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UNIVERSITATEA DE MEDICINĂ ŞI FARMACIE
IULIU HAŢIEGANU
CLUJ-NAPOCA

Facultatea de Medicină Cluj

Fetal and Postnatal Impact of Diabesity

PROF. DR. DANIEL MURESAN
IST DEPT OF OBSTETRIC & GYNECOLOGY
UNIVERSITY OF MEDICINE “IULIU HATIEGANU” CLUJ-NAPOCA
ROMANIA

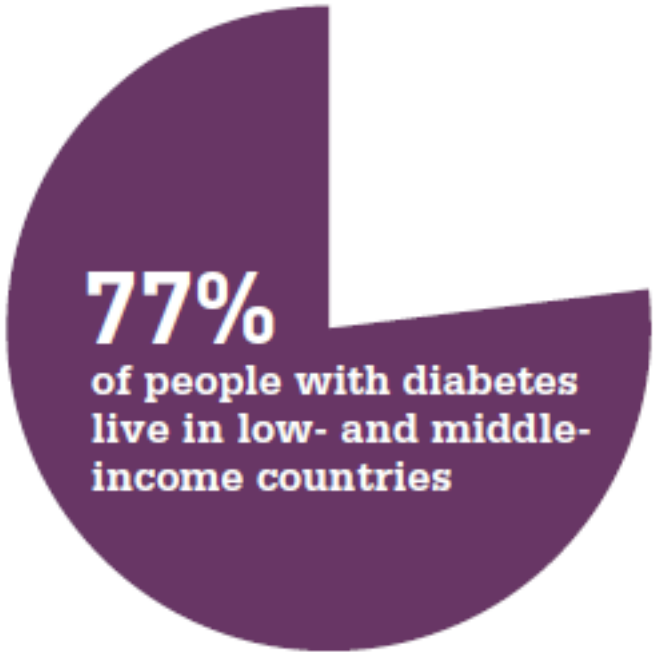
Diabetes and obesity represent today an almost epidemic condition.

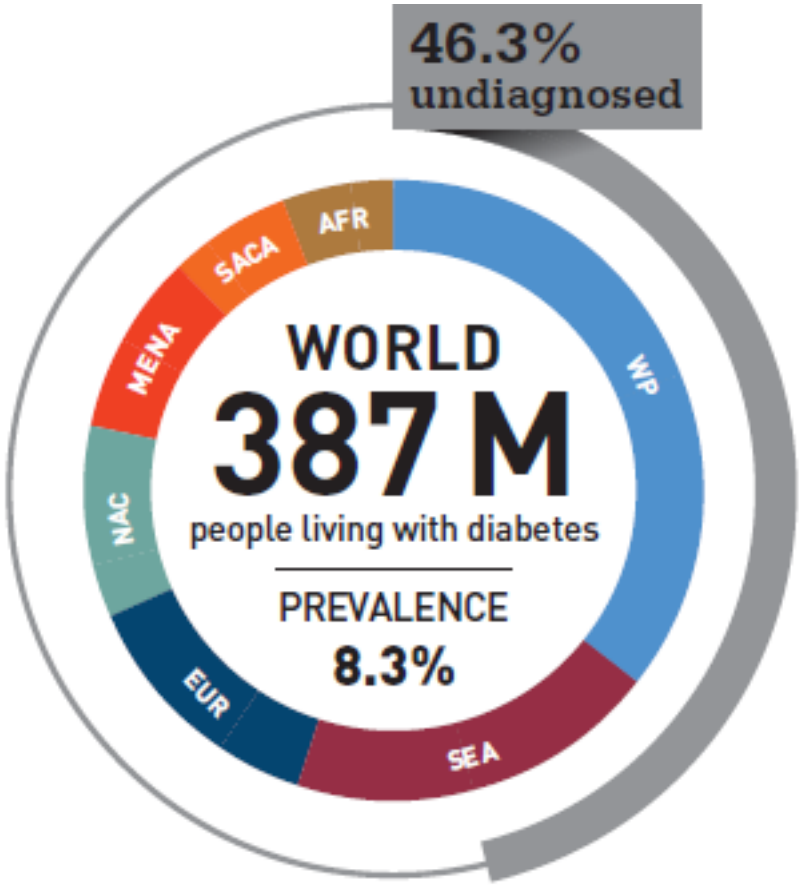
Many pregnant women present both these conditions, and due to their common pathways they are now known as **Diabesity**.

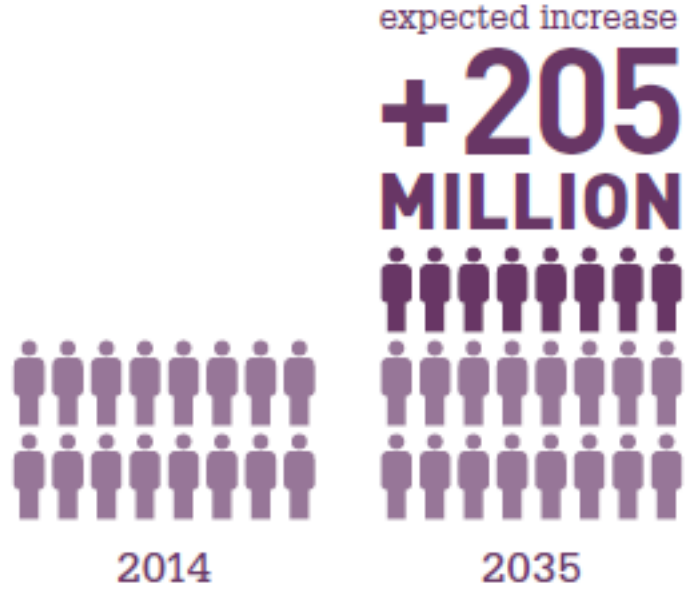
The evolution of pregnancies in these conditions is altered by complications developing

- from the embryonic period,
- during the second and third trimester,
- in the neonatal period
- **metabolic and developmental problems in childhood and adult life**.

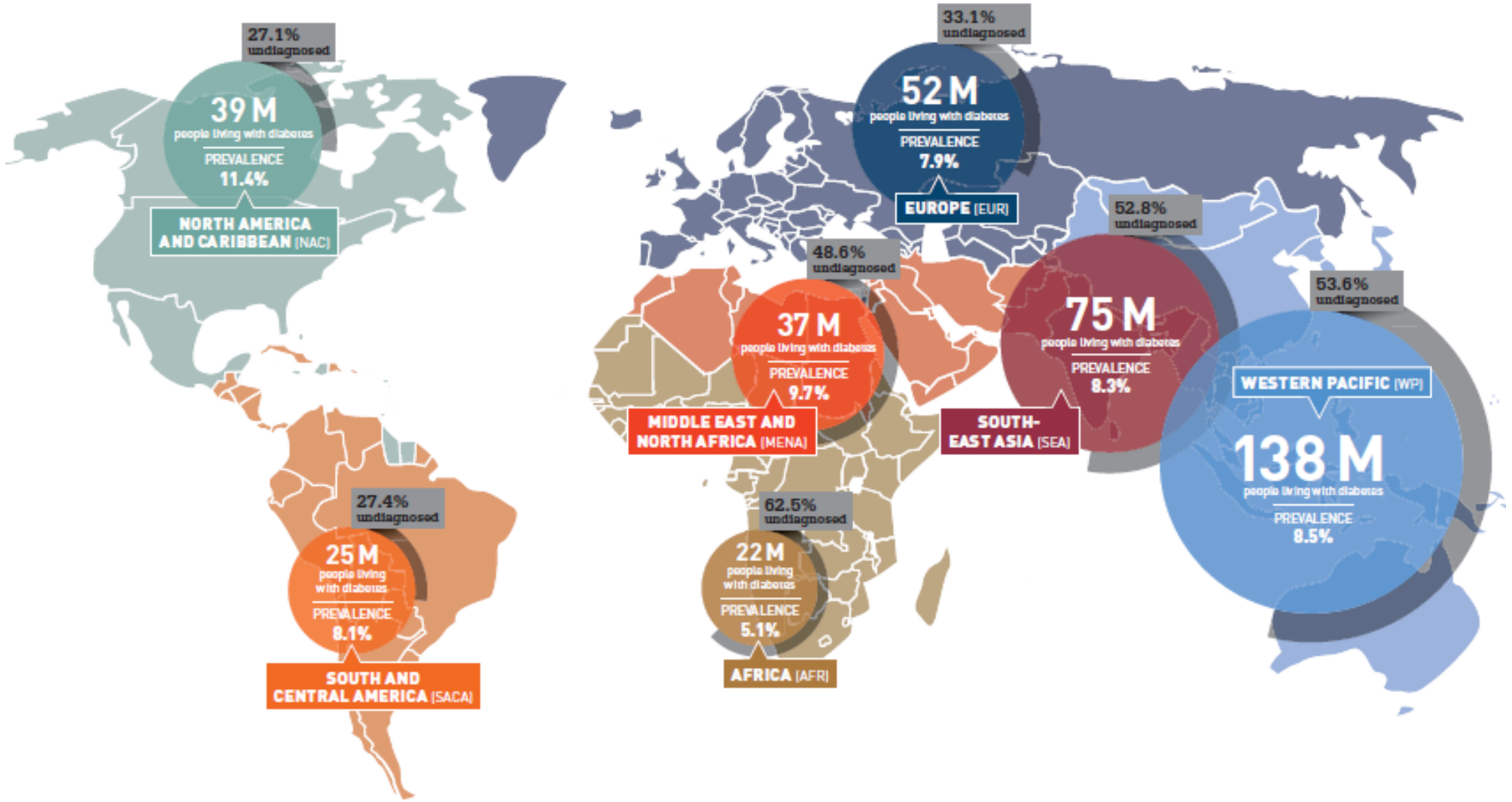
Epidemiology of Diabetes

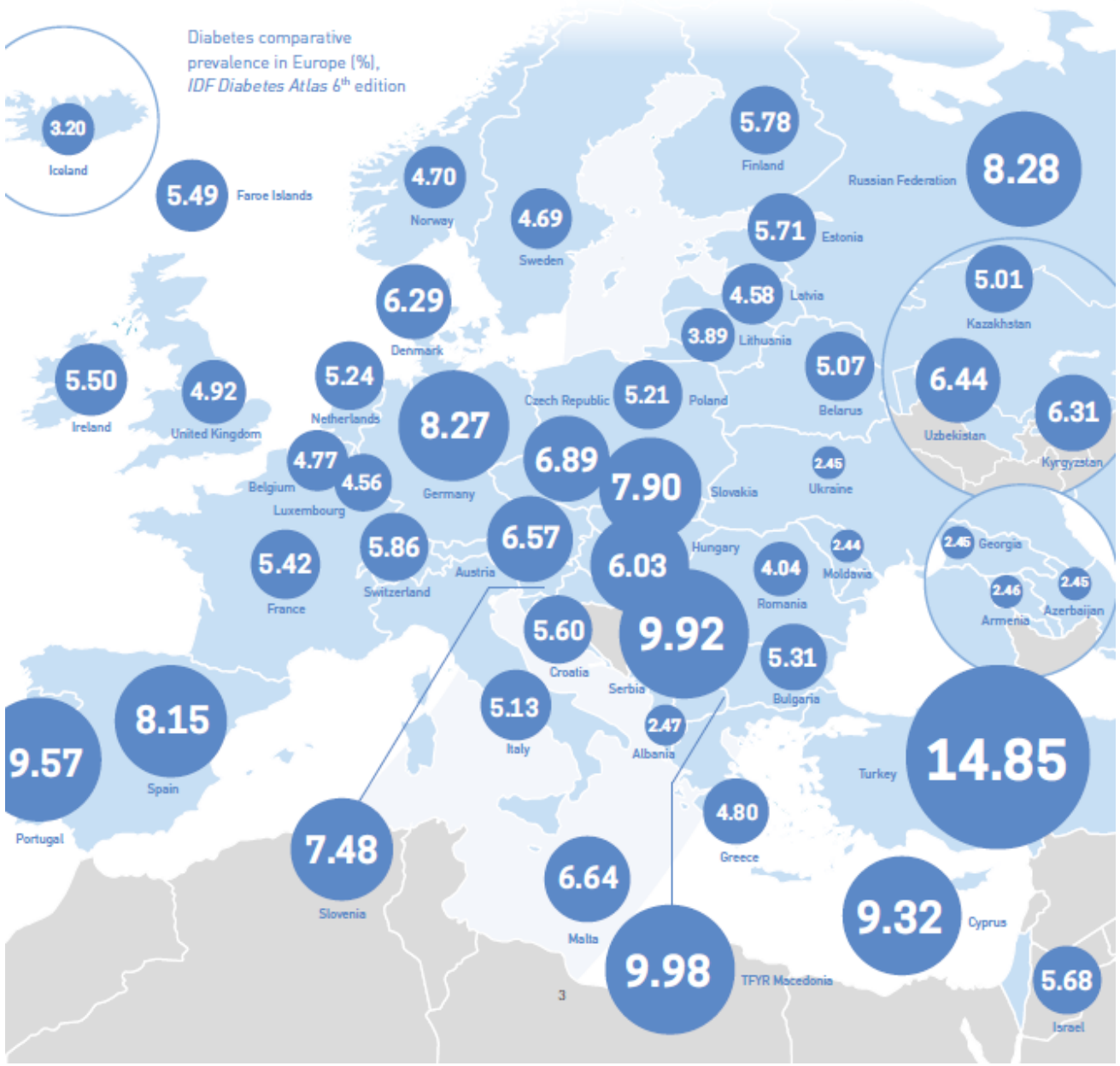






In 2014 the global prevalence of diabetes was estimated to be around 9% among adults aged 18+ years


27.1% undiagnosed
39 M
people living with diabetes
PREVALENCE
11.4%
NORTH AMERICA AND CARIBBEAN (NAC)
27.4% undiagnosed
25 M
people living with diabetes
PREVALENCE
8.1%
SOUTH AND CENTRAL AMERICA (SACA)
33.1% undiagnosed
52 M
people living with diabetes
PREVALENCE
7.9%
EUROPE (EUR)
48.6% undiagnosed
37 M
people living with diabetes
PREVALENCE
9.7%
MIDDLE EAST AND NORTH AFRICA (MENA)
62.5% undiagnosed
22 M
people living with diabetes
PREVALENCE
5.1%
AFRICA (AFR)
52.8% undiagnosed
75 M
people living with diabetes
PREVALENCE
8.3%
SOUTH-EAST ASIA (SEA)
53.6% undiagnosed
WESTERN PACIFIC (WP)
138 M
people living with diabetes
PREVALENCE
8.5%



The IDF data indicates that 56.3 million European adults were living with diabetes in 2013 – 8.5% of the region's adult population. This number is set to rise to 68.9 million by 2035.

Turkey has the highest prevalence with 14.8% of the adult population, Macedonia (10.0%) and Serbia (9.9%).

Countries with the lowest prevalence are the Republic of Moldova (2.4%), Azerbaijan (2.5%), Georgia (2.5%), and Ukraine (2.5%).

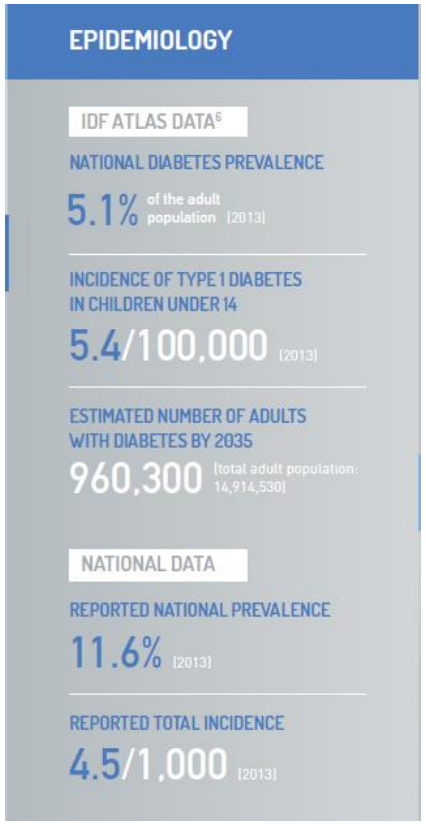
Epidemiology of Diabetes

Preexisting diabetes complicates ~1 % of pregnancies.

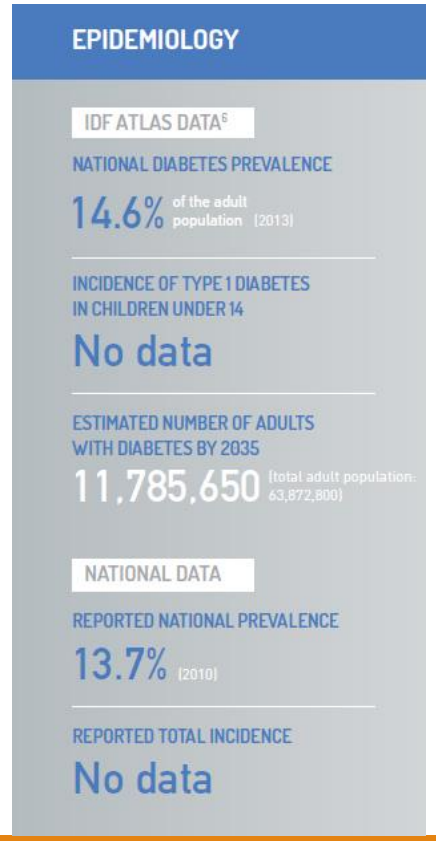
Overweight and obesity (BMI over 25 kg/m2) have been estimated to account for about 65–80% of new cases of type 2 diabetes.

Type 2 diabetes is increasing in all age groups and is now also reported among children and adolescents.

ROMANIA



TURKEY



WHO 2015 Report, NCHS 2013, ACOG 2013

Epidemiology of Gestational Diabetes

The prevalence of GDM is between **4.6% and 9.2**% of all pregnancies

GDM represents 90% of diabetic cases during pregnancies

- Within 10-20 years after delivery, approximately 50% of women who had gestational diabetes will develop type 2 diabetes
- Is frequently associated with Obesity

DM type 2 and GDM – "lifestyle diabetes"

GDM is also associated with increased risk of obesity and abnormal glucose metabolism during childhood and adult life in the offspring.

Prevalence Estimates of Gestational Diabetes Mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007–2010 Carla L. DeSisto, MPH; Shin Y. Kim, MPH; Andrea J. Sharma, CDC – vol 11, june 2014

Prevalence of Diabetes in UK NICE 2012

	Prevalence	**Number of pregnancies in England**
Total singleton pregnancies		600,200
Type 1 diabetes	0.3%	1,800
Type 2 diabetes	0.2%	1,200
Gestational diabetes	3.5%	20,400
Total diabetes in pregnancy		**23,400**

eurostat | newsrelease

203/2016 - 20 October 2016

Epidemiology of Obesity

In 2014,

- more than 1.9 billion adults - 39% of adults aged 18 years and over (38% of men and 40% of women), were overweight.
- about 13% of the world's adult population (11% of men and 15% of women) - over 600 million - were obese.

Worldwide prevalence of obesity more than doubled between 1980 and 2014

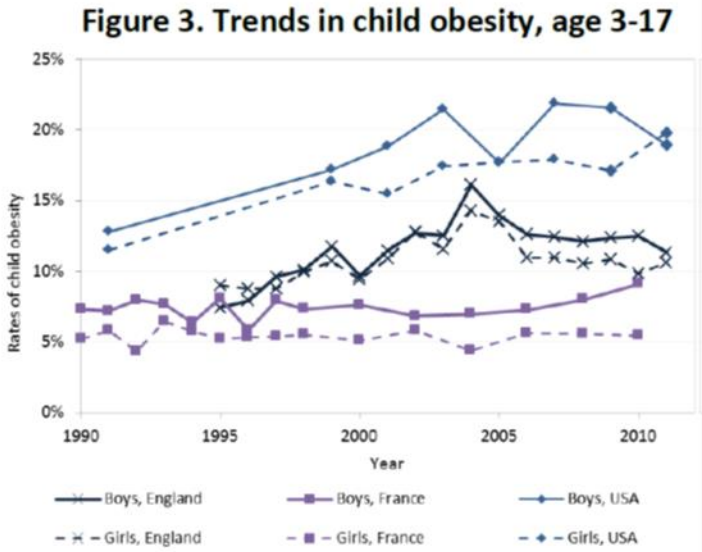
Most of the world's population live in countries where overweight and obesity kills more people than underweight.

41 million children under the age of 5 were overweight or obese in 2014.

EMERGENCE OF ADULT METABOLIC disease epidemics **in children** is an advancing public health concern, with childhood obesity, diabetes, cardiovascular disease, and nonalcoholic fatty liver disease (NAFLD) all increasing at alarming rates

Epidemiological studies have revealed statistical correlation between nutritional excess during pregnancy and later development of diseases such as obesity and type 2 diabetes childhood and adulthood.

The in utero environment can substantially modify how the fetal genome is expressed, which can exert stimulatory or inhibitory effects on fetal growth and adiposity



Boney CM et al. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* 2005.

Metabolic modifications in normal pregnancy

Contents lists available at ScienceDirect

Placenta

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

Current topic

Inflammation in maternal obesity and gestational diabetes mellitus
P. Pantham [a,*], I.L.M.H. Aye [b], T.L. Powell [a]

[a] Department of Pediatrics, Section of Neonatology, University of Colorado Anschutz Medical Campus, Aurora, CO, USA
[b] Department of Obstetrics & Gynecology, University of Colorado Anschutz Medical Campus, Aurora, CO, USA

The most important modifications during pregnancy affect the carbohydrates and lipid metabolism:

Carbohydrates metabolism

- **Periferic insulin resistance** due to placental hormones: E2, P, PRL, HPL mainly after 26-28 weeks
- **Increased insulin secretion**

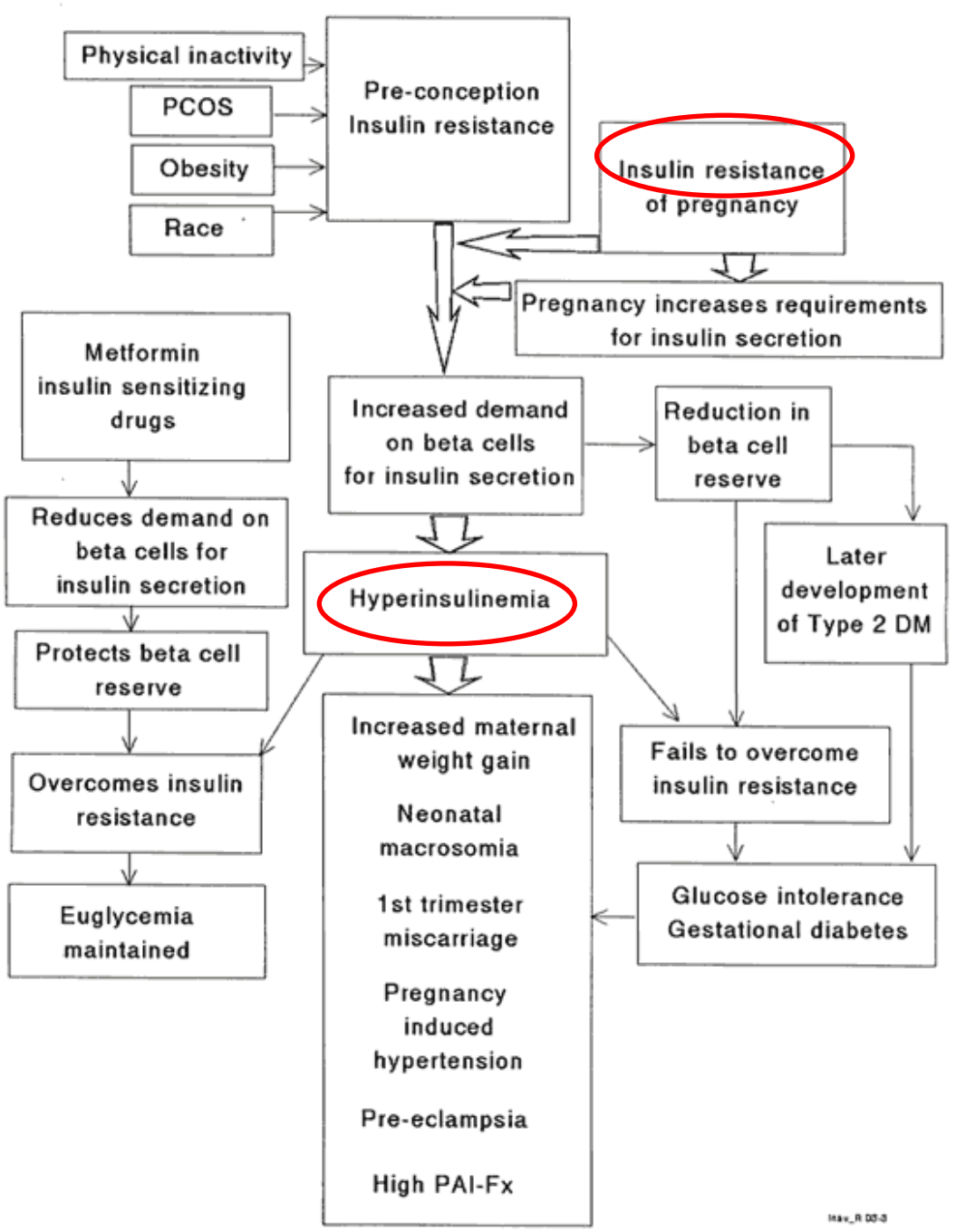
Lipid metabolism

- **increased adipose tissue lipolysis** and hepatic **VLDL secretion**
- **excess lipid transfer to the developing fetus that may impact the liver, skeletal muscle, adipose tissue, brain, and pancreas** to **increase the risk for metabolic disease in childhood**

Meta-inflammation

- metabolically induced by excessive consumption of nutrients in obese pregnant woman
- leads to systemic insulin resistance
- *These inflammatory environement may be **one mechanism** by with, offspring of obese woman are programed to develop insulin-resistance in adult life = **Developmental origins of adult disease***

Gestational Diabetes (GDM)



Mechanism of epigenetic programming

Epigenetic regulation of gene expression is characterized by stable changes to DNA and chromatin structure that alter gene expression independent of gene sequence.

DNA metilation

Posttranslational histone modifications

Micro RNAs

During embryonic development and organogenesis alterations to the “in utero” environment can have epigenetic consequences

Lipids and their pro-inflammatory derivatives can be transcriptional activators of multiple nuclear receptors

Potential Mechanisms for Fetal Metabolic Programming

In utero exposure to excess maternal glucids and lipids can impact some pathways in developing organs: liver, skeletal muscle, adipose tissue, brain , pancreas

Pathways affected:

- Energy storage
- Oxidation
- Celular death
- Differentiation
- Inflammation

Maternal obesity and high-fat diet also appear to profoundly alter offspring feeding behavior

- composition
- total caloric energy

Why to diagnose and treat Diabesity ?

Fetal outcome remains suboptimal

GDM and Obesity have an additive negative impact on obstetric outcomes.

Maternal prognosis is affected by de development of the metabolic syndrome

Intrauterine imprinting with consequences in childhood and adult life

Organogenesis

Morphogenesis

Hyperglicemy of pregestational Diabetes

Hyperglicemy of Gestational Diabetes

The prognosis of the Pregnancy with Diabesity

Optimal metabolic control before and during pregnancy

Complex ultrasound assesement

Congenital malformations in pregnancies with DM

Incidence 4X higher than in general population (4-12%)

Linked to poor preconceptional glucose control and to the metabolic environment in the first trimester

Most significant remaining cause of fetal death is congenital malformation

Due to frequent association with obesity the ultrasound diagnostic is especially difficult

Diabetes and obesity have an independent and additional risk of malformations

Prenatal diagnostic is mandatory

Table 4. Major Congenital Anomalies in Infants Born of Mothers With and Without Diabetes, 1988–2002

Type of Congenital Anomaly	IDM (n=516)	Non-IDM (n=150,589)	IDM Compared With non-IDM	*P*
Total	47 (9.1)	4,625 (3.1)	2.97 (2.25–3.90)	<.001
Adjusted total*			3.10 (2.28–4.22)*	<.001
Cardiac	25 (4.8)	1,147 (0.8)	6.36 (4.32–9.36)	<.001
Dextrocardia	2 (0.4)	31 (0.0)	18.83 (4.52–78.47)	.010
Patent ductus arteriosis	4 (0.8)	135 (0.1)	8.65 (3.21–23.29)	.010
Ventricular septal defect	10 (1.9)	511 (0.3)	5.71 (3.07–10.61)	<.001
Musculoskeletal	14 (2.7)	1,609 (1.1)	2.54 (1.51–4.27)	<.001
Caudal regression	3 (0.6)	4 (0.0)	218.88 (49.11–975.55)	<.001
Central nervous system	7 (1.4)	275 (0.2)	7.43 (3.54–15.65)	<.001
Spina bifida	1 (0.2)	17 (0.0)	17.17 (2.29–128.76)	.060
Ear, nose, and throat	5 (1.0)	368 (0.2)	3.97 (1.65–9.54)	.010
Genitourinary	3 (0.6)	659 (0.4)	1.33 (0.43–4.12)	.500
Hypospadias complex	6 (1.2)	626 (0.4)	2.80 (1.26–6.22)	.020

Yang et all, ACOG, vol 108, nr 3, 2006

Malformations of the Central Nervous System

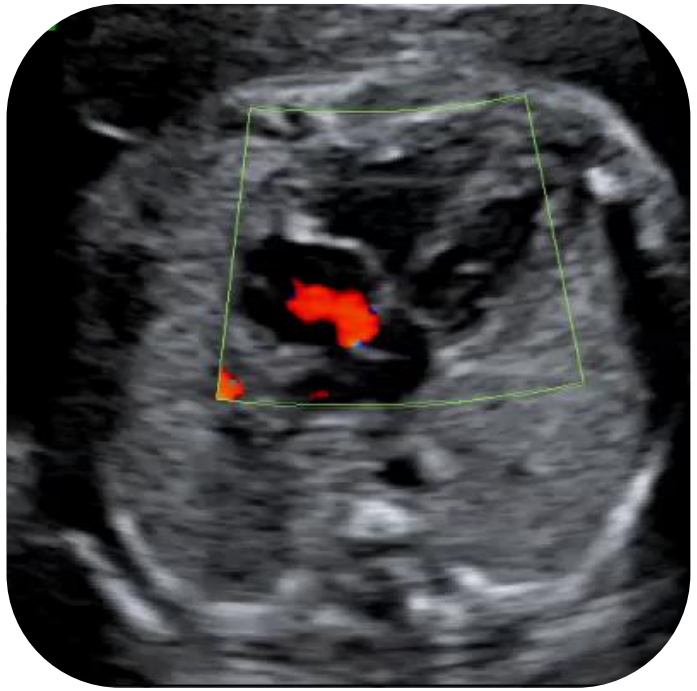
Frequency 2%, **OR 20**

- Anencephaly, holoprosencephaly , spina bifida, hidrocephaly, meningomielocel, microcephaly, septo-optic dysplasia

Cardiac Malformations

Frequency. 4%, **OR 5**

- Transposition of great arteries, Fallot tetralogy, Ventricular septal defect, Aortic coartation, pulmonary stenosis, Ventricular septal defect, hypertrophic obstructive cardiomyopathy



Digestive malformations

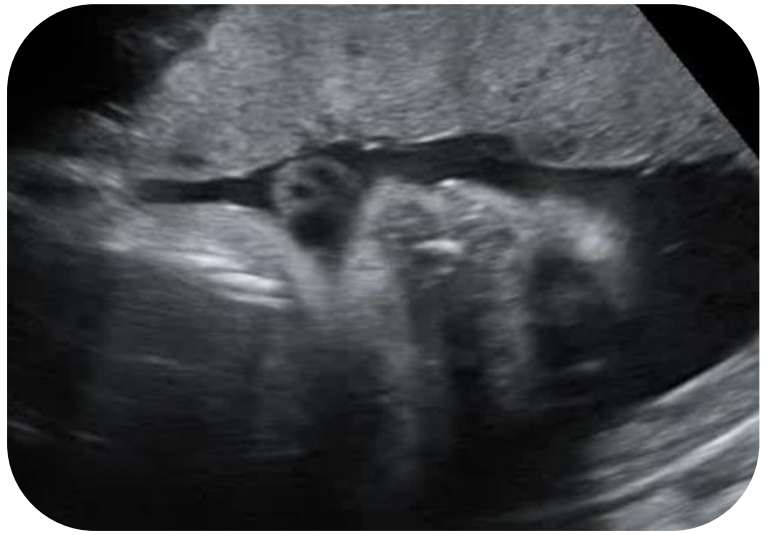
Laparoschisis, diaphragmatic hernia, duodenal atresia, esophagial atresia, omphalocelus, malrotation, volvulus, anal imperforation.

Others malformations

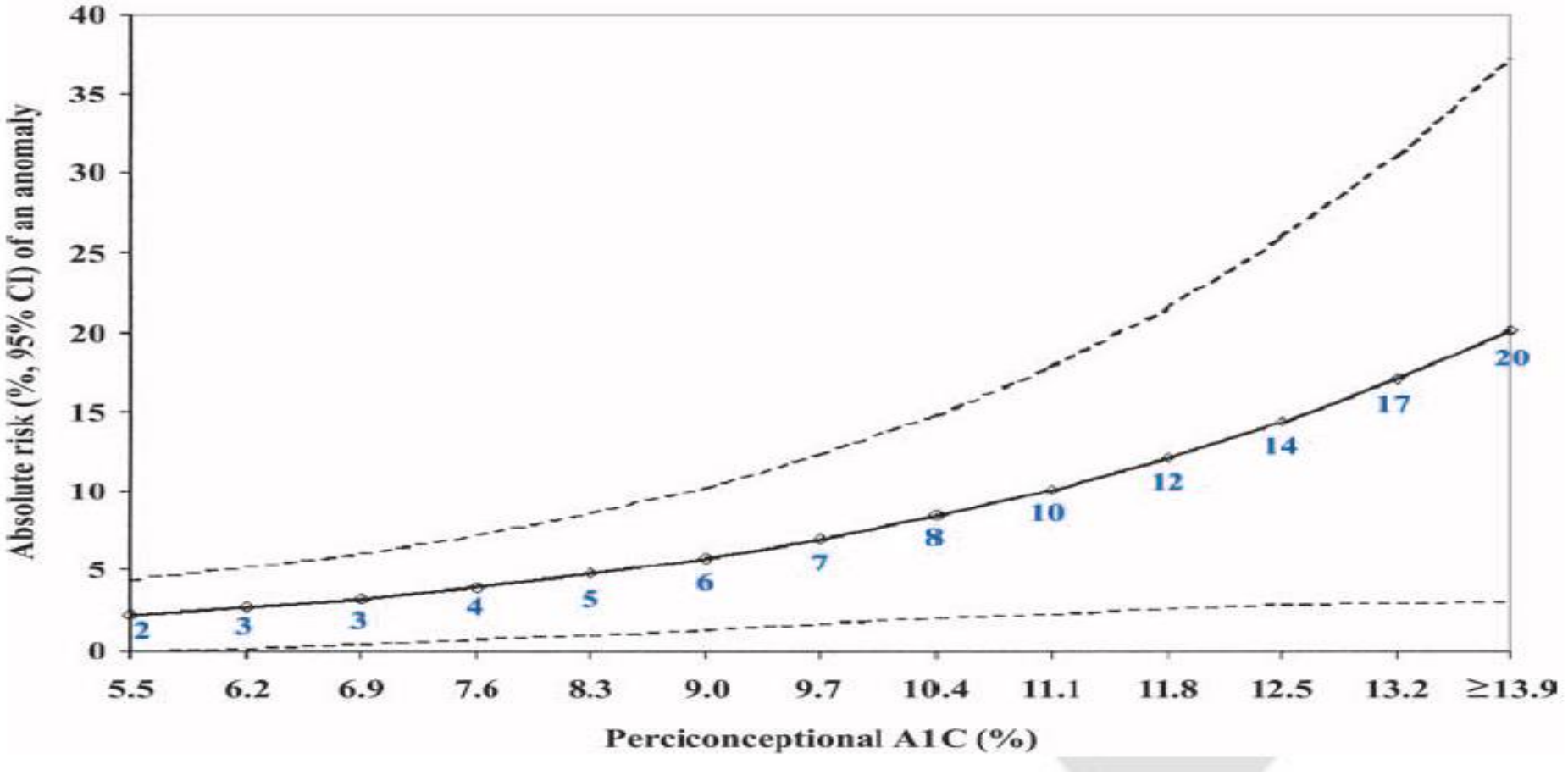
S**cheletal** : caudal regression syndrome, polidactily, hemivertebra, sindactily, limb hypoplasia, short femur

Urogenital - polycystic kidney, renal agenesis, hydronephrosis, uretheral duplications

Face: cheilognatopalatoschizis, anomalies of the ear, lens congenital cataracts



Risk of Fetal Anomaly Relative to Periconceptional HbA1C



Guerin A et al. *Diabetes Care* 2007;30:1-6.

Congenital malformations in pregnancies with Obesity

The ultrasound diagnosis is more difficult

The best period for diagnostic: 12-16 weeks

The frequency of congenital malformations is increased

- Neural tube defects OR 1.7-3.5 **proportional** with the BMI
- Cardiac OR 1.2-6.5
- Omphalocel OR 1.5-4.2
- Anorectal OR 1.46
- Limbs OR 1.36

Reference	*Congenital anomaly*	*BMI category**	*Study design*	*Odds ratio*	*95% CI*
Rasmussen *et al.*[45] (2008)	Spina bifida	Obese	Meta-analysis	1.70	1.34–2.15
Waller *et al.*[22] (2007)	Spina bifida	Obese	Case–control	2.10	1.63–2.71
Waller *et al.*[19] (1994)	Spina bifida	Obese	Case–control	2.60	1.50–4.50
Watkins *et al.*[21] (2003)	Spina bifida	Obese	Case–control	3.50	1.20–10.3
Shaw *et al.*[25] (1996)	NTD	Obese	Case–control	1.90	1.30–2.90
Watkins *et al.*[26] (1996)	NTD	Obese	Case–control	1.92	1.08–3.40
Hendricks *et al.*[27] (2001)	NTD	Obese	Case–control	1.73	1.03–2.92
Queisser-Luft *et al.*[28] (1998)	Encephalocele	Obese	Case–control	7.30	1.70–50.6
Waller *et al.*[19] (1994)	Other CNS	Obese	Case–control	4.20	1.20–14.6
Queisser-Luft *et al.*[28] (1998)	Eye anomalies†	Obese	Case–control	5.00	1.30–20.0
Waller *et al.*[22] (2007)	Heart defects	Obese	Case–control	1.40	1.24–1.59
Waller *et al.*[22] (2007)	Heart defects	Overweight	Case–control	1.13	1.01–1.26
Watkins *et al.*[21] (2003)	Heart defects	Obese	Case–control	2.00	1.20–3.40
Watkins *et al.*[21] (2003)	Heart defects	Overweight	Case–control	2.00	1.20–3.10
Mikhail *et al.*[29] (2002)	Heart defects	BMI > 27	Retrospective cohort	6.50	1.20–34.9
Cedergren and Kallen[23] (2003)	Heart defects	Obese	Case–control	1.41	1.22–1.64
Cedergren and Kallen[23] (2003)	Heart defects	Overweight	Case–control	1.18	1.09–1.27
Waller *et al.*[19] (1994)	GA defect	Obese	Case–control	6.20	1.40–27.4
Queisser-Luft *et al.*[28] (1998)	GA defect	Obese	Case–control	4.40	1.10–17.7
Queisser-Luft *et al.*[28] (1998)	CAT	Obese	Case–control	6.30	1.60–24.8
Waller *et al.*[22] (2007)	Anorectal atresia	Obese	Case–control	1.46	1.10–1.95
Queisser-Luft *et al.*[28] (1998)	Urogenital system	Obese	Case–control	1.70	1.10–2.80
Waller *et al.*[22] (2007)	Hypospadia‡	Obese	Case–control	1.33	1.03–1.72
Waller *et al.*[22] (2007)	Hypospadia‡	Overweight	Case–control	1.25	1.01–1.54
Waller *et al.*[22] (2007)	Limb reduction	Obese	Case–control	1.36	1.05–1.77
Waller *et al.*[22] (2007)	CDH	Obese	Case–control	1.42	1.03–1.98
Waller *et al.*[22] (2007)	Omphalocele	Obese	Case–control	1.63	1.07–2.47
Waller *et al.*[22] (2007)	Omphalocele	Overweight	Case–control	1.50	1.04–2.17
Waller *et al.*[19] (1994)	Omphalocele	Obese	Case–control	4.20	1.20–14.6

Ultrasound surveillance of fetuses with DM & Obesity

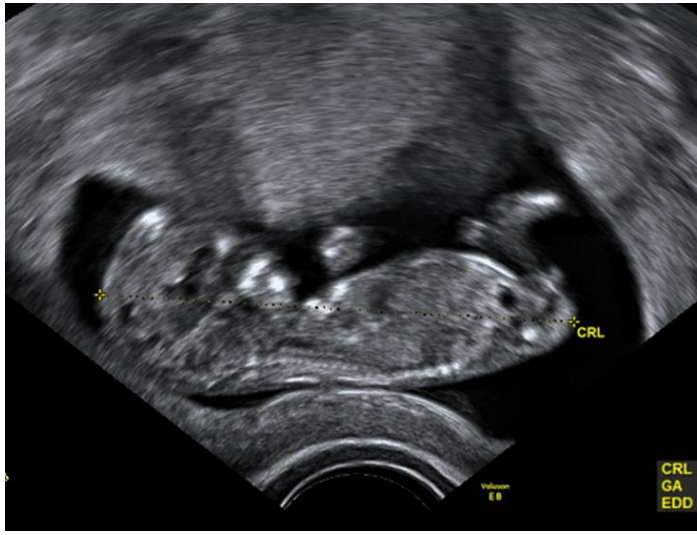
11-14 weeks
- Early diagnostic of pregnancy
- Early morphology scan
- If anomaly suspected control at 16-18 weeks

20-22 weeks - complete morphology scan
- echocardiography

32-34 weeks - repeat biometry in order to detect abnormal growth
- Different patterns of fetal growth
- Mandatory to have an individual growth curve

Doppler examination with reduced value for the 3rd trimester
- Umbilical and uterine IP does not correlate with maternal glycemia and HbA1c

Doppler examination is useful if preeclampsia and/or IUGR develops



Langer O, UOG 2005

Complications during pregnancy in Diabetes

Increase frequency of

- Fetal macrosomia OR 2
  - Due to poor metabolic control from the 1st trimester – early programming of the fetus and subsequent accelerated growth rate
- Preeclampsia
- Spontaneous abortion
- Hydramnios
- Premature birth
- IUGR
- Unexplained intrauterine fetal demise in the IIIrd trimester **OR 5** (Typically LGA, die before labor < 35 weeks)
- Low Apgar scores

Pregnancy Outc… Scotia from 1988 to 2002 in Women with and without Pregestational Diabetes

Factor	Diabetic (n = 516) %	Nondiabetic (n = 150,598) %	*p* value
Gestational hypertension	28	9	< .001
Preterm birth	28	5	< .001
Macrosomia	45	13	< .001
Fetal-growth restriction	5	10	< .001
Stillbirth	1.0	0.4	.06
Perinatal death	1.7	0.6	.004

Yang et all, ACOG, vol 108,nr 3, 2006 Wong S.F. UOG 2006

REVIEW ARTICLE

Published online 3 November 2014

Role of ultrasound in the management of diabetes in pregnancy

Badreldeen Ahmed[1], Mandy Abushama[1], Majeda Khraisheh[2], and J. Dudenhausen[3,4]

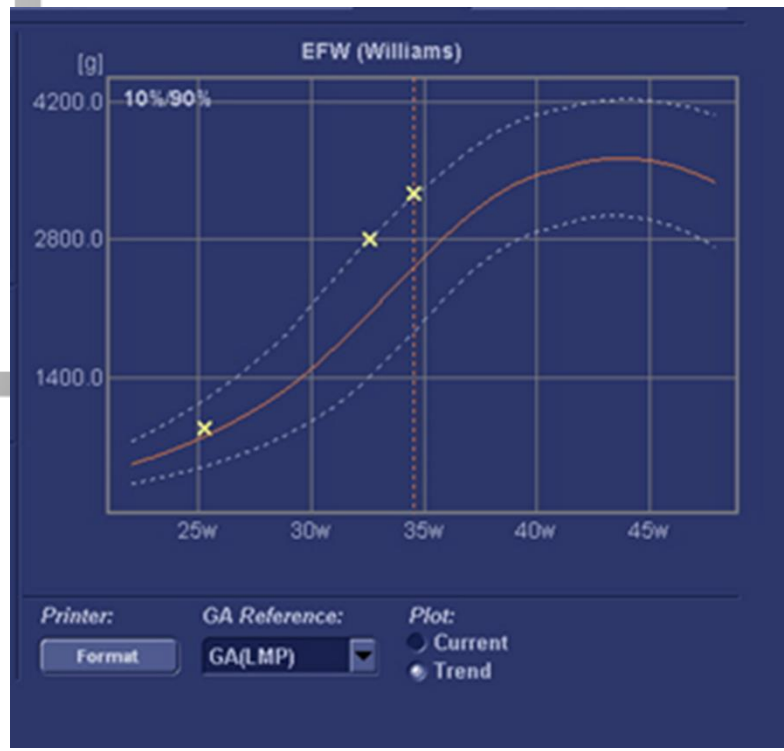
[1]Weill Cornell Medical College, Fetal Medicine Centre, Doha, Qatar, [2]Department of Chemical Engineering, Qatar University, Doha, Qatar, [3]Sidra Medical and Research Center, Ar-Rayyan, Qatar, and [4]Department of Obstetrics, Charité, Universitaetsmedizin Berlin, Berlin, Germany

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE

Ultrasound is not very accurate in estimation of fetal weight, regardless of the formulae used. The fact that the morphology of infant of Diabetic mother is different from non-diabetic mother will only add to this inaccuracy.

Compared to other US parameters used in estimation of fetal weight, fetal abdominal circumference is the most effective predictor of fetal weight.

When the abdominal circumference is greater than 90th centile, macrosomia is found to be present in approximately 80% of neonates



Fetal cardiac anomalies in DM and GD

Increase risk of CHD

Even in normal structured hearts

- Ventricular diastolic filling anomalies beginning in the first trimester
- Accelerated myocardial growth
- Cardiac hypertrophy

Specific

- Thickening of the interventricular septum and right ventricle free wall > 2.4 mm
- Hypertrophic subaortic stenosis – transient after birth after relief of maternal hyperglycemia
- Left outflow obstruction
- Congestive heart failure

Cardiac dysfunction with risk of intrauterine fetal demise in the IIIrd trimester: **OR 4-5**

Cardiac rhythm anomalies

These complications may arise even in the situation of o good glycemic control

Langer O, UOG, 2005

EXPERT REVIEWS

The effect of pregestational diabetes on fetal heart function

Expert Rev. Cardiovasc. Ther. 13(1), 67–74 (2015)

Table 1. Gestational diabetes and the fetal heart.

	Pregestational DM type 1	Pregestational DM type 2	Gestational DM
Incidence	<0.1%	Nearly 2%	7–8%
Cardiac malformations (embryopathy)	>5%	>5%	≤1%
Fetal hypertrophic cardiomyopathy	Possible	Possible	Possible
Fetal cardiac dysfunction	Possible	Possible	Possible
Long-term impact on child health	Possible	Possible	Possible

Diabetes in Pregnancy

Table 2. Risk of Stillbirth (GDM vs. No GDM)

Author	Gestational age cutoff	Population (n)	Absolute stillbirth rate in GDM (per 1000 pregnancies)	RR or OR (95% CI)	Policy management
Hutcheon et al.[6]	≥ 20 weeks	2 001 749	4.2	0.88 (0.79 to 0.99)	Not available
Peticca et al.[7]	≥ 20 weeks	120 604	2.0	0.31 (0.11 to 0.67)	Induction rate: 38% vs 24%
Karmon et al.[8]	≥ 20 weeks	184 256	4.0	0.5 (0.4 to 0.7)	Routine induction at 40 weeks
Ohana et al.[9]	≥ 20 weeks	228 293	0.32	0.7 (0.5 to 0.8)	Not available
Fadl et al.[3]	> 28 weeks	1 260 297	4.0	1.18 (0.87 to 1.60)	Not available
Hutcheon et al.[6]	> 28 weeks	1 988 320	3.5	1.25 (1.11 to 1.41)	Not available
Rosenstein et al.[10]	≥ 36 weeks	4 190 953	1.71	1.34 (1.2 to 1.5)	At > 39 weeks risk higher if expectant management

Complications during pregnancy in Obesity

Obesity

- acts as an independent risk for developing GDM, with a risk of about 20%
- significant and independent and additive contributor impacting fetal size

		Increased Complications (Odds Ratio[a])	
	Normal BMI 2024.9 (n = 176,923)	*Overweight BMI 2529.9* (*n* = 79,014)	*Obese BMI* > 30 (*n* = 31,27)
Gestational diabetes	0.8	1.7	3.6
Preeclampsia	0.7	1.5	2.1
Postterm pregnancy	0.13	1.2[b]	1.7
Emergency cesarean	7.8	1.3	1.8
Elective cesarean	4.0	1.2	1.4
Postpartum hemorrhage	10.4	1.2	1.4
Pelvic infection	0.7	1.2	1.3
Urinary tract infection	0.7	1.2	1.4
Wound infection	0.4	1.3	2.2
Macrosomia	9.0	1.6	2.4
Stillbirth	0.4	1.1[b]	1.4

BMI = body mass index.

[a]Odds ratios (99% CI) are significant except when denoted.

[b]Not significantly different.

Sebire 2001

GDM associated with Obesity

Gante et al. BMC Pregnancy and Childbirth (2015) 15:249
DOI 10.1186/s12884-015-0692-z

BMC Pregnancy & Childbirth

RESEARCH ARTICLE Open Access

Impact of gestational weight gain on obstetric and neonatal outcomes in obese diabetic women

Inês Gante[1*], Njila Amaral[2], Jorge Dores[3] and Maria C. Almeida[1]

In patients with GDM , maternal BMI and Excessive gestational weight gain is an independent risk factor, and more important for fetal macrosomia than glucose intolerance (Mission 2013, Stuebe 2013)

GDM prevalence increase with 1% for every 1kg/m2 increase in BMI

Excessive weight gain during pregnancy has long term effects on offspring adiposity (Lavlor DA – Am J Clin Nutr 2011)

The cesarean rate was significantly higher, Apgar score was lower and perinatal morbidity was higher in cases with excessive weight gain

GDM, obesity and excessive GWG represent, individually and additively, high-risk conditions associated with adverse maternal and neonatal outcomes

Activities directed in reducing GWG (from early pregnancy) can improve fetal outcome

Complications during delivery

IN DIABETES

Shoulder dystocia

Increase rate of cesarean section

Increase rate of operative vaginal delivery

Increase rate of neonatal complications

IN OBESITY

Increase dystocia

Increase rate of cesarean section

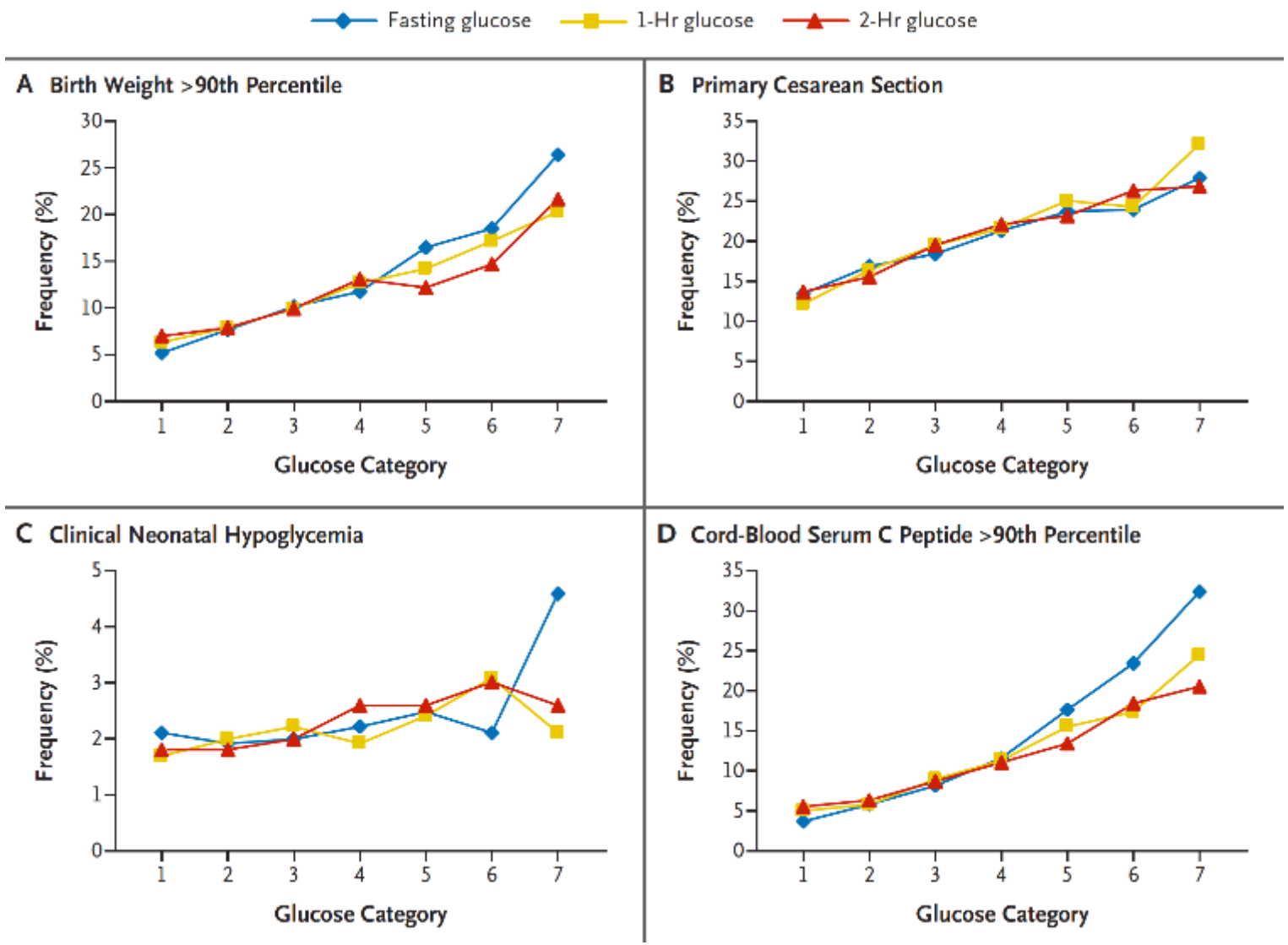
Lower Apgar scores

Increase rate of neonatal complications

Pregravid obesity and diabetes independently increase the risk of cesarian delivery

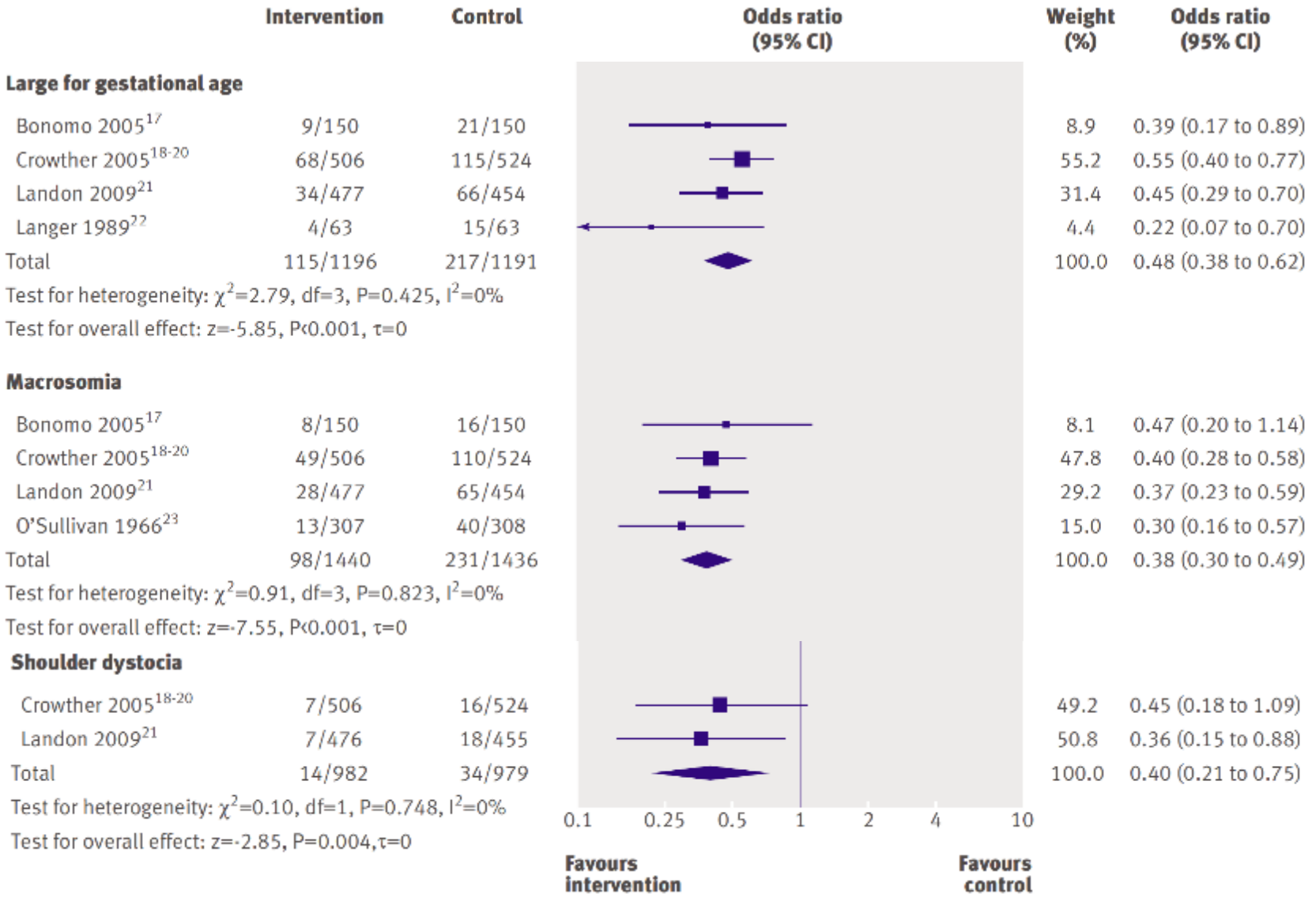
Cameron CM, IJ of Obesity 2014, Ehrenberg 2004

HAPO: Incidence of Adverse Outcomes Increases Along Continuum



Metzger BE, et al. Hyperglycemia and Adverse Pregnancy Outcomes. *NEJM* 2008;358(19):1991-2002.

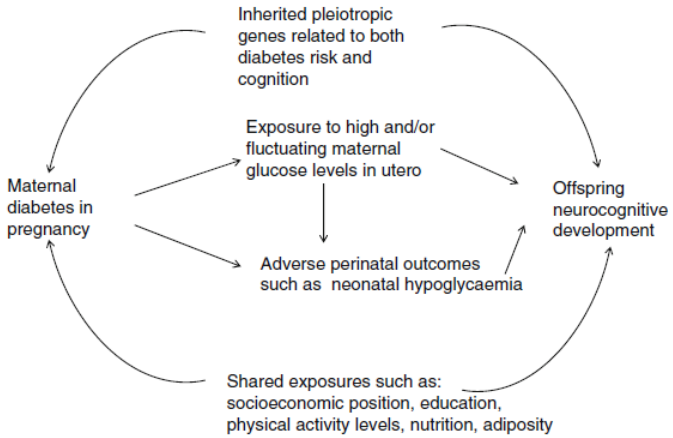
Benefits of Treatment of GDM



	Intervention	Control	Odds ratio (95% CI)	Weight (%)	Odds ratio (95% CI)
Large for gestational age					
Bonomo 2005[17]	9/150	21/150		8.9	0.39 (0.17 to 0.89)
Crowther 2005[18-20]	68/506	115/524		55.2	0.55 (0.40 to 0.77)
Landon 2009[21]	34/477	66/454		31.4	0.45 (0.29 to 0.70)
Langer 1989[22]	4/63	15/63		4.4	0.22 (0.07 to 0.70)
Total	115/1196	217/1191		100.0	0.48 (0.38 to 0.62)
Test for heterogeneity: χ^2=2.79, df=3, P=0.425, I^2=0%					
Test for overall effect: z=-5.85, P<0.001, τ=0					
Macrosomia					
Bonomo 2005[17]	8/150	16/150		8.1	0.47 (0.20 to 1.14)
Crowther 2005[18-20]	49/506	110/524		47.8	0.40 (0.28 to 0.58)
Landon 2009[21]	28/477	65/454		29.2	0.37 (0.23 to 0.59)
O'Sullivan 1966[23]	13/307	40/308		15.0	0.30 (0.16 to 0.57)
Total	98/1440	231/1436		100.0	0.38 (0.30 to 0.49)
Test for heterogeneity: χ^2=0.91, df=3, P=0.823, I^2=0%					
Test for overall effect: z=-7.55, P<0.001, τ=0					
Shoulder dystocia					
Crowther 2005[18-20]	7/506	16/524		49.2	0.45 (0.18 to 1.09)
Landon 2009[21]	7/476	18/455		50.8	0.36 (0.15 to 0.88)
Total	14/982	34/979		100.0	0.40 (0.21 to 0.75)
Test for heterogeneity: χ^2=0.10, df=1, P=0.748, I^2=0%					
Test for overall effect: z=-2.85, P=0.004, τ=0					

Horvath K et al. BMJ 2010;340:c1935

Long-Term Development of infants born by Diabetic mothers



Lower intelligence quotient (*Fraser A, Diabetologia 2014*)

Impaired memory performance at age 1

Autism spectrum disorders more frequent (*CHARGE study*)

Adiposity into early adulthood (*Lawlor DA, Circulation 2011*)

- this association is likely to be via intrauterine mechanisms, and is independent of maternal BMI in early pregnancy – Developemental overnutrition

Type 2 diabetes during adolescence

LGA offspring of diabetic mothers are at significant risk of developing metabolic syndrome in childhood (*Boney CM, Pediatrics 2005*)

Inheritance of Diabetes

- 1 parent with DM type 1 – 3-4% risk
- 2 parents with DM type 2 – 40% risk of type 2 DM
- After GDM increase risk of type 2 DM

Long-Term Development of infants born by Obese mothers

Offspring of the overweight/obese patients at the beginning of pregnancy have a higher body fat % and fat mass and lower fat-free mass

Children of obese women with GDM are more likely to have increased adiposity ant to be insulin rezistent

Childhood obesity

Type 2 diabetes during adolescence

LGA of obese mothers are at an increased risk of developing metabolic syndrome during childhood

Increased risk of all-cause hospital admissions in the first 5 years of life

Cardiovascular disease in adulthood

These modifications have implications for **perpetuating the cycle of obesity, insulin resistance, and their consequences to the next generations**

Hull HR, AJOG 2008, Pantham P. 2015, Cameron CM 2014

Table 2. Child hospital admissions from birth to 5 years of age by maternal pregravid BMI, overall and by 1-year time intervals: number of hospitalisations (excluding birth admission), rates reported per 10 PYs ($n = 2807$)

	Underweight		*Normal weight*		*Overweight*		*Obese*	
	n	*Rate*	n	*Rate*	n	*Rate*	n	*Rate*
Year 1	38	1.83	275	1.98	95	1.63	128	2.73
Year 2	22	1.25	120	1.03	48	1.00	58	1.49
Year 3	15	1.13	74	0.83	38	1.08	14	0.52
Year 4	7	0.80	55	0.86	27	1.14	52	2.96
Year 5	10	1.73	35	0.82	13	0.85	88	7.34
Total 5 years	92	1.39	557	1.24	220	1.22	327	2.30

Abbreviations: BMI, body mass index; PYs, person years.

Table 3. Unadjusted and adjusted RRs for all-cause child hospital admissions in the first 5 years of life by maternal pregravid BMI status

	Crude RR (95% CI)	*Adjusted RR (95% CI)*[a]
Maternal BMI		
Underweight	1.06 (0.75–1.52)	1.00 (0.65–1.54)
Normal weight	Reference	Reference
Overweight	0.94 (0.74–1.20)	0.95 (0.71–1.28)
Obese	1.69 (1.32–2.15)*	1.48 (1.10–1.98)*

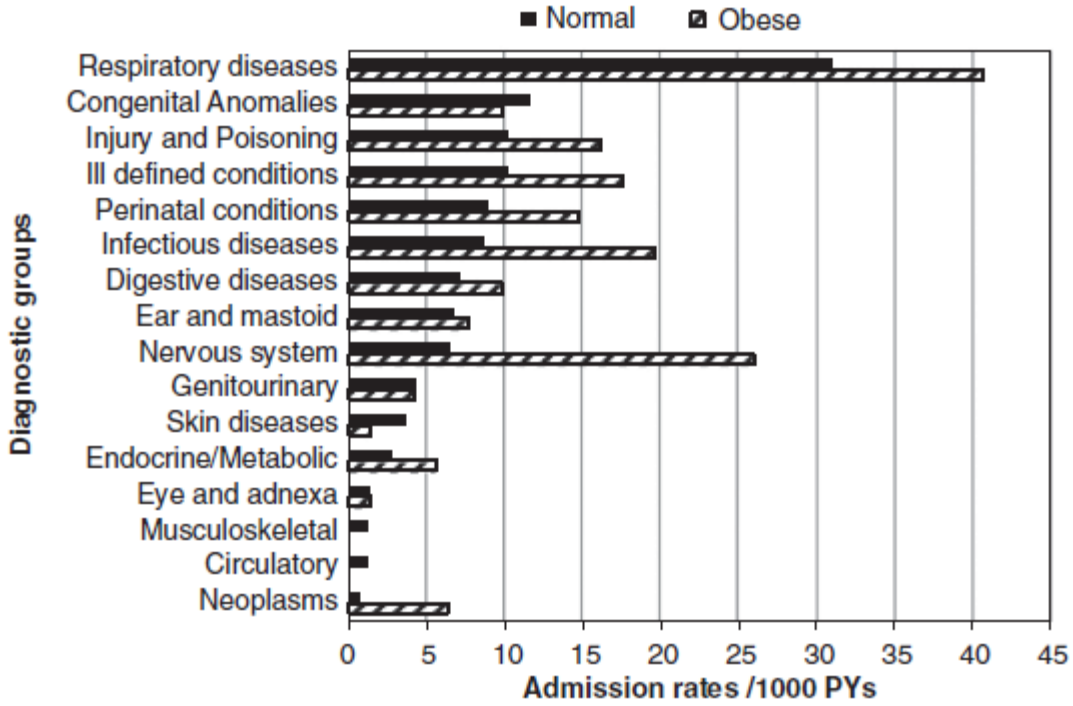
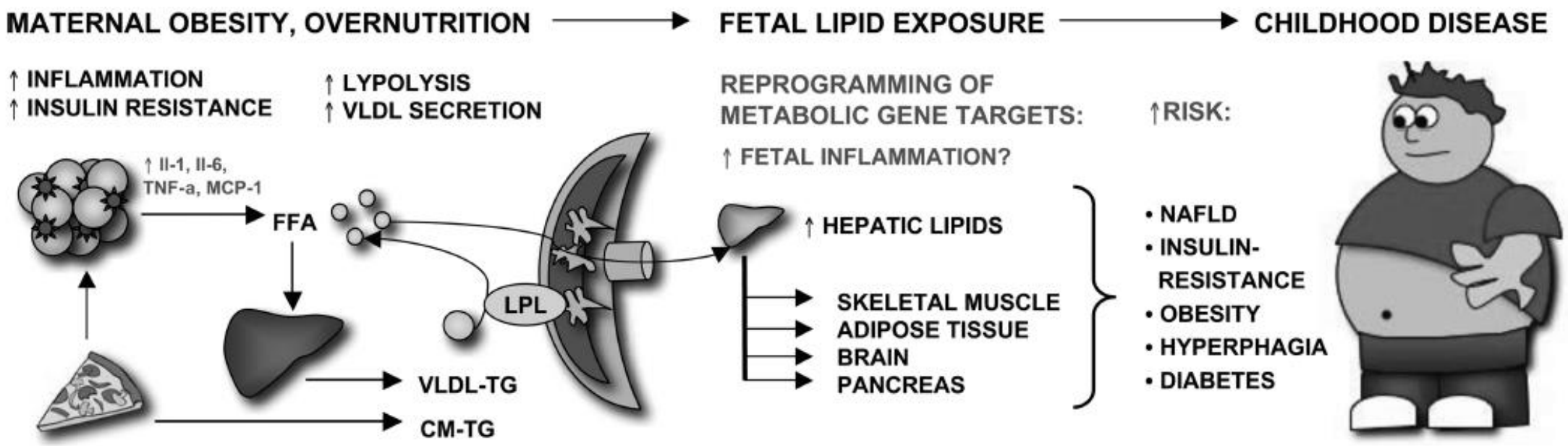


Figure 1. Five year rates of ICD-10 diagnostic grouping of hospital admissions per 1000 PYs, for children of maternal pregravid obese BMI group compared with normal BMI group.

Cameron CM, Int J of Obesity, 2014

Transgenerational impact



Given the multiple metabolic gene pathways that may be targeted by excess fetal metabolits exposure, the question is:

HOW DO WE REVERSE THE PROGRAM ?

- supplementation with folate or choline can promote DNA methylation

perhaps the most attractive mechanisms to prevent fetal metabolic programming in cases of maternal obesity is at the source - prevention of

- initial hyperlipidemia
- insulin resistance
- maternal inflammation

Possible interventions

To reduce the prevalence of diabetes and obesity – public health policies !

To assure euglycemia from the beginning of the pregnancy

To try to normalize the weight before pregnancy

To control the weight gain from the beginning of pregnancy

To improve the metabolic environement of obese mothers from the first trimester

To identify GDM in pregnancy

Appropriate date of delivery

To modify the inflammatory reponse in obese/GDM patients ?

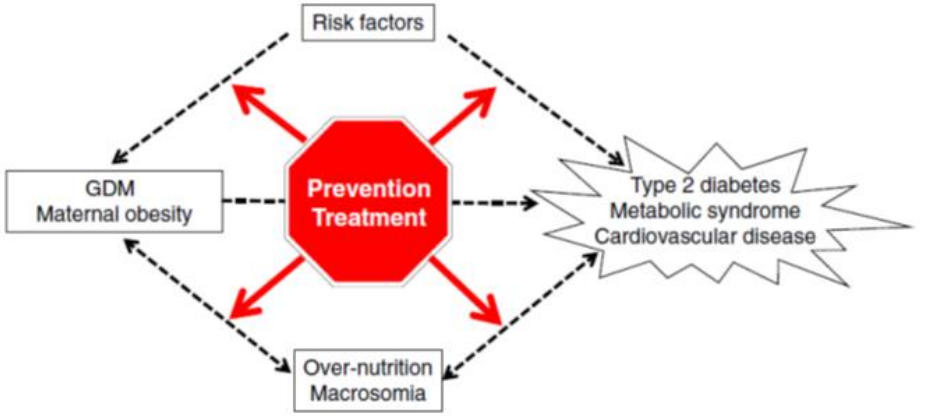
Conclusions

Diabesity affect the short and long term fetal outcome – intrauterine origin hypothesis of adult diseases

Pregnancies with Diabesity needs a complex follow-up from the preconceptional period until delivery

Actions intended to reduce the global prevalence of Diabesity will

- improve the results of these pregnancies
- break the propagation of these modifications to the next generations and the long-term intergenerational impact
- improve the children health
- diminish the cost of child health care



Thank you