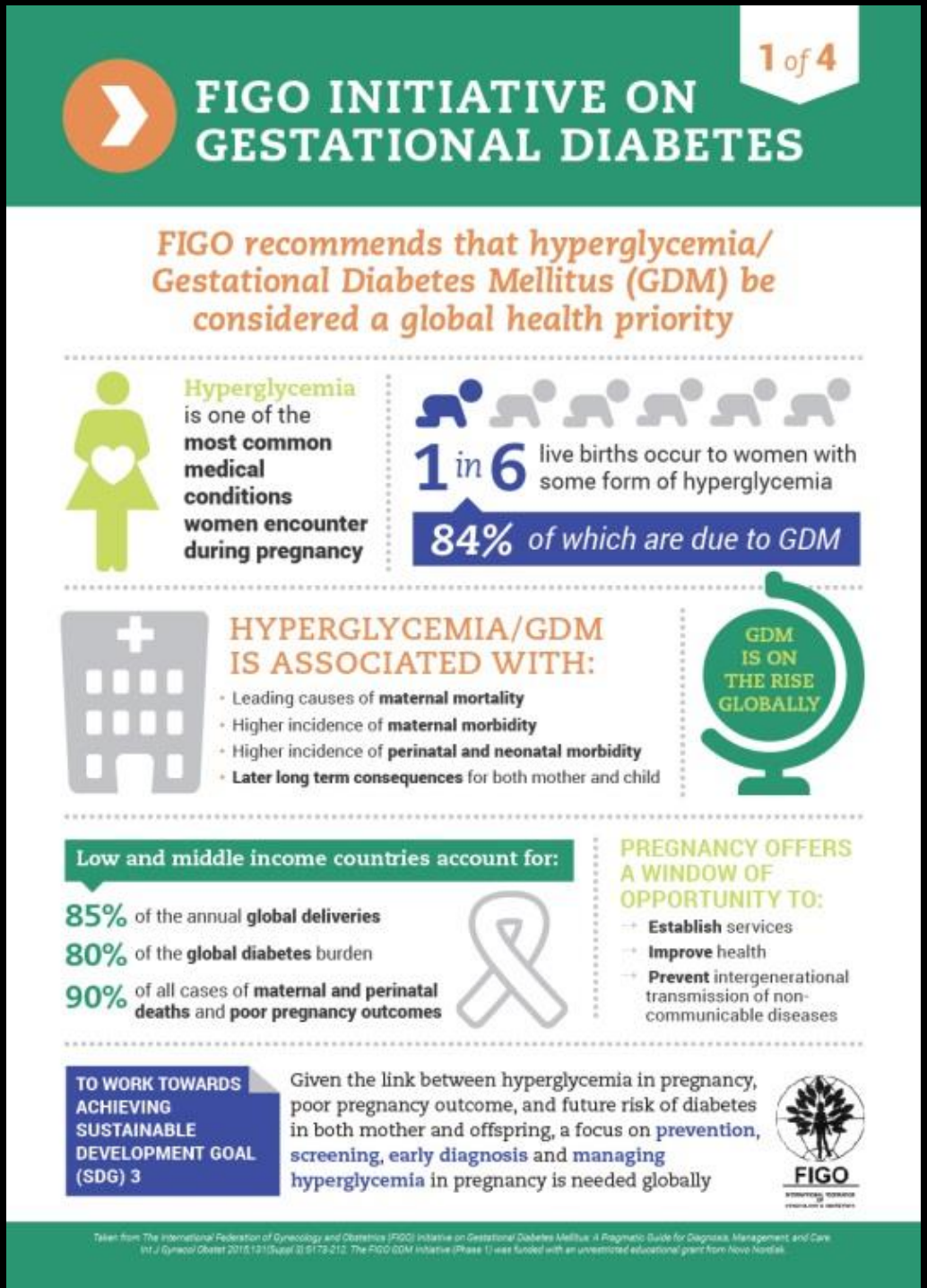
Infographics

The basics



Infographics

Diagnosis

Infographics

Management

Infographics

Postpartum

FIGO INITIATIVE ON GESTATIONAL DIABETES

FIGO recommends using the postpartum period for increased engagement to improve health for mother and child

POSTPARTUM AIMS

- Early **DETECTION** of infections
- **SUPPORT** of breastfeeding
- **ADVICE** on pregnancy spacing
- **RETEST** all women with GDM at 6-12 weeks postpartum
- Future blood glucose **TESTS**

The postpartum period is an important platform to **initiate early preventive health** for both the mother and the child who are both at higher risk of:

- **Future Obesity**
- **Metabolic Syndrome**
- **Diabetes**
- **Hypertension**
- **Cardiovascular Disorders**

Both **lifestyle intervention** and **metformin** can be effective in **delaying** or **preventing diabetes** in women with impaired glucose tolerance and a history of GDM

Obstetricians to link with other healthcare providers to support postpartum follow-up through **child vaccination/ regular health visits**

AIMS FOR PRECONCEPTION & INTER-PREGNANCY INTERVALS

Increase acceptance and access to **preconception services**

Universal pre-conception screening for malnutrition, anemia, overweight and obesity, hypertension, diabetes and thyroid dysfunction

FIGO
INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS

Taken from The International Federation of Gynecology and Obstetrics (FIGO) Initiative on Gestational Diabetes Mellitus: A Pragmatic Guide for Diagnosis, Management, and Care. Int J Gynecol Obstet 2015;131(Suppl 3):S173-212. The FIGO GDM Initiative (Phase 1) was funded with an unrestricted educational grant from Novo Nordisk.

EARLY PREDICTORS?

Early detection of GDM

Principal findings:

1. Elevated **tissue plasminogen** (t-PA) and low high-density cholesterol (HDL) levels were shown to be indipendent predictors of GDM;

2. A combination of serum **visfatin** and maternal characteristics identified >65% of pregnant women who developed GDM, at a false positive rate of 10%;

3. **Glycosylated fibronectin** predicted GDM occurence with a positive predictive value of 63% with a negative predictive value of 95%;

4. The connection between miRNAs and adipose tisssue, and insulin resistance may have a role in GDM pathophysiology, such as miR-29 and miR-222 that were significantly decreased in GDM women.

GYNECOLOGICAL ENDOCRINOLOGY

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 DOI: 10.3109/09513590.2014.958994

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healthcare

ORIGINAL ARTICLE

Body mass index associated to rs2021966 ENPP1 polymorphism increases the risk for gestational diabetes mellitus

Federica Tarquini[1], Elena Picchiassi[1], Michela Centra[1], Luana Pennacchi[1], Vittorio Bini[2], Benito Cappuccini[3], Elisabetta Torlone[4], Giuliana Coata[1], Giancarlo Di Renzo[1], and Stefano Brancorsini[5]

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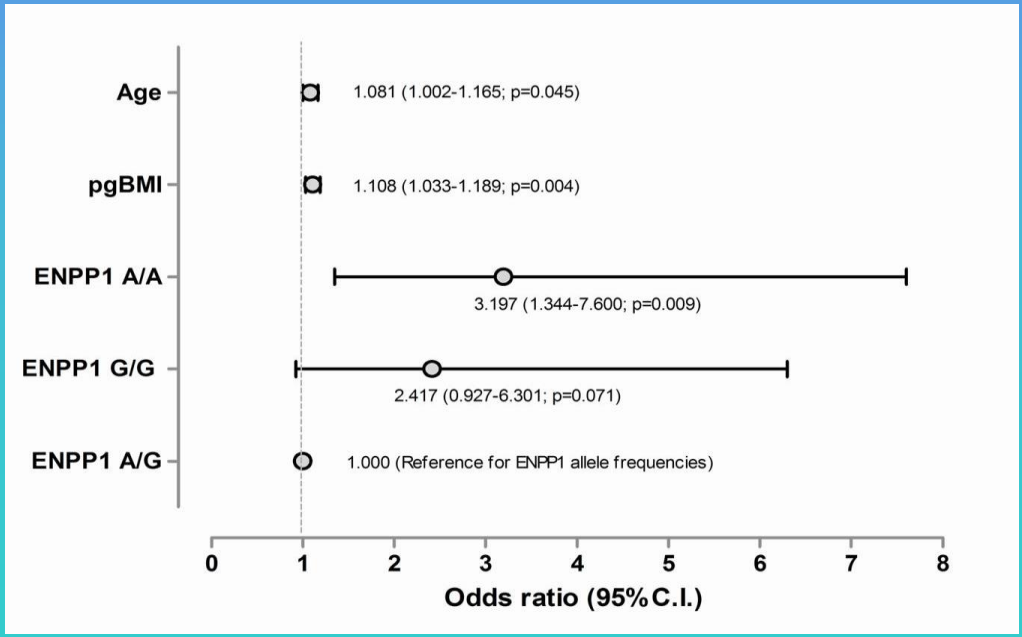
Genotype distribution of rs2021966

	n	G-dominant model			
		AA	AG+GG	OR (95% CI)	P value
-OGTT	240	62 (25.8%)	178 (74.2%)	0.433 (0.213-0.868)	0.027
+OGTT	38	17 (44.7%)	21 (55.3%)		

- Homozygous genotype for allele A was associated with increased risk of +OGTT, while opposing effects were observed with heterozygous and homozygous genotype for allele G.

Multivariate logistic analysis



- High values of pre-gestational BMI and age were independently associated to +OGTT.

- The GG homozygous genotype did not reach the statistical significance, while a significant increase were found in women carrying the AA genotype.

- ENPP1 **may play an important role in the pathophysiology of GDM in genetically predisposed pregnant women;**

- **A novel polymorphism (rs2021966) is strictly correlated to insulin resistance during pregnancy;**

- **The combination of a high pre-pregnancy BMI with a genotype homozygous for the allele 1(A) for ENPP1 could be useful to discriminate women with high risk to develop GDM;**

The early detection of maternal conditions that lead to harmful pregnancy complications, such as GDM, would enable reliable accurate diagnosis and close monitoring, which can lower the risk for the mother as well as for the fetus.

Other potential marker for GDM

Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) secreted from duodenal and jejunal K-cells are two potent insulinotropic incretin hormones that stimulate insulin release after food intake in humans. In addition, patients with DM2 or in late pregnancy have a depressed B cell response to GIP compared with healthy individuals, and GIP antagonism has been proposed as a strategy for the treatment of obesity. **(Di Renzo et al, 2016)**

Other potential marker for GDM

In pregnancy there is a physiological phenomenon of decreased insulin sensitivity, which under normal circumstances is compensated for by increased pancreatic insulin secretion, so that normal glucose tolerance is maintained.

In some women this effect causes gestational diabetes.

Normal pregnancy induces insulin resistance through the diabetogenic effects of placenta hormones and progesterone.

Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) secreted from duodenal and jejunal K-cells are two potent insulinotropic incretin hormones that stimulate insulin release after food intake in humans. In addition, patients with DM2 or in late pregnancy have a depressed B cell response to GIP compared with healthy individuals, and GIP antagonism has been proposed as a strategy for the treatment of obesity.

Aim of the study

Evaluate whether an impaired secretion of glucagon-like peptide-1 (GLP-1) and/or glucose-dependent insulinotropic polypeptide (GIP) could play a role in the development of carbohydrate disorders during pregnancy.

Material and methods

The study group (GDM) consisted of 41 gestational women with diabetes mellitus in whom GDM was diagnosed according to the World Health Organization criteria (75-g oral glucose tolerance test (OGTT). The control group consisted of 35 pregnant women with normal glucose tolerance (NGT). For all patients, plasma insulin, glucagon, C-Peptide, GIP and GLP-1 concentrations were evaluated before glucose load using Bio-Plex Pro Human Diabetes 10-Plex Assay (BIO-RAD, CA,USA).

Results

– Demographic and metabolic characteristics of subjects at study

	Control subjects	GDM subjects	*p-value*
n	35	41	
Age (y)*	32.0 (24.0-39.0)	35.5 (24.0-44.0)	**0.004**
Gestational age at blood collection (w)*	27.0 (19.0-36.0)	28.0 (12.0-38.0)	0.062
Pre-gravidic BMI (Kg/m^2)*	21.3 (17.6-32.5)	24.9 (17.9-40.0)	**<0.0001**
BMI at blood collection (Kg/m^2)*	24.8 (19.8-34.3)	29.1 (20.0-38.9)	**0.001**
Family history of type 2 diabetes (n; %)	10 (28.6%)	26 (63.4%)	**0.002**
Insulin (pg/ml)*	142.6 (63.4-255.1)	216.7 (73.9-1174.9)	**<0.0001**
Glucagon (pg/ml)*	555.2 (429.9-949.8)	536.1 (398.2-864.8)	0.272
C peptide (pg/ml)*	528.9 (80.3-981.3)	882.0 (333.4-4405.0)	**<0.0001**
GIP (pg/ml)*	129.8 (50.5-236.8)	153..3 (56.6-711.3)	**0.013**
GLP (pg/ml)*	211.6 (145.0-427.9)	216.0 (170.5-361.9)	0.921

* Data are expressed as median (min-max)

Results

· Spearman's rho correlation coefficients

	Control subjects				GDM subjects			
	GIP		GLP		GIP		GLP	
	rho	*p-value*	rho	*p-value*	rho	*p-value*	rho	*p-value*
GIP	-	-	**0.448**	**0.007**	-	-	0.093	0.560
GLP	**0.448**	**0.007**	-	-	0.093	0.560	-	-
Insulin	0.026	0.881	0.145	0.407	**0.502**	**0.001**	0.071	0.611
C peptide	-0.264	0.192	-0.154	0.454	**0.546**	**0.001**	-0.100	0.567
Glucagon	**0.813**	**<0.0001**	**0.782**	**<0.0001**	-0.101	0.529	**0.811**	**<0.0001**
Age	0.075	0.667	0.268	0.119	0.263	0.110	0.125	0.454
Pre-gravidic BMI	0.297	0.088	0.208	0.239	**0.394**	**0.013**	0.238	0.081

Results

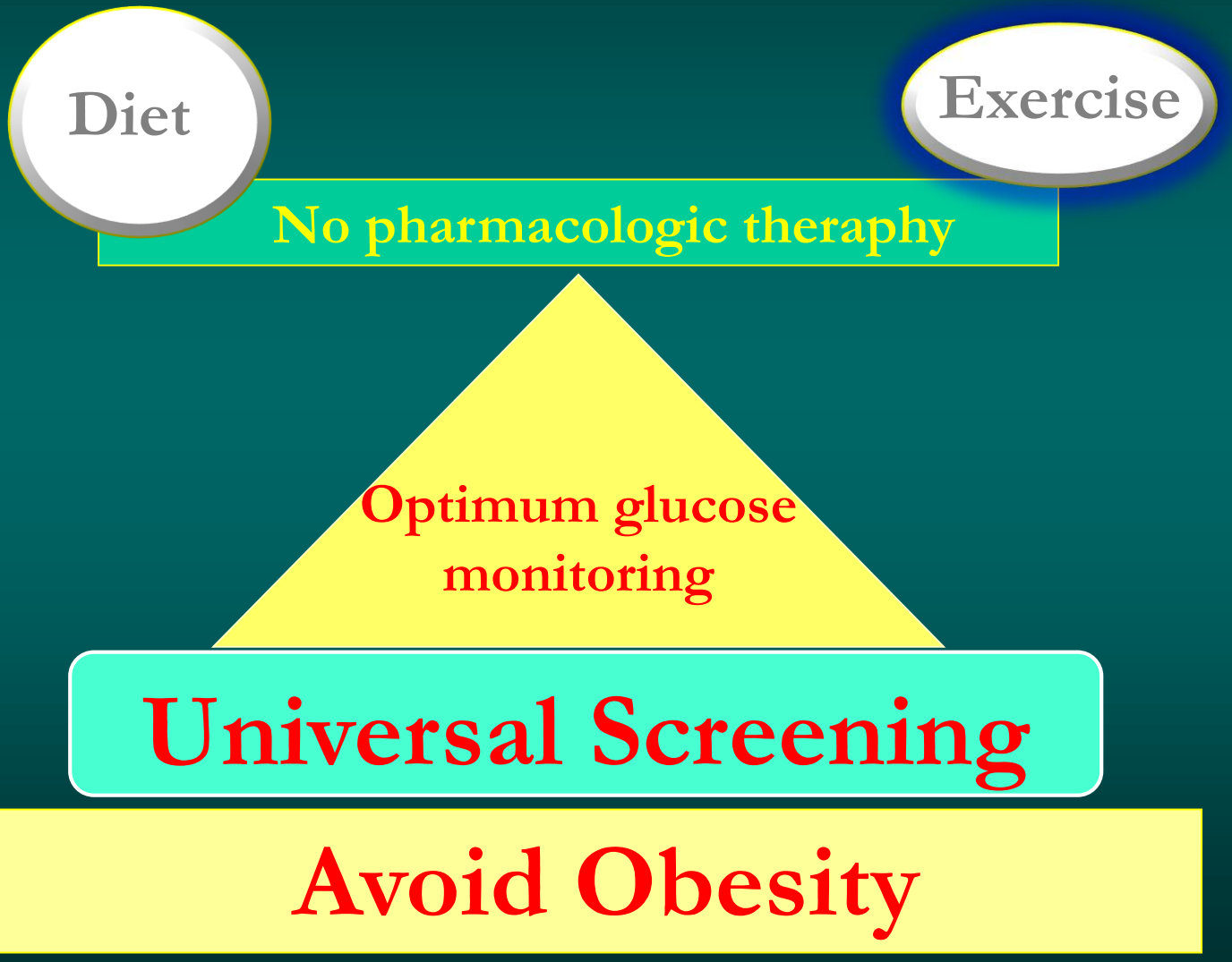
· Logistic regression model for the prediction of GDM at start of pregnancy

	OR	95% C.I.	*p-value*
Age (y)	1.053	0.876-1.265	0.584
Gestational age at blood collection (w)	1.050	0.870-1.266	0.613
Pre-gravidic BMI (Kg/m^2)	1.102	0.877-1.386	0.405
Family history of type 2 diabetes (y/n)	1.544	0.330-7.220	0.581
C peptide (pg/ml)	**1.004**	**1.001-1.008**	**0.016**
GIP (pg/ml)	0.998	0.983-1.013	0.778

Only C-Peptide was a significant and independent predictor of the GDM, with an OR of 1.004 (95% C.I.: 1.001-1.008).

ANY PREVENTION?

Prevention Strategies



Prevention

Prevention of gestational diabetes could be an important strategy in curbing the obesity and diabetes epidemic in this and future generations

Identify potentially modifiable risk factors and to quantify their potential impact on this common condition

Several potentially modifiable factors before pregnancy have been related to a lower risk of gestational diabetes. These include maintaining :

- healthy body weight,
- adapting a healthy diet,
- regular physical activity,
- abstinence from cigarette smoking

Zhang C. BMJ 2014

Estimates of the relative risk among women in the combined categories of low risk lifestyle compared with all other women

Table 3| **Combined low risk lifestyle factors and risk of gestational diabetes in 20 136 pregnancies in Nurses' Health Study II**

Low risk group	Percentage of pregnancies	No of pregnancies with gestational diabetes	Relative risk* (95% CI)	Population attributable risk percentage† (95% CI)
3 factors in low risk category (current non-smoker, moderate/vigorous physical activity ≥150 min/week, healthy eating‡)	20.3	112	0.59 (0.48 to 0.71)	35.4 (25.1 to 44.9)
All 4 factors in low risk category (BMI <25.0, current non-smoker, moderate/vigorous physical activity ≥150 min/week, healthy eating‡)	16.3	71	0.48 (0.38 to 0.61)	47.5 (35.6 to 56.6)

*Estimated from generalized estimating equation models and adjusted for age, parity, family history of diabetes, history of infertility, race/ethnicity, questionnaire period, total energy intake, and alcohol intake. Reference group for relative risk is all other pregnancies not in low risk group as defined in table.

†Percentage of cases of gestational diabetes in population theoretically attributable to non-adherence to particular factors.

‡Alternate Healthy Eating Index-2010 diet score in upper two fifths.

Zhang C. BMJ 2014

Conclusions

In this large prospective cohort study of women of reproductive age, it has been observed that a **low risk lifestyle** before pregnancy that is

- ✓ **maintaining a healthy body weight,**
- ✓ **consuming a healthy diet,**
- ✓ **exercising regularly,**
- ✓ **not smoking**

was **strongly and inversely associated with the risk of gestational diabetes**

Women at low risk for all four lifestyle factors had more than 80% lower risk than those without any of the low risk factors.

Zhang C. BMJ 2014

Diet
Physical exercise

Probiotics

Inositols

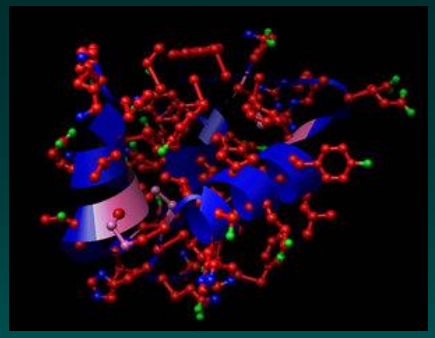
Antioxidants

INOSITOLS

Among strategies to reduce the occurrence of GDM in high-risk pregnancies, **insulin sensitizing substances**, such as metformin, have been used throughout the pregnancy with contrasting results.

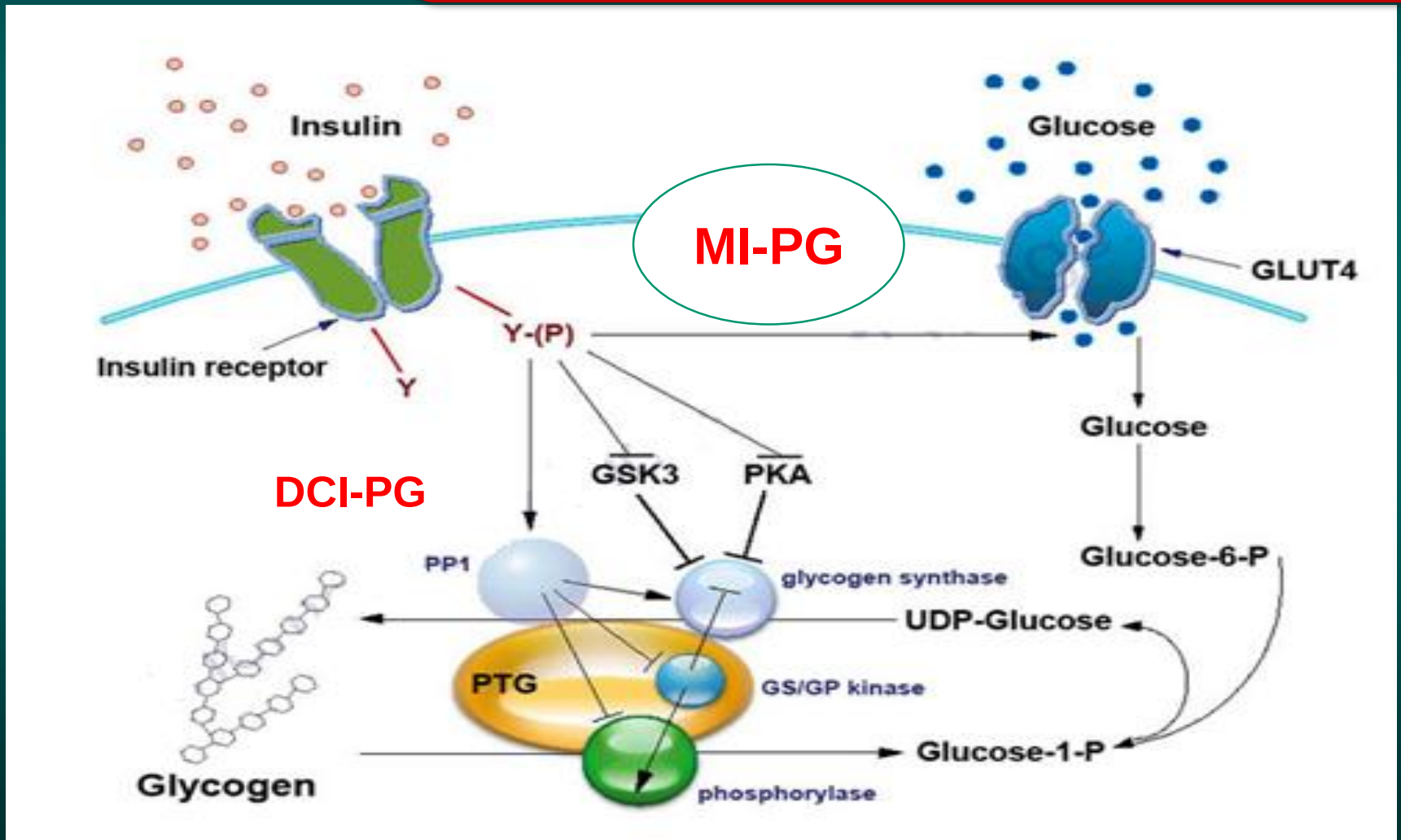
Another substance primarily used in polycystic ovary syndrome (PCOS), with the aim of lowering hyperinsulinemia and restoring ovarian function, was **inositol**; it was given either in the two forms:

- ✓ **D-chiroinositol isomer**
- ✓ **Myo-inositol isomer**



Inositol & insulin

The binding between insulin and its receptor mediates the production of low molecular weight inositol-phosphoglycans that act as second messengers



Recent reports have supported the involvement of inositol in the mechanisms of glycemic control. They showed an increased urinary excretion of inositol-phosphoglycans in women affected by GDM, which was positively correlated with blood glucose levels. Inositol phosphoglycans may play a role not only in glycemic control but also in the fetal growth of GDM women.

✓Myo-inositol may reduce insulin resistance by ~70% in postmenopausal women affected by the metabolic syndrome.

✓ Insulin resistance may be significantly reduced in GDM women.

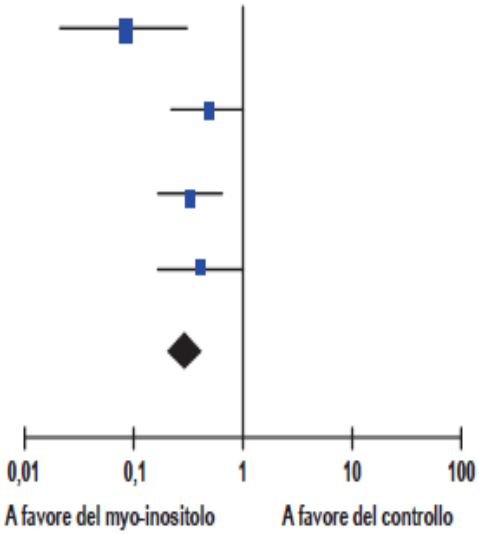
✓ In pregnant women affected by PCOS, myo-inositol intake, through the whole pregnancy, may reduce the prevalence of GDM

MYOINOSITOL: REDUCED INCIDENCE OF GDM

INCIDENZA DI DGM:

Studio o sottogruppi	MYO-INOSITOLO Eventi	MYO-INOSITOLO Totale	CONTROLLO Eventi	CONTROLLO Totale	Peso	RAPPORTO TRA I RISCHI M-H, fissato, IC 95%
Barbara Matarrelli 2013	2	35	27	38	32,6%	0,08 [0,02; 0,31]
Fabio Facchinetti 2013	6	31	24	60	20,6%	0,48 [0,22; 1,06]
Rosario D'Anna 2012	8	46	20	37	27,9%	0,32 [0,16; 0,65]
Rosario D'Anna 2013	6	99	15	98	19,0%	0,40 [0,16; 0,98]
Totale IC 95%		**211**		**233**	**100%**	**0,29 [0,19; 0,44]**
Totale eventi	22		86			

Test per effetto complessivo: Z=5,72 (P<0,00001)



✓ ***MI SIGNIFICANTLY REDUCES THE INCIDENCE OF GDM***

MYOINOSITOL: REDUCED INCIDENCE OF GDM

STUDY	POPOLATION	BMI	DURATION	
Rosario D'Anna 2015	110 110	≥30	Dal primo trimestre al parto	→ **MI:14% CTRL:33,6% *p*=0,001**

Obstet Gynecol.2015 Aug;126(2):310-5..

Angelo Santamaria 2015	110 110	25≤BM ≤30	Dal primo trimestre al parto	→ **MI:11,6% CTRL:27,4% *p*=0,004**

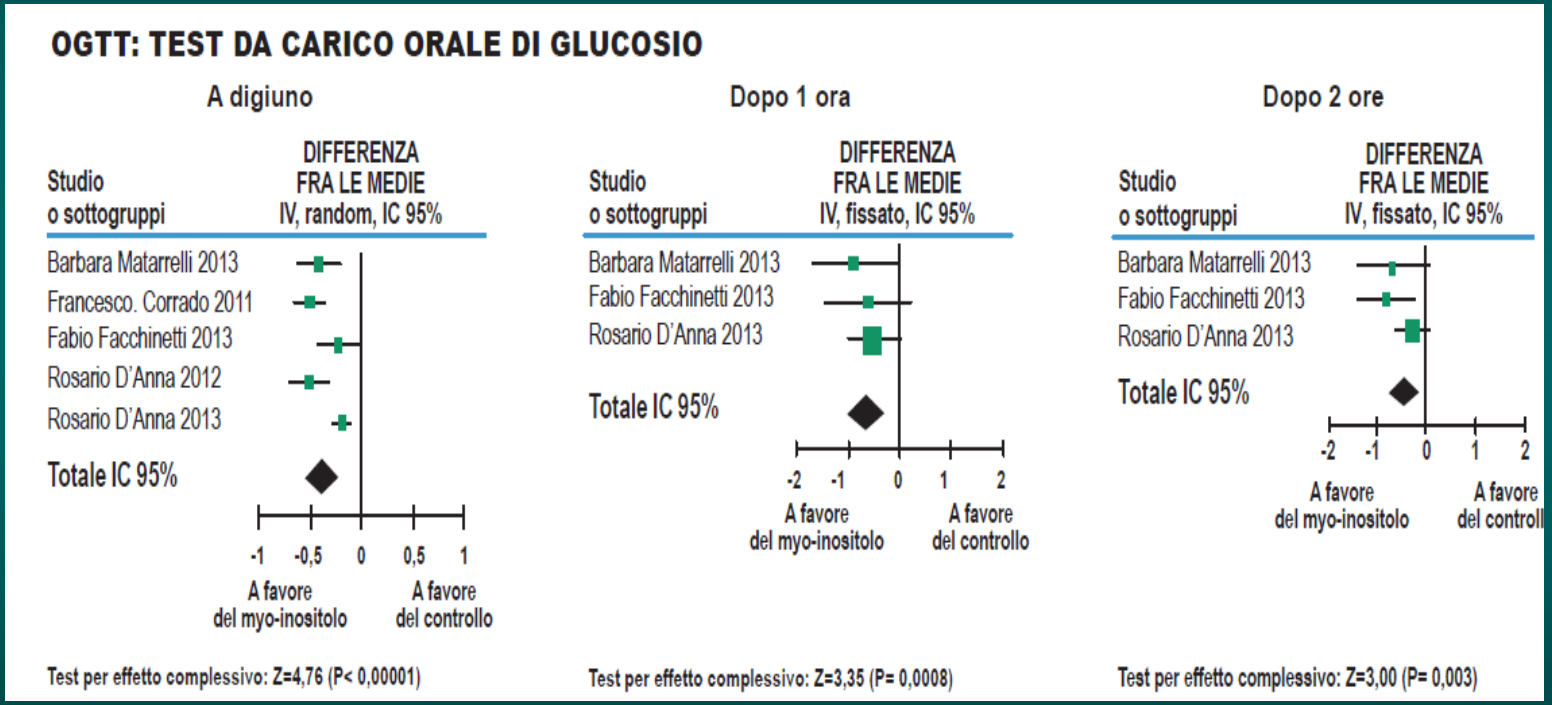
J Matern Fetal Neonatal Med, 2015 Nov, Early Online: 1–4

✓ ***MYO INOSITOL REDUCES INCIDENCE OF GDM IN WOMEN WITH BMI > 25***

MYOINOSITOL & GLYCEMIA IN GDM

Relationship Between Myo-Inositol Supplementary and Gestational Diabetes Mellitus

A Meta-Analysis



✓ ***MI REDUCES LEVELS OF GLUCOSE IN GDM PREGNANT PATIENTS***

Medicine Volume 94, Number 42, October 2015

MYOINOSITOL: COMPLICATIONS OF GDM

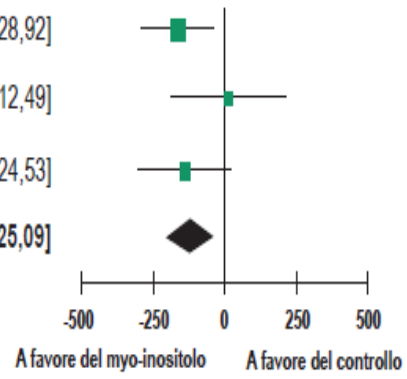
Relationship Between Myo-Inositol Supplementary and Gestational Diabetes Mellitus

A Meta-Analysis

PESO ALLA NASCITA:

	MYO-INOSITOLO			CONTROLLO				DIFFERENZA FRA LE MEDIE	DIFFERENZA FRA LE MEDIE
Studio o sottogruppi	Media	DS	Totale	Media	DS	Totale	Peso	IV, fissato, IC 95%	IV, fissato, IC 95%
Rosario D'Anna 2013	3,111	447	99	3,273	504	98	47,7%	-162,00 [-295,08; -28,92]	
Barbara Matarrelli 2013	3,267	33,7	35	3,251	617	38	21,9%	16,00 [-180,49; 212,49]	
Rosario D'Anna 2012	3,089	424	46	3,231	350	37	30,4%	-142,00 [-308,53; 24,53]	
Totale IC 95%			180			173	100%	**116,98 [-2087,87; -25,09]**	

Test per effetto complessivo: Z=2,50 (P=0,01)

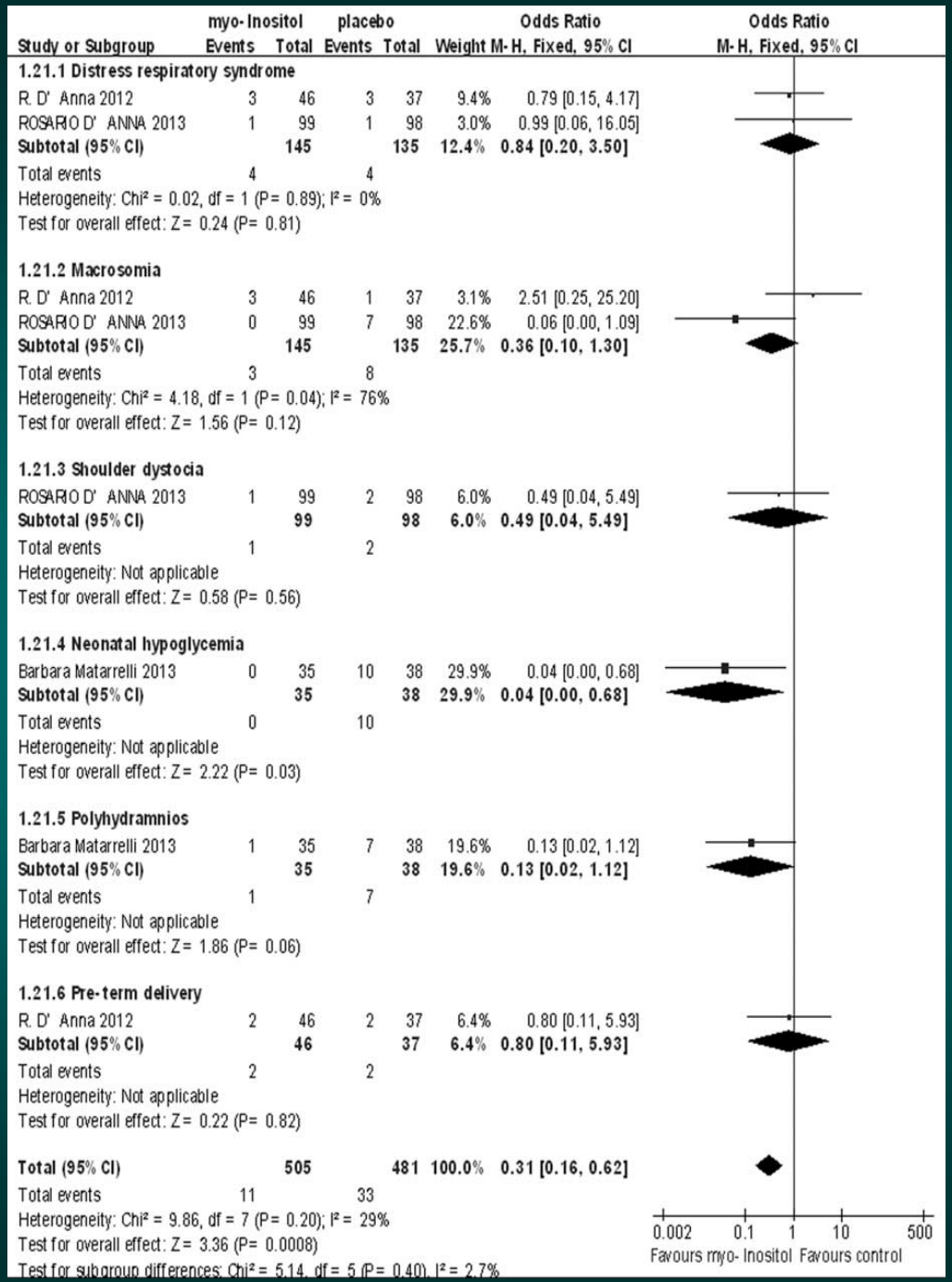


✓

MI REDUCES BIRTHWEIGHT SIGNIFICANTLY

Medicine Volume 94, Number 42, October 2015

MYOINOSITOL: COMPLICATIONS OF GDM



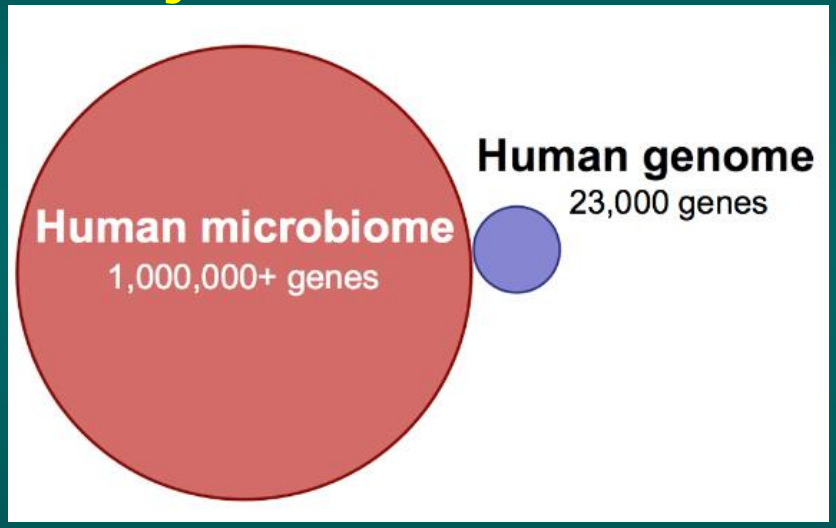
Facts & speculations

- **Myo-inositol prophylaxis reduce the incidence of Gestational Diabetes in women at risk, namely in overweight and obese population.**
- **Myo-inositol may improve insulin resistance in the obese pregnant women, as well as in PCOS**
- **Correction of insulin resistance is associated with reduced gestational hypertension and preterm birth in the obese pregnant women**
- **Preliminary data on Myo/D-chiro combination indicate a synergy among the two stereoisomers**

PROBIOTICS

What is the microbiome?

- **Microbiome commensal microorganisms living within the human body**
  - **Colonize all "exposed" tissues (oral, respiratory, digestive, skin, uro-genital**



- **10 times more organisms than human cells; 100 times more DNA**

The observed pronounced effect of probiotics on glucose metabolism is most probably attributable to their immunoregulatory properties. Probiotics elicit powerful antiinflammatory capabilities by inhibiting the NF-kB pathway, which mediates microbial activation of the immune system through toll-like receptors. Regulation of inflammatory pathways by probiotics may be of particular importance due to the fundamental involvement that inflammation plays in insulin resistance. The concomitance of elevated blood glucose concentrations, insulin resistance and dyslipidaemia with activation of inflammation pathways is related to an enhanced risk of a range of metabolic disorders, including obesity and CVD.

- ✓ Balanced glucose metabolism during pregnancy reduces the risk of pregnancy-related complications and confers long-term health benefits on both the mother and the child.

- ✓ Combined dietary counselling and probiotics intervention yielded consistently improved glucose metabolism and insulin sensitivity in healthy women, providing **the first clinical evidence of an active dialogue between host and microbiota in glucose metabolism**.

- ✓ Combined dietary counselling and probiotic intervention with *L. rhamnosus GG* and *B. lactis Bb12* moderated plasma glucose concentrations and afforded glycaemic control in healthy young females during and after pregnancy.

Laitinen BJN 2009

Modification of gut microbiota composition by probiotics, thereby altering the intestinal immunological milieu, may be seen as a novel means of attaining regulation of glucose metabolism. This dietary approach would offer a cost-effective tool for both prophylaxis and therapy in the metabolic disorders that constitute the metabolic syndrome.

The benefit is expected to be most pronounced during the critical period of human development in view of the programming of later diseases by events in the uterus

- ✓ Combined dietary counselling and probiotic intervention to target maternal glucose metabolism, in view of the importance to maintain normoglycaemia throughout pregnancy.

- ✓ Previous dietary interventions with primarily reduced energy and fat intakes as well as increased fibre intakes have resulted in improved glucose tolerance test results

- ✓ The approach may also be justified by the demonstration that diet and microbiota may exert their effects via similar signalling pathways in regulating immune responses.

- ✓ Immunoinflammatory processes and prevailing systemic low-grade inflammation may contribute to the metabolic conditions affecting glucose metabolism.

Laitinen K. BJN 2009

Effects of probiotics on glucose metabolism and diabetes

Study	Outcome	Results
Brantsaeter 2011	Pre-eclampsia	reduced risk especially severe pre-eclampsia (OR=0.79, 95% CI: 0.66–0.96) vs control
Laitinen 2009*	Maternal blood glucose	significantly lower (4.45 vs 4.6 mmol/L; p=0.025) vs placebo
	Insulin concentration	Significant lower (7.55 vs 9.32 mU/l; p=0.032) vs placebo
Luoto 2010*	Incidence of GDM	Significant reduction (13% v. 36%; p=0.003) vs placebo
Ilmonen 2011*	central adiposity at six months post-partum	Significant reduction (OR 0.30, 95% CI 0.11–0.85, p=0.023 adjusted for BMI) vs placebo
Asemi 2011a**	C-reactive protein (hs-CRP)	significant reduction (10.44±1.56 to 7.44± 1.03 μg/ml; p=0.041) vs control
Asemi 2011b**	Lipid profiles	No statistically significant effect
Asemi 2012**	biomarkers of oxidative stress	No statistically significant effect

ANTIOXIDANTS

Protection against oxidative stress

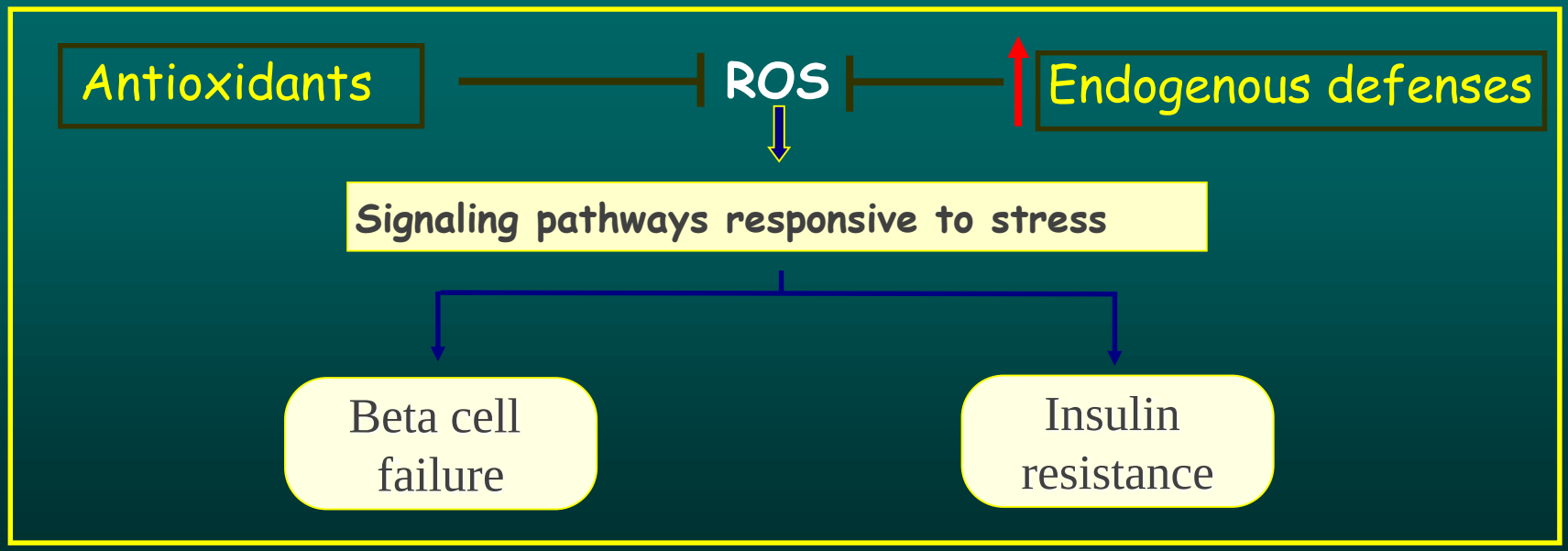
Strategies of protection against oxidative stress

1.- Antioxidant Supplementation

N- acetylcysteine (NAC), Vit. E, Vit. C, Lipoic acid

2.- Increase antioxidant defenses

Overexpression of antioxidant enzymes



ANTIOXIDANT CAPACITY

ORAC* units/ 100g	
Dark chocolate	13120
Milk chocolate	6700
Prunes	5770
Nuts	5715
Chestnuts	3300
Raisins	2830
Bilberry	2400
Balckberry	2036
Cauliflowers	1770
Strawberry	1540
Plums	949
* Oxigen Radical Absorbance Capacity	

BIOLOGICALLY ACTIVE SUBSTANCES in COCOA DERIVED PRODUCTS

Flavo noids

Theobro mine

Caffeine

Poly phenols

Phenyl ethylami ne (PEA)

Methyl xanthines

Tyrami ne

Biogenic amines

Tryptam ine

Seroto nin

Minerals

Magnesi um

Iron

Ananda mide

Cacao (or cocoa) tree (*Theobroma cacao*)

Chocolate

Cocoa powder

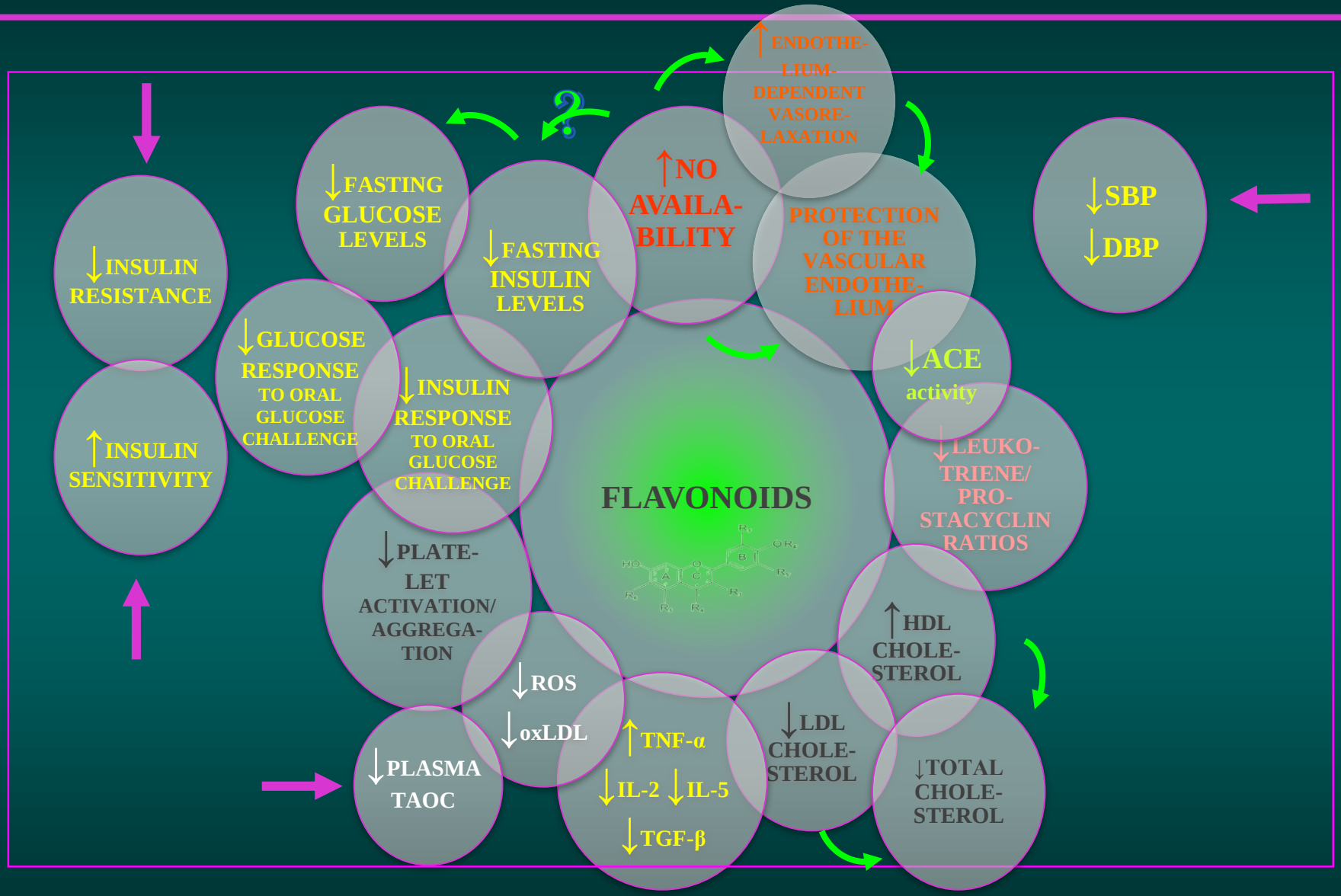
Cocoa liquor

Cacao fruit (cacao pod or cocoa pod)

Cocoa beans

Cocoa beans are the dried and fully fermented fatty seeds of *Theobroma cacao*

BIOLOGICAL EFFECTS of COCOA FLAVONOIDS



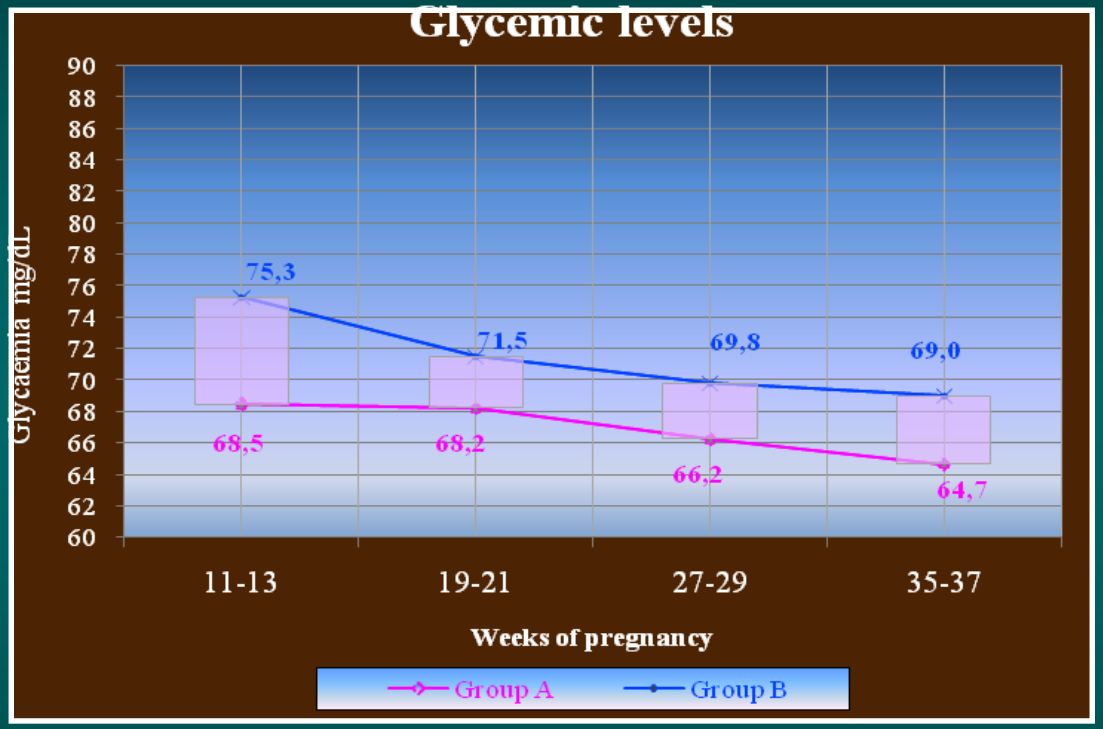
ACE: Angiotensin-Converting Enzyme; DBP: Diastolic Blood Pressure; HDL: High Density Lipoprotein; IL: Interleukin; LDL: Low Density Lipoprotein; oxLDL: oxidized LDL; SBP: Systolic Blood Pressure; TAOC: Total Antioxidant Capacity; TGF: Transforming Growth Factor; TNF: Tumor Necrosis Factor.

CHOCOLATE EFFECTS on HOMEOSTASIS MODEL ASSESSMENT OF INSULIN RESISTANCE (HOMA-IR)

in HEALTY SUBJECTS

Before values = baseline; NS: No Significant Differences

GLYCEMIC LEVELS



Group A: intervention group; Group B: control group
Statistically significant different averages ($p < 0.05$) according to Tukey's test

Di Renzo et al JMFNM 2012

CONCLUSIONS

Fetal or Maternal perspective?

CONCLUSIONS

SCREENING: YES

implementation of HAPO guidelines of FIGO

PREDICTION : POSSIBLE

specific markers under evaluation

PREVENTION: OPEN POSSIBILITY

inositols, antioxidants and probiotics under evaluation

SERIES IN
MATERNAL-FETAL
MEDICINE

TEXTBOOK OF DIABETES AND PREGNANCY

THIRD EDITION

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CRC Press
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"In every forest, every farm, every garden on the planet, what is under the ground creates what's above. That is why focusing on the ripe fruit is useless. Those already on the trees you can not change".

T. Harv Eker,2005

PREIS SCHOOL

Permanent International and European School in Perinatal, Neonatal and Reproductive Medicine

GRAZIE

merci

gracias

thank you

谢谢

DZIĘKUJEMY

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Баярлалаа

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спасибо

고맙습니다 o 감사합니다.

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