Maternal obesity or GDM; which is the real problem?

And what about GDM screening?

Gerard H.A.Visser

Obesity and GDM

BMI	Odds ratio	GDM
20-25	1	10%
25-30	1.6-1.7	
>30	3.6-4	35%
>40	10	100%

Sebire et al, 2001; Baeten et al, 2001, Kumari, 2007

Overweight and pregnancy

- GDM
- Macrosomia
- C.section
- Hypertension
- Preterm delivery
- Post operative complications
- Congenital malformations
- Fetal death
- Neonatal morbidity
- Autism

Odds ratios 2-3

After Jensen et al, 2003

Obesity without diabetes

Body Mass index	<25	25-30	>30
PIH	1	1.7	5.6
Birth weight>p90	1	1.1	2.5
CS	1	1.6	2.7
Induction of labour	1	1.5	3.2

Jensen et al, 2003. 2459 'glucose tolerant'women

Correction for 2 h glucose level, age, parity, ethnicity, smoking, gest weight gain, gest age at delivery

BOTERO

Obesity and GDM; direct perinatal outcome
independent risk factors with synergistic effects

	Control	GDM	Obesity	GDM and Obesity
Birth weight>90th centile	1	2.19	1.73	3.62
Cord C-peptide>90th centile	1	2.49	1.77	3.61
Primary Caesarean section	1	1.25	1.51	1.71
Preeclampsia	1	1.74	3.91	5.98
Newborn % body fat>90th centile	1	1.98	1.65	3.69
Shoulder dystocia/birth injury	1	1.14	1.03	1.8

Adapted from Catalano et al, 2012

Obesity and GDM

- Both have an (synergistic) effect on early perinatal outcome

- But what about long term outcome of the children?

Mat Diabetes and Childhood obesity meta-analysis, Philipps et al, Diabetologia 2011

All types of diabetes:

Study or subgroup (first author, year, ref.)	All diabetes Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Catalano, 2009 [29]	0.9	1.4	37	0.31	1.16	52	7.3	0.59 (0.04, 1.14)
Gillman, 2003 [23]	0.33	1.01	465	0.15	1.02	14,416	18.3	0.18 (0.09, 0.27)
Hunter, 2004 [50]	1.6	2.4	27	−0.2	2.3	15	1.5	1.80 (0.33, 3.27)
Krishnaveni, 2010 [22]	0.79	1	35	−0.06	1.06	381	11.7	0.85 (0.50, 1.20)
Lawlor, 2009 [27]	0.228	1.253	93	−0.006	0.991	10,126	14.2	0.23 (−0.02, 0.49)
Lindsay, 2010 [15]	0.69	1.2	100	0.28	0.78	45	12.2	0.41 (0.08, 0.74)
Manderson, 2002 [14]	0.59	1.35	61	0.6	1.21	57	9.0	−0.01 (−0.47, 0.45)
Whitaker, 1998 [13]	0.39	0.94	58	0.45	0.93	257	13.9	−0.06 (−0.33, 0.21)
Wright, 2009 [46]	0.47	1.22	51	0.44	1.02	1,035	11.9	0.03 (−0.31, 0.37)
Total (95% CI)			927			26,384	100.0	0.28 (0.09, 0.47)

Fig. 2 Forest plot showing the unadjusted association between all types of maternal diabetes and offspring BMI z score. Heterogeneity: $\tau^2=0.05$; $\chi^2=27.02$, $df=8$ ($p=0.0007$); $I^2=70\%$. Test for overall effect: $z=2.90$ ($p=0.004$). IV, inverse variance; ref., reference

GDM:

| Study or subgroup (first author, year, ref.)	Gestational diabetes Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Catalano, 2009 [29]	0.9	1.4	37	0.31	1.16	52	10.2	0.59 (0.04, 1.14)
Gillman, 2003 [23]	0.33	1.01	465	0.15	1.02	14,416	23.5	0.18 (0.09, 0.27)
Krishnaveni, 2010 [22]	0.79	1	35	−0.06	1.06	381	15.7	0.85 (0.50, 1.20)
Lawlor, 2009 [27]	0.302	1.225	53	−0.006	0.991	10,126	16.2	0.31 (−0.02, 0.64)
Whitaker,1998 [13]	0.39	0.94	58	0.45	0.93	257	18.4	−0.06 (−0.33, 0.21)
Wright, 2009 [46]	0.47	1.2	51	0.44	1.02	1,035	16.1	0.03 (−0.31, 0.37)
Total (95% CI)			699			26,267	100.0	0.28 (0.05, 0.51)

Fig. 3 Forest plot showing the unadjusted pooled analysis of offspring BMI z score of mothers with gestational diabetes mellitus and controls. Heterogeneity: $\tau^2=0.06$; $\chi^2=25.54$, $df=5$ ($p=0.001$); $I^2=76\%$. Test for overall effect: $z=2.39$ ($p=0.02$). IV, inverse variance; ref., reference

Mat Diabetes and Childhood obesity meta-analysis, Philipps et al, Diabetologia 2011

Adjusted for maternal BMI:

All types of diabetes:

Study or subgroup (first author, year, ref.)	Mean difference	SE	Weight (%)	Mean difference IV, fixed, 95% CI
Lawlor, 2009 [27]	0.01	0.32	11.9	0.01 (0.62, 0.64)
Lindsay, 2010 [15]	0.34	0.193	32.6	0.34 (−0.04, 0.72)
Wright, 2009 [46]	−0.08	0.148	55.5	−0.08 (−0.37, 0.21)
Total (95% CI)			100.0	0.07 (−0.15, 0.28)
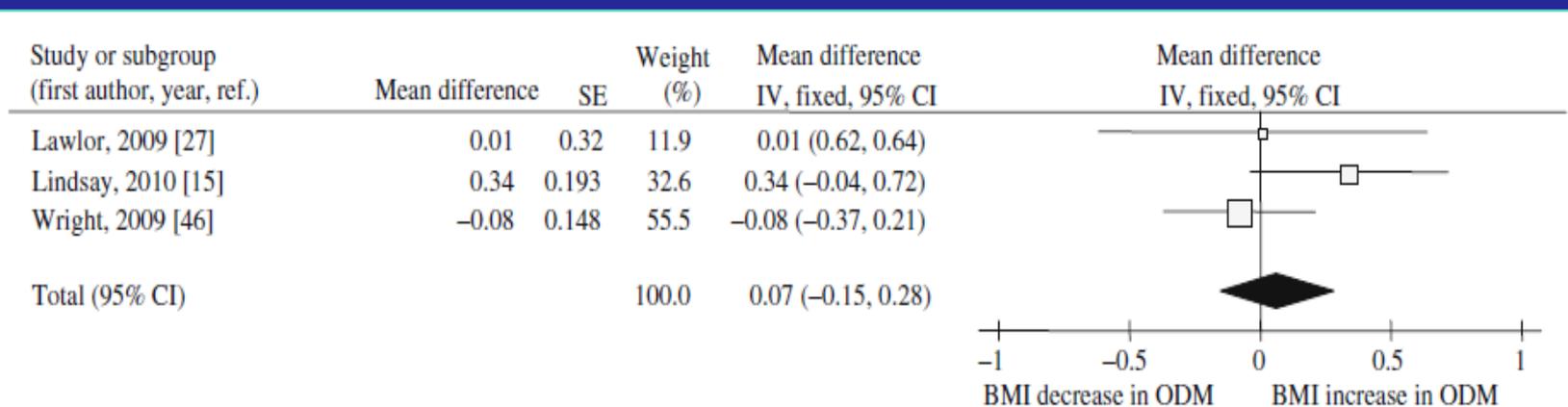
Fig. 5 Forest plot showing the adjusted association between all types of maternal diabetes and offspring BMI z score. Heterogeneity: $\chi^2 = 3.02$, $df = 2$ ($p = 0.22$); $I^2 = 24\%$. Test for overall effect: $z = 0.61$ ($p = 0.54$). IV, inverse variance; ref., reference

Maternal overweight is the main problem and not GDM

overweight and abdominal obesity in 16 y old adolescents

Risk population:

-GDM 84

-Normal OGTT 657

Control 3.427

■ = mat BMI> 25

Overweight (n=530)

	GDM	OGTT normal	Control
	40	27.9	
	8.2	13.5	11.7

Abdominal obesity (n=347)

	GDM	OGTT normal	Control
	25.7	19.5	
	8.2	9.1	7.5

Pirkola et al, Diab Care 2010
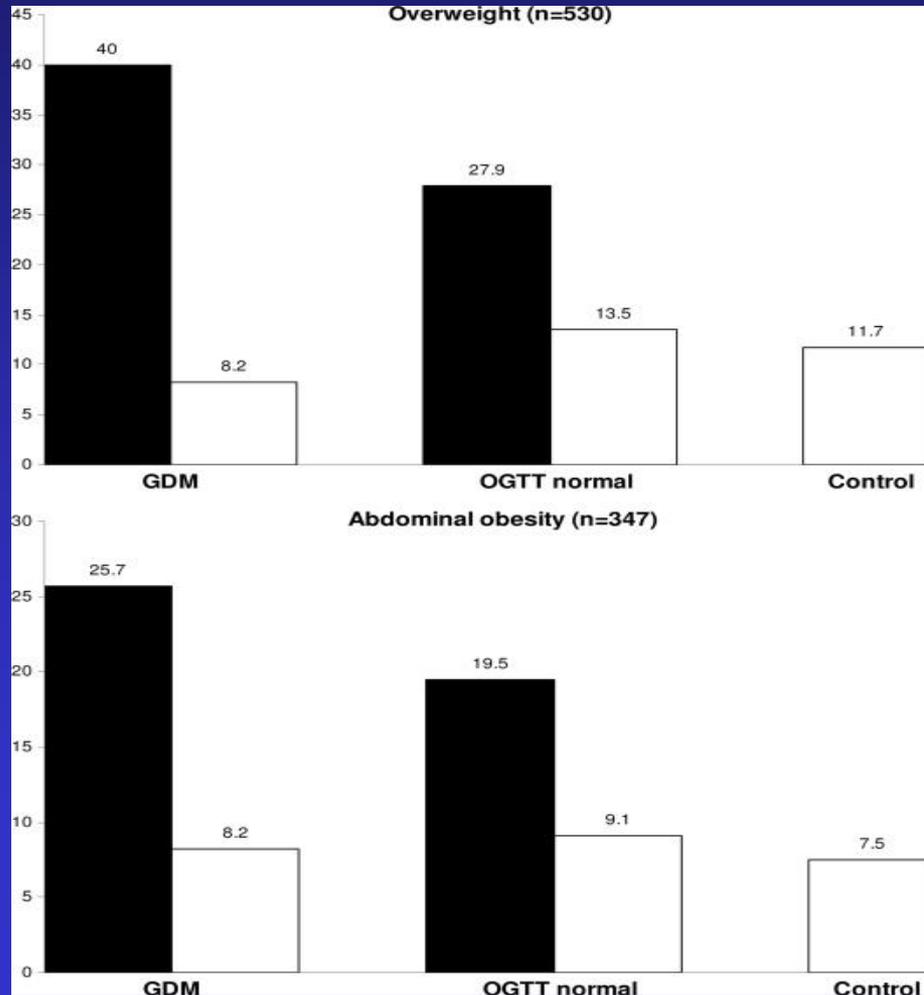
Metabolic syndrome in 175 infants age 7-11, according to birth weight and GDM

TABLE 4. Hazard Ratio for the Risk of MS ($n = 175$)			
Variables	Hazard Ratio	P Value	95% CI for Hazard Ratio
LGA versus AGA	2.19	.006	1.25–3.82
Maternal obesity* versus nonobese	1.81	.039	1.03–3.19
GDM versus control	1.44	.191	0.83–2.50
Male versus female	1.52	.133	0.88–2.61

* Prepregnancy BMI of >27.3 kg/m².

Boney, Pediatrics 2005

A 'typical' US situation

- 9.835 untreated women, without severe GDM at screening, but with an abnormal OGTT according to the IADPSG classification in 19.2%:

- Normal weight 40%, overweight 32%, obese 28%

- 21.6% of LGA was attributable to overweight/obesity
- 23.3% of LGA was attributable to overweight/obesity+GDM
- 2.9% was attributable to GDM in normal weight women

MH Black et al, Diabetes Care 2013;36:56-62

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- 2.9% was attributable to GDM in normal weight women

MH Black et al, Diabetes Care 2013;36:56-62

Review Article

Does exposure to hyperglycaemia *in utero* increase the risk of obesity and diabetes in the offspring? A critical reappraisal

L. E. Donovan[1] and T. Cundy[2]

[1]Department of Medicine, Division of Endocrinology and Metabolism and Department of Obstetrics and Gynaecology, University of Calgary, Alberta, Canada and [2]Department of Medicine, Faculty of Medical & Health Sciences, University of Auckland, New Zealand

Results Some animal studies support a relationship between exposure to hyperglycaemia *in utero* and future development of obesity and diabetes, but the results are inconsistent. Most of the human studies claiming to show a relationship have not taken into account important known confounders, such as maternal and paternal BMI. Evidence supporting a dose–response relationship between maternal hyperglycaemia exposure and obesity and diabetes in the offspring is weak, and there is no convincing evidence that treating gestational diabetes reduces the later risk of offspring obesity or glucose intolerance.

Conclusions Exposure to hyperglycaemia *in utero* has minimal direct effect on the later risk of obesity and Type 2 diabetes. The increased risk of obesity in the offspring of women with Type 2 or gestational diabetes can be explained by confounding factors, such as parental obesity.

Maternal obesity during pregnancy and premature mortality from cardiovascular event in adult offspring; Reynolds et al, BMJ 2013
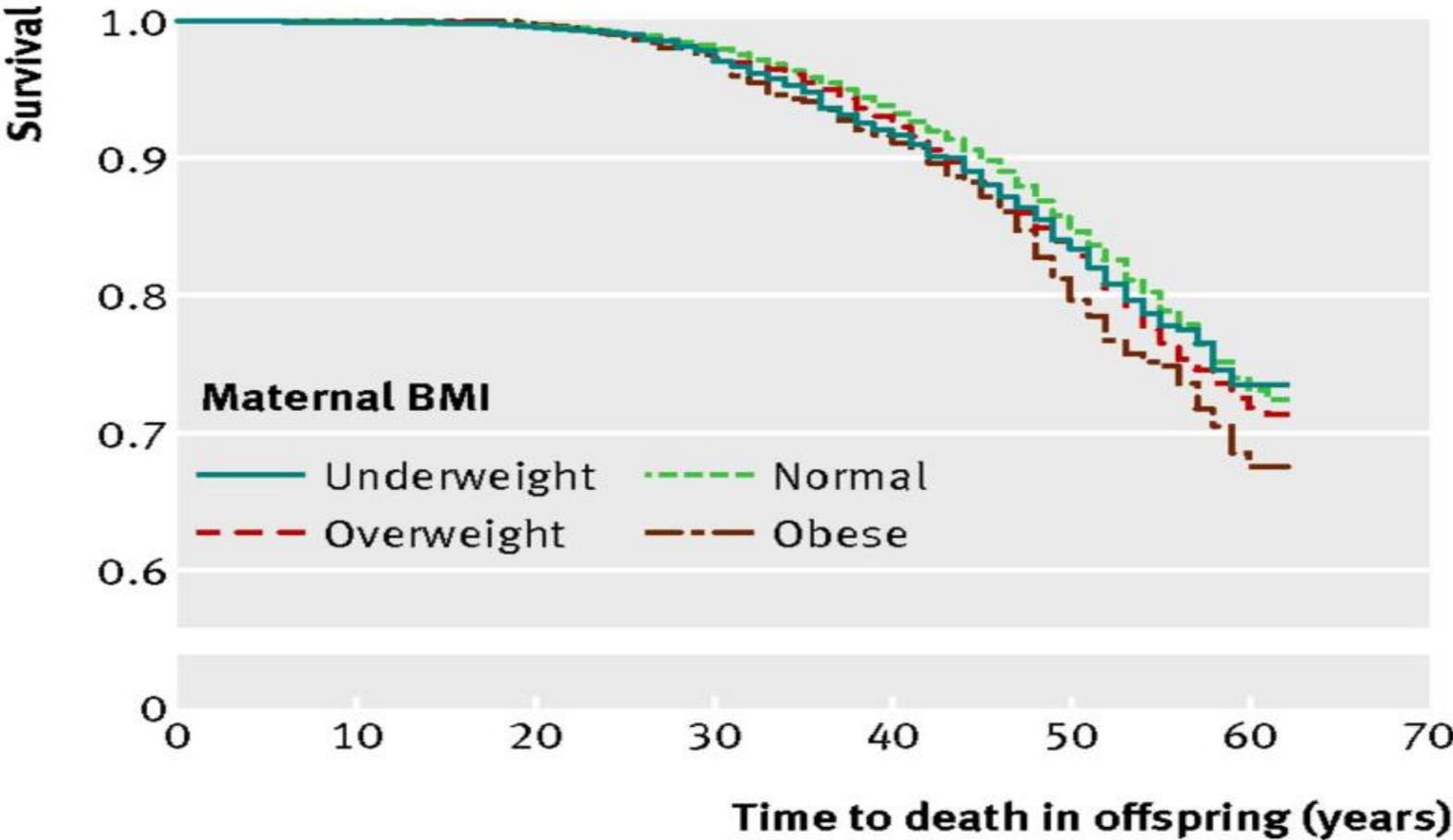
Adjusted for mat age at delivery, socioeconomic status, birth weight, gestation at delivery

Obesity and GDM

- Both have an (synergistic) effect on early perinatal outcome

- Obesity seems to have the most important effect on long term development of the offspring (especially childhood obesity)

So, which infants are likely to develop obesity/diabetes and what about prevention?

- Genetic predisposition (thrifty genotype)
- High maternal BMI
- High weight gain in pregnancy
- Macrosomia at birth

Maternal diabetes

- And……excessive weight gain > 2 y of age

Weight gain during pregnancy in obese glucose tolerant women (BMI>30 ; multivariate analysis)

	< 5kg	5-10	10-15	>15
Hypertension	1	2.1	3.6	4.8
CS	1	2.4	3.0	3.6
Ind.labour	1	2.7	2.8	3.7
LGA	1	2.4	2.1	4.7
SGA	no difference			
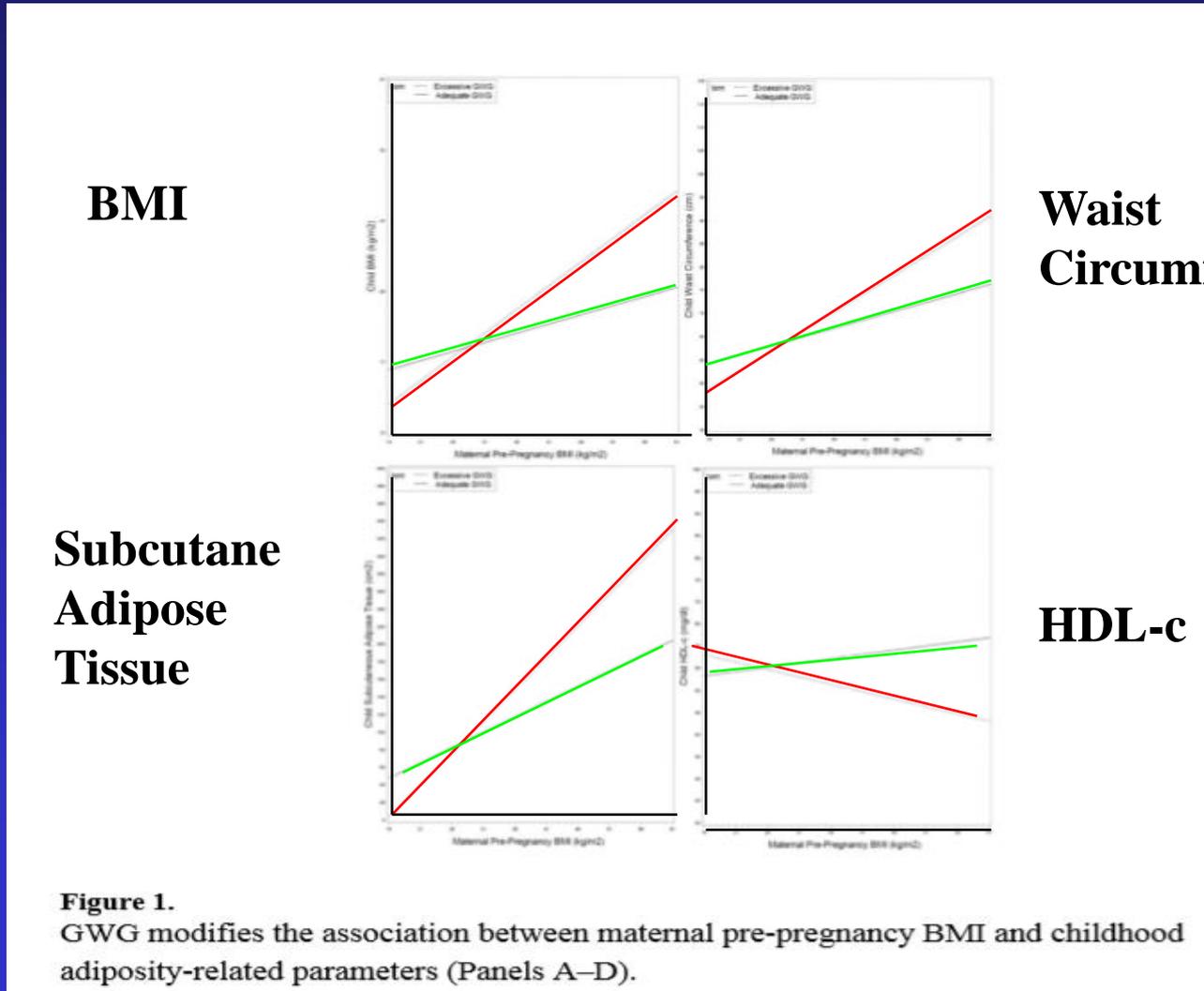
Jensen et al, Diab Care 2005

Prepregnancy BMI and Gest Weight Gain in relation to childhood obesity

BMI

Waist Circumf

Subcutane Adipose Tissue

HDL-c

Adequate W gain

Excessive W gain

Figure 1.
GWG modifies the association between maternal pre-pregnancy BMI and childhood adiposity-related parameters (Panels A–D).

Kaar et al, P Pediatr, 2014

Optimal weight gain during pregnancy

Table 17.1   Recommended weight gain in pregnancy according to the Institute of Medicine Guidelines

BMI	Recommended weight gain	
	kg	lb
<18.5	12–18	28–40
18.5–25	11.5–16	25–35
25–30	6.8–11.4	15–25
>30	5–9	11–20

Source: Rasmussen, K.M. et al., *Curr. Opin. Obstet. Gynecol.*, 21, 521, 2009.

Optimal weight gain during pregnancy

Table 17.1 Recommended weight gain in pregnancy according to the Institute of Medicine Guidelines

BMI	Recommended weight gain	
	kg	lb
<18.5	12–18	28–40

So,..involve a dietician !!

Source: Rasmussen, K.M. et al., *Curr. Opin. Obstet. Gynecol.*, 21, 521, 2009.

RCT real-time CGM
for 6 days at 8, 12, 21, 27 and 33 wks

	CGM	Controls*
• N	79	75
• HbA1c baseline	6.6%	6.8%
• HbA1c 33 wks	6.1%	6.1%
• Severe hypo glyc.	16%	16%
• LGA infant	45%	34%

RCT real-time CGM in GDM
2nd half of pregnancy; n=236

Continuous Glucose Monitoring Effects on Maternal Glycemic Control and Pregnancy Outcomes in Patients With Gestational Diabetes Mellitus: A Prospective Cohort Study

JCEM 2015

Fan Yu,* Lijuan Lv, Zhijiang Liang, Yi Wang, Jiying Wen, Xiaohong Lin, Yuheng Zhou, Caiyuan Mai, and Jianmin Niu*

and returned to the hospital for a visit on day 3. Visits included downloads and analysis of data in meter and sensor (only for patients in CGM group), nutrition consultation, education of information on blood glucose testing and self-care activities, and getting an individualized diabetes care prescription, which was arranged by the same obstetric diabetes team. After the first visit, patients adhered strictly to their new diet and lifestyle, and SMBG was performed every day.

LGA 13.6% vs 25.6%; PE & CSs sign lower

Birthweight, Infant growth & Type-2 diabetes

Mean Z-score

(Eriksson et al, Diab Care 2003; 26: 2006-10)
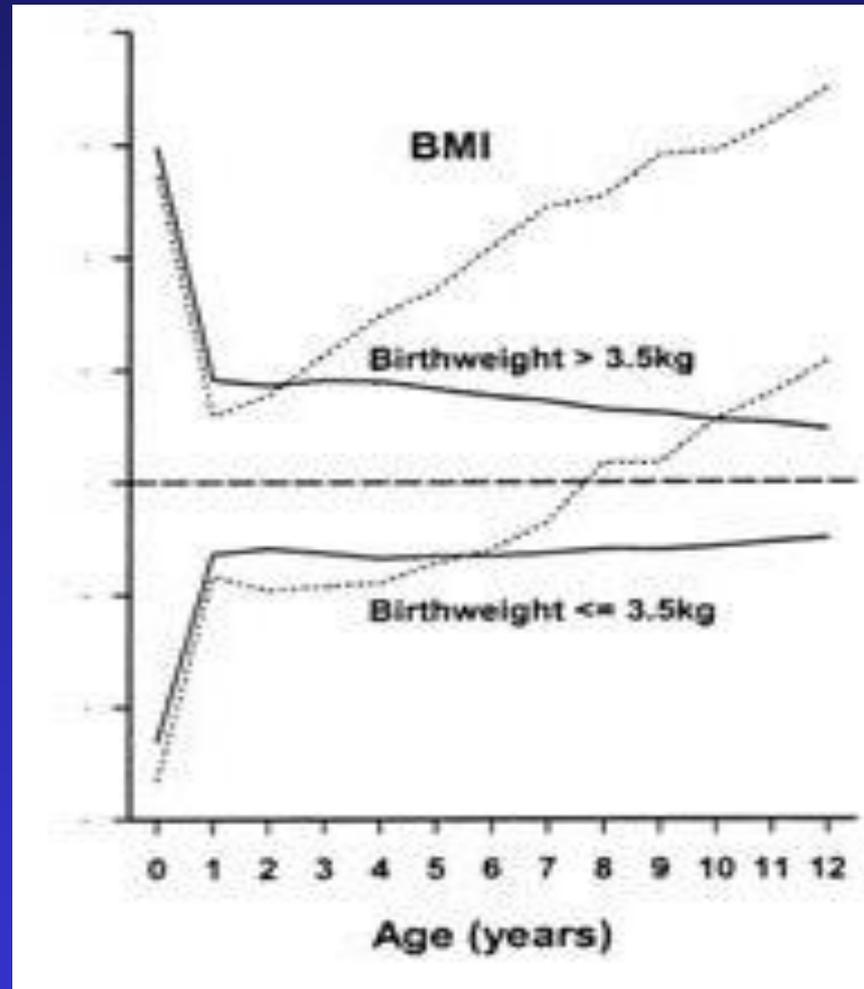
Birthweight, Infant growth & Type-2 diabetes

Mean Z-score

diabetes

(Eriksson et al, Diab Care 2003; 26: 2006-10)
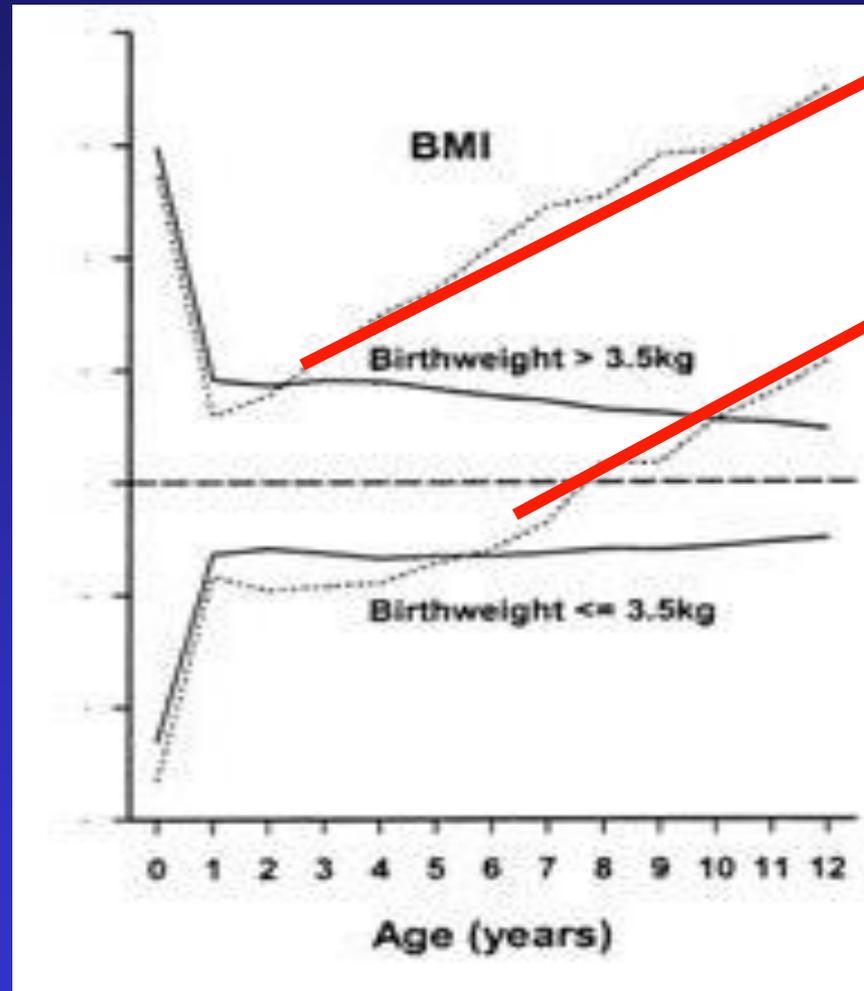
Prevention of impaired outcome

- Prevent overgrowth of the young infant (2-7 yrs)

Prevention

-- Healthy diet

-- Excercise

-- Folic acid

(may prevent epigenetic changes)

(Eriksson; Lillycrop et al, 2005)

So, which infants are likely to develop obesity/diabetes

- Genetic predisposition (thrifty genotype)
- High maternal BMI
- High weight gain in pregnancy
- Macrosomia at birth

Maternal diabetes

- And……excessive weight gain > 2 y of age

Type-1, type-2 diabetes and GDM
which infants have the highest risk of becoming obese during childhood?

LGA at birth

Type-1

Type 2

GDM

Type-1, type-2 diabetes and GDM
which infants have the highest risk of becoming obese during childhood?

	LGA at birth
Type-1	50%
Type 2	35%
GDM	20%

Fetal growth profiles in diabetic pregnancies Head to abdomen circumf. ratio (N. Hammoud et al, UOG 2012)
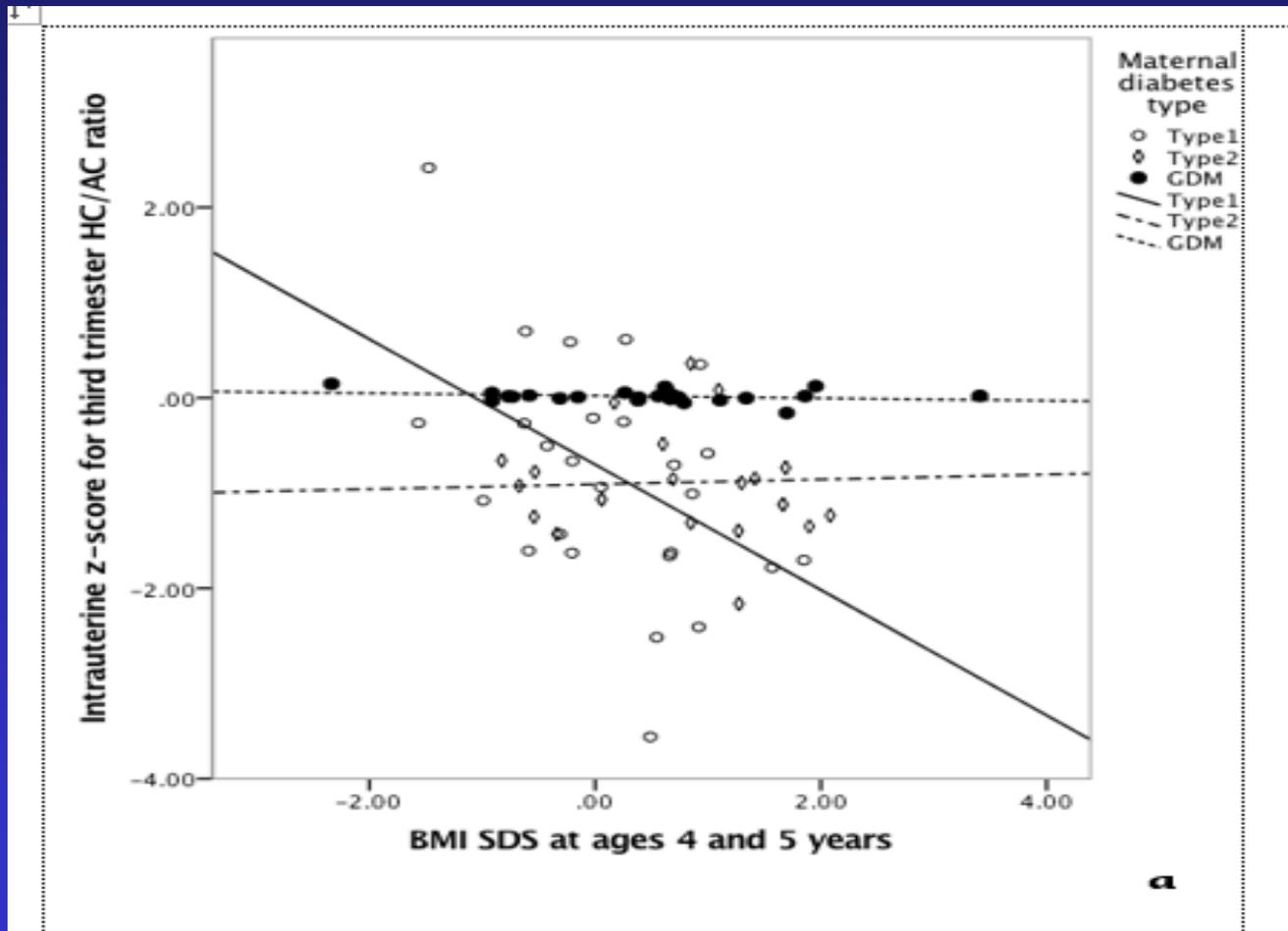
Fetal growth profiles in diabetic pregnancies

Relationship HC/AC ratio with BMI at 4-5 y

Relationship HC/AC ratio with BMI at 4-5 y

And who were the biggest infants at 4-5 y of age?

Hammoud et al, Neonatology in press

Relationship HC/AC ratio with BMI at 4-5 y

And who were the biggest infants at 4-5 y of age?

	type-1	type-2	GDM
Overweight	7%	36%	17%
Obese	0	18%	4%
BMI SDs	+0.15	+1.7	+0.65

Hammoud et al, Neonatology in press

Type-1, type-2 diabetes and GDM
which infants have the highest risk of becoming obese during childhood?

	LGA at birth	Overw 4-5y	BMI SDs at 14y
Type-1	50%	7% (0.15)	
Type 2	35%	36% (1.7)	
GDM	20%	17% (0.65)	

Childhood growth of infants of women with type-1, type-2 and Gest diabetes (Hammoud et al,Ped Res in press)

Figure: (non)-LGA ODM1; ODM2; OGDM. SDS for BMI versus Offspring age (years). Type-2, Type-1. Legend: ODM1 non-LGA, ODM1 LGA, ODM2 non-LGA, ODM2 LGA, OGDM non-LGA, OGDM LGA.
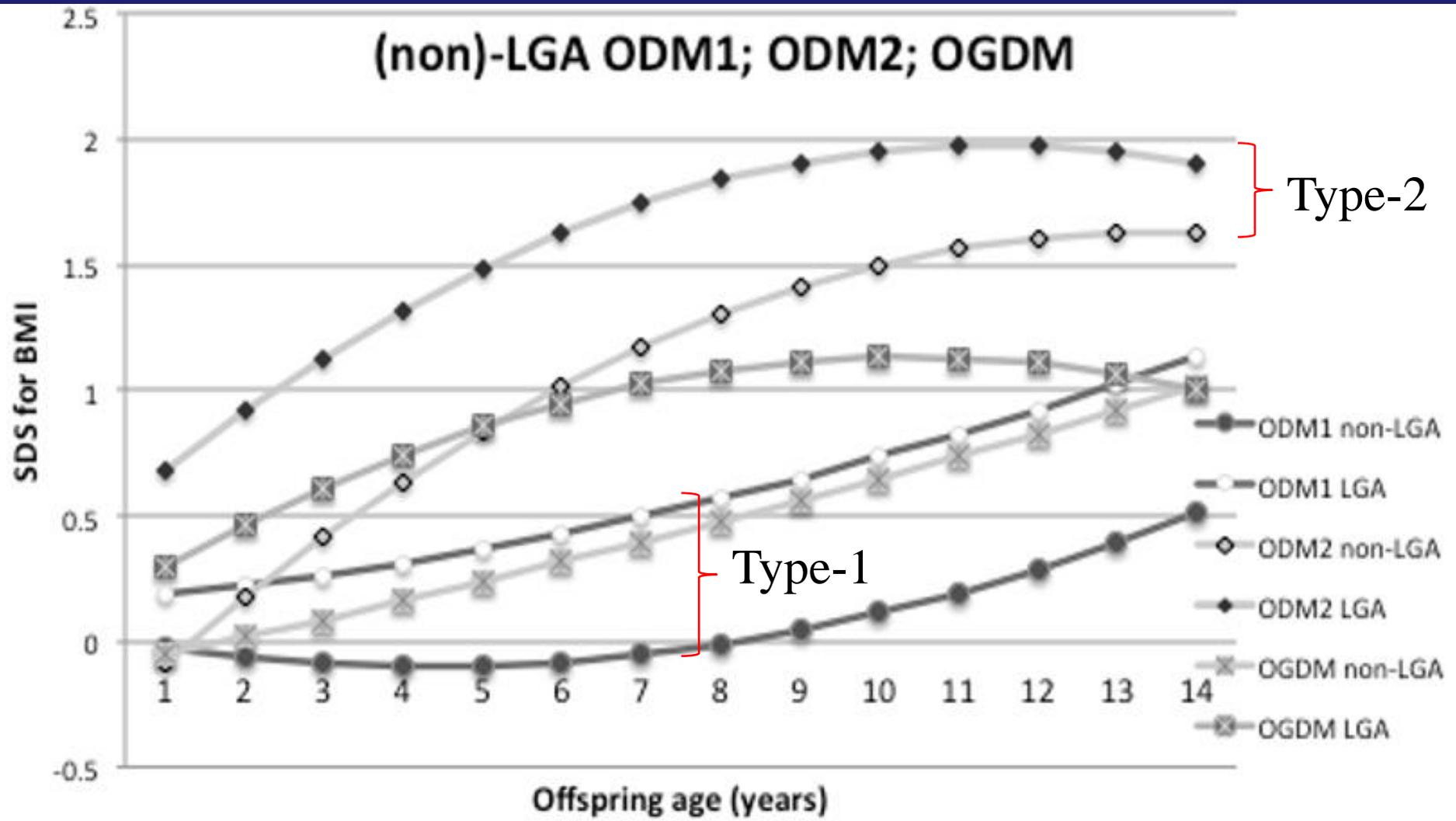
Type-1, type-2 diabetes and GDM
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	LGA at birth	Overw 4-5y	BMI SDs at 14y
Type-1	50%	7% (0.15)	+0.8
Type 2	35%	36% (1.7)	+1.8
GDM	20%	17% (0.65)	+1.1

Childhood growth of infants of women with type-1, type-2 and Gest diabetes (Hammoud et al, Ped Res in press)
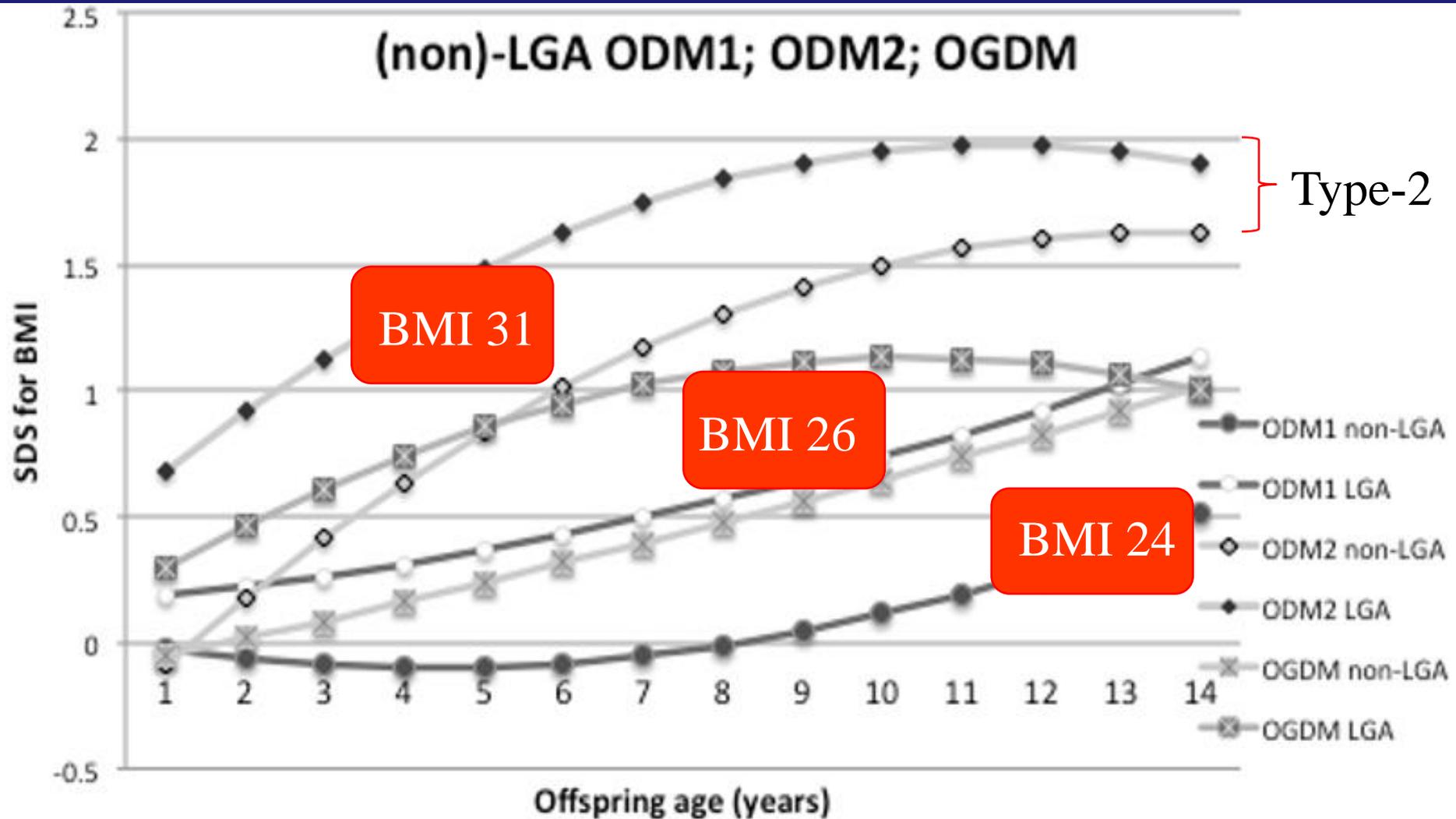
Lifestyle and Nutrition, offspring 10y

	type-1	type-2	GDM
Breakfast>3wk	98%	81%	98%
No snacks	4%	28%	12%
Member sportsclub	90%	67%	84%

Hammoud et al, in preparation

Maternal obesity or GDM; which is the real problem?
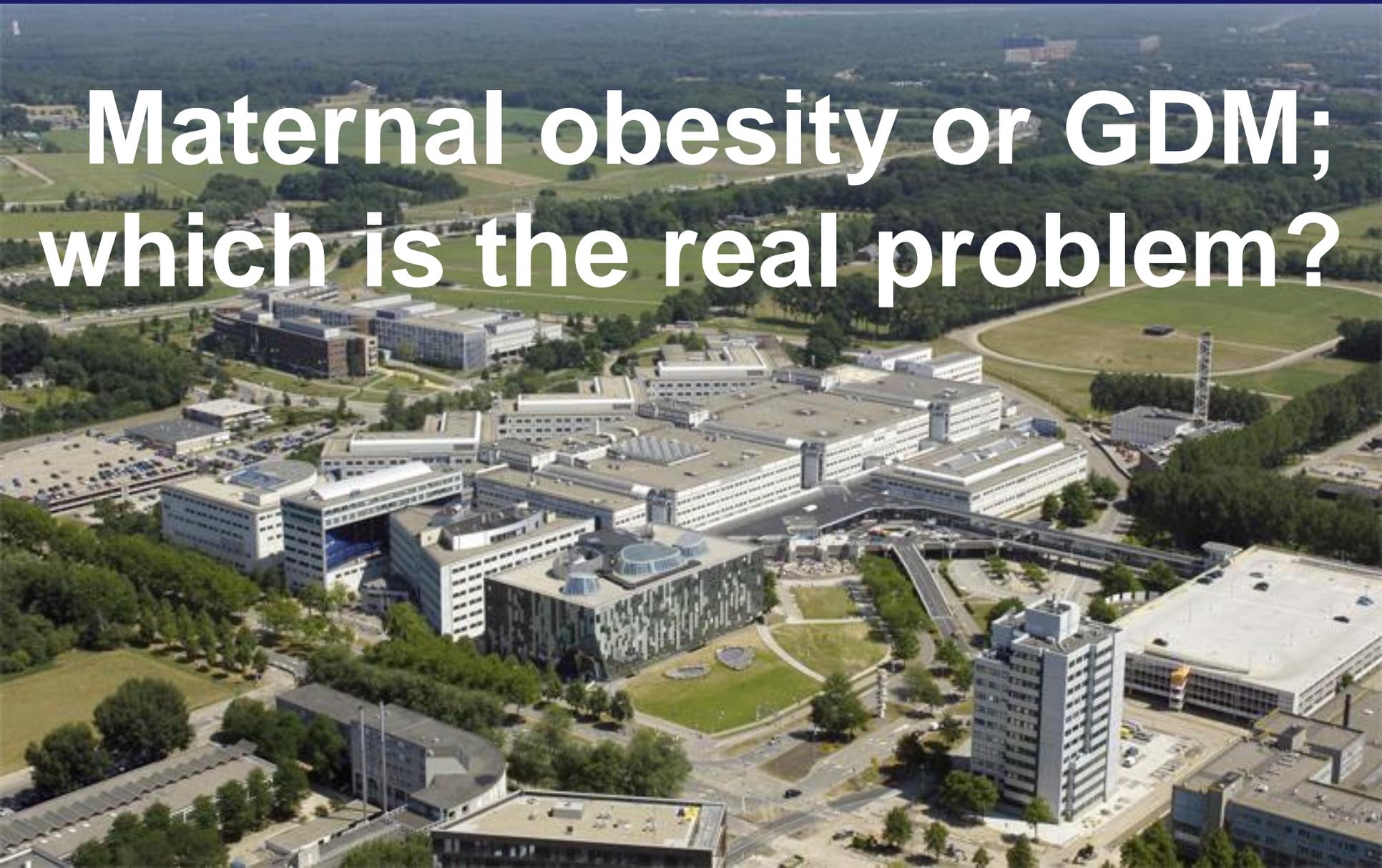
And what about GDM screening?

Should we screen for GDM?

- Treatment improves outcome (screening is therefore useful)

- Mortality
- Birth trauma   } 50% reduction
- LGA
- % CS   (Landon et al, only)

Crowther et al, 2005; n=1000; London et al, 2010, n=958

Outcome after screening is better than outcome following symptoms

	screening	symptoms
• N	175	74
• BMI	30	26
• GA at diagnosis (wks)	27	31
• HbA1c at diagnosis (%)	5.4	5.5
• FAC> 90th centile (%)	33	68
• Birthweight> 90th centile (%)	17	36
• Birthweight > 97.7th centile (%)	5	16

Should we screen for GDM?

- So, screening for GDM in the total population

- Preferably one-step procedure

- At 24-28 wks gestation

Gestational diabetes
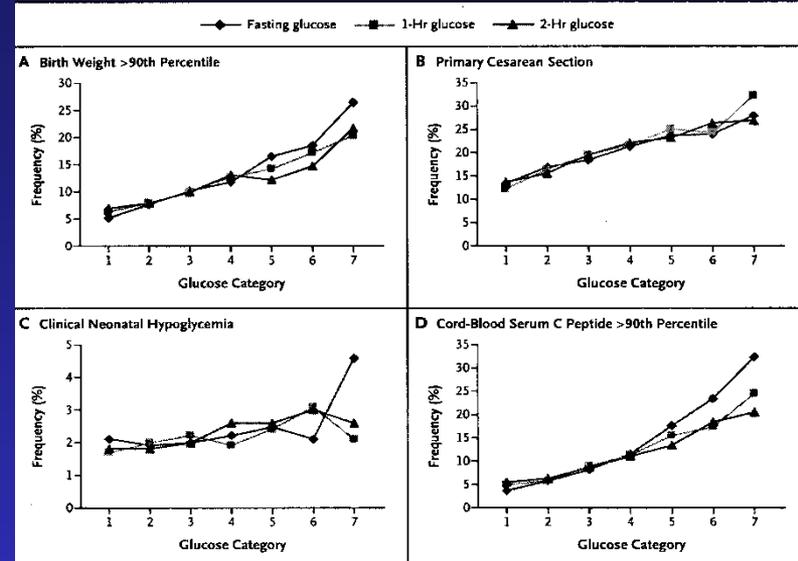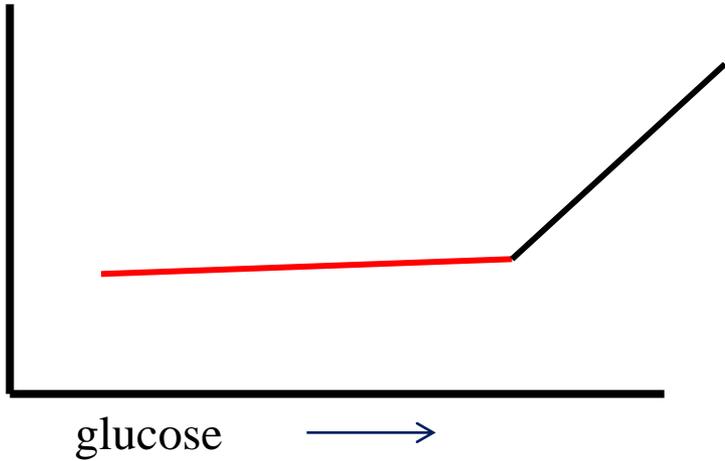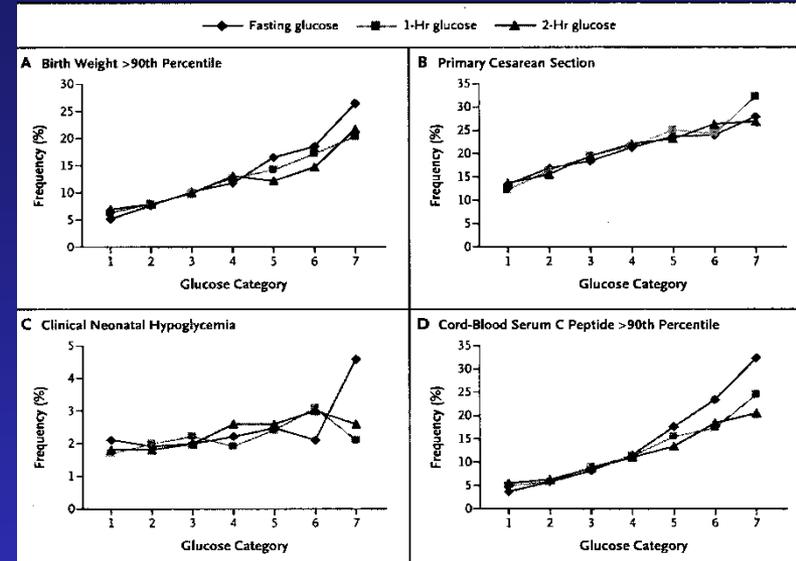
Gestational diabetes

oGTT threshold values will –by definition – be arbitrary, given the linear relationship between glucose values and impaired outcome

Gestational diabetes

75 g OGTT: fasting => 5.1 mmol/l

1 hour => 10.0

2 hour => 8.5

Diagnostic criteria based on 1.75 fold increase in LGA infant

(Metzger et al, Diab Care, 2010;33:676-682)

Prevalence of GDM of

17.8%

75 g OGTT: fasting =>5.3 mmol/l

1 hour => 10.6

2 hour => 9.0

Diagnostic criteria based on 2 fold increase in LGA infant

(E.A.Rian, Diabetologia 2011;54:480-486)

Prevalence of GDM 0f

10.5%

It is the question if are we ready for such an increase in GDM?

- Don't we make the healthy sick

(stop harming the healthy, Moynihan et al, BMJ 2012)

- Does outcome really improve

- Shouldn't we look more for women with risk factors

- Etc

- etc

GDM and Obesity; practical considerations

- Use strict threshold values for obese women (according to IADPSG criteria)

- Use higher values in non-obese women

Use strict oGTT criteria in obese women

- Glucose values in obese women with a normal oGTT are higher than those in women with normal weight, and GDM is usually more severe
- Obesity by itself has a negative effect on outcome
- Obesity and GDM have a synergistic effect on direct outcome
- Diet, treatment and frequent visits may reduce weight gain, which by itself has a positive effect on outcome

Management of the obese patient

- Lose weight before pregnancy

- Healthy lifestyle

- Restrict weight gain during pregnancy (dietician, frequent antenatal visits)

- First trimester screening for unrecognized type-2 diabetes (OGTT or HbA1c)

- Metformin for PE prevention?

- Second trimester OGTT

- Beware of large baby and 3rd trimester onset of GDM

RCTs metformin in Obese non-diabetic women, started in 1st trimester

Author	Inclusion	N	MWG	BW	PE	Weight at 1y
Carlsen 2012	PCO mean BMI 30	258	-1 kg	-	?	+0.5kg
Chiswick 2015	BMI>30 Cauc.only	449	-	-	-	
Syngelaki 2016	BMI>35	400	-3 kg	-	4fold reduction	

Carlsen et al, Pediatrics, 2012; Chiswick et al, Lancet July 2015; Syngelaki et al JEJM, 2016

And what about the development of type-2 diabetes in women who had a GDM during pregnancy?

Incidence of diabetes following GDM
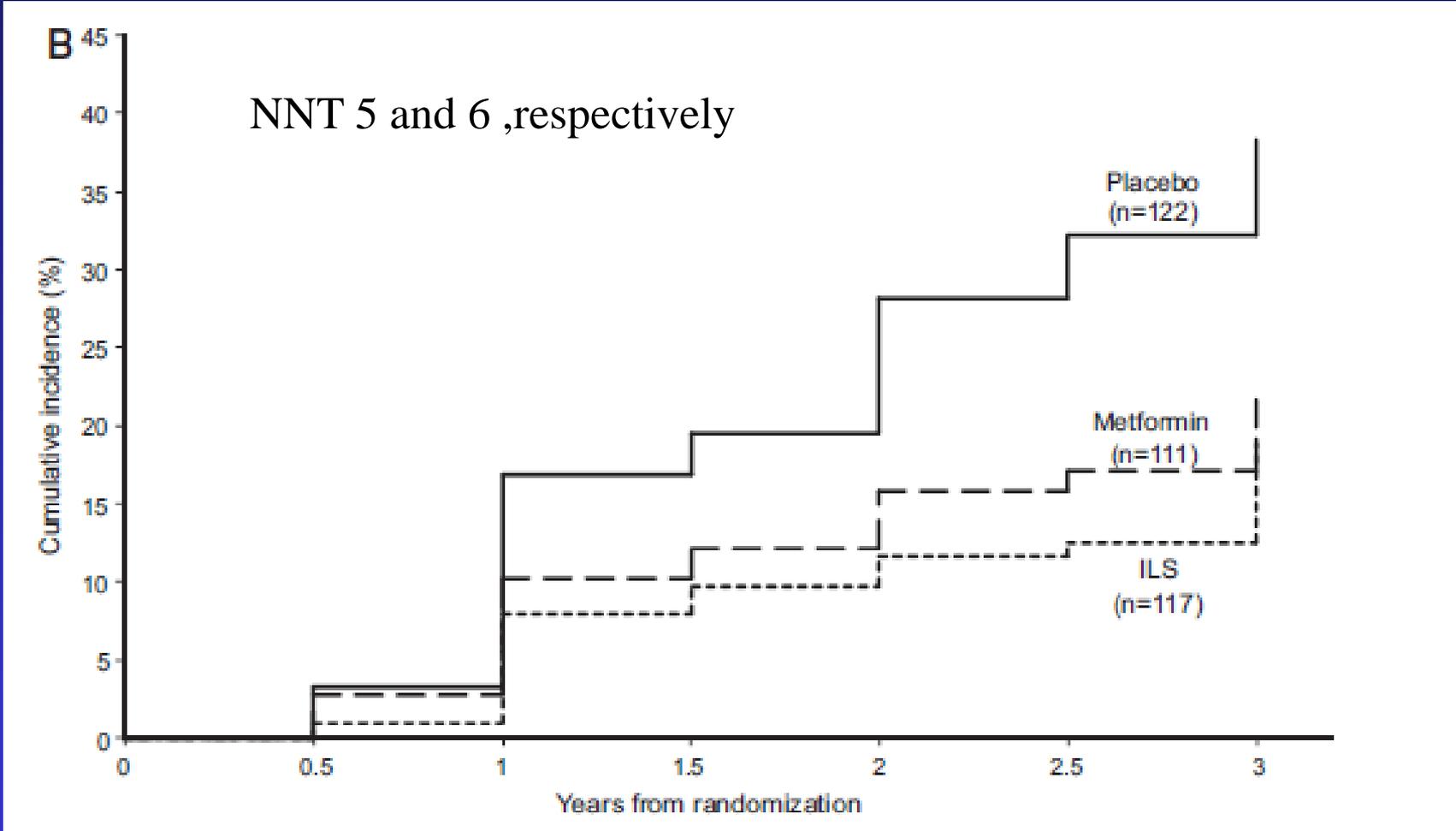
Ratner et al, JCEM 2008

Post partum testing following GDM

- Systemic review; 54 articles

- Postpartum testing on average in 33% of patients (9-71%)

- With proactive patient contact programs: 60% (14-95%)

Carson MP et al, Prim Care Diabetes, Oct 2013

Post partum testing following GDM

- Systemic review; 54 articles

- Postpartum t... patie... ...ntact programs:

So, please arrange an adequate follow-up especially in obese women !!

Carson MP et al, Prim Care Diabetes, Oct 2013

Thank you

Screening for gestational diabetes:

- Yes, the whole population; but that does not happen yet ! (Even in countries with 'universal' screening only 10-90% of women will actually be screened; Jiwani et al JMFNM 2012)

- Tell me how many GDM you want and I will give you the formula

- No clear advantages of a one-step approach

- Use strict criteria in obese women

- Implement an adequate postpartum screening follow-up program in women with GDM

Screening for gestational diabetes:

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- Tell me how many GDM you want and I will give you the formula

- Use strict criteria in obese women

- First trimester risk assessment?

So we may conclude that…….

- oGTT threshold values will –by definition- be arbitrary, given the linear relationship between glucose values and impaired outcome

Which factors affect outcome in offspring

- Genetic predisposition
- Maternal BMI
- Weight gain in pregnancy
- (Gestational) diabetes mellitus
- Macrosomia at birth
- Cesarean Delivery
- Excessive weight gain > 2 y of age
- Socio-economic circumstances

For the time being, however, I guess that big babies are going to stay

And which can we change/influence?

- Genetic predisposition
- Maternal BMI
- Weight gain in pregnancy
- (Gestational) diabetes mellitus
- Macrosomia at birth
- Cesarean Delivery
- Excessive weight gain in infants > 2 y of age
- Socio-economic circumstances

Obesity and GDM

- Both have an (synergistic) effect on early perinatal outcome

- Obesity seems to have the most important effect on long term development of the offspring (especially childhood obesity)

- Consequences for screening and management?

Prepregnancy counseling

- Information to the whole population

Do you want to become pregnant?

Than first lose weight, and than we will tell you were your puppy is……..

Prepregnancy BMI and Gest Weight Gain in relation to childhood obesity
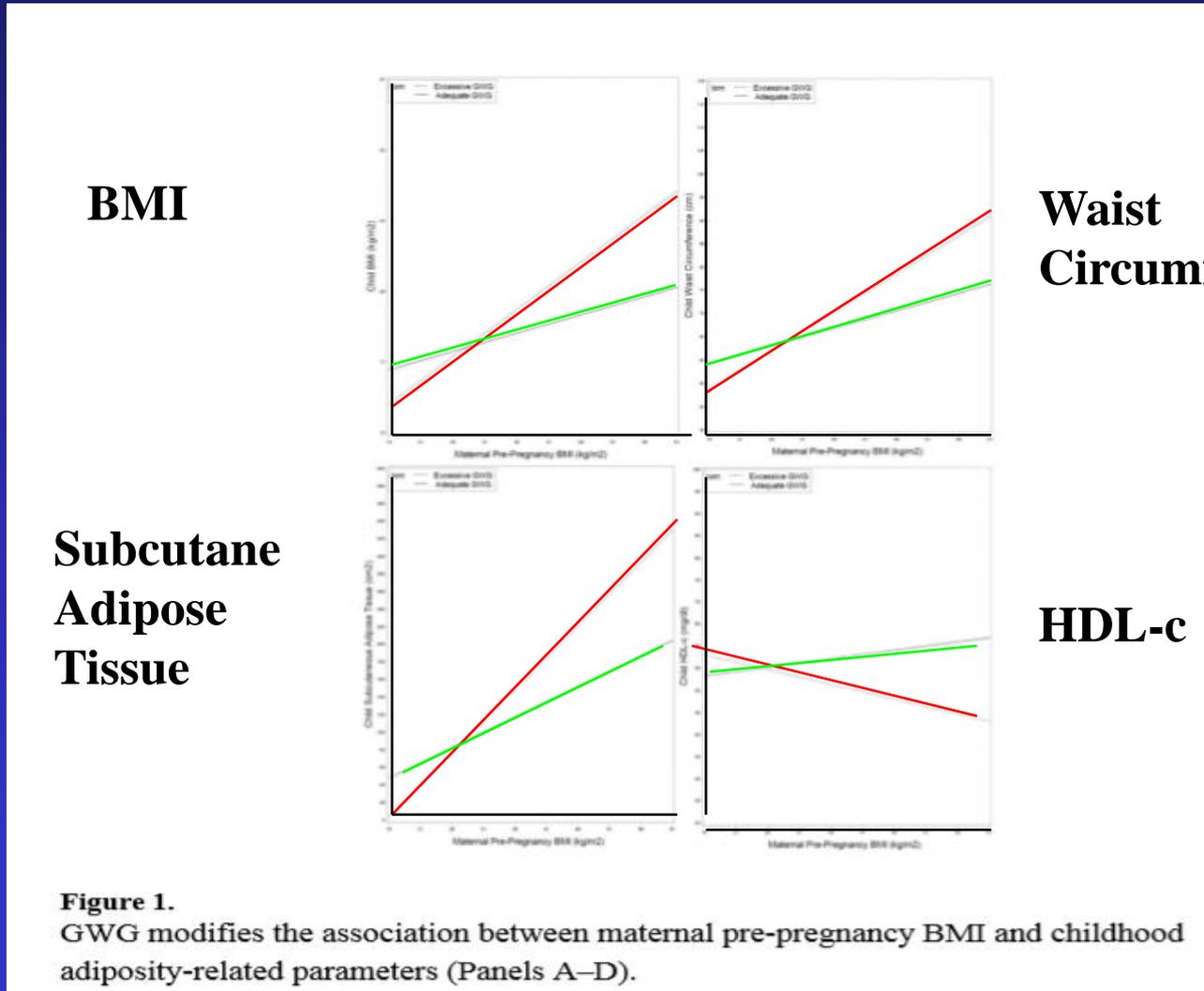
BMI

Waist Circumf

Subcutane Adipose Tissue

HDL-c

Adequate W gain

Excessive W gain

Figure 1.
GWG modifies the association between maternal pre-pregnancy BMI and childhood adiposity-related parameters (Panels A–D).

Kaar et al, P Pediatr, 2014

Prepregnancy counseling

- Information to the whole population

- In case of PCOS: first lose weight and than we will treat you

Prepregnancy counseling

- Information to the whole population

- In case of PCOS: first lose weight and than we will treat you
- Consider bariatric surgery

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- Maternal BMI
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- Maternal BMI
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Childhood obesity in relation to gestational weight gain
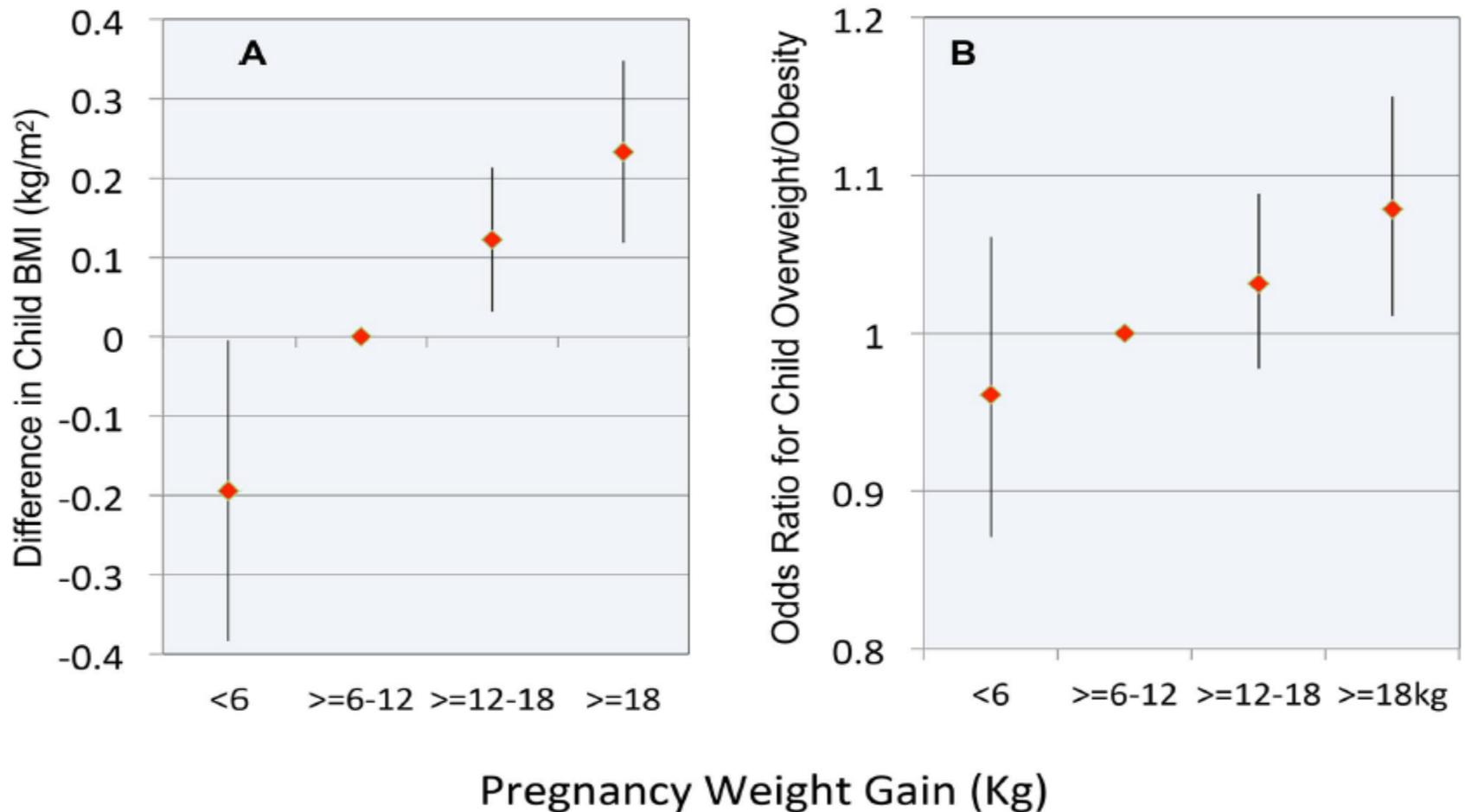
Figure 3. Relationship between pregnancy weight gain and body weight in childhood. (A) Difference in child BMI; (B) OR for child overweight or obesity. Reference range for pregnancy weight gain is ≥6 to 12 kg. Error bars are 95% confidence intervals.
doi:10.1371/journal.pmed.1001521.g003
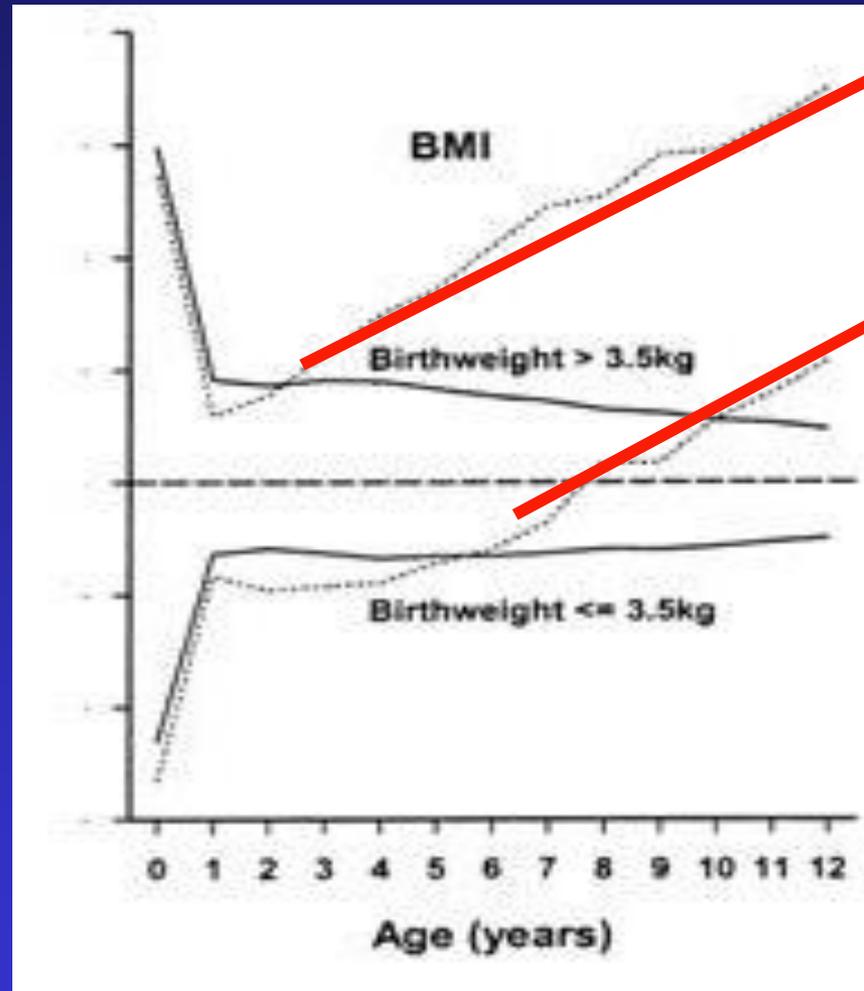
Ludwig et al. PLOS Medicine, Oct 1, 2013

Birthweight, Infant growth & Type-2 diabetes

Mean Z-score

(Eriksson et al, Diab Care 2003; 26: 2006-10)

Childhood obesity in relation to macrosomia at birth and diabetes type

Hammoud et al, in preparation

Childhood obesity in relation to macrosomia at birth and diabetes type

Hammoud et al, in preparation
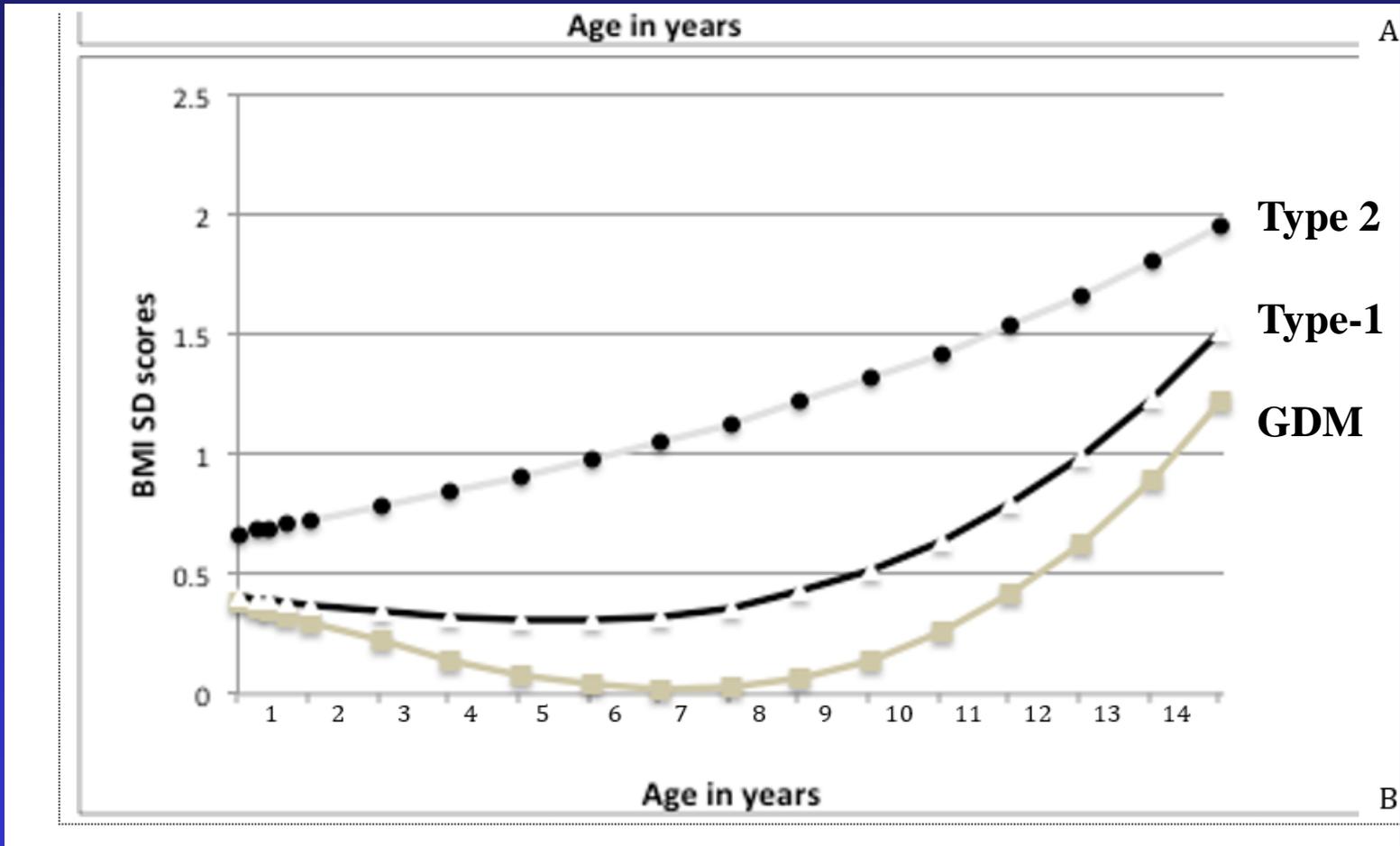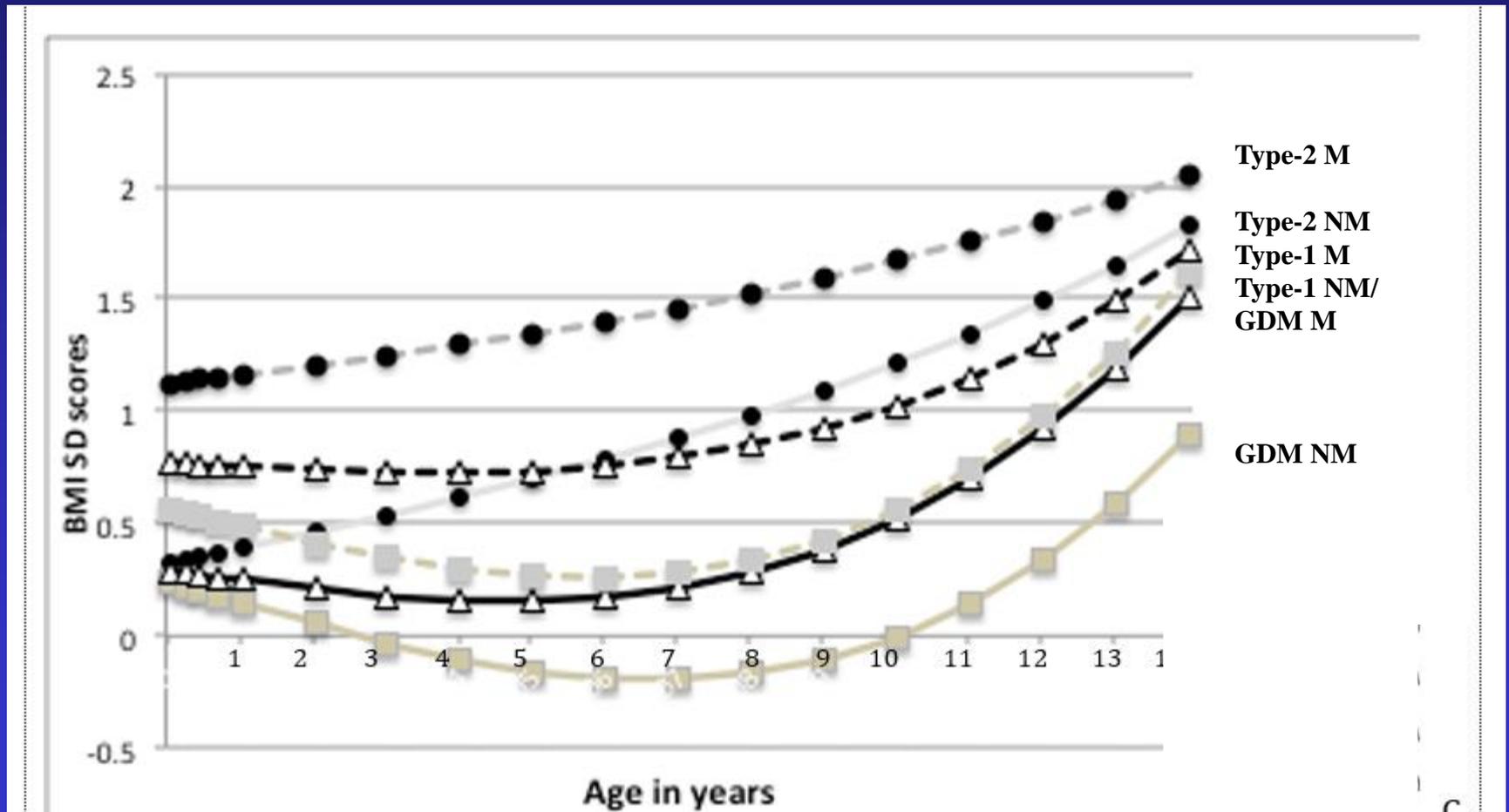
Prevention of impaired outcome

- Prevent overgrowth of the young infant (2-7 yrs)

The descent of Man
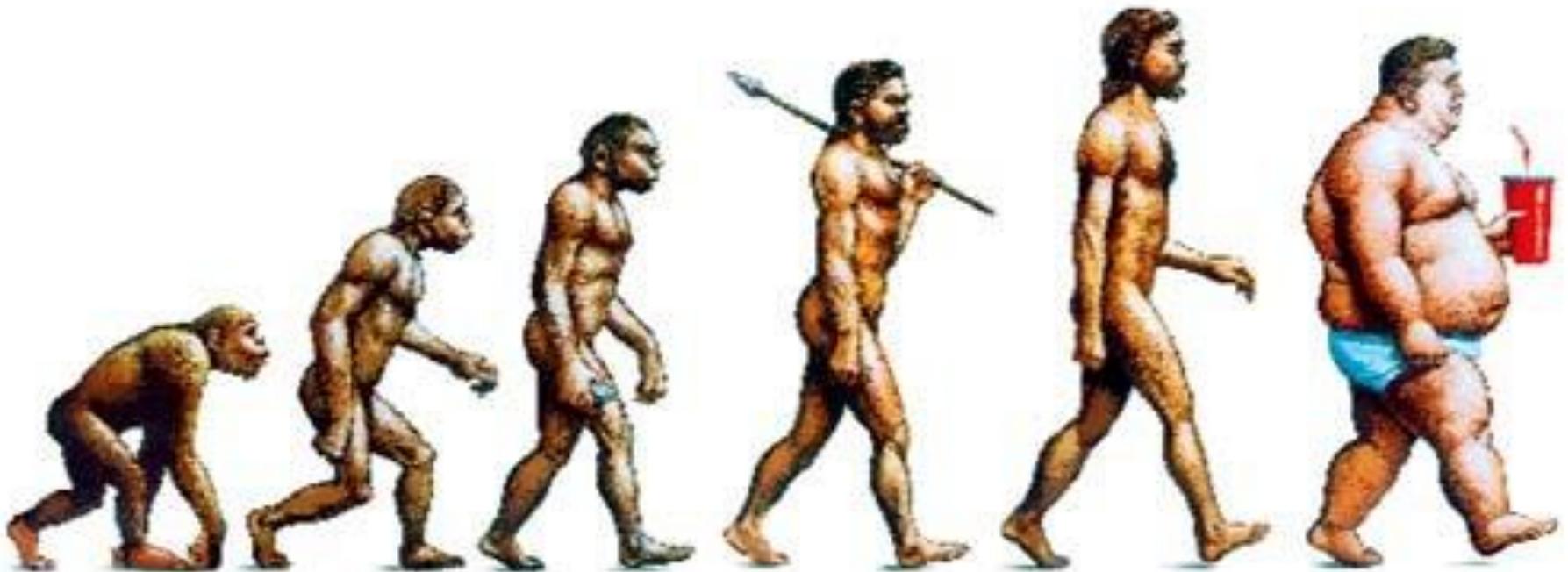
Thank you

Thank you

Incidence of diabetes following GDM
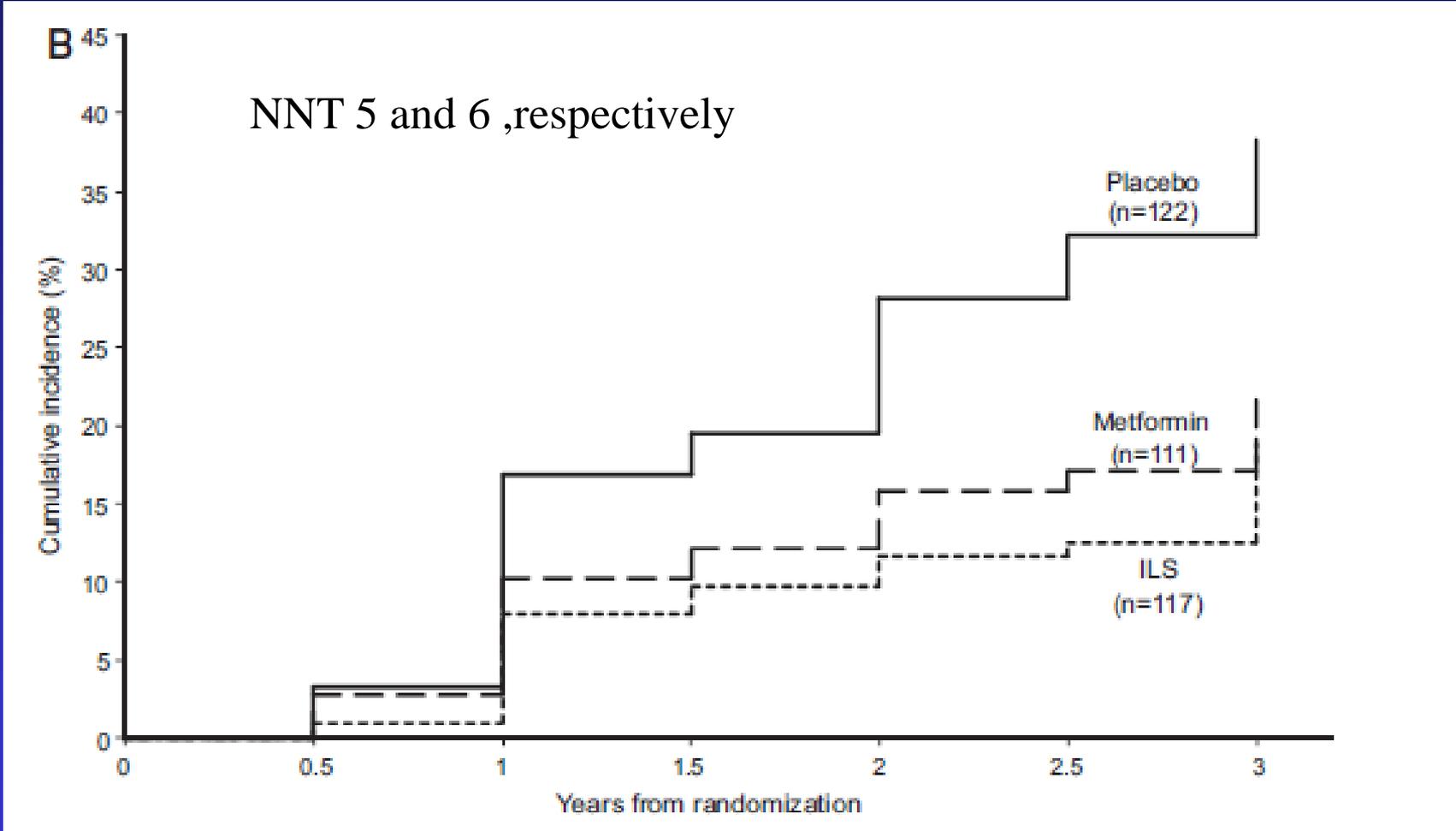
Ratner et al, JCEM 2008

Post partum testing following GDM

- Systemic review; 54 articles

- Postpartum testing on average in 33% of patients (9-71%)

- With proactive patient contact programs: 60% (14-95%)

Carson MP et al, Prim Care Diabetes, Oct 2013

Post partum testing following GDM

- Systemic review; 54 articles

- Postpartum t~~~~~~~~~
  pati~~~~~~~~~~~~~~~~~~~~~~~ntact programs:

In other words, we do not seem ready for an increase in GDM

Carson MP et al, Prim Care Diabetes, Oct 2013

In conclusion

- Obesity/metabolic syndromy increases maternal and perinatal risks

- It also affects long term fetal outcome, either directly or through an increased Cesarean Delivery rate

- Treatment/prevention is difficult and requires a nationwide (gouvermental) approach

Metabolic Syndrome
Syndrome X, Insulin resistance syndrome, CHAOS

with _>3 of the following conditions:

- Abdominal (central obesity)
- Elevated blood pressure
- Elevated fasting plasma glucose
- High serum triglycerides
- Low high-density cholesterol (HDL)

Metabolic Syndrome
Syndrome X, Insulin resistance syndrome, CHAOS

with ≥ 3 of the following conditions:

- Abdominal (central obesity) : BMI>30
- Elevated blood pressure
- Elevated fasting plasma glucose
- High serum triglycerides
- Low high-density cholesterol (HDL)

The Epidemic of Diabesity, 2000 and 2030
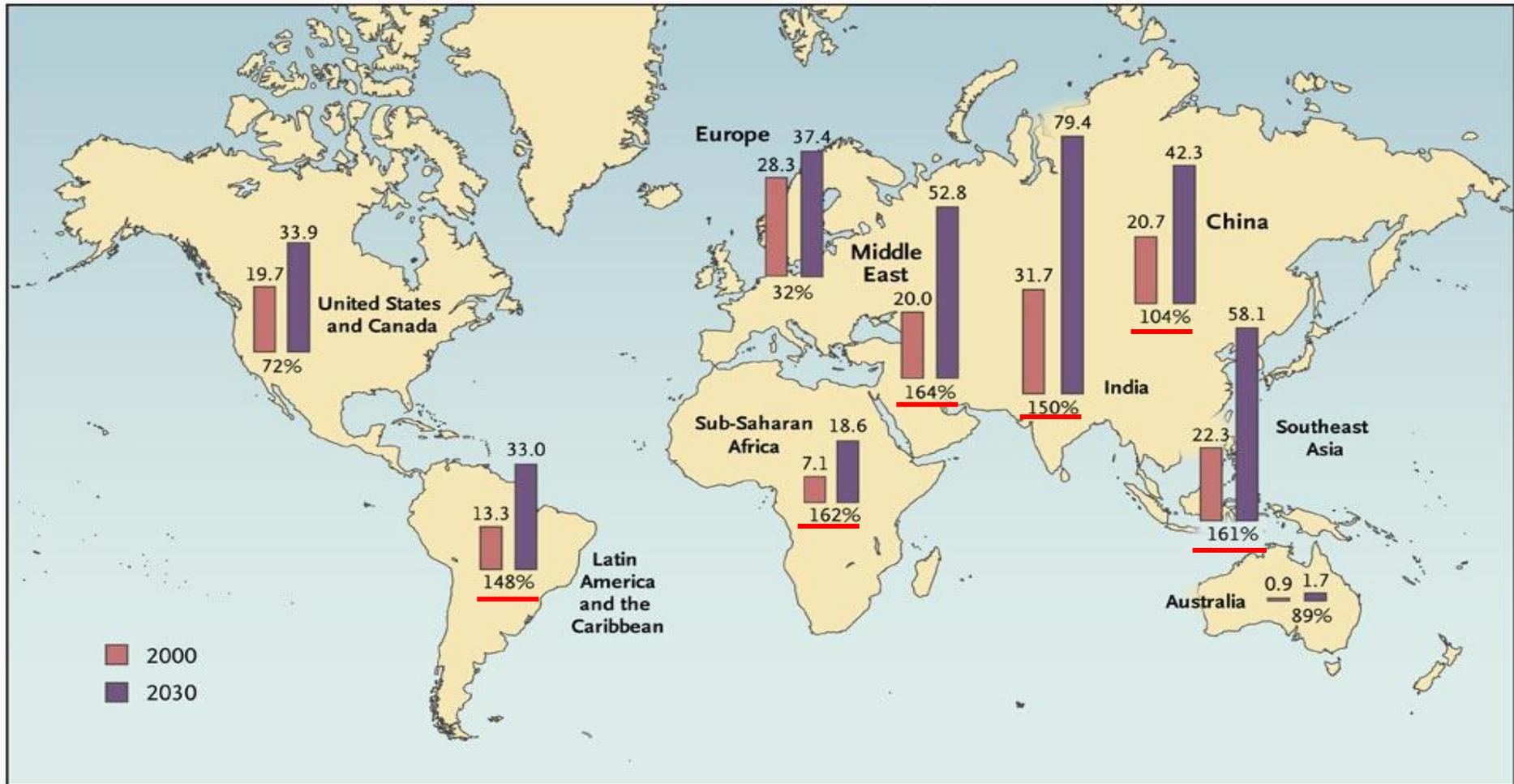
Hossain et al NEJM, 2007
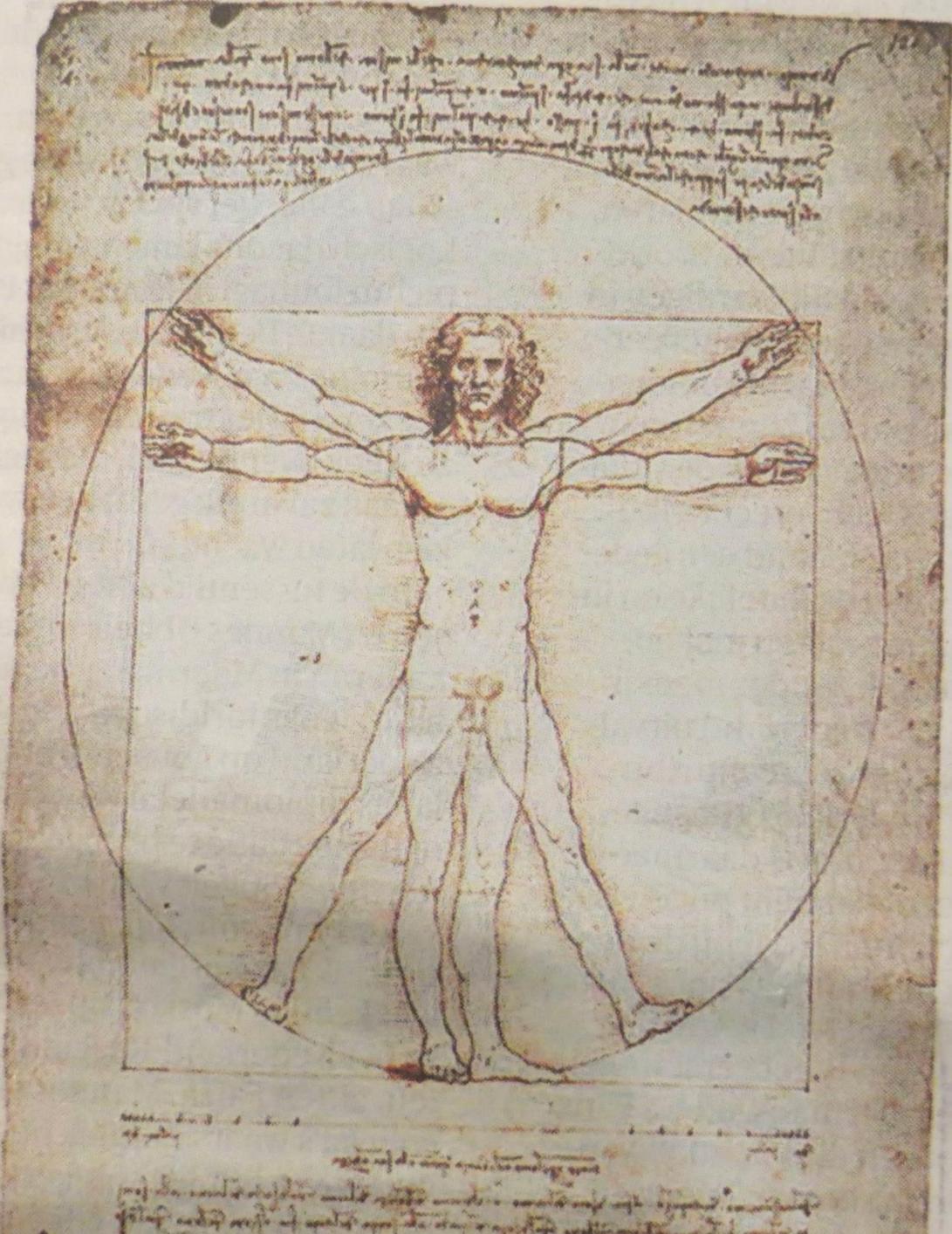
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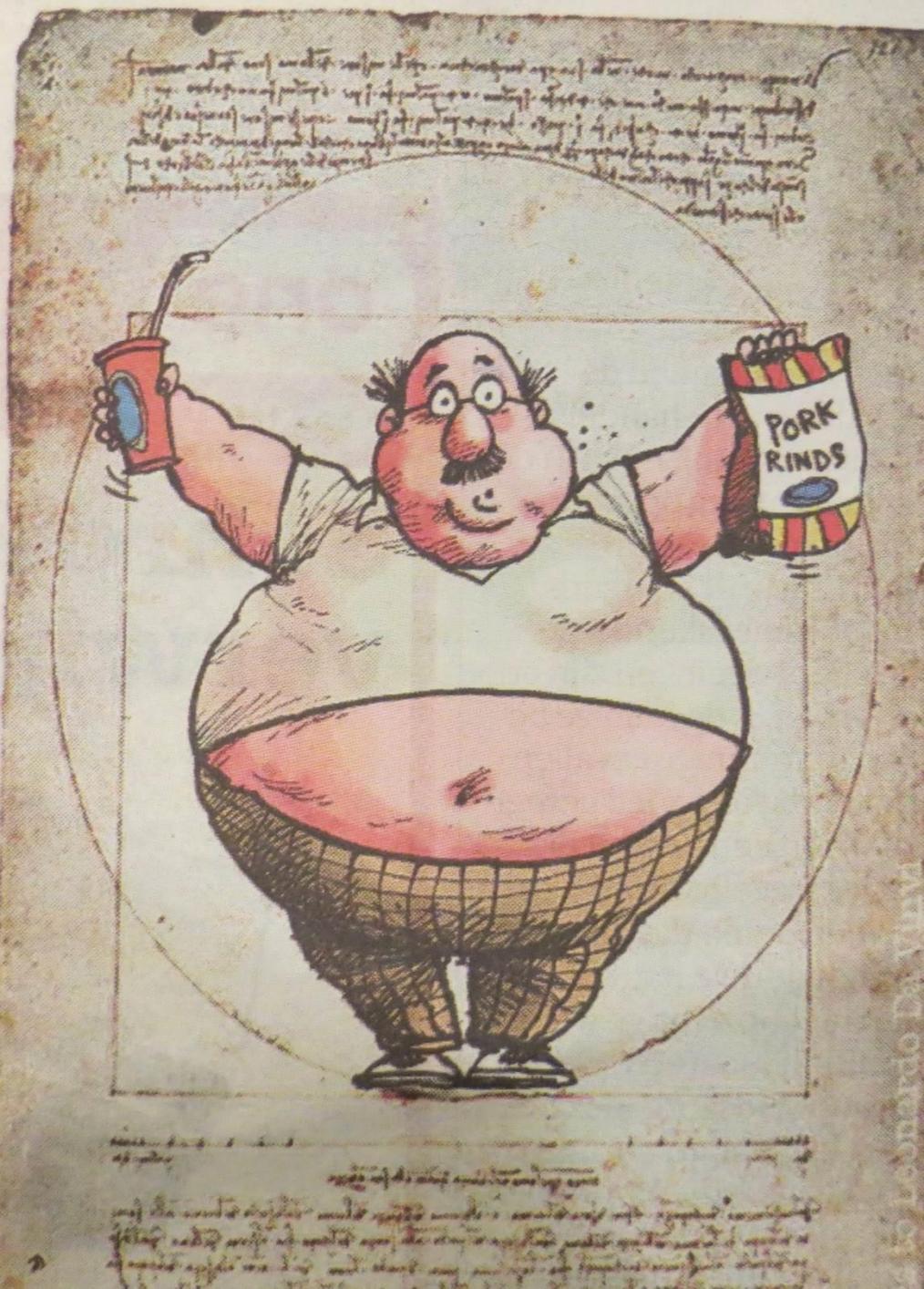
Rosanne Hert
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Birthweight, Infant growth & Type-2 diabetes

Mean Z-score

(Eriksson et al, Diab Care 2003; 26: 2006-10)
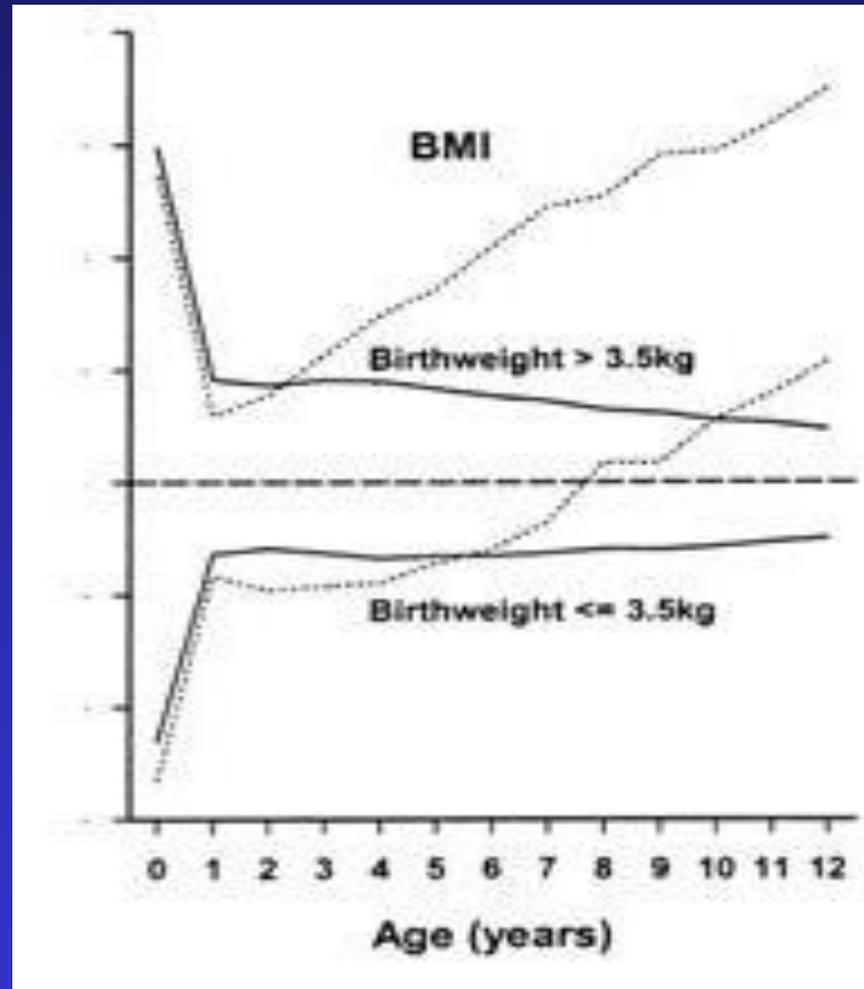
How strict should the oGTT threshold values be?

And should they be similar for obese-/non-obese women

Gerard H.A.Visser

CLINICAL OPINION

OBSTETRICS

Is the evidence strong enough to change the diagnostic criteria for gestational diabetes now?

Gerard H. A. Visser, MD; Harold W. de Valk, MD, PhD

In 2008, the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study group published the results of a large international observational study on the relationship between second-trimester oral glucose tolerance test (oGTT) values and outcome.[1] Unfortunately, but not surprisingly, there was a linear relationship among fasting, 1-hour and 2-hour glucose values, and the frequency of primary cesarean delivery, fetal macrosomia (birth weight >90th centile), clinical neonatal hypo-

The International Association of the Diabetes and Pregnancy Study Groups has proposed new thresholds for oral glucose tolerance test that are based on the large observational Hyperglycemia and Adverse Pregnancy Outcomes study. By using these criteria about 18% of pregnant women will be diagnosed as having gestational diabetes mellitus. The question arises if we are ready for such an enormous increase in gestational diabetes mellitus patients, if outcome would really by using these criteria, and if additional studies are necessary before deciding on new diagnostic thresholds. In this clinical opinion, the pros and cons will be discussed.

Key words: adverse pregnancy outcome, diabetes mellitus, glucose intolerance, metabolic syndrome, oral glucose tolerance test

NIH Consensus Development Conference:

DIAGNOSING GESTATIONAL DIABETES MELLITUS

March 4-6, 2013
Bethesda, Maryland

1. What are the current screening and diagnostic approaches for gestational diabetes mellitus, what are the glycemic thresholds for each approach, and how were these thresholds chosen?

2. What are the effects of various diabetes mellitus screening/diagnostic approaches for patients, providers, and U.S. healthcare systems?

3. In the absence of treatment, how do health outcomes of mothers who meet various criteria for gestational diabetes mellitus and their offspring compare with those who do not?

4. Does treatment modify the health outcomes of mothers who meet various criteria for gestational diabetes mellitus and their offspring?

5. What are the harms of treating gestational diabetes, and do they vary by diagnostic approach?

6. Given all of the above, what diagnostic approach(es) for gestational diabetes mellitus should be recommended, if any?

7. What are the key research gaps in the diagnostic approach of gestational diabetes mellitus?

7. What are the key research gaps in the diagnostic approach of gestational diabetes mellitus?

The panel identified the following research needs for GDM diagnosis:

- Evaluate diagnostic thresholds associated with an adverse outcome of 2.0 in the HAPO study as opposed to 1.75
- Determine whether women, normal in a two-step strategy and abnormal in the IADPSG model, benefit from treatment (RCT?)
- Conduct cost-benefit analyses
- Conduct research to understand patient preferences
- Study the impact of GDM treatment on care utilization
- Assess lifestyle interventions and effects of obesity
- Assess impact that a label of GDM may have on future reproductive career
- Assess long-term outcome of GDM on offspring
- Assess interventions to decrease subsequent signs of metabolic syndrome, diabetes and cardiovascular disease in women with GDM

7. What are the key research gaps in the diagnostic approach of gestational diabetes mellitus?

The panel identified the following research needs for GDM diagnosis:

- Evaluate diagnostic thresholds associated with an adverse outcome of 2.0 in the HAPO study as opposed to 1.75
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Too early to adopt the stringent IADPSG oGTT criteria for universal screening

- Assess long-term outcome of GDM on offspring
- Assess interventions to decrease subsequent signs of metabolic syndrome, diabetes and cardiovascular disease in women with GDM

Pregnancy Weight Gain and Childhood Body Weight: A Within-Family Comparison

David S. Ludwig[1]*, Heather L. Rouse[2], Janet Currie[3]

1 New Balance Foundation Obesity Prevention Center, Boston Children's Hospital, Boston, Massachusetts, United States of America, 2 Arkansas Center for Health Improvement, University of Arkansas for Medical Sciences, Little Rock, Arkansas, United States of America, 3 Center for Health and Wellbeing, Princeton University, Princeton, New Jersey, United States of America

Abstract

Background: Excessive pregnancy weight gain is associated with obesity in the offspring, but this relationship may be confounded by genetic and other shared influences. We aimed to examine the association of pregnancy weight gain with body mass index (BMI) in the offspring, using a within-family design to minimize confounding.

Methods and Findings: In this population-based cohort study, we matched records of all live births in Arkansas with state-mandated data on childhood BMI collected in public schools (from August 18, 2003 to June 2, 2011). The cohort included 42,133 women who had more than one singleton pregnancy and their 91,045 offspring. We examined how differences in weight gain that occurred during two or more pregnancies for each woman predicted her children's BMI and odds ratio (OR) of being overweight or obese (BMI$\geq$85th percentile) at a mean age of 11.9 years, using a within-family design. For every additional kg of pregnancy weight gain, childhood BMI increased by 0.0220 (95% CI 0.0134–0.0306, $p<0.0001$) and the OR of overweight/obesity increased by 1.007 (CI 1.003–1.012, $p=0.0008$). Variations in pregnancy weight gain accounted for a 0.43 kg/m^2 difference in childhood BMI. After adjustment for birth weight, the association of pregnancy weight gain with childhood BMI was attenuated but remained statistically significant (0.0143 kg/m^2 per kg of pregnancy weight gain, CI 0.0057–0.0229, $p=0.0007$).

Conclusions: High pregnancy weight gain is associated with increased body weight of the offspring in childhood, and this effect is only partially mediated through higher birth weight. Translation of these findings to public health obesity prevention requires additional study.

Please see later in the article for the Editors' Summary.

No data on maternal BMI

Lowest risk of SGA/LGA, preterm delivery

6.500 obese women, California

Weight gain	Class 1	Class 2	Class 3
< 2.2 kg			X (Black women)
2.2-5			X (white women)
5-9		x	
9.1-13.5	x		

Bodnar et al, Am J Clin Nutr, 2010

Lowest risk of SGA/LGA, preterm delivery

6.500 obese women, California

Weight gain	Class 1	Class 2	Class 3

With an increase in Preterm delivery in case of weight loss, in all 3 categories

Bodnar et al, Am J Clin Nutr, 2010

Adjusted effects of gestational weight loss, according to maternal BMI; Bavaria, n=445.000

BMI:	normal	overwt	Obese I	II	III
• PE	-	-	-	⬇	⬇
• Em CS	-	⬇	⬇	-	⬇
• PT del	⬆	⬆	-	-	-
• SGA	⬆	⬆	⬆	⬆	(1.3)
• LGA	-	-	-	⬇	⬇
• PNMort	3.1*	1.6	1.4	1.7	0.92

Beijerlein et al, BJOG 2010; * sign, corrected, but not for PTB

Adjusted effects of gestational weight loss, according to maternal BMI; Bavaria, n=445.000

| BMI:	normal	overwt	Obese I	II	III

> The association of GWL with a decreased risk of pregnancy complications appears to be outweighed by increased risk of prematurity and SGA in all but obese class III mothers

-

(1.3)

- PNMort   3.1*   1.3   1.25   1.65   0.88

Beijerlein et al, BJOG 2010; * sign, corrected, but not for PTB

- Nog te includeren:

- Baric surgery

- Beperkte gewichtstoename tijdesn zwangerschap; lange termijn gevolgen sterke weight gain tijdends zwangerschap

- Metformine- gewichtsloss

Antenatal interventions for overweight or obese pregnant women: a systematic review of RCTs
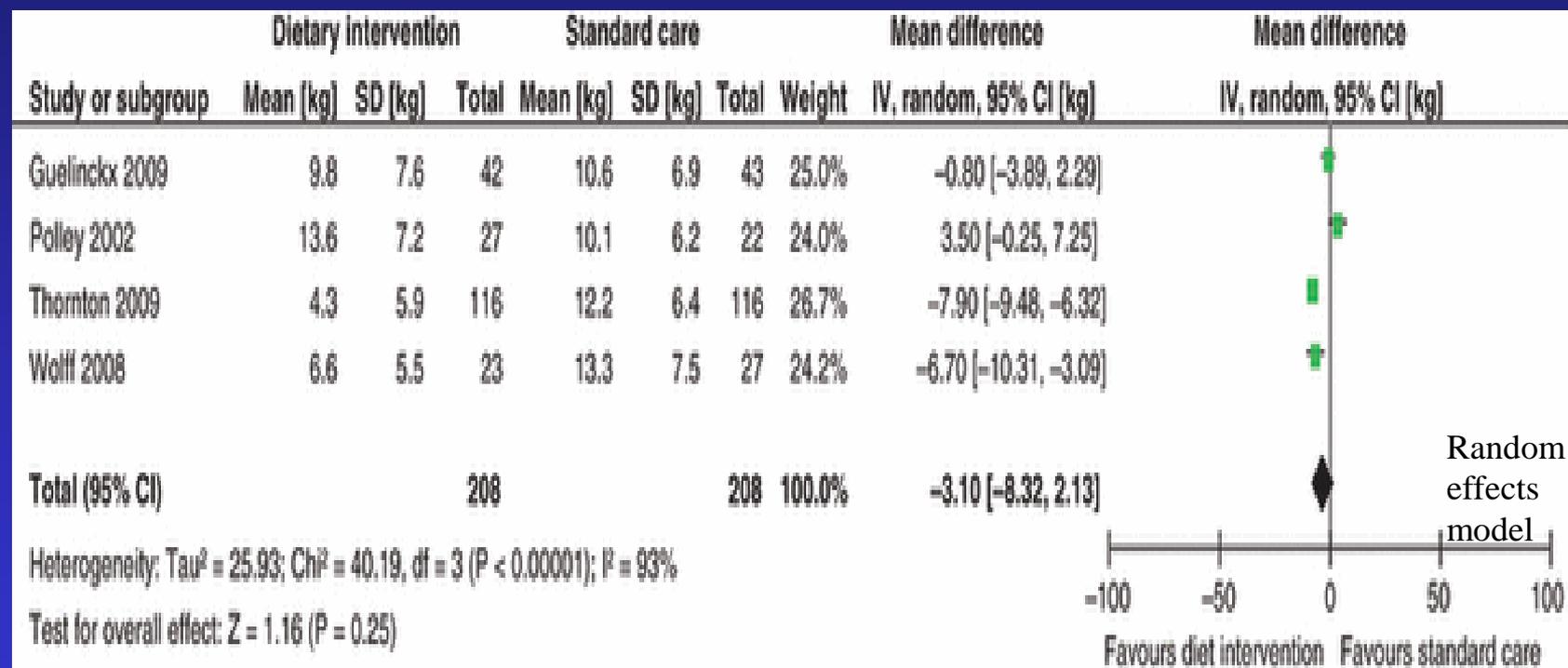
Adjusted effects of gestational weight loss, according to maternal BMI; Bavaria, n=445.000

Dataset of 710.000 singleton deliveries in Bavaria (2000-2007)

Gest Weight Loss   Normal WG   Excessive WG

Underweight > 18 kg

Normal weight >16 kg

Overweight > 11.5 kg

Obese > 9 kg

Beijerlein et al, BJOG 2010; adjusted for Pregest diab.,f.sex, parity, mat age and preterm delivery

Adjusted effects of gestational weight loss, according to maternal BMI; Bavaria, n=445.000

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Beijerlein et al, BJOG 2010; adjusted for Pregest diab.,f.sex, parity, mat age and preterm delivery

The potential hazards of GWL cannot be underestimated and the practice cannot be recommended

Dodd & Robinson, Evid Based Med, Aug 2011

Commentary to the German study

Antenatal interventions for overweight or obese pregnant women: a systematic review of randomised trials
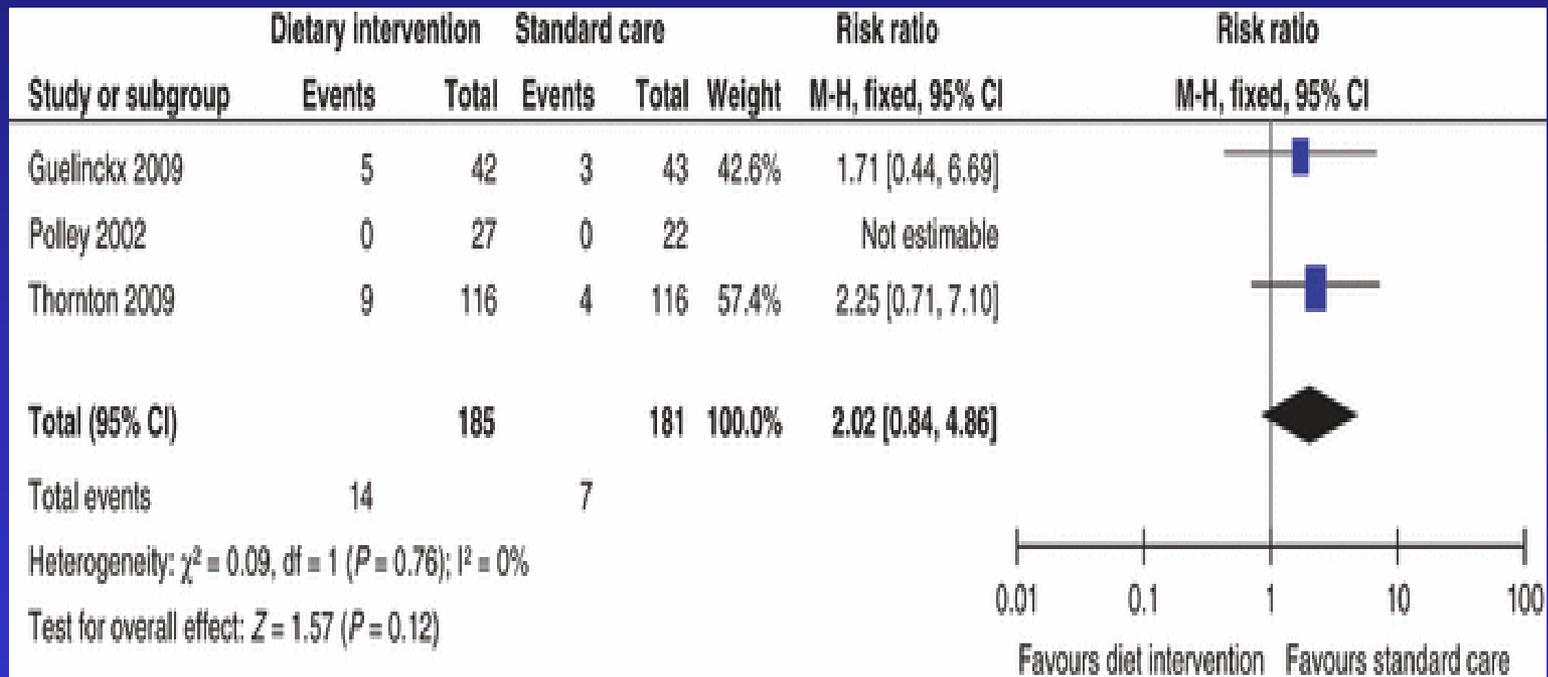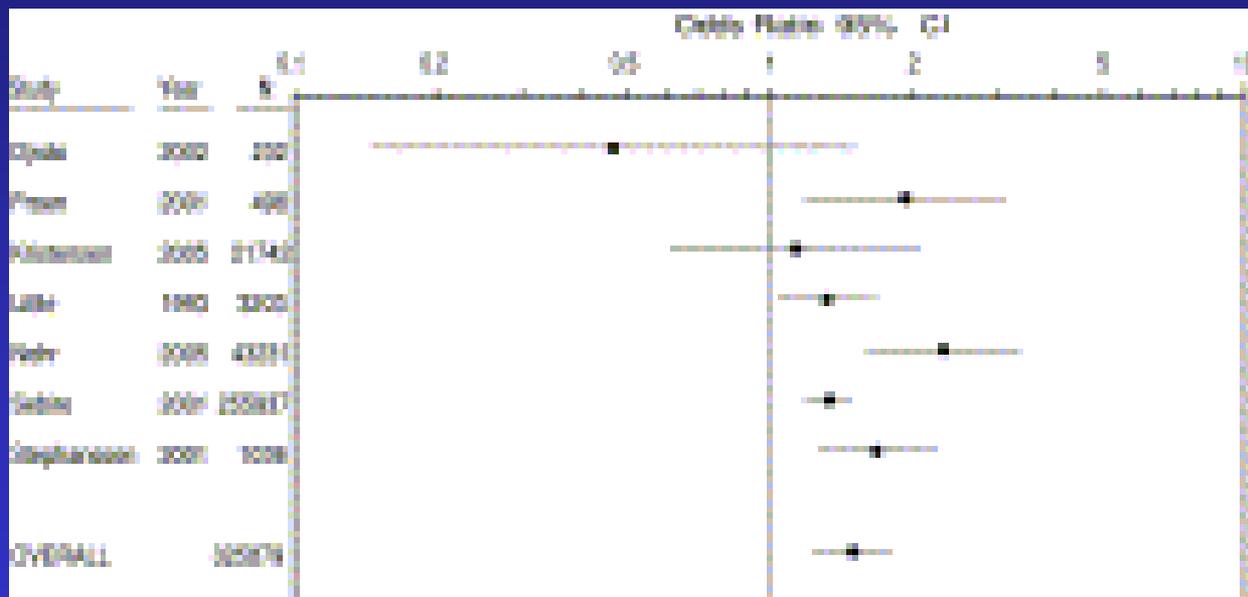
It used to be quiet on the GDM front

- GDM a diagnosis still looking for a disease
- Just another routine test to tell 2.3% of pregnant women that they have a disease
- GDM is the mere interpretation of a laboratory test
- Antenatal scare, not care

Liu et al, 2000; Odent 2008

Treatment of GDM improves outcome

- Mortality
- Birth trauma   } 50% reduction
- LGA
- % CS   (Landon et al, only)

Crowther et al, 2005; n=1000; London et al, 2010, n=958

HAPO
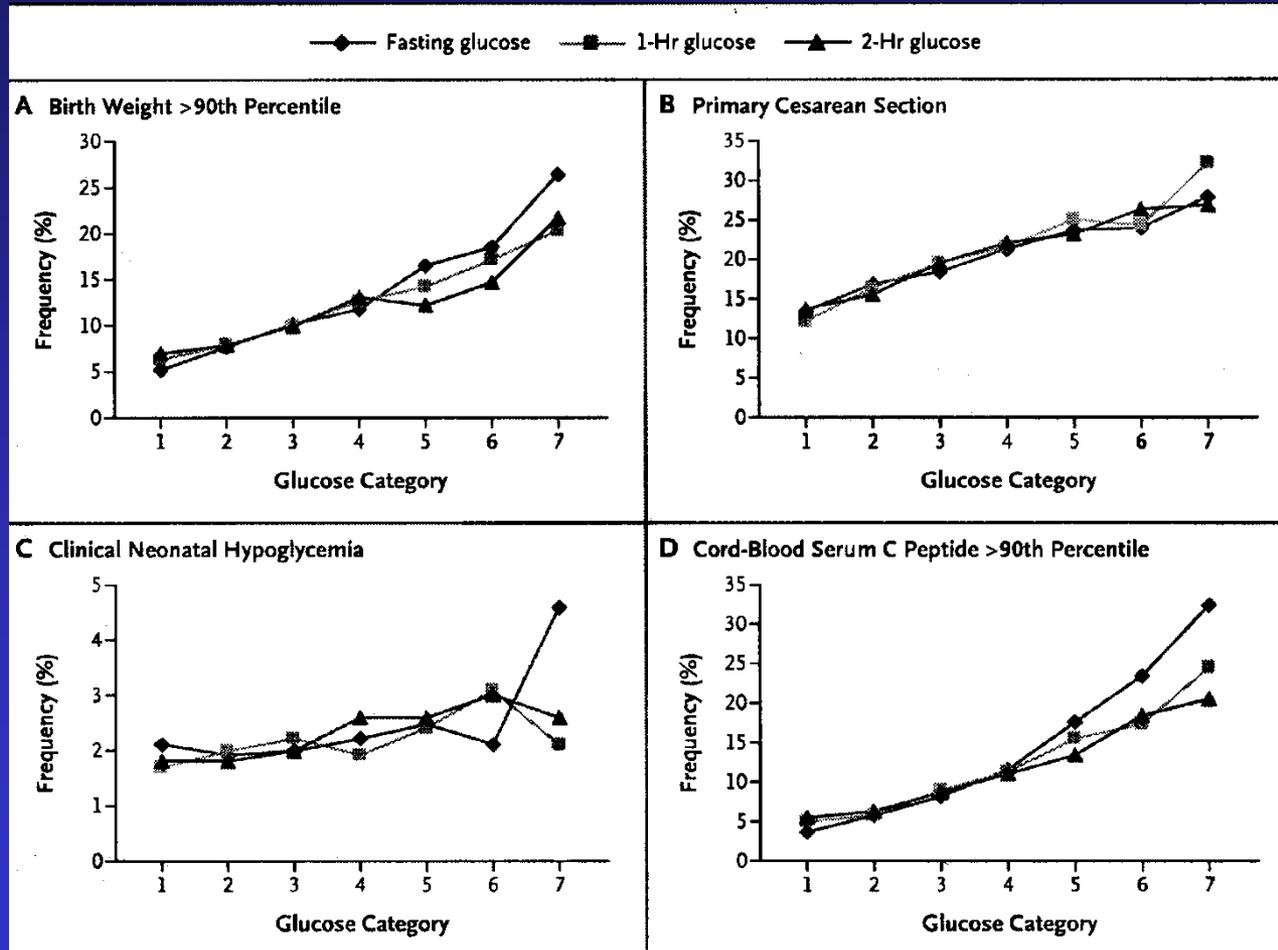
Gestational diabetes according to the IADPSG

75 g OGTT: fasting => 5.1 mmol/l

1 hour => 10.0

2 hour => 8.5

Diagnostic criteria based on 1.75 fold increase in LGA infant

(Metzger et al, Diab Care, 2010)

Prevalence of GDM of

17.8%

'Preventing overdiagnosis: how to stop harming the healthy' Moynihan et al, BMJ 2012

Drivers for overdiagnosis:

- Technological changes detecting even smaller abnormalities
- Commercial and professional vested interests
- Conflicting panels producing expanded disease definitions and writing guidelines
- Legal incentives that punish underdiagnosis but not overdiagnosis
- Health system incentives favoring more tests and treatments
- Cultural belief that more is better

Gestational diabetes

75 g OGTT: fasting => 5.1 mmol/l

                   1 hour => 10.0

                   2 hour => 8.5

Diagnostic criteria based on 1.75 fold increase in LGA infant

(Metzger et al, Diab Care, 2010;33:676-682)

Prevalence of GDM of

17.8%

75 g OGTT: fasting =>5.3 mmol/l

                   1 hour   => 10.6

                   2 hour =>   9.0

Diagnostic criteria based on 2 fold increase in LGA infant

(E.A.Rian, Diabetologia 2011;54:480-486)
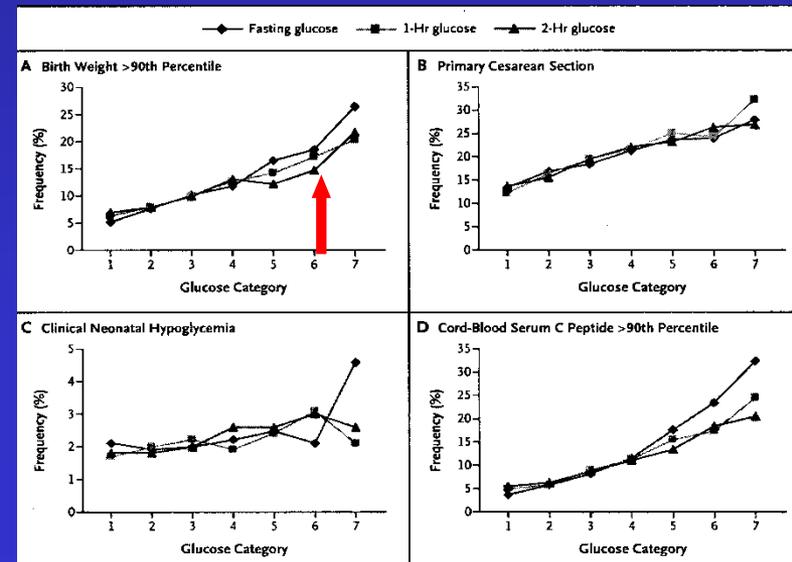
Change diagnostic criteria for GDM?

TABLE 1

Arguments in favor and against use of International Association of Diabetes and Pregnancy Study Groups threshold glucose values for diagnosing gestational diabetes mellitus

Arguments in favor

- Previous oGTT thresholds were set in such a way that about 2.5% of population would classify as GDM, irrespective of relationship of glucose values with prerinatal outcome

- Striking increase in obesity and type 2 diabetes in general population may well correspond to GDM incidence of about 20%

- Treatment of GDM improves perinatal outcome

- Treatment of GDM is generally easy with insulin treatment in only 8-20% of women

- Adequate diagnosis is cost-effective

Arguments against

- oGTT has poor reproducibility

- Even with very strict threshold values, only a minority of fetal macrosomia will be identified

- GDM is related to childhood obesity, but mainly in case of maternal obesity

- Overdiagnosis of GDM may well result in overtreatment

- Stricter oGTT criteria will result in increasing workload

GDM, gestational diabetes mellitus; *oGTT*, oral glucose tolerance test.

Visser. Is evidence strong enough to change diagnostic criteria for gestational diabetes now? Am J Obstet Gynecol 2012.

Change diagnostic criteria for GDM?

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Visser & de Valk, AJOG, 2012

Change diagnostic criteria for GDM?

Arguments in favor

√ - Previous oGTT thresholds were set in such a way that about 2.5% of population would classify as GDM, irrespective of relationship of glucose values with prerinatal outcome

- Striking increase in obesity and type 2 diabetes in general population may well correspond to GDM incidence of about 20%

- Treatment of GDM improves perinatal outcome

√ - Treatment of GDM is generally easy with insulin treatment in only 8-20% of women

- Adequate diagnosis is cost-effective

Change diagnostic criteria for GDM?

6% GDM; Obesity 10 to 30%
Odds ratio for GDM= 3-4

Overall incidence GDM 10.4%

Arguments in favor

- Previous oGTT thresholds were se... classify as GDM, irrespective of relationship of glucose values with prerinatal outcome

- Striking increase in obesity and type 2 diabetes in general population may well correspond to GDM incidence of about 20%

Yes, but also for very mild cases??

- Treatment of GDM improves perinatal outcome

- Treatment of GDM is generally easy wit...

- Adequate diagnosis is cost-effective

Only if post delivery care would reduce the incidence of diabetes in these women, or if PE and CSs would be reduced by 0.5 and 2.7%, respectively (Werner et al, Diab Care 2012; Mission et al, AJOG 2012

Visser & de Valk, AJOG, 2012

Change diagnostic criteria for GDM?

Arguments against

- oGTT has poor reproducibility

- Even with very strict threshold values, only a minority of fetal macrosomia will be identified

- GDM is related to childhood obesity, but mainly in case of maternal obesity

- Overdiagnosis of GDM may well result in overtreatment

- Stricter oGTT criteria will result in increasing workload

GDM, gestational diabetes mellitus; oGTT, oral glucose tolerance test.

Visser. Is evidence strong enough to change diagnostic criteria for gestational diabetes now? Am J Obstet Gynecol 2012.

Metabolic syndrome in 175 infants age 7-11, according to birth weight and GDM
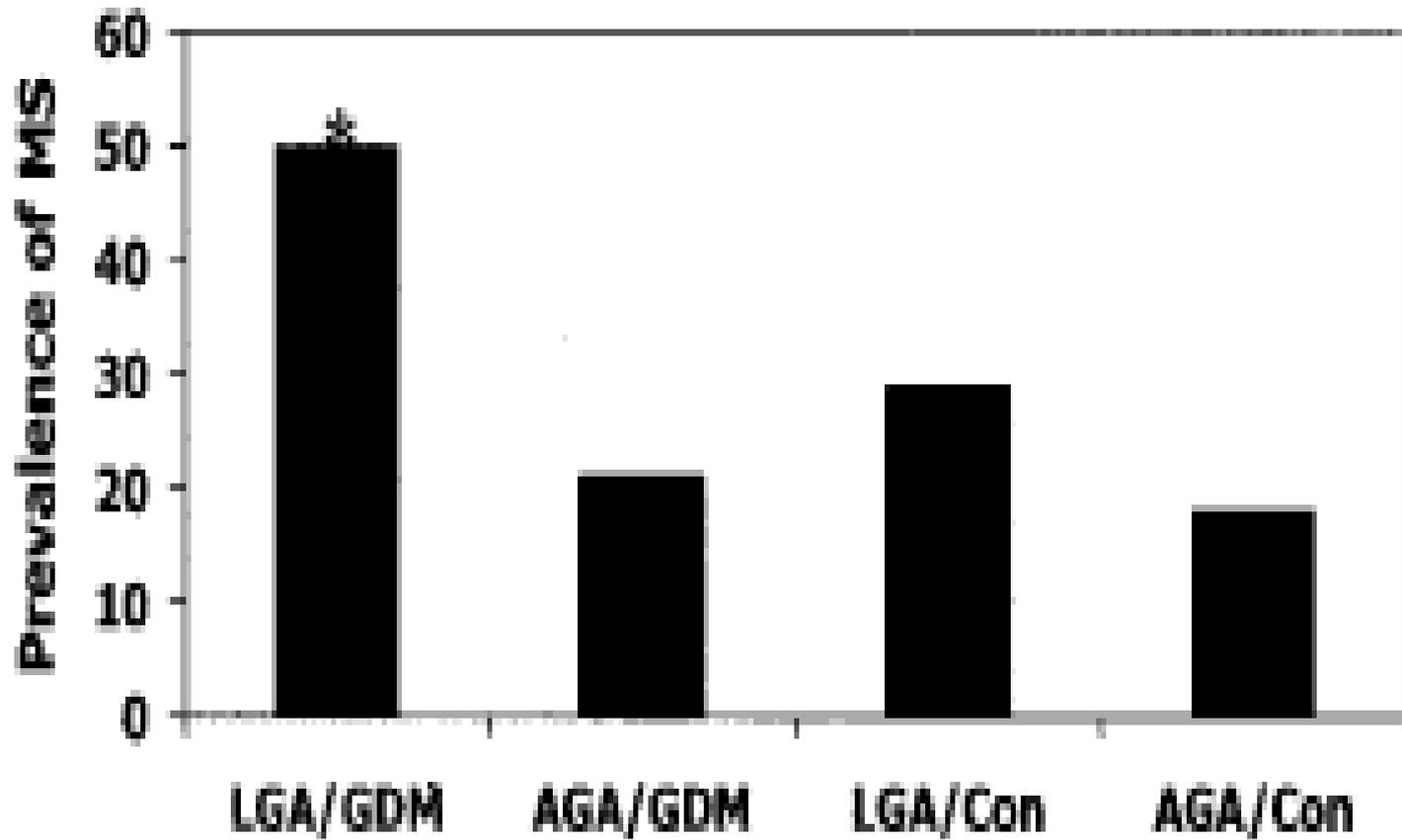
Boney, Pediatrics 2005

Obesity and GDM

- Obesity seems to have the most important effect on long term development of the offspring (especially childhood obesity)

Adopt the IADPSG oGTT threshold values

- You want to be on the safe side, but you realise that you will most likely overtreat the 'healthy'.

- Moreover you realise that the oGTT has a poor reproducibility, whereby GDM still may emerge during the 3rd trimester

Adopt the 'Ryan' oGTT threshold values (based on 2-fold increase in LGA)

- You realise that GDM has gone up due to an increase in maternal obesity

- However, you consider evidence insufficient for treatment of very mild increases of glucose, apart from that in obese women

- You are prepared to participate in a RCT treating half of the women with glucose values in between both diagnostic threshold values and stratifying for BMI

Study the safety of oral antidiabetic drugs

Metformin: a new drug to kill the 'dandelion root'
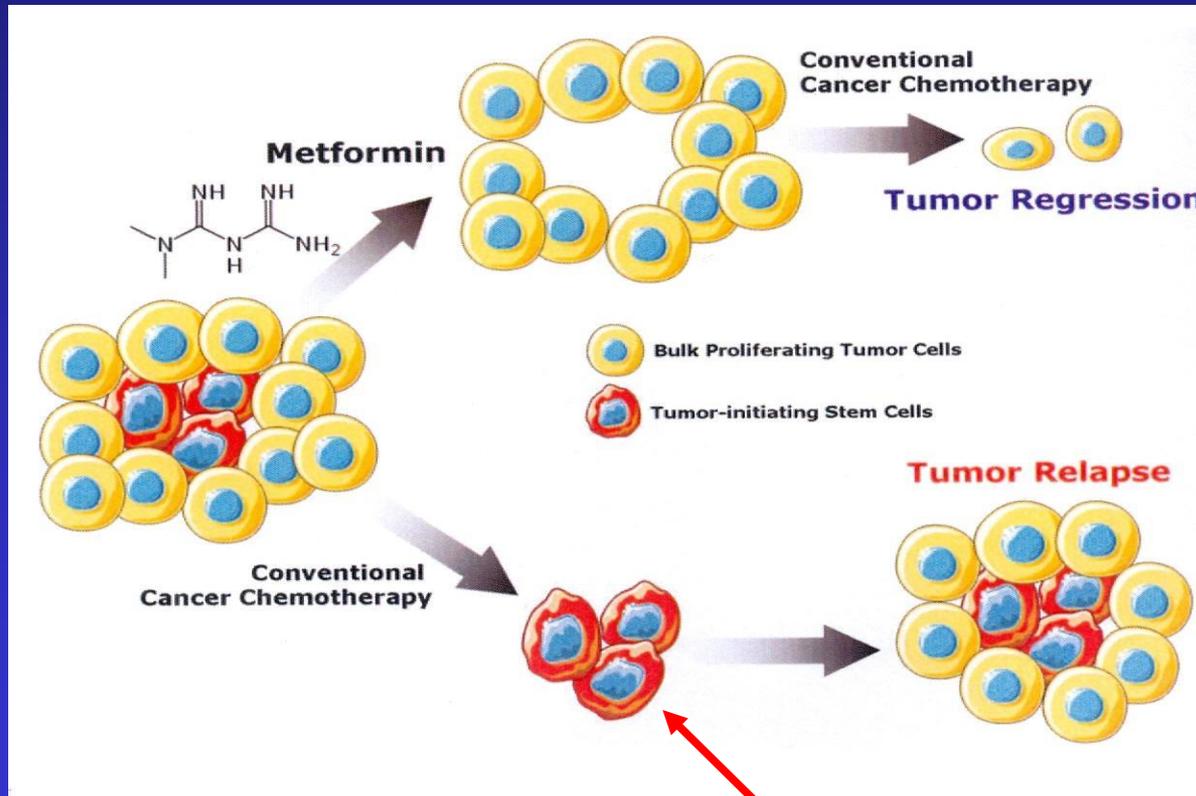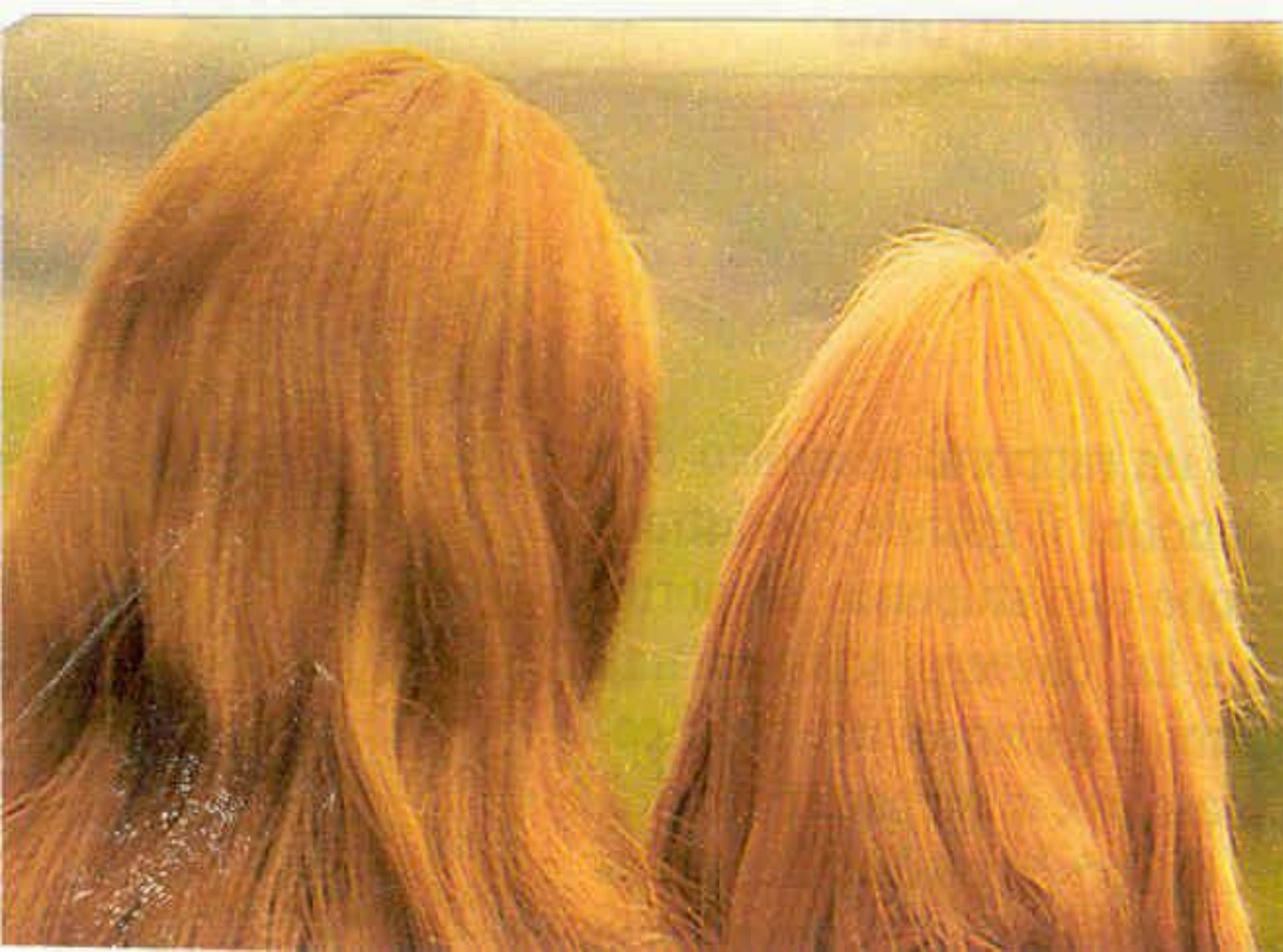
Martin-Castello et al, Cell Cycle 2010

Tumor- initiating stem cells

Maternal obesity during pregnancy and premature mortality from cardiovascular event in adult offspring; **Reynolds et al, BMJ 2013**
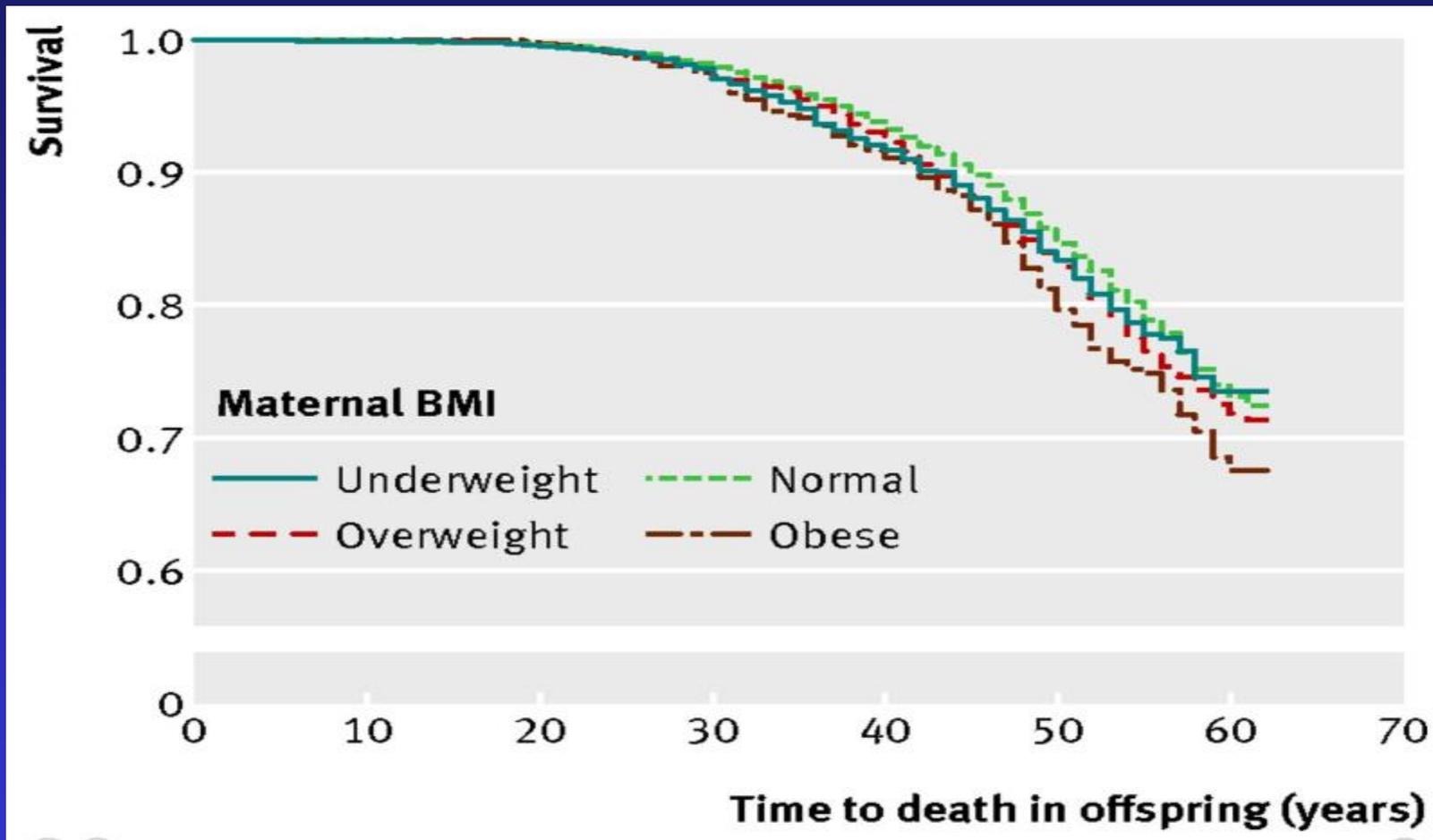
Adjusted for mat age at delivery, socioeconomic status, birth weight, gestation at delivery

TABLE 2

Which recommendations for oral glucose tolerance test threshold values during pregnancy should be adopted: those of International Association of Diabetes and Pregnancy Study Groups or less strict ones as proposed by Ryan[4]?

Follow IADPSG recommendations: you want to be on safe side and realize that number of GDM patients most likely will double. Be aware that if 24-wk oGTT result is negative, GDM may still emerge during third trimester of pregnancy, due to poor reproducibility of oGTT, especially in case of minor abnormalities and due to increasing placental hormone levels. With this approach outcome might be somewhat improved, although definite proof is lacking.

Follow Ryan[4] recommendations (2-fold increase in LGA; overall incidence of GDM around 10%): you realize that incidence of GDM most likely has gone up due to increase in maternal obesity. However, you consider 18% incidence too high. You will create database to collect all cases with oGTT values in between IADPSG and threshold values of Ryan[4] and compare outcome to that of women who were negative according to both tests, after correcting for maternal body mass index.[13] Even better, you may consider starting RCT treating half of women with glucose values in between both diagnostic thresholds. Alternatively you may decide to treat only obese women by using IADPSG thresholds, given symbiotic effect of obesity and GDM on outcome. Diet, treatment, and frequent visits may reduce weight gain in these women, which by itself may have positive effect on outcome.

GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups; LGA, XX; oGTT, oral glucose tolerance test; RCT, randomized controlled trial.

Visser. Is evidence strong enough to change diagnostic criteria for gestational diabetes now? Am J Obstet Gynecol 2012.

Meta- Analysis - Definition

"Meta-analysis is like a sausage:
Only God and the butcher know what it contains
And both are not going to eat it "

Prof. Yariv Yogev, Lisbon, 2012

Adopt less stringent thresholds

75 g OGTT: fasting =>5.3 mmol/l

1 hour => 10.6

2 hour => 9.0

Diagnostic criteria based on 2 fold increase in LGA infant

(E.A.Rian, Diabetologia 2011;54:480-486)

Prevalence of GDM 0f

10.5%

- Create a database of women with oGTT values in between the IADPSG thresholds and the current one, to compare outcome with IADPSG negative women. (Bodmer-Roy et al O&G Oct 2012)
- Or better, do a RCT, with treatment or not, in women with values in between both definitions (clinical outcome, cost-effectiveness)
- Alternatively, one may decide to classify obese women according to the IADPSG definitions, given the synergistic effect of both conditions (and considering that frequent visits and diet may improve outcome)

Obesity and GDM

BMI	Odds ratio
20-25	1
25-30	1.6-1.7
>30	3.6-4
>40	10

Sebire et al, 2001; Baeten et al, 2001, Kumari, 2007

Obesity – Global prevalence

European Region
Albania 36%
Malta 35%
Turkey 29%
Slovakia 28%
Czech Republic 26%

Eastern Mediterranean
Jordan 60%
Qatar 45%
Saudi Arabia 44%
Israel 43%
Lebanon 38%

North America
USA 33%
Barbados 31%
Mexico 29%
St Lucia 28%
Bahamas 28%

South Central America
Panama 36%
Paraguay 36%
Peru (urban) 23%
Chile (urban) 23%
Dominican Republic 18%

Africa
Seychelles 28%
South Africa 28%
Ghana 20%
Mauritania 19%
Cameroon (urban) 14%

South East Asia & Pacific Region
Nauru 78%
Tonga 70%
Samoa 63%
Niue 46%
French Polynesia 44%

% Obese	
	0-9.9%
	10-14.9%
	15-19.9%
	20-24.9%
	25-29.9%
	≥30%
	Self Reported data

Obesity

Prevalence - Europe

Male and female obesity levels in selected European countries
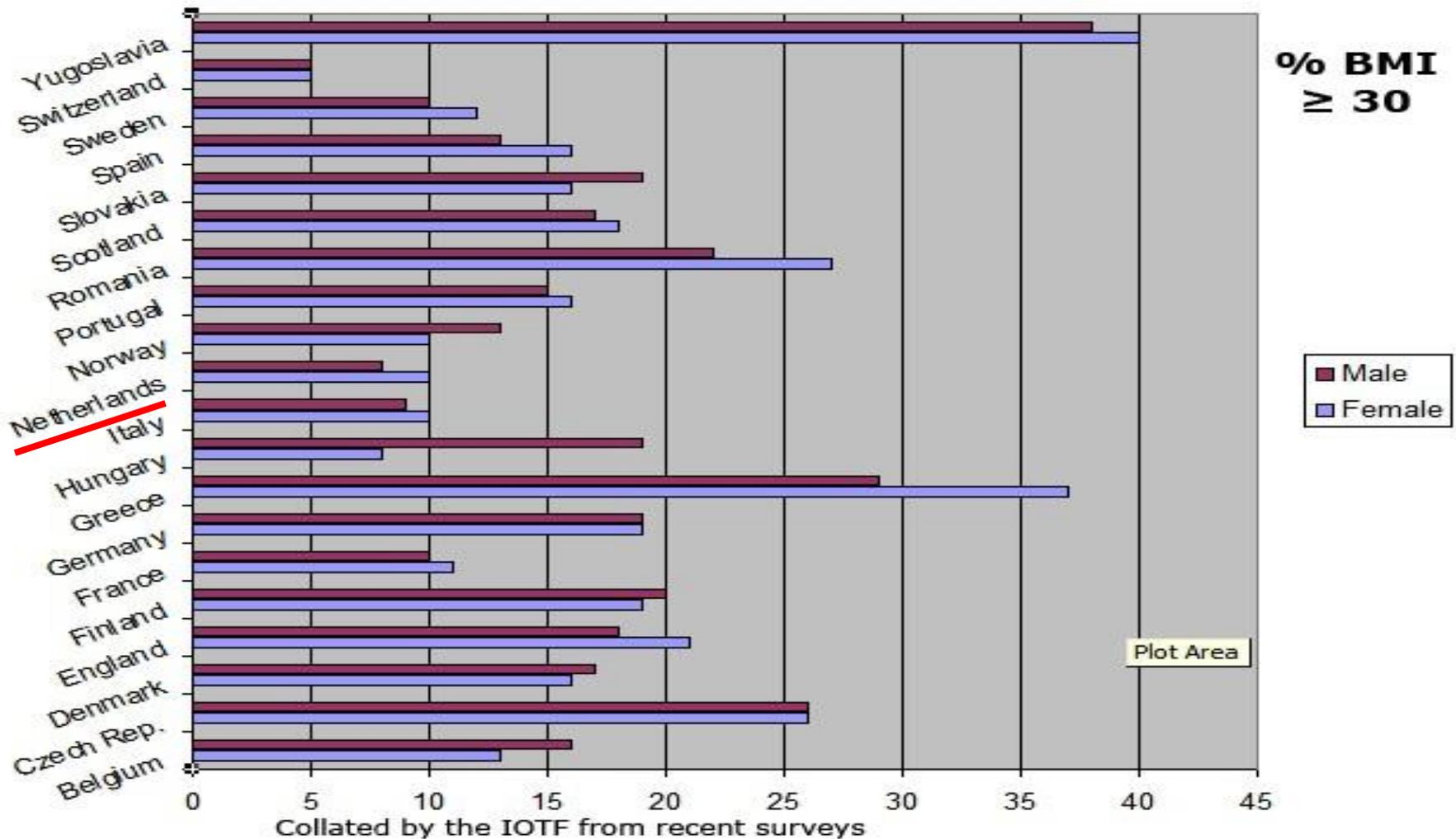
% BMI ≥ 30

Collated by the IOTF from recent surveys

Obesity and Diabetes in the USA

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

The Epidemic of Diabesity, 2000 and 2030

Hossain et al NEJM, 2007
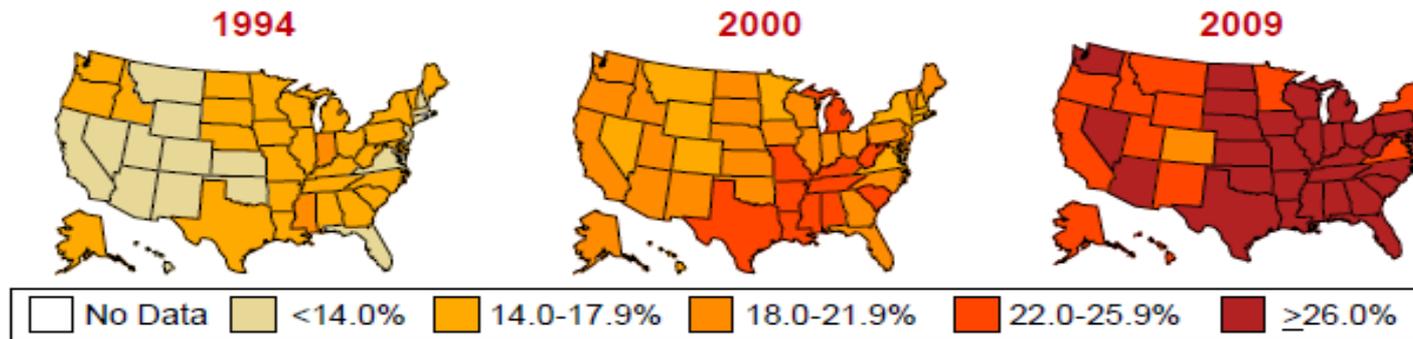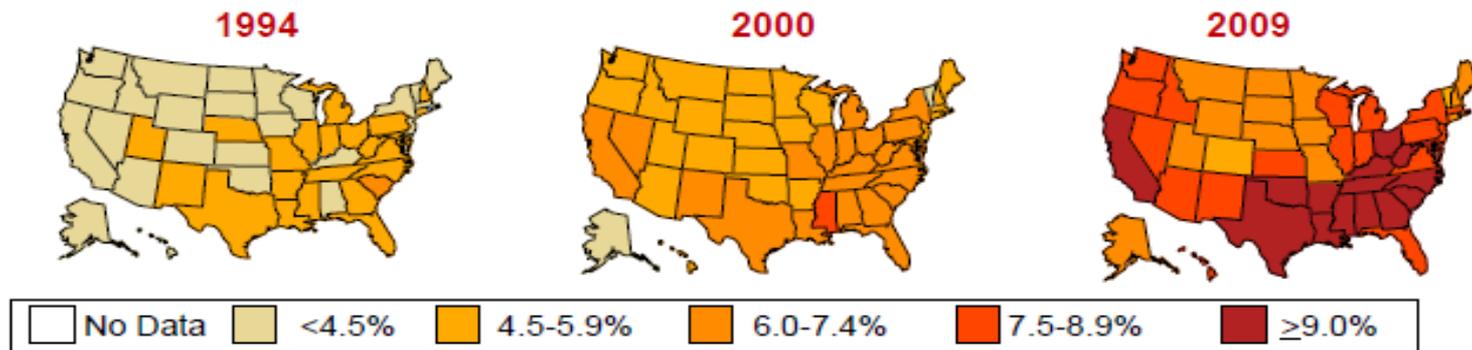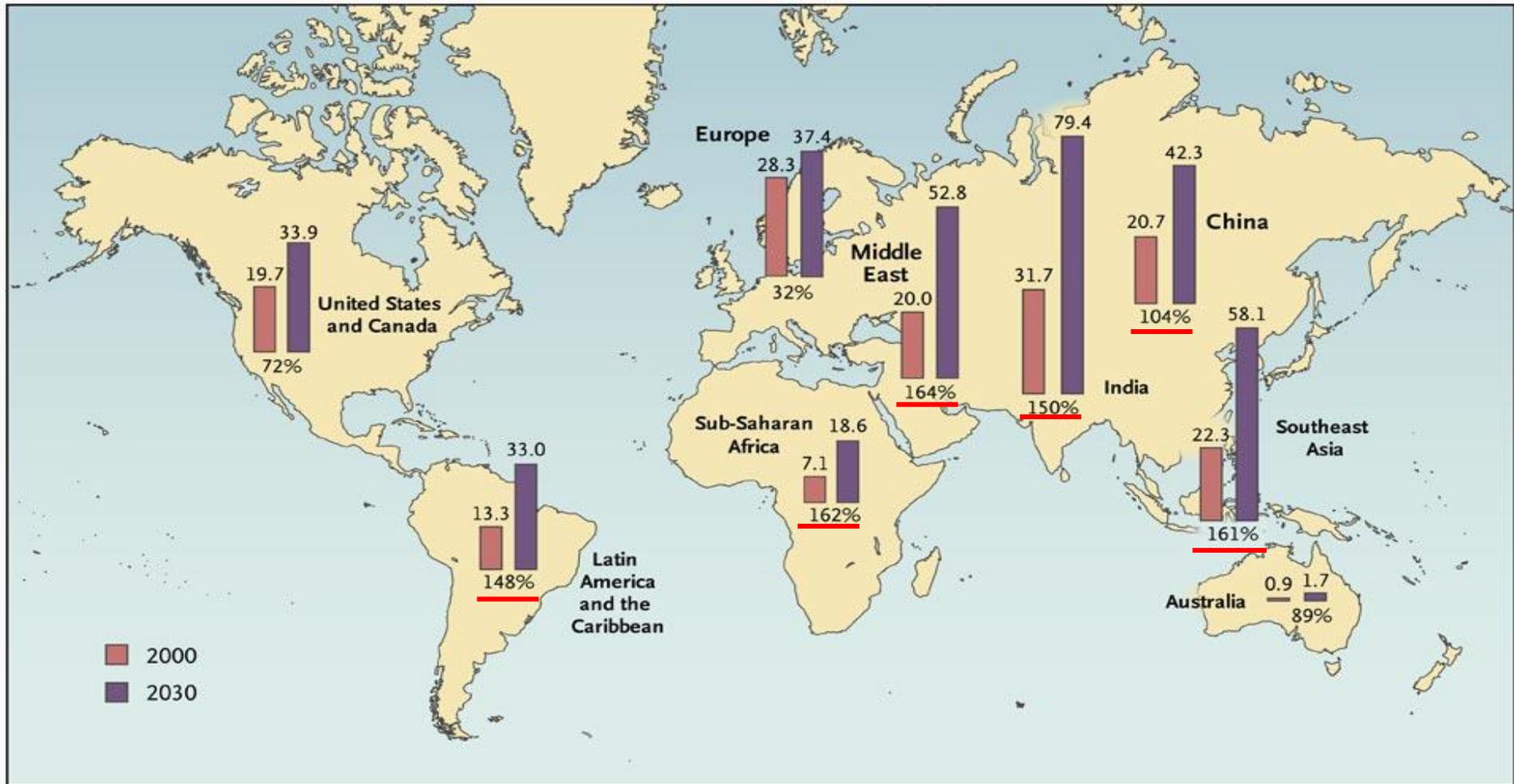
More diabetes, more gestational diabetes

TABLE 2

Which recommendations for oral glucose tolerance test threshold values during pregnancy should be adopted: those of International Association of Diabetes and Pregnancy Study Groups or less strict ones as proposed by Ryan[4]?

Follow IADPSG recommendations: you want to be on safe side and realize that number of GDM patients most likely will double. Be aware that if 24-wk oGTT result is negative, GDM may still emerge during third trimester of pregnancy, due to poor reproducibility of oGTT, especially in case of minor abnormalities and due to increasing placental hormone levels. With this approach outcome might be somewhat improved, although definite proof is lacking.

Visser & de Valk, AJOG 2012

Follow Ryan[4] recommendations (2-fold increase in LGA; overall incidence of GDM around 10%): you realize that incidence of GDM most likely has gone up due to increase in maternal obesity. However, you consider 18% incidence too high. You will create database to collect all cases with oGTT values in between IADPSG and threshold values of Ryan[4] and compare outcome to that of women who were negative according to both tests, after correcting for maternal body mass index.[13] Even better, you may consider starting RCT treating half of women with glucose values in between both diagnostic thresholds. Alternatively you may decide to treat only obese women by using IADPSG thresholds, given symbiotic effect of obesity and GDM on outcome. Diet, treatment, and frequent visits may reduce weight gain in these women, which by itself may have positive effect on outcome.

GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups; LGA, XX; oGTT, oral glucose tolerance test; RCT, randomized controlled trial.

Alternatives for insulin; type-2; gest diabetes

-Glibenclamide (glyburide) **(Langer et al, NEJM 2000)**

FDA Category C

-Metformin **(Rowan et al, NEJM 2008)**

Metformin crosses the placenta (fetal concentration 50% of maternal). It has been used in women with PCOS and/or type-2-diabetes in the first half of pregnancy and there is thus far no evidence that it may induce congenital malformations.

However, long term follow-up data are lacking, especially in IUGR infants

Metformin and the risk of cancer

- Anti-angiogenetic effects, including negative effects on VEGF
- Anti-inflammatory effects
- Growth inhibitory effects
- Anti-oxidative effects
- Decreases(tumor-initiating) stem cells

Tan et al, J.Clin Endocr Metab, Dec 2010; Ersoy et al, Diab Care, 2008; Martin-Castillo Cell Cycle, 2010

Metformin and the risk of cancer

- Anti-angiogenetic effects, including negative effects on VEGF
- Anti-inflammatory effects
- Growth inhibitory effects
- Anti-oxidative effects
- Decreases (tumor-initiating) stem cells

That appears to be good for the prevention and/or treatment of cancer

Tan et al, J.Clin Endocr Metab, Dec 2010; Ersoy et al, Diab Care, 2008; Martin-Castillo Cell Cycle, 2010

Metformin and the risk of cancer

- Anti-angiogenetic effects, including negative effects on VEGF
- Anti-inflammatory effects
- Growth inhibitory effects
- Anti-oxidative effects
- Decreases (tumor-initiating) stem cells

But what about a nine months exposition of the fetus ??

Tan et al, J.Clin Endocr Metab, Dec 2010; Ersoy et al, Diab Care, 2008; Martin-Castillo Cell Cycle, 2010

MICHELIN MAN DENIES PATERNITY SUIT...... CLAIMS CHILD IS NOT HIS

Pima Indians NIDDM

Incidence of NIDDM in 20-24 y old offspring of:

- nondiabetic women   1.4 %
- women developing NIDDM after pregnancy   8.6 %
- women with NIDDM during pregnancy   45 %

differences persist taking into account paternal diabetes, age at onset diabetes in parents, birth weight

(Pettitt et al, Diabetes 1988;37:622-8)

Type-2 diabetes or impaired glucose intolerance in 18-27 y offspring (total study group 597)

- Women with gest diabetes   21%
- Genet predisposed women   12%

  (but no diabetes in pregnancy)

- Women with type-1 diabetes   11%
- Control group   4%

Clausen et al, Diab Care 2008;31:340-6

Type-2 diabetes or impaired glucose intolerance in 18-27 y offspring (total study group 597)

- Women with gest diabetes   21%   **9%**
- Genet predisposed women   12%

  (but no diabetes in pregnancy)

- Women with type-1 diabetes   11%   **7%**
- Control group   4%

So, diabetes during pregnancy results in an almost 10% incidence of diabetes in offspring

Clausen et al, Diab Care 2008;31:340-6

So,

- Abnormal intrauterine environment induces DM and obesity in offspring

- Most studies were not controlled for maternal BMI

- Is remains uncertain whether GDM or Obesity is the factor most strongly related to obesity in offspring

However,

- Given the synergistic effect of Obesity and GDM, be very strict in diagnosing and treating Obese women who have GDM

More diabetes, more gestational diabetes

75 g OGTT: fasting => 5.1 mmol/l

1 hour => 10.0

2 hour => 8.5

Diagnostic criteria based on 1.75 fold increase in LGA infant

(Metzger et al, Diab Care, 2010;33:676-682)

75 g OGTT: fasting =>5.3 mmol/l

1 hour   => 10.6

2 hour =>   9.0

Diagnostic criteria based on 2 fold increase in LGA infant

(E.A.Rian, Diabetologia 2011;54:480-486)

-Poor reproducibility of OGTT

-Glucose weak predictor of LGA

-Obesity is a stronger predictor

-GDM is only related to childhood obesity in case of maternal obesity (Pirkola et al, 2010)

-Economic factors

-On the other hand: treatment is relatively easy (insulin in only 8-20 % of women)

(Rian, 2011; RCOG SACO paper 23, January 2011)

1. What are the current screening and diagnostic approaches fo
   what are the glycemic thresholds for each approach, and how

2. What are the effects of various diabetes mellitus screening/di
   providers, and U.S. healthcare systems?

3. In the absence of treatment, how do health outcomes of moth
   gestational diabetes mellitus and their offspring compare with

4. Does treatment modify the health outcomes of mothers who m
   diabetes mellitus and their offspring?

5. What are the harms of treating gestational diabetes, and do th

6. Given all of the above, what diagnostic approach(es) for gesta
   recommended, if any?

7. What are the key research gaps in the diagnostic approach of

More diabetes, more gestational diabetes

75 g OGTT: fasting => 5.1 mmol/l

1 hour => 10.0

2 hour => 8.5

Diagnostic criteria based on 1.75 fold increase in LGA infant (IADPSD)

(Metzger et al, Diab Care, 2010)

# Obesity – Global prevalence
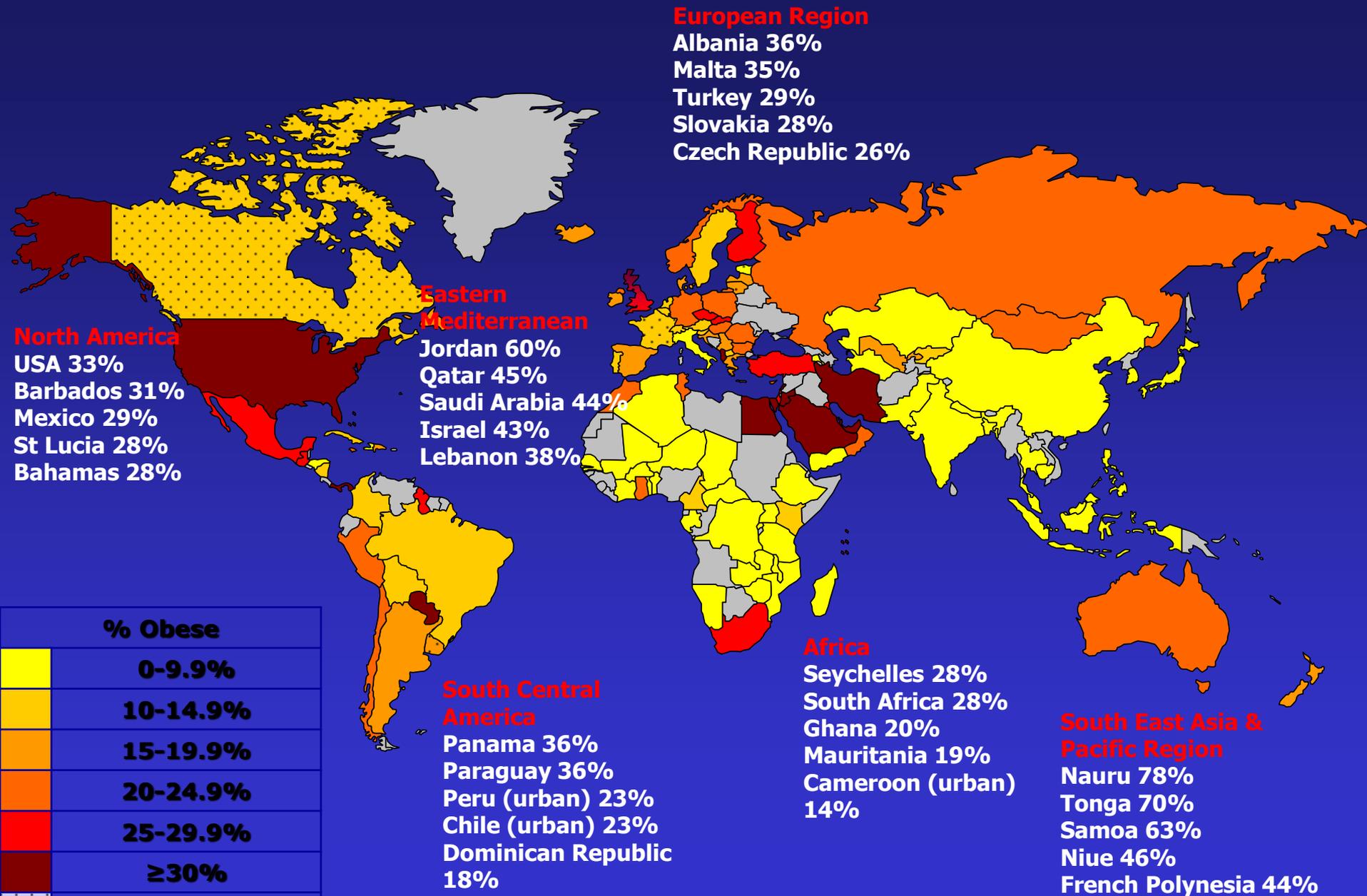
European Region
Albania 36%
Malta 35%
Turkey 29%
Slovakia 28%
Czech Republic 26%

Eastern Mediterranean
Jordan 60%
Qatar 45%
Saudi Arabia 44%
Israel 43%
Lebanon 38%

North America
USA 33%
Barbados 31%
Mexico 29%
St Lucia 28%
Bahamas 28%

South Central America
Panama 36%
Paraguay 36%
Peru (urban) 23%
Chile (urban) 23%
Dominican Republic 18%

Africa
Seychelles 28%
South Africa 28%
Ghana 20%
Mauritania 19%
Cameroon (urban) 14%

South East Asia & Pacific Region
Nauru 78%
Tonga 70%
Samoa 63%
Niue 46%
French Polynesia 44%

% Obese	
	0-9.9%
	10-14.9%
	15-19.9%
	20-24.9%
	25-29.9%
	≥30%
	Self Reported data

Obesity and Diabetes in the USA

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

Maternal overweight is the main problem and not GDM

overweight and abdominal obesity in 16 y old adolescents

Risk population:

-GDM 84

-Normal OGTT 657

Control 3.427

■ = mat BMI> 25



Pirkola et al, Diab Care 2010

Obesity and GDM

- Obesity seems to have the most important effect on long term development of the offspring (especially childhood obesity)

Obesity and GDM

- Both have an (synergistic) effect on early perinatal outcome

# Childhood obesity in relation to macrosomia at birth and diabetes type
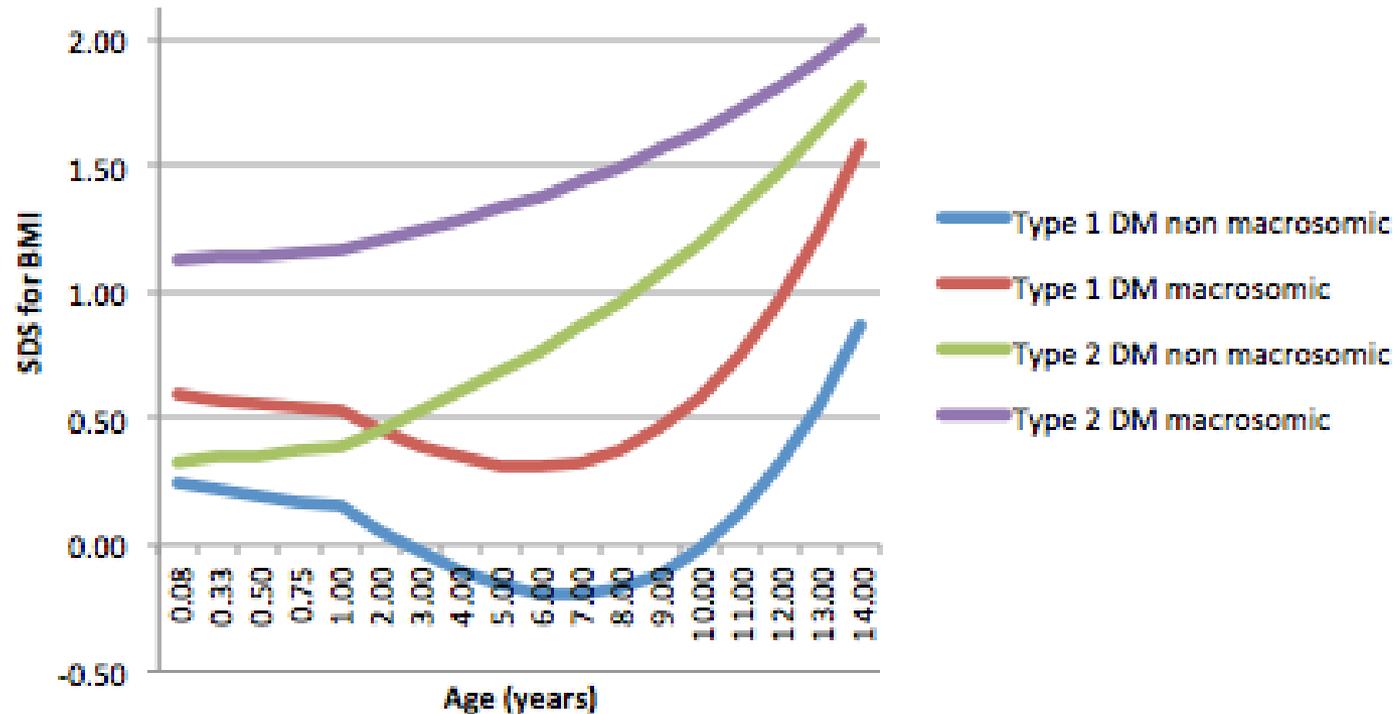
Model: lineair mixed model, leeftijd als lineaire variabele

Hammoud et al, in preparation

University Medical Center, Utrecht, the NL

The impact of diabetes, obesity and hypertension in pregnancy

Gerard H.A.Visser
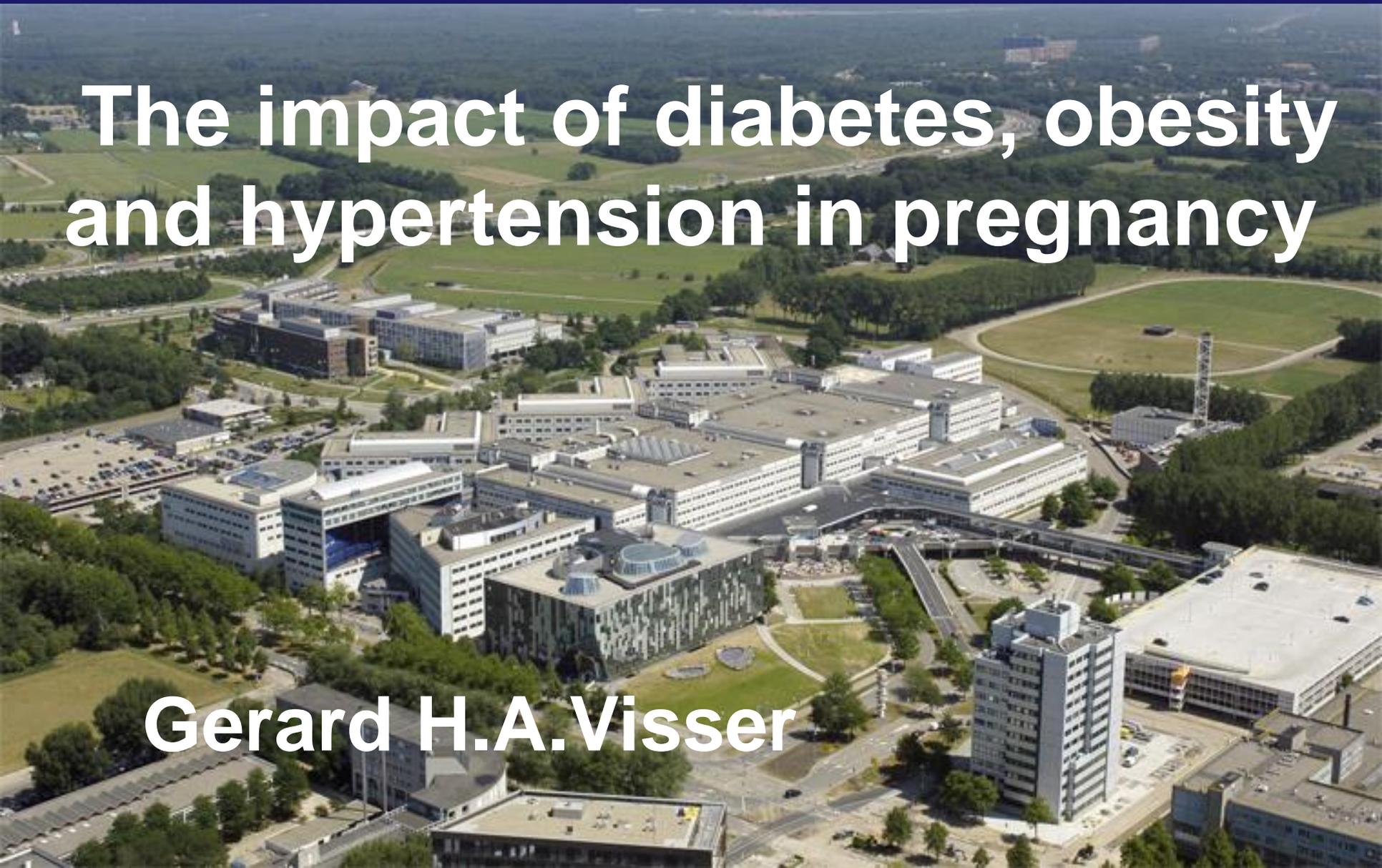
Diabetes and Pregnancy

	Cong malf	PN death	Macrosomia	Mat death
GDM	?	?	?	?
Type- 2	?	?	?	?
Type -1	?	?	?	?

Diabetes and Pregnancy

	Cong malf	PN death	Macrosomia	Mat death
GDM	-	+/-	+	-
Type- 2	++	+++	++	-
Type -1	++	++	+++	+

Infant weight at age 14…………

	Cong malf	PN death	Macrosomia	Mat death	
GDM	-	+/-	+	-	?
Type- 2	++	+++	++	-	?
Type -1	++	++	+++	+	?

Metabolic Syndrome
Syndrome X, Insulin resistance syndrome, CHAOS

with _>3 of the following conditions:

- Abdominal (central obesity)
- Elevated blood pressure
- Elevated fasting plasma glucose
- High serum triglycerides
- Low high-density cholesterol (HDL)

Metabolic Syndrome

Syndrome X, Insulin resistance syndrome, CHAOS

with _>3 of the following conditions:

- Abdominal (central obesity) : BMI>30
- Elevated blood pressure
- Elevated fasting plasma glucose
- High serum triglycerides
- Low high-density cholesterol (HDL)