XIVè CONGRÉS ACD, 16 i 17 de març 2017, Badalona

Gestació i diabetes: l'escola de Barcelona, 30 anys després

Rosa Corcoy Pla
Hospital de la Santa Creu i Sant Pau

GDM and the incidence of type 2 diabetes: a systematic review

Kim C. Diabetes Care. 2002;25:1862-8

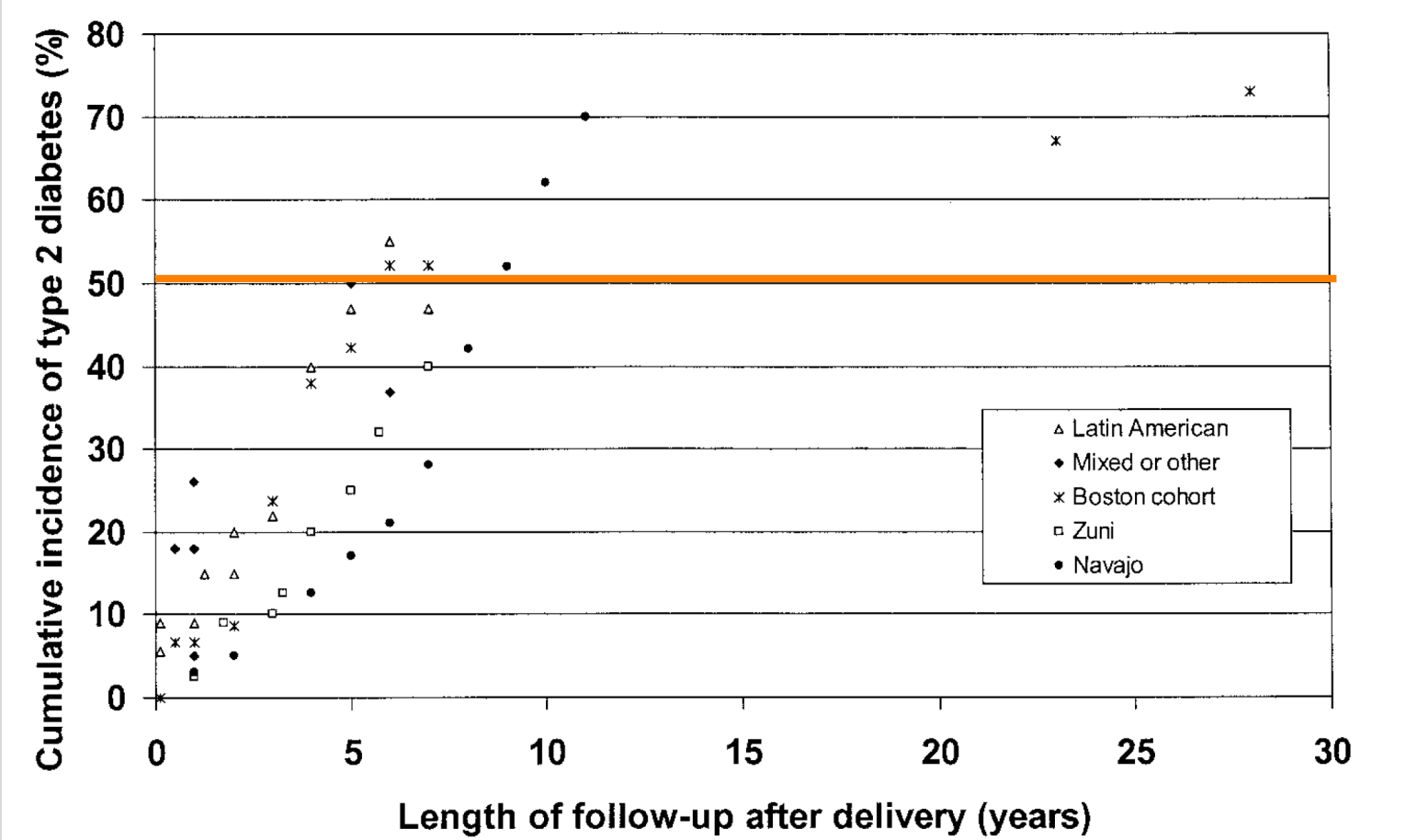
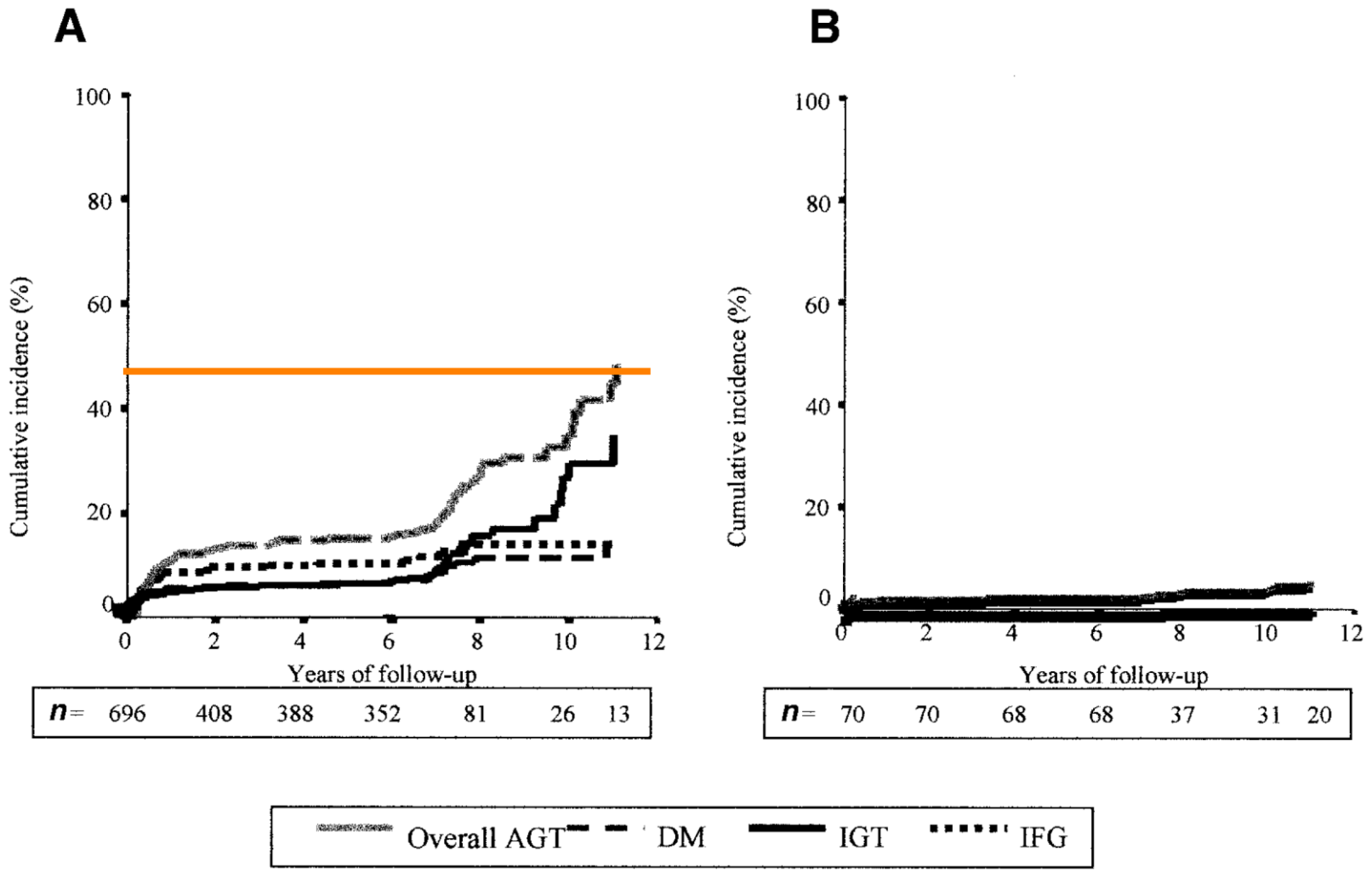


Figure 2—*Cumulative incidence of type 2 diabetes by ethnicity and length of follow-up, adjusted for retention. Studies using local criteria or WHO criteria for GDM diagnosis are not illustrated.*

Diabetes and abnormal glucose tolerance in women with previous gestational diabetes

Albareda M. Diabetes Care 2003;26:1199-205



Islet cell antibodies identify a subset of GDM women with higher risk of developing DM shortly after pregnancy

D Mauricio. Diab Nutr Metab 1992; 5: 237-241

+ ICA 12,4%

Table 2 - *Results of the 75 g post-partum oral glucose tolerance test in 184 women with previous gestational mellitus, according to ICA status.*

Glycemia	ICA- (n=158)	ICA<20 JDF U (n=18)	ICA>20 JDF U (n=8)
0 min	5.4 ± 0.7	5.7 ± 1.0	6.0 ± 0.4*
30 min	8.9 ± 1.6	8.6 ± 2.7	10.3 ± 1.0
60 min	8.5 ± 2.4	8.3 ± 3.4	10.7 ± 3.9
120 min	6.0 ± 2.0	6.0 ± 3.2	8.9 ± 5.4**

Footnote: Values are mean±SD. Glucose is expressed in mM/l.

* $p<0.03$. ** $p<0.01$. p values refer to difference between the three groups.

Diabetes and abnormal glucose tolerance in women with previous gestational diabetes

Albareda M. Diabetes Care 2003;26:1199-205

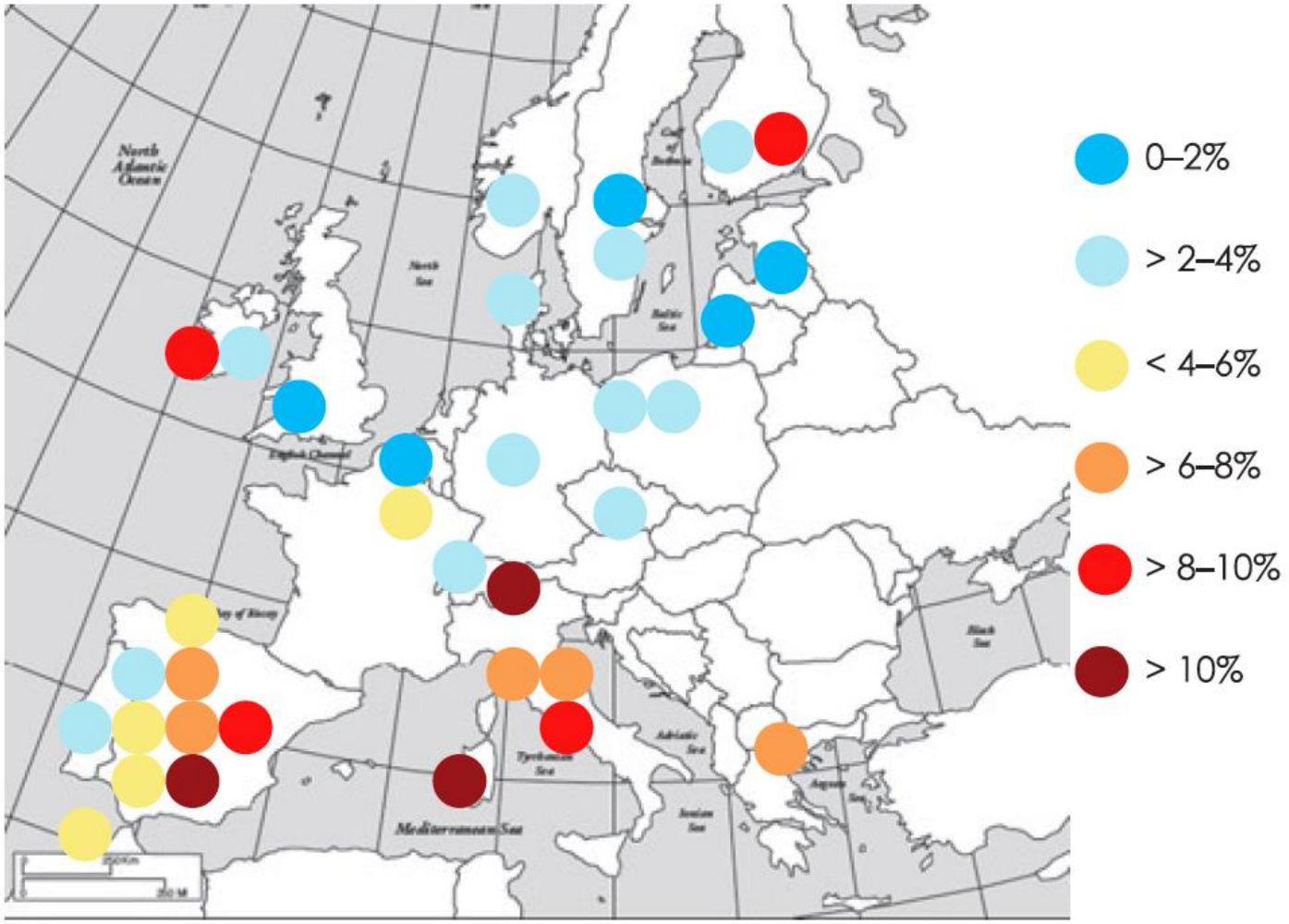
Independent predictors were

- **previous hyperglycemia (RR 2.49, CI 1.22– 5.07)**
- **four abN values in the dx OGTT or overt DM during pregnancy (RR 3.92, CI 1.86 – 8.28)**
- **2-h BG in the dx OGTT >=11.7 mmol/l (RR 2.67, CI 1.35–5.28)**
- **GA at dx <24 weeks (RR 2.25, CI 1.21–4.18)**
- **prepregnancy BMI >=26.4 kg/m2 (RR 3.02, CI 1.61– 5.65)**

Vitamin D and Lifestyle Intervention for Gestational Diabetes Prevention

GDM in Europe: prevalence, current screening practice and barriers to screening. A review

Buckley BS. Diabet Med 2012;29:844-54



Effect of physical activity and/or healthy eating on GDM risk: The DALI Lifestyle Study

Simmons D. J Clin Endocrinol Metab. 2016

RESULTS:

We randomized

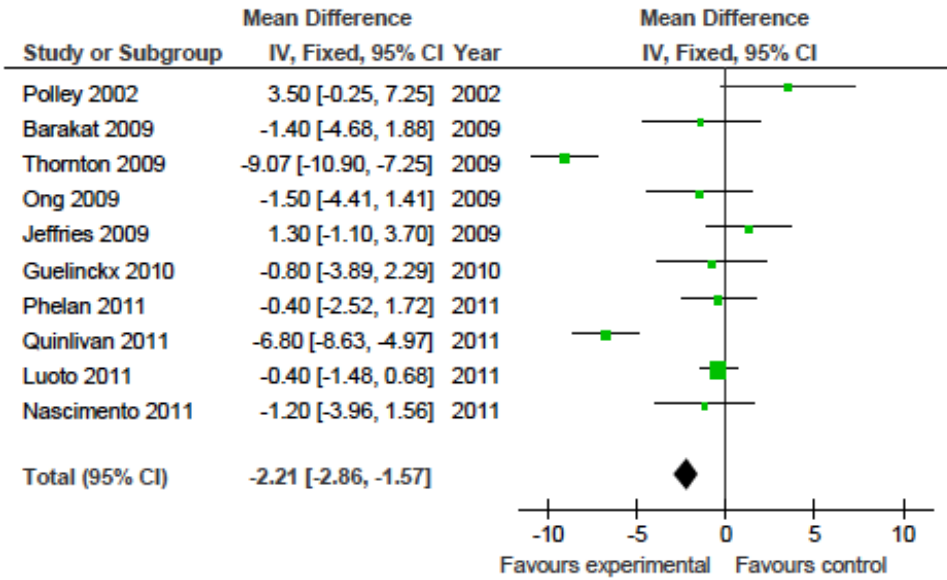
- **108 women to HE&PA**
- **113 to HE**
- **110 to PA**
- **105 to control**

In the HE+PA group, but not HE or PA alone, women achieved substantially less GWG than controls by 35-37 weeks (-2.02 (95% CI -3.58; -0.46 kg). … there were no improvements in fasting or post-load glucose or, insulin [ ] or HOMA-IR.

BW, LGA and SGA rates were similar.

Lifestyle interventions for OW and OB pregnant women to improve outcomes: systematic review and meta-analysis

Oteng-Ntim E. BMC Med 2012;10:47



GDM, RR 1.51 (0.72, 3.16)

Brit. J. prev. soc. Med. (1969), **23**, 218–225

CONGENITAL MALFORMATIONS AND ENVIRONMENTAL INFLUENCES IN PREGNANCY

BY

I. D. GERALD RICHARDS, M.D. (Wales), D.P.H.[1]

Department of Social and Occupational Medicine, Welsh National School of Medicine, Cardiff

Group C: Employment, Accommodation, Water Supply, Height, and Weight in the First Trimester

Factors Investigated	Particulars Recorded
Employment	Nature, duration and whether sedentary or non-sedentary
Accommodation	Type (own, shared or other, *e.g.*, caravan)
Bedroom density	Ratio bedrooms used: number of occupants
Water supply	Type of supply (tap, well, other)
Height	Mother's statement
Weight	Mother's statement of weight before pregnancy or during first trimester*

*Confirmed, whenever possible, from the mother's 'pregnancy continuity card' (this fact recorded)

GROUP C

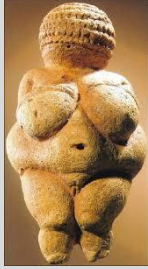
The bedroom density (ratio of bedrooms: occupants) differed significantly for miscellaneous defects ($P < 0.01$), there being more cases than controls with high ratios.

For individual defects there were significant differences for the following:

Anencephaly: maternal weight—heavier than controls ($P < 0.05$)

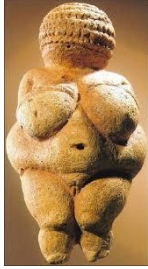
Talipes: bedroom density—more cases with low ratios ($P < 0.05$)

"In none of the defects investigated was there a significantly lower weight …. In fact the mothers of anencephalics were significantly heavier than matched controls"



30 anys més tard ….

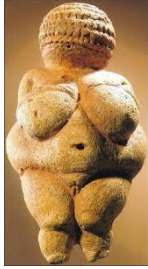
- **Risk of NTD-affected pregnancies among obese women**
  Shaw GM. JAMA 1996; 275: 1093–1096
- **Is maternal obesity a risk factor for anencephaly and spina bifida?**
  Watkins ML. Epidemiology 1996; 7: 507–512
- **Maternal smoking, BMI and NTD**
  Kallen K. Am J Epidemiol 1998; 147: 1103–1111
- **Prepregnancy BMI and the risk of multiple congenital anomalies**
  Shaw GM. Am J Med Genet 2002; 107: 253–255
- **Is maternal obesity a risk factor for open NTD?**
  Haddow JE. Am J Obstet Gynecol 1995; 172: 245–247
- **Maternal prepregnancy weight and congenital heart defects in the offspring**
  Watkins ML. Epidemiology 2001; 11: 439–446
- **A prospective study of the risk of congenital defects associated with maternal obesity and DM**
  Moore LL. Epidemiology 2000; 11: 689–694
- **Does maternal obesity increase the risk of fetal abnormalities? Analysis of 20,248 newborn infants of the Mainz Birth Register for detecting congenital abnormalities.**
  Queisser-Luft. Ultraschall Med 1998; 19: 40–44



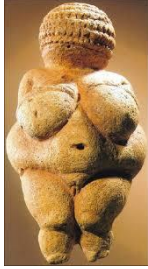
In human GDM, CM are related to prepregnancy BMI and to severity of GDM

García-Patterson A; Diabetologia 2004;47: 509-514

Predictive variable	>=1 MCM	Heart	Renal/urinary	Skeletal
Prepregnancy BMI				
• 1st T (<21.91)	1.00	1.00	1.00	
• 2nd T (21.92, 24.47)	2.54*	19.67*	1.47	
• 3rd T (>24.78)	2.67*	5.58*	5.22*	
Maternal age				
• 1st + 2nd T			1.00	
• 3rd T			2.60	
GA at dx				
• 1st T	1.00	1.00		
• 2nd + 3rd T	0.64	0.28*		
Fasting BG at dx				
• 1st T				1.00
• 2nd T				1.48
• 3rd T				3.99
1h BG at dx				
• 1st T	1.00			
• 2nd T	1.78			
• 3rd T	1.13			
2h BG at dx				
• 1st T		1.00		
• 2nd T		0.218*		
• 3rd T		0.620		
N of abN values				
• 2-3		1.00		
• 4/overt DM		4.82*		

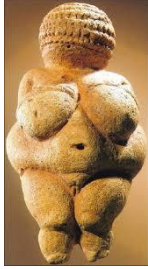


Origin Year Endorsed by... Glucose dose	O'Sullivan plasma 1980-1991 NDDG 1st - 3rd WC 100 gr	C & C 1982 4th WC, 1998 5th WC, 2005 100 gr
Fasting	105 mg/dl 5.8 mmol/l	95 mg/dl 5.3 mmol/l
1h	190 mg/dl 10.6 mmol/l	180 mg/dl 10.0 mmol/l
2h	165 mg/dl 9.2 mmol/l	155 mg/dl 8.6 mmol/l
3h	145 mg/dl 8.1 mmol/l	140 mg/dl 7.8 mmol/l
N points	2	2



Toronto Trihospital GDM project		
Women screened		3836
GDM prevalence		3.8
↑with CC criteria		50
↑Macrosomia		
Control		13.7
CC-only	*	28.7
NDDG-GDM		10.5
Cesarean Section		
Control		20.2
CC-only	*	29.6
NDDG-GDM	*	33.6
Hypertension		Preeclampsia
Control		4.9
CC-only	*	8.7
NDDG-GDM	*	8.4

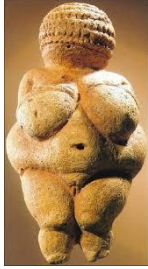
M. Sermer The Toronto Tri-Hospital GDM Project. A preliminary review. Diabetes Care. 1998; Suppl 2:B33-42
M. Sermer. Impact of increasing CHO intolerance on maternal-fetal outcomes in 3637 women without GDM. The Toronto Tri-Hospital GDM Project. Am J Obstet Gynecol. 1995;173(1):146-56



Potential impact of ADA (2000) criteria for diagnosis of GDM in Spain

Ricart W. Diabetologia. 2005; 48(6):1135-41

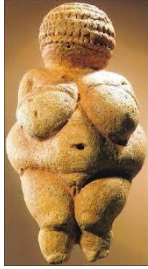
- prospective study
- 2002
- 16 hospitals belonging to the Spanish National Health Service
- singleton pregnancies without pregestational DM
- primary outcomes:
  - macrosomia
  - CS
- secondary outcomes:
  - LGA
  - preterm birth
  - PIH
  - Apgar <7 at 1 & 5 min
  - MCM
  - PNM
- sample size (n=9,741) calculated to detect a x2 ↑ in macrosomia and a 40% ↑ in CS in women fulfilling ADA-only-GDM criteria (α=0.05 and β=0.80)



	Toronto	Spain
Women screened	3836	9270
GDM prevalence	3.8	8.8
↑with CC criteria	50	32
↑Macrosomia		
Control	13.7	4.6
CC-only	28.7 *	8.0 *
NDDG-GDM	10.5	7.4 *
Cesarean Section		
Control	20.2	19.2
CC-only	29.6 *	22.5
NDDG-GDM	33.6 *	24.8 *
Hypertension	Preeclampsia	PIH
Control	4.9	1.7
CC-only	8.7 *	3.8 *
NDDG-GDM	8.4 *	4.2 *

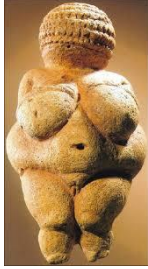
* significant vs the reference category of the study

Multivariate analysis for the prediction of 1ary & 2ary outcomes (OR)



Predictive variable	Macrosomia	LGA	PIH
Glucose tolerance			
• Neg Sc	1.00	1.00	1.00
• FP Sc	1.33*	1.15	1.25
• ADA-only GDM	1.45	1.44*	2.34*
• NDDG-GDM	1.47*	1.10	2.03*
Maternal BMI (kg/m^2)			
• Q1 <21.5	1.00	1.00	1.00
• Q2 21.5-23.6	1.51*	1.24*	2.69*
• Q3 23.7-26.1	1.66*	1.44*	2.21*
• Q4 >26.1	2.52*	2.08*	5.77*
Male sex (Y/N)	2.58*	1.16*	1.27
Gestational age	1.62*	0.89*	0.82*
Maternal age	1.00	1.01	0.98
Macrosomia (Y/N)	-	-	0.32
PIH (Y/N)	0.32	0.43*	-

Multivariate analysis for the prediction of 1ary & 2ary outcomes (OR)



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• NDDG-GDM	1.47*	1.10	2.03*
Maternal BMI (kg/m^2)			
• Q1 <21.5	1.00	1.00	1.00
• Q2 21.5-23.6	1.51*	1.24*	2.69*
• Q3 23.7-26.1	1.66*	1.44*	2.21*
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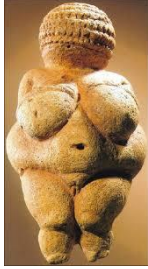
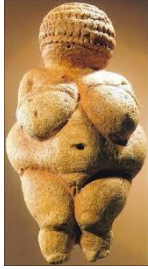
Macrosomia (Y/N)	-	-	0.32
PIH (Y/N)	0.32	0.43*	-

Population-attributable fractions and preventive fractions



Predictive variable	Macrosomia		LGA		PIH	
	OR	Afp/PFp	OR	Afp/PFp	OR	Afp/PFp
Glucose tolerance						
• Neg Sc	1.00		1.00		1.00	
• FP Sc	1.33*	6.4	1.15	2.9	1.25	4.4
• ADA-only GDM	1.45	1.3	1.44*	1.0	2.34*	2.8
• NDDG-GDM	1.47*	3.8	1.10	0.9	2.03*	9.1
Maternal BMI (kg/m^2)						
• Q1 <21.5	1.00		1.00		1.00	
• Q2 21.5-23.6	1.51*	7.5	1.24*	4.2	2.69*	15.1
• Q3 23.7-26.1	1.66*	6.3	1.44*	7.9	2.21*	11.6
• Q4 >26.1	2.52*	23.0	2.08*	17.6	5.77*	50.0
Male sex (Y/N)	2.58*	42.0	1.16*	7.5	1.27	12.1
Gestational age	1.62*		0.89*		0.82*	
Maternal age	1.00		1.01		0.98	
Macrosomia (Y/N)	-		-		0.32	35.6
PIH (Y/N)	0.32	2.1	0.43*	1.9	-	

Population-attributable fractions and preventive fractions



Predictive variable	Macrosomia		LGA		PIH	
	OR	Afp/PFp	OR	Afp/PFp	OR	Afp/PFp
Glucose tolerance						
• Neg Sc	1.00		1.00		1.00	
• FP Sc	1.33*	6.4	1.15	2.9	1.25	4.4
• ADA-only GDM	1.45	1.3	1.44*	1.0	2.34*	2.8
• NDDG-GDM	1.47*	3.8	1.10	0.9	2.03*	9.1
Maternal BMI (kg/m^2)						
• Q1 <21.5	1.00		1.00		1.00	
• Q2 21.5-23.6	1.51*	7.5	1.24*	4.2	2.69*	15.1
• Q3 23.7-26.1	1.66*	6.3	1.44*	7.9	2.21*	11.6
• Q4 >26.1	2.52*	23.0	2.08*	17.6	5.77*	50.0
Male sex (Y/N)	2.58*	42.0	1.16*	7.5	1.27	12.1
Gestational age	1.62*		0.89*		0.82*	
Maternal age	1.00		1.01		0.98	
Macrosomia (Y/N)	-		-		0.32	35.6
PIH (Y/N)	0.32	2.1	0.43*	1.9	-	

Diabetes y embarazo. Guía asistencial (3ª edición)

Grupo Español de Diabetes y Embarazo. Av Diabetol 2006; 22: 73-87

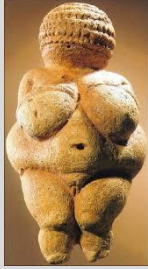
Diabetes y embarazo. Guía asistencial (3ª edición)

Grupo Español de Diabetes y Embarazo. Prog Obstet Ginecol. 2007;50(4):249-64

- Se considerará diagnóstico de DG el hallazgo de dos o más puntos ≥ a los siguientes valores[1]:

Basal	105 mg/dl	5,8 mmol/l
1 h	190 mg/dl	10,6 mmol/l
2 h	165 mg/dl	9,2 mmol/l
3 h	145 mg/dl	8,1 mmol/l

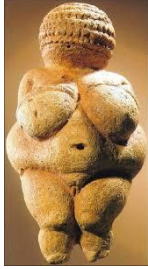
Estos criterios corresponden a los recomendados por el 3er Workshop-Conference on Gestational Diabetes Mellitus, no habiéndose adaptado a los del 4º Workshop a raíz de los estudios realizados por el grupo[22,23]



HAPO Study: associations with maternal BMI

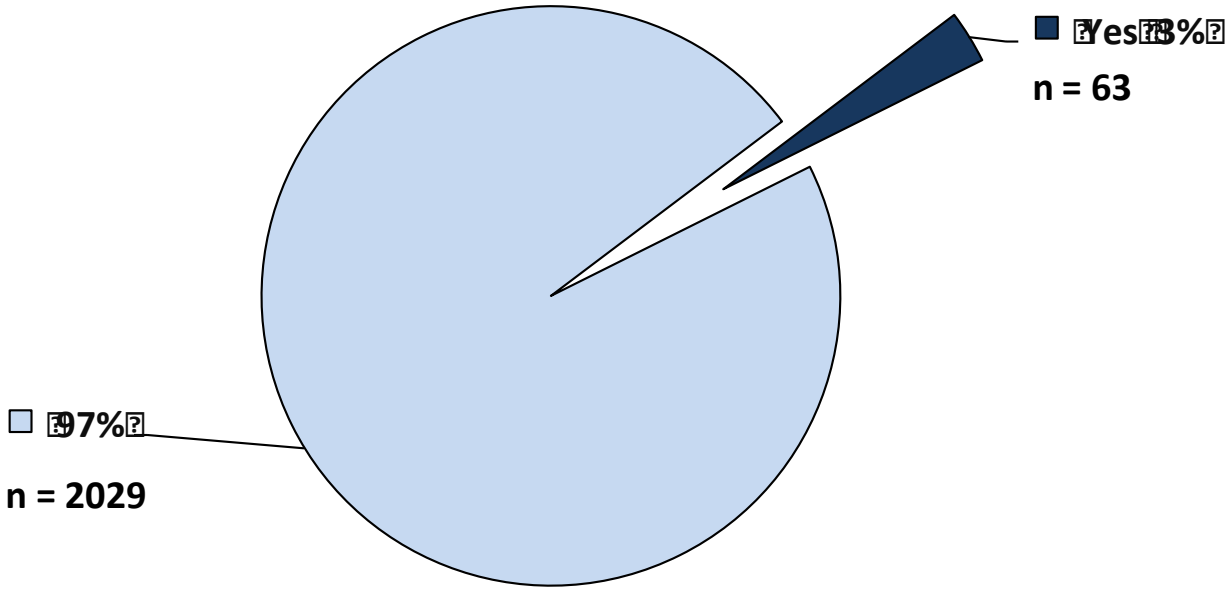
HAPO Study Cooperative Research Group. BJOG. 2010 ;117(5):575-84

BMI (Kg/m^2)	Cord CP > P90			Clinical NN hypoglycemia		
	N	%	OR	N	%	OR
<22.6	2633	4.7	1.00	2978	2.5	1.00
22.6-28.4	10317	7.1	1.46*	11938	1.9	0.81
28.5-32.9	4355	10.3	2.18*	5123	1.9	0.89
33.0-37.4	1683	13.8	3.11*	2068	2.4	1.08
37.5-41.9	599	13.9	3.04*	737	2.4	1.19
>=42	298	18.1	4.30*	383	3.4	1.74

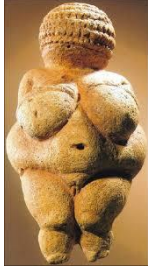


Maternal BMI is a predictor of NN hypoglycemia in GDM

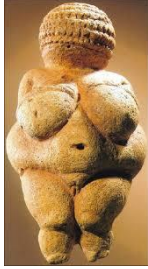
García-Patterson A. JCEM 2012; 97: 1623–1628



Maternal and fetal characteristics according to the presence of NN hypo



	No n = 2029	Yes n = 63 (3%)	p
Age (years)	33	33	ns
BMI (Kg/m^2)	23.2	24.5	< 0.02
Family history of DM (%)	56.1	51.6	ns
Poor obstetric outcome (%)	12.2	19.4	ns
Smoking habit (%) • Active • Quitters	 24.6 11.5	 25.5 9.8	 ns ns
Prior GDM/Abnormal glucose (%)	14.4	12.9	ns
Gestational age at diagnosis (weeks)	30	30	ns
Glucose values at diagnosis (mmol/l) 0h 1h 2h 3h N AbN points	 4.70 11.55 10.20 7.90 2	 4.90 11.50 10.10 7.95 2	 ns ns ns ns ns
Delay between dx and treatment (weeks)	2	2	ns
Mean blood glucose (mg/dl) 1st trimester 2nd trimester 3rd trimester	 92.0 92.0 90.0	 - 91 86	 ns ns <0.01

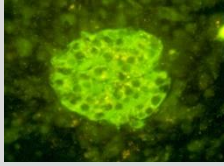


Logistic regression analysis to predict NN hypoglycemia (BW)

Variables	OR	
	Intermediate variables	Intermediate variables
BMI >= 25 kg/m^2	2.66*	2.11*
Male sex	–	–
Maternal HT		3.37*
GA at Dx	–	1.06
FPG at Dx	–	–
N abN points	1.52	–
HbA1c 3rd T	0.46*	0.47*
Cesarean delivery		2.56*
Delay between Dx & Tx	–	–
3rd T MBG	–	–
Weight increase	–	–
Twin pregnancy	–	–
Preterm birth		–
SGA		–
LGA		–
Abnormal Apgar		–
Respiratory distress		–

Tipus de diabetis

What's in a name?



Type 2 vs Type 1 DM

- **Poor pregnancy outcome in women with 2 DM**
  Clausen TD. Diabetes Care 2005; 28: 323-8

- **The pregnancies of women with type 2 DM: poor outcomes but opportunities for improvement**
  Roland JM. Diabet Med 2005; 22:1774–1777

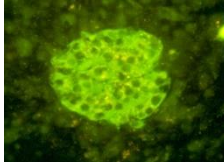
- **Similar outcome in pregnancies from Type 1 and Type 2 diabetic patients**
  De Leiva A. 37th Annual Meeting of the DPSG, 2005, Mykonos

- **PNM and congenital anomalies in babies of women with type 1 or type 2 DM in England, Wales, and Northern Ireland: population based study**
  Macintosh MC BMJ 2006; 333:177

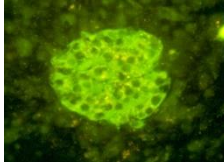
- **Is Pregnancy Outcome Worse in Type 2 Than in Type 1 Diabetic Women?**
  Hillman N. Diabetes Care 2006; 29: 2557-2558

Maternal and fetal outcome in women with type 2 versus type 1 DM: a systematic review and metaanalysis

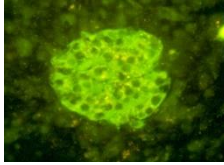
Balsells M. J Clin Endocrinol Metab. 2009;94(11):4284-91



Reference	Year	Country	Study design	Type 2 DM	Type 1 DM
Langer O	1988	USA	SC cohort	40	63
Botta RM	1990	Italy	SC cohort	25	31
Diabetes and Pregnancy Group	1991	France	MC cohort	78	232
Huddle K	1993	South Africa	SC cohort	85	122
Sidibe EH	1994	Senegal	SC cohort	50	35
Sachon C	1994	France	MC cohort	34	76
Hawthorne G	1994	UK	SC cohort	28	138
Sacks DA	1997	USA	SC cohort	113	46
Botta RM	1997	Italy	MC cohort	130	362
Zhu L	1997	Japan	SC cohort	244	178
Jouatte F	1999	France	SC cohort	38	105
Brydon P	2000	UK	SC cohort	(57)	(196)
Gunton JE	2000	Australia	SC cohort	19	74
Farrell T	2002	N. Zealand	SC cohort	(315)	(221)
Diabetes and Pregnancy Group	2003	France	MC cohort	146	289
Abdelgadir M	2003	Sudan	SC cohort	31	38
Hiéronimus S	2004	France	SC cohort	20	40
Ozumba BC	2004	Nigeria	SC cohort	44	34
Chaudry T	2004	UK	MC cohort	72	314
Roland JM	2005	UK	MC cohort	146	389
33 articles				3781	7966

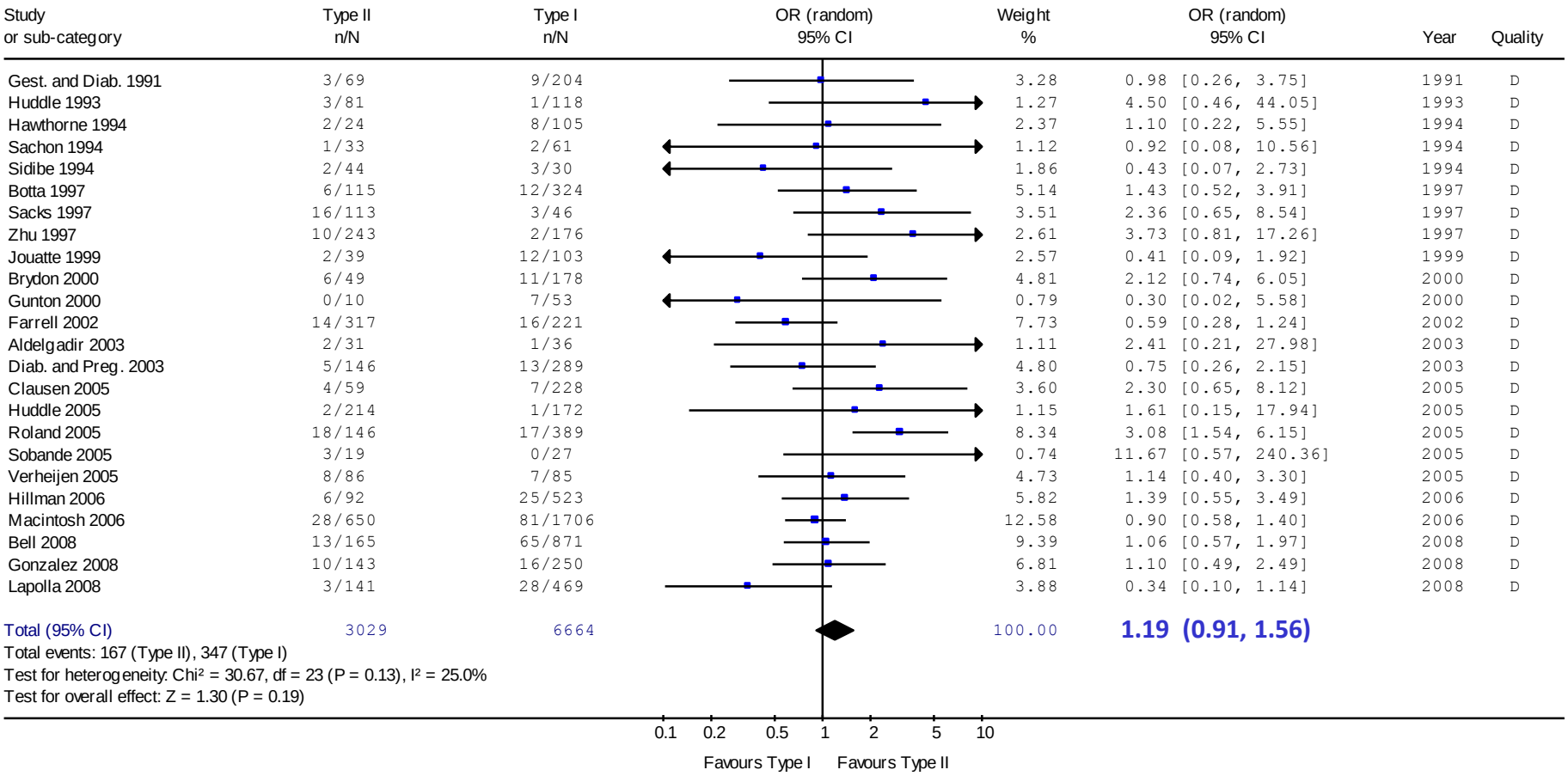


Maternal characteristics	n	Type 2 DM	Type 1 DM
Age (years)	23	33.9	28.8
BMI (Kg/m^2)	12	30.2	24.2
DM duration (years)	15	5.9	11.9
Chronic hypertension (%)	6	11.2	5.5
Retinopathy (%)	13	6.2	25.3
Micro/Macroalbuminuria (%)	10	2.9	6.8
Prepregnancy care (%)	11	18.8	34.8
GA at booking (weeks)	12	16.2	15.2
HbA1c at booking (%)	9	7.20	8.06
HbA1c 2nd trimester (%)	4	5.70	6.23
HbA1c 3rd trimester (%)	7	5.69	6.00

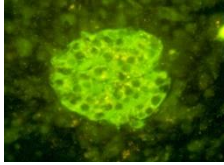


Major congenital malformations

Review: Gestació i diabetes
Comparison: 02 Type II vs Type I
Outcome: 03 maCM



Total events: 167 (Type II), 347 (Type I)
Test for heterogeneity: Chi² = 30.67, df = 23 (P = 0.13), I² = 25.0%
Test for overall effect: Z = 1.30 (P = 0.19)

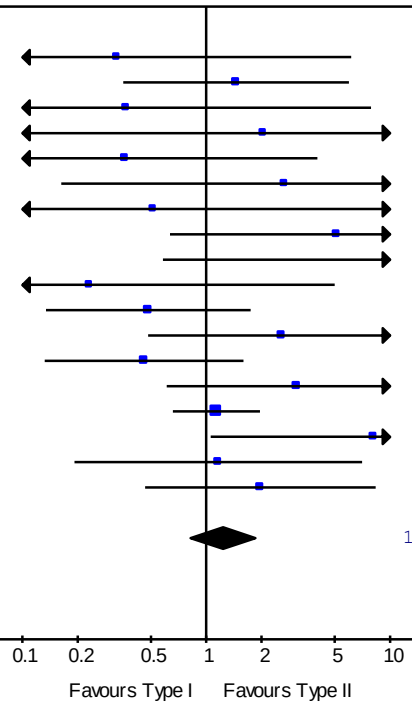


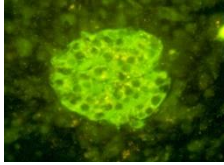
Stillbirth

Review: Gestació i diabetes
Comparison: 02 Type II vs Type I
Outcome: 01 Stillbirth

Study or sub-category	Type II n/N	Type I n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI	Year	Quality
Langer 1988	0/40	0/63			Not estimable	1988	D
Gest. and Diab. 1991	0/69	4/208		1.86	0.33 [0.02, 6.15]	1991	D
Huddle 1993	4/85	4/122		7.30	1.46 [0.35, 5.99]	1993	D
Sachon 1994	0/33	2/63		1.71	0.37 [0.02, 7.87]	1994	D
Sacks 1997	2/115	0/46		1.72	2.05 [0.10, 43.49]	1997	D
Zhu 1997	1/244	2/178		2.72	0.36 [0.03, 4.03]	1997	D
Jouatte 1999	1/40	1/105		2.04	2.67 [0.16, 43.68]	1999	D
Brydon 2000	0/49	3/181		1.81	0.52 [0.03, 10.14]	2000	D
Cundy 2000	8/256	1/160		3.57	5.13 [0.64, 41.40]	2000	D
Gunton 2000	1/11	0/53		1.51	15.29 [0.58, 401.49]	2000	D
Aldelgadir 2003	0/31	2/38		1.70	0.23 [0.01, 5.01]	2003	D
Diab. and Preg. 2003	3/146	12/289		8.69	0.48 [0.13, 1.74]	2003	D
Ozumba 2004	6/41	2/32		5.40	2.57 [0.48, 13.70]	2004	D
Huddle 2005	4/218	7/179		9.13	0.46 [0.13, 1.59]	2005	D
Verheijen 2005	6/86	2/85		5.66	3.11 [0.61, 15.88]	2005	D
Macintosh 2006	19/650	44/1706		29.70	1.14 [0.66, 1.96]	2006	D
Cundy 2007	13/544	1/333		3.74	8.13 [1.06, 62.42]	2007	D
Gonzalez 2008	2/145	3/253		4.71	1.17 [0.19, 7.06]	2008	D
Lapolla 2008	3/144	5/469		7.04	1.97 [0.47, 8.36]	2008	D
Total (95% CI)	2947	4563		100.00	**1.23 (0.82, 1.85)**		

Total events: 73 (Type II), 95 (Type I)
Test for heterogeneity: Chi² = 18.65, df = 17 (P = 0.35), I² = 8.9%
Test for overall effect: Z = 1.01 (P = 0.31)



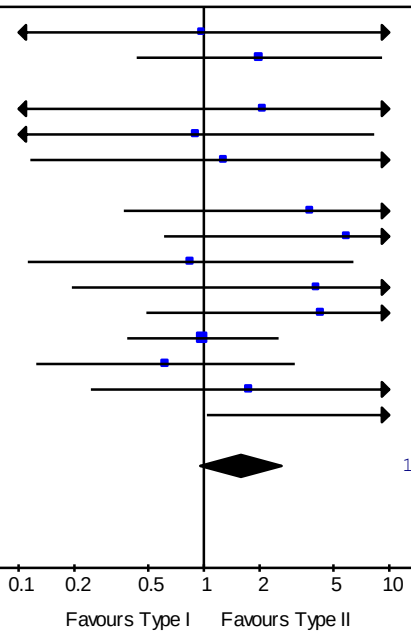


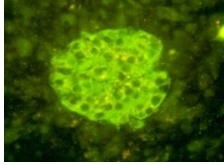
Neonatal Mortality

Review: Gestació i diabetes
Comparison: 02 Type II vs Type I
Outcome: 04 MN

Study or sub-category	Type II n/N	Type I n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI	Year	Quality
Gest. and Diab. 1991	0/69	1/204		2.47	0.98 [0.04, 24.24]	1991	D
Huddle 1993	4/81	3/118		10.98	1.99 [0.43, 9.15]	1993	D
Sachon 1994	0/33	0/61			Not estimable	1994	D
Sacks 1997	2/113	0/46		2.73	2.09 [0.10, 44.28]	1997	D
Brydon 2000	1/49	4/178		5.20	0.91 [0.10, 8.30]	2000	D
Cundy 2000	2/248	1/159		4.40	1.28 [0.12, 14.28]	2000	D
Gunton 2000	0/10	0/53			Not estimable	2000	D
Aldelgadir 2003	3/31	1/36		4.75	3.75 [0.37, 38.05]	2003	D
Diab. and Preg. 2003	3/143	1/277		4.94	5.91 [0.61, 57.38]	2003	D
Ozumba 2004	2/35	2/30		6.23	0.85 [0.11, 6.42]	2004	D
Huddle 2005	2/214	0/172		2.76	4.06 [0.19, 85.11]	2005	D
Mc Elduff 2005	5/96	1/79		5.43	4.29 [0.49, 37.47]	2005	D
Macintosh 2006	6/631	16/1662		28.71	0.99 [0.38, 2.54]	2006	D
Cundy 2007	3/531	3/331		9.89	0.62 [0.12, 3.10]	2007	D
Gonzalez 2008	2/143	2/250		6.57	1.76 [0.25, 12.62]	2008	D
Lapolla 2008	3/141	1/464		4.95	10.07 [1.04, 97.54]	2008	D
Total (95% CI)	2568	4120		100.00	**1.58 (0.96, 2.62)**		

Total events: 38 (Type II), 36 (Type I)
Test for heterogeneity: Chi² = 8.71, df = 13 (P = 0.79), I² = 0%
Test for overall effect: Z = 1.78 (P = 0.07)



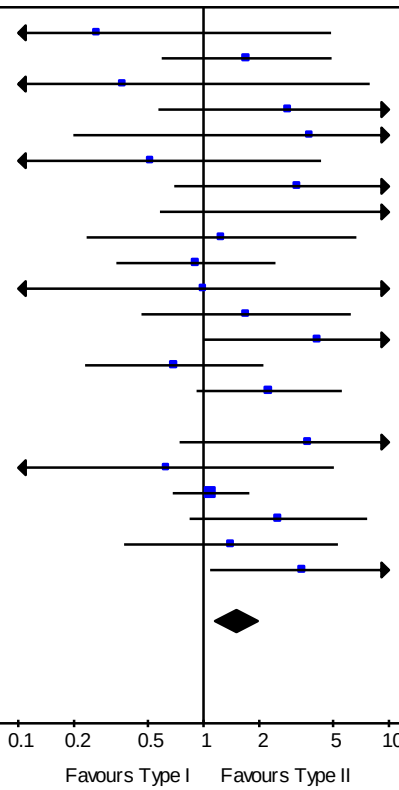


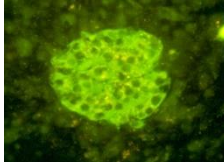
Perinatal mortality

Review: Gestació i diabetes
Comparison: 02 Type II vs Type I
Outcome: 02 PNM

Study or sub-category	Type II n/N	Type I n/N	Weight %	OR (random) 95% CI	Year	Quality
Gest. and Diab. 1991	0/69	5/208	0.83	0.27 [0.01, 4.88]	1991	D
Huddle 1993	8/85	7/122	6.32	1.71 [0.59, 4.90]	1993	D
Sachon 1994	0/33	2/63	0.75	0.37 [0.02, 7.87]	1994	D
Botta 1997	3/115	3/324	2.70	2.87 [0.57, 14.41]	1997	D
Sacks 1997	4/115	0/46	0.81	3.75 [0.20, 71.12]	1997	D
Brydon 2000	1/49	7/181	1.56	0.52 [0.06, 4.31]	2000	D
Cundy 2000	10/256	2/160	3.00	3.21 [0.69, 14.85]	2000	D
Gunton 2000	1/11	0/53	0.66	15.29 [0.58, 401.49]	2000	D
Aldelgadir 2003	3/31	3/38	2.50	1.25 [0.23, 6.68]	2003	D
Diab. and Preg. 2003	6/146	13/289	7.19	0.91 [0.34, 2.45]	2003	D
Hiéronimus 2004	1/20	2/40	1.16	1.00 [0.09, 11.74]	2004	D
Ozumba 2004	8/41	4/32	4.15	1.70 [0.46, 6.24]	2004	D
Clausen 2005	4/61	4/240	3.51	4.14 [1.01, 17.06]	2005	D
Huddle 2005	6/218	7/179	5.72	0.70 [0.23, 2.11]	2005	D
Roland 2005	9/146	11/389	8.63	2.26 [0.92, 5.57]	2005	D
Sobande 2005	0/19	0/27		Not estimable	2005	D
Verheijen 2005	7/86	2/85	2.74	3.68 [0.74, 18.24]	2005	D
Hillman 2006	1/93	9/532	1.63	0.63 [0.08, 5.05]	2006	D
Macintosh 2006	25/650	60/1706	31.08	1.10 [0.68, 1.77]	2006	D
Cundy 2007	16/535	4/333	5.76	2.54 [0.84, 7.65]	2007	D
Gonzalez 2008	4/145	5/253	3.97	1.41 [0.37, 5.33]	2008	D
Lapolla 2008	6/144	6/478	5.34	3.42 [1.09, 10.77]	2008	D
Total (95% CI)	3068	5778	100.00	**1.50 (1.15, 1.96)**		

Total events: 123 (Type II), 156 (Type I)
Test for heterogeneity: Chi² = 19.25, df = 20 (P = 0.51), I² = 0%
Test for overall effect: Z = 3.01 (P = 0.003)





Secondary Outcomes	N	OR (95% CI)	P value
Maternal			
PIH	9	0.87	ns
Preeclampsia	7	0.85	ns
Hypoglycemic coma	3	0.17	0.06
Diabetic ketoacidosis	5	0.09	<0.001
Caesarean section	18	0.80	<0.01
Fetal			
Miscarriages	7	1.36	0.07
Pregnancy terminations	6	1.02	ns
Preterm birth	17	0.85	ns
SGA	10	1.30	ns
LGA	14	0.98	ns
Macrosomia	6	1.02	ns
Minor congenital malformations	2	1.00	ns
Hypoglycemia	11	0.85	ns
Jaundice	7	0.82	ns
Respiratory distress	10	0.67	ns






Dades poblacionals

- **Perinatal outcomes among Asian American and Pacific Islander women**
  Rao AK. Am J Obstet Gynecol. 2006; 195:834-8
- **Ethnicity modifies the effect of obesity on insulin resistance in pregnancy: a comparison of Asian, South Asian, and Caucasian women**
  Retnakaran R. J Clin Endocrinol Metab. 2006; 91:93-7
- **Maternal race/ethnicity and predictors of pregnancy and infant outcomes**
  Shiao SY. Biol Res Nurs. 2005;7:55-66
- **Ethnicity and birth outcome: New Zealand trends 1980-2001: Part 4. Pregnancy outcomes for European/other women**
  Craig ED. Aust N Z J Obstet Gynaecol. 2004;44:545-8

DMG

- **Ethnic differences in perinatal outcome of GDM**
  Silva JK. Diabetes Care. 2006; 29:2058-63
- **Perinatal outcomes in patients with GDM by race/ethnicity**
  Esakoff TF. J Maternal-Fetal and Neonatal Medicine. 2011; 24: 422-26

GDM and maternal ethnicity: high prevalence of fetal macrosomia in non-Caucasian women

A. Aulinas. Med Clin 2013; 141: 240-5

	1986-1992	1993-1997	1998-2002	2003-2007	Total
%	0.3	1.1	3.1	9.7	2.5

Maternal characteristics	Caucasian GDM N=2480	Non Caucasian GDM N=63	p
Family Hx DM (%)	56.3	50	ns
Personal Hx AGT (%)	13.9	7.9	ns
Chronic Hx (%)	2.1	3.2	ns
Prior pregnancies (%)	61	82.5	<0.05
Unfavourable obstetric Hx (%)	12.6	22.2	<0.05
Prior macrosomia (%)	5.2	14.3	<0.05
Age (years)	33	33	ns
Prepregnancy BMI (Kg/m^2)	23.2	24.8	<0.05
Smoking habit (%)			<0.05
• Stop during pregnancy	11	8.3	
• Active	25	8.3	
GA at dx (weeks)	29	28	0.052
GA at clinic entry (weeks)	32	32	ns
Delay in clinic entry (weeks)	2	3	<0.001
Dx OGTT (mmol/l)			
• 0h	4.7	5.16	<0.001
• 1h	11.6	11.3	ns
• 2h	10.2	10.2	ns
• 3h	7.9	8.1	ns
Insulin Tx (%)	48.3	49.2	ns
1st HbA1c (%)	5.01	5.4	<0.001
Mean 3rd T HbA1c (%)	5.08	5.45	<0.001
Weight gain (kg)	10.2	10.7	ns

Perinatal outcome	Caucasian GDM N=2480	Non Caucasian GDM N=63	p
PIH	5	6.7	ns
Preterm birth (%)	10.6	3.2	0.056
CS (%)	24.9	33.3	ns
Apgar <7			
• 1’	6.1	6.5	ns
• 5’	0.5	0	ns
Macrosomia (>= 4000 g)	4.3	19.4	<0.05
LGA (%)	9.5	32.3	<0.05
SGA (%)	10.6	8.1	ns
Obstetric trauma (%)	2.2	0	ns
Malformations			
• major (%)	3.8	5	ns
• minor (%)	7.4	11.7	ns
Hypoglycemia (%)	2.7	1.7	ns
Hypocalcemia (%)	1.6	0	ns
Polycythemia (%)	1.7	0	ns
Hyperbilirrubinemia (%)	5.3	8.3	ns
Respiratory distress (%)	3.6	3.3	ns
Perinatal mortality (%)	0.8	0	ns

Maternal ethnicity as a predictor of perinatal outcome

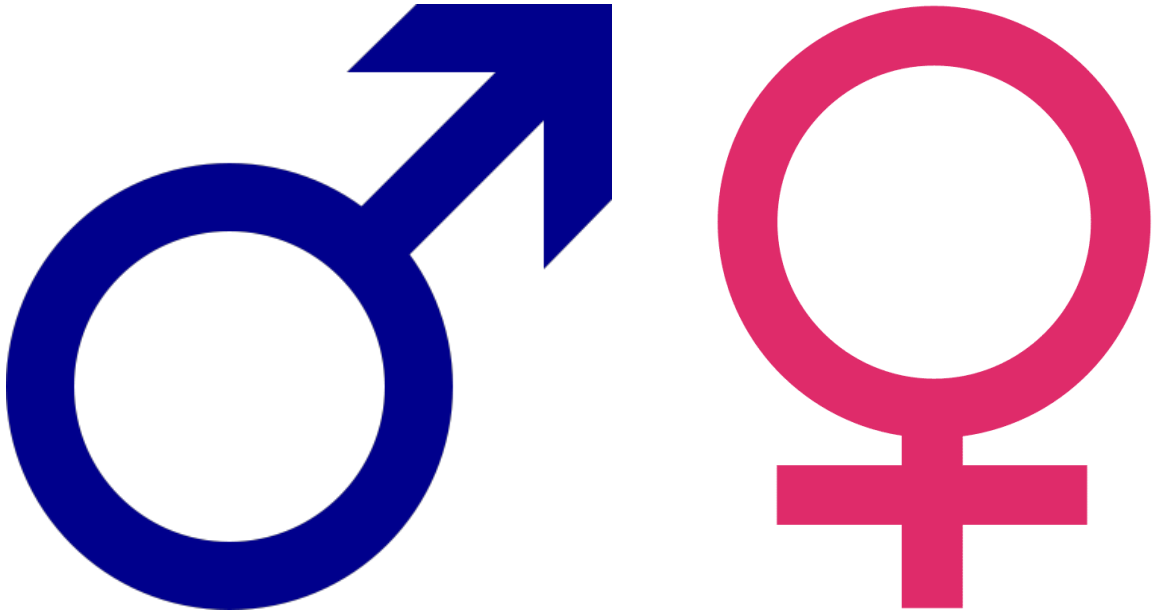
(multiple logistic regression analysis, BW)

Outcome	OR (95 CI)
PIH	ns
Preterm birth	ns
CS	ns
Apgar <7 • 1' • 5'	 ns ns
Macrosomia (>= 4000 g)	2.994 *
LGA	2.767 *
SGA	ns
Obstetric trauma	ns
Malformations • Major • Minor	ns ns
Hypoglycemia	ns
Hypocalcemia	ns
Polycythemia	ns
Hyperbilirrubinemia	3.629 *
Respiratory distress	ns
Perinatal mortality	no predictive model

genotip estalviador?

fenotip estalviador?

etnia asiàtica?



Differences in BW regulation in boys and girls

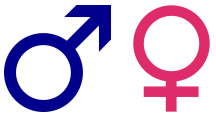
- **Maternal CHO and its relationship to fetal growth and body composition**
  Catalano P. Am J Obstet Gynecol 1995;172:1464–70

- **Girls at five are intrinsically more insulin resistant than boys: The Programming Hypotheses Revisited--The EarlyBird Study (EarlyBird 6)**
  Murphy MJ; EarlyBird Study (EarlyBird 6). Pediatrics. 2004 113(1 Pt 1):82-6

- **Sexual Dimorphism in the GH and IGF-I Axis at Birth**
  Geary MPP. J Clin Endocrinol Metab 2003;88:3708–14

- **Sex-based differences in serum leptin concentrations from umbilical cord blood at delivery**
  Tome MA. Eur J Endocrinol. 1997 Dec;137(6):655-8

- **Gender specificity of body adiposity and circulating adiponectin, visfatin, insulin, and IGF-I at term birth: relation to prenatal growth**
  Ibáñez L. J Clin Endocrinol Metab. 2008 Jul;93(7):2774-8.



Maternal glucose tolerance status influences the risk of macrosomia in male but not in female fetuses

Ricart W. J Epidemiol Community Health 2009;63;64-68

Maternal characteristic	Male N=4793	Female N=4477	p
Age (years)	29.4	29.4	ns
BMI (Kg/m^2)	23.9	24.0	ns
Glucose tolerance • Neg Sc • FP Sc • ADA-only GDM • NDDG-GDM	 68.3 22,8 8.9 0.9	 69.0 22.5 8.5 0.8	ns
Chronic hypertension (%)	0.9	0.8	ns
PIH (%)	2.2	1.8	ns
GA (weeks)	39.5	39.5	ns
BW (g)	3301	3174	<0.001
LGA (%)	15.4	13-8	<0.02
SGA (%)	7.3	6.4	<0.05

Multivariate logistic regression models to predict BW categories in boys and girls (E)

Maternal characteristic	Macrosomia		LGA		SGA	
	Female	Male	Female	Male	Female	Male
BMI categories						
• UW (<18.5 kg/m^2)	0.66	0.36	0.61	0.54	1.50	1.92*
• NW (18.5-24.9 kg/m^2)	1.00	1.00	1.00	1.00	1.00	1.00
• OW (25-24.9 kg/m^2)	1.47*	1.37*	1.52*	1.37*	0.82	0.85
• OB (>=30 kg/m^2)	3.27*	1.97*	1.89*	2.37*	0.66	0.56*
Glucose tolerance						
• Neg Sc	1.00	1.00	1.00	1.00	1.00	1.00
• FP Sc	0.98	1.53*	1.10	1.25*	1.01	0.77
• NDDG-GDM	1.04	1.67*	1.16	1.01	1.04	1.41

Background population

- **Sex differences in the prevalence of human birth defects: A population-based study**
  Lary JM. Teratology. 2001; 64:237-251
- **Male predominance in fetal distress during labor**
  Bekedam DJ. Am J Obstet Gynecol 2002; 187:1605-1607
- **Offspring sex and pregnancy outcome by length of gestation**
  Vatten LJ.Early Hum Dev 2004; 76: 47-54
- **RF and outcome of failure to progress during the first stage of labor: a population-based study**
  Sheiner E. Acta Obstet Gynecol Scand 2002; 81: 222–226

DM

- **Effect of gender on perinatal outcome in pregnancies complicated by DM**
  Bracero LA. Gynecol Obstet Invest 1996; 41:10-14
- **Congenital anomalies among infants of diabetic mothers in Emilia Romagna (North Italy) between 1982 and 2002**
  Cocilovo G. 4th International Symposium on Diabetes & Pregnancy Istambul, Turkey; 2007; 48A
- **Male predominance of congenital malformations in infants of women with type 1 DM**
  Evers IM. Diabetes Care 2009; 32:1194-1195
- **GDM alters the male bias for CS**
  Knights S. Diabetes Care 2000; 23: 425-6

Poorer perinatal outcome in male newborns of women with pregestational DM

García-Patterson A. Diabet Med. 2011;28(4):436-9

Maternal characteristic	Female N=220	Male N=235	p
Age (years)	30	30	ns
BMI (Kg/m^2)	23.1	23.4	ns
Diabetes duration (years)	10	10	ns
Preconception care (%)	50.9	46.4	ns
GA at first visit (week)	6	6	ns
Hypertension (%)	22.1	21.7	ns
Smoking (%) • quitters • smokers	 12.8 26.0	 13.6 28.5	ns
Prior adverse outcome (%)	18.3	12.8	ns
First trimester HbA1c (%)	6.30	6.20	ns
Second trimester HbA1c (%)	5.83	5.70	ns
Third trimester HbA1c (%)	5.74	5.73	ns

Perinatal outcome	Female N=220	Male N=235	p
Perinatal mortality (%)	1.8	1.7	ns
Major CM (%)	5.5	7.7	ns
LGA (%)	30.6	35.9	ns
SGA (%)	2.7	4.7	ns
Preterm delivery (%)	20.9	23.8	ns
Composite outcome (%)	46.4	56.2	0.039

Logistic regression analysis to predict composite fetal outcome (BW method)

Variable	OR (CI 95)
Age (years)	ns
BMI (Kg/m^2)	ns
Diabetes duration (years)	ns
Preconception care (Y/N)	ns
GA at first visit (week)	ns
Hypertension (Y/N)	1.81 *
Smoking • quitters (Y/N) • smokers (Y/N)	 1.05 0.49 *
Prior adverse outcome (Y/N)	ns
First trimester HbA1c (%)	ns
Second trimester HbA1c (%)	ns
Third trimester HbA1c (%)	1.78 *
Male sex (Y/N)	1.61 *

Perinatal Maternal and Neonatal Outcomes in Women With GDM According to Fetal Sex

D. Tundidor. Gender Medicine 2012; 9: 411-7

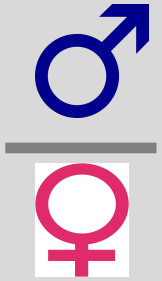
Conclusions: In this group of women with GDM, perinatal outcomes in pregnancies of male newborns differ in only 2 of 16 evaluated variables:

- **an increased frequency of CS** **OR 1.48**
- **and neonatal hypoglycemia** **OR 2.13**

Male newborns of mothers with GDM could benefit from increased awareness of neonatal hypoglycemia.

Environmental factors influencing sex ratio

- **The sex ratio at birth (proportion of males in liveborn fetus) in the general population has been established as 1.06 (51.5%)**



- **Different factors can modify this ratio as:**
  - ✓ **Industrialization** (Davis 1998)
  - ✓ **Parental age** (Juntunen 1997, Nicolich 2000)
  - ✓ **Smoking** (Fukuda 2002)
  - ✓ **Season of conception** (Cagnacci 2003)
  - ✓ **Geographical latitude** (Savona-Ventura 2000)
  - ✓ **Maternal nutritional status** (Gibson 2004, Cagnacci 2004)
  - ✓ **Hormonal environment during conception** (James 1996, 2004)
  - ✓ **Endocrinological diseases:**
    - **Congenital adrenal hyperplasia** (Haegnfeldt 2008)
    - **Diabetes mellitus** (Rjasanowski, 1998, Moller 1998)

Sex ratio at birth is associated with type 1 diabetes characteristics

García-Patterson A. Acta Diabetol 2016;53(6):1025-1035

- **The observed SRB (238 males/468 live births = 0.509) did not differ from expected**
- **In the logistic regression analysis, SRB was significantly associated with three diabetes characteristics (ORs for a live male newborn):**
  - ✓ **DM duration:**
    - **OR 1.22 for ≤5 years**
    - **OR 1.0 for 5-20 years**
    - **OR 2.79 for >20 years**
  - ✓ **1st trimester HbA1c:**
    - ✓ **OR 1.98 for ≤6.7 %**
    - ✓ **OR 1.0 for 6.7-8.2 %**
    - ✓ **OR 2.61 for >8.2 %**
  - ✓ **1st trimester insulin dose:**
    - ✓ **OR 0.70 for ≤0.5 IU/kg/day**
    - ✓ **OR 1.0 for 0.5-1.0 IU/kg/day**
    - ✓ **OR 0.18 for >1.0 IU/kg/day**


INSULI
50 Units — 5 C.C.
10 Units per C.C.
CONNAUGHT LABORATO
UNIVERSITY OF TORO

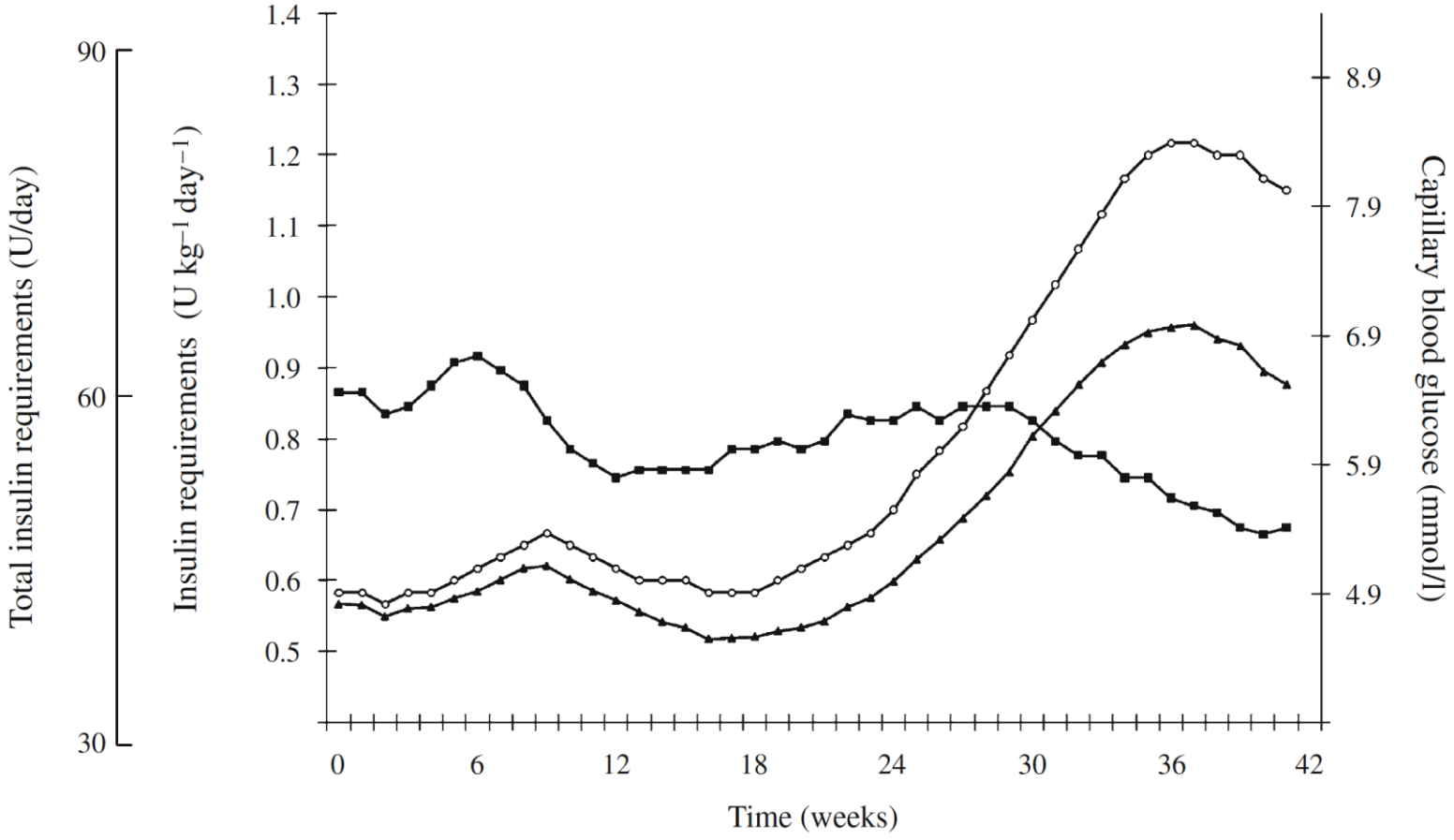
CONCEPTT

CONCEPTT: Continuous Glucose Monitoring in Women with Type 1 Diabetes in Pregnancy Trial

2017

Insulin requirements throughout pregnancy in women with type 1 diabetes mellitus: three changes of direction

García-Patterson A. Diabetologia 201;53(3):446-51



The New England Journal of Medicine

VOLUME 343 OCTOBER 19, 2000 NUMBER 16

A COMPARISON OF GLYBURIDE AND INSULIN IN WOMEN WITH GESTATIONAL DIABETES MELLITUS

ODED LANGER, M.D., DEBORAH L. CONWAY, M.D., MICHAEL D. BERKUS, M.D., ELLY M.-J. XENAKIS, M.D., AND OLGA GONZALES, R.N.

Conclusions In women with gestational diabetes, glyburide is a clinically effective alternative to insulin therapy. (N Engl J Med 2000;343:1134-8.)

Langer and his colleagues are to be congratulated for prudently defying conventional wisdom and showing the way to an alternative treatment for women with gestational diabetes

Michael Greene, accompanying editorial

Original Research

Trends in Glyburide Compared With Insulin Use for Gestational Diabetes Treatment in the United States, 2000–2011

Wendy Camelo Castillo, MD, PhD, Kim Boggess, MD, Til Stürmer, MD, PhD, M. Alan Brookhart, PhD, Daniel K. Benjamin Jr, MD, PhD, and Michele Jonsson Funk, PhD

OBSTETRICS & GYNECOLOGY VOL. 123, NO. 6, JUNE 2014

Table 1. Distribution of Women Treated With Glyburide (n=5,873) Among Women Treated With Glyburide or Insulin, by Calendar Year and Region

	Glyburide (%)*	Total (N=10,778)
Calendar year		
2001	7.4	68
2002	13.5	155
2003	22.7	361
2004	33.1	631
2005	41.1	869
2006	48.4	881
2007	56.4	1,090
2008	59.4	1,278
2009	60.8	1,966
2010	62.3	1,807
2011	64.5	1,672

BMJ 2015;350:h102 doi: 10.1136/bmj.h102 (Published 21 January 2015)

Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis

Montserrat Balsells *registrar in endocrinology and nutrition*[1], Apolonia García-Patterson *registrar in endocrinology and nutrition*[2], Ivan Solà *associate researcher*[3 4 5], Marta Roqué *associate researcher*[3 4 5], Ignasi Gich *associate researcher*[5 6 7], Rosa Corcoy *assistant professor in endocrinology and nutrition*[2 8 9]

Abstracts retrieved 911

→ **872 excluded after abstract revision**

Full text reviewed 39

→ **24 excluded**
- **18 no RCT**
- **3 data overlap**
- **3 addressing T2DM or T2DM & GDM**

15 studies included
- **7 GLY vs INS**
- **6 MET vs INS**
- **2 MET vs GLY**

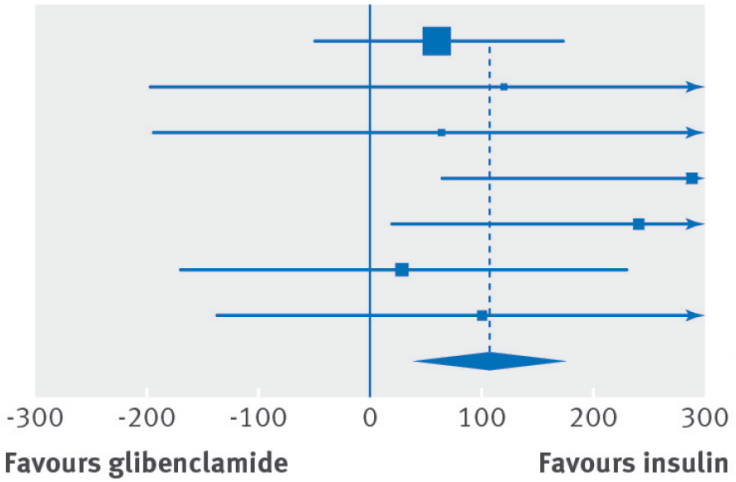
Outcomes measures:
- **14 primary (6 maternal, 8 fetal)**
- **16 secondary (5 maternal, 11 fetal)**

Glibenclamide vs Insulin

Study or subgroup	Glibenclamide Mean (SD) birth weight (g)	Glibenclamide No of births	Insulin Mean (SD) birth weight (g)	Insulin No of births	Mean difference (95% CI)*	Weight (%)
Glibenclamide *v* insulin						
Langer et al 2000[2]	3256 (543)	201	3194 (598)	203		42.6
Anjalakshi et al 2007[21]	2720 (340)	10	2600 (430)	13		5.3
Ogunyemi et al 2007[22]	3460.5 (741)	48	3395.6 (542)	49		7.9
Silva et al 2007[20]	3372.18 (501.04)	32	3082.78 (423.23)	36		10.7
Lain et al 2009[3]	3603.7 (607)	41	3363.2 (385)	41		10.9
Mukhopadhyay et al 2012[23]	3010 (400)	30	2980 (390)	30		13.2
Tempe et al 2013[24]	3200 (420)	32	3100 (540)	32		9.4
Total		394		404		100.0

Test for heterogeneity: χ^2=5.32, df=6, P=0.50, I^2=0%

Test for overall effect: z=2.93, P=0.003



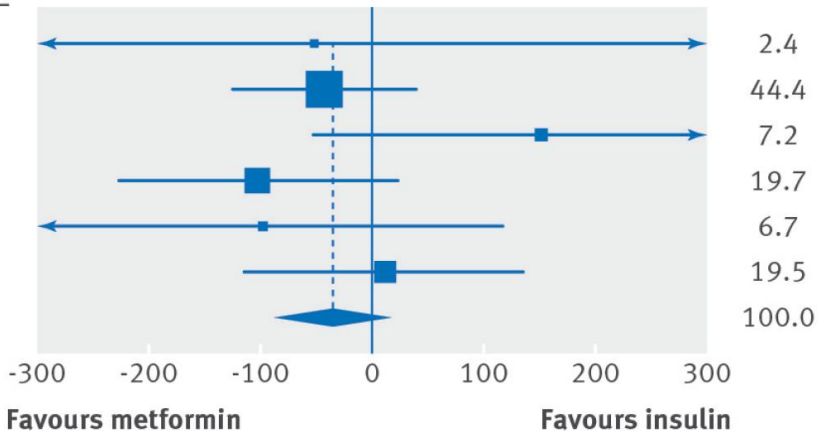
- **Birtweight** **MD 108.5 g**
- **Macrosomia** **RR 2.62**
- **NN hypoglycemia** **RR 2.04**

Metformin vs Insulin

Study or subgroup	Mean (SD) birth weight (g)	No of births	Mean (SD) birth weight (g)	No of births	
	Metformin		Insulin		
Metformin *v* insulin					
Moore et al 2007[25]	3451.8 (727.5)	32	3500.2 (700.5)	31	2.4
Rowan et al 2008[4]	3372 (572)	363	3413 (569)	370	44.4
Ijas et al 2011[26]	3712 (432)	47	3558 (593)	50	7.2
Niromanesh et al 2012[27]	3300 (400)	80	3400 (400)	80	19.7
Spaulonci et al 2013[29]	3143.7 (446.6)	46	3237.6 (586.8)	46	6.7
Tertti et al 2013[28]	3604 (488)	110	3589 (448)	107	19.5
Total		678		684	100.0

Test for heterogeneity: χ^2=5.22, df=5, P=0.39, I^2=4%

Test for overall effect: z=1.12, P=0.26



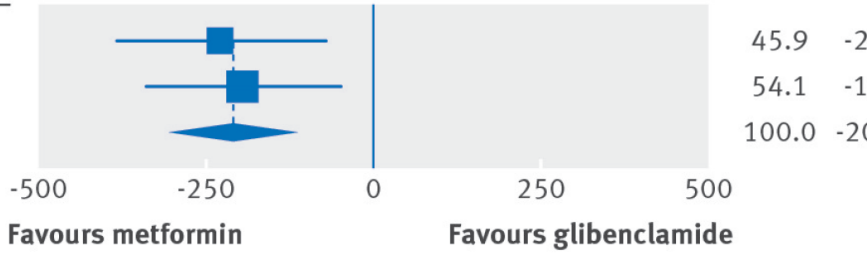
- **Weight gain MD -1.14 kg**
- **GA at delivery -0.16 wk**
- **Preterm birth RR 1.50**
- **SMBG 2h pp -0.14 mmol/l**
- **Weight gain since entry -1.23 kg**
- **PIH RR 0.53**
- **Severe NN hypo RR 0.62**

Metformin vs Glibenclamide

Study or subgroup	Mean (SD) birth weight (g)	No of births	Mean (SD) birth weight (g)	No of births
Metformine *v* glibenclamide	**Metformin**		**Glibenclamide**	
Moore et al 2010[30]	3103 (600)	75	3329.6 (334)	74
Silva et al 2012[5]	3193.87 (521.22)	104	3387.98 (512.16)	96
Total		179		170

Test for heterogeneity: χ^2=0.09, df=1, P=0.76, I^2=0%

Test for overall effect: z=3.89, P<0.001



- **Weight gain MD -2.06 kg**
- **Birthweight -209.01 kg**
- **Macrosomia RR 0.33**
- **LGA RR 0.44**
- **SMBG fasting 0.15 mmol/l**

Alberto de Leiva
Agueda Caballero
Agustina Prados
Analía Ramos
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Apolonia García-Patterson
Bettina Biagetti
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Manel Puig
M José Barahona
M José Cerqueira
Marta Roqué
Mercè Albareda
Mercedes Codina
Mercedes Rigla
Miguel Angel María
Montserrat Balsells
Nuria Gascón
Orenci Altirriba
Paquita Montaner
Raquel Campos
Sandra Piquer
Teresa Puig
Wifredo Ricart
Xisca Caimari

Què ens falta?

- **Dades epidemiològiques poblacionals**
  - ✓ **prevalença ≠ tipus**
  - ✓ **condicions associades**
  - ✓ **resultats perinatals**
  - ✓ **a llarg termini**

- **DMG**
  - ✓ **criteris IADPSG**
  - ✓ **cribrat i dx 1er trimestre**

- **Tx**
  - ✓ **dieta**
  - ✓ **monitorització**
  - ✓ **fàrmacs orals**
  - ✓ **anàlegs, bomba**

The Toronto Tri-Hospital Gestational Diabetes Project
A preliminary review
Sermer M. Diabetes Care. 1998 Aug;21 Suppl 2:B33-42

Study subjects	**3836**
GDM prevalence (NDDG, %)	**3.8**
↑ after CC criteria (%)	**50**
Macrosomia (%)	
Control	**13.7**
Only CC	**28.7**
GDM-NDDG	**10.5**
Cesarean section (%)	
Control	**20.2**
Only CC	**29.6**
GDM-NDDG	**33.6**
Preeclampsia (%)	
Control	**4.9**
Only CC	**8.7**
GDM-NDDG	**8.4**

Hyperglycemia and Adverse Pregnancy Outcomes

N Engl J Med 2008;358:1991-2002

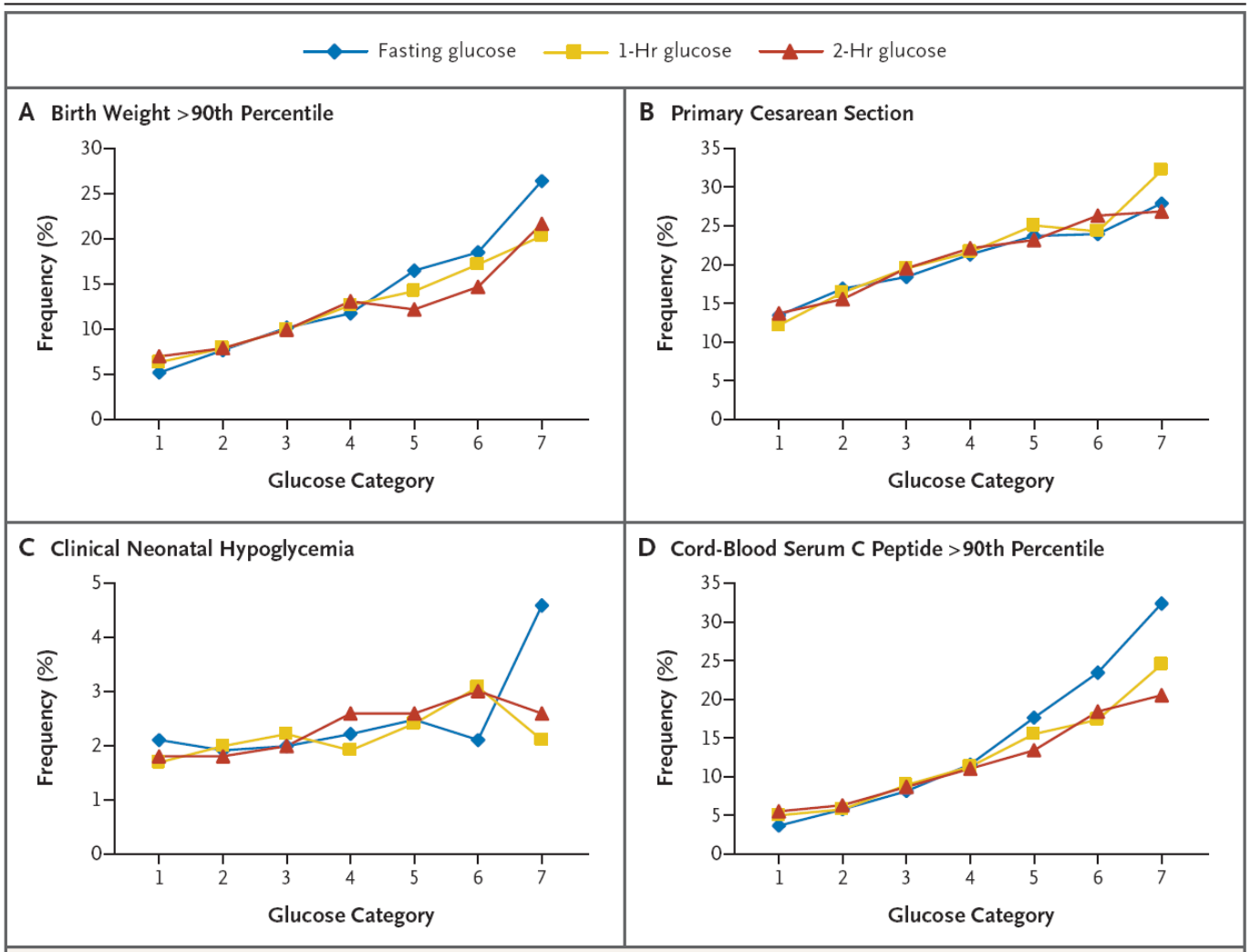

Figure 1. Frequency of Primary Outcomes across the Glucose Categories.

IADPSG recommendations on the diagnosis and classification of hyperglycemia in pregnancy

Metzger BE. Diabetes Care 2010;33(3):676-82

Consensus in:

- **Relevant variables:**
  - **LGA newborn (BW >P90)**
  - **s.c. adiposity (s.c. fat >P90)**
  - **hiperinsulinism (cord CP >P90)**

- **define cut-off as the glucose value identifying the group of pregnant women with a risk over the mean:**
  - **OR 1.50**
  - **OR 1.75**
  - **OR 2.0**

- **Dx if >=1 value >= cut-off**

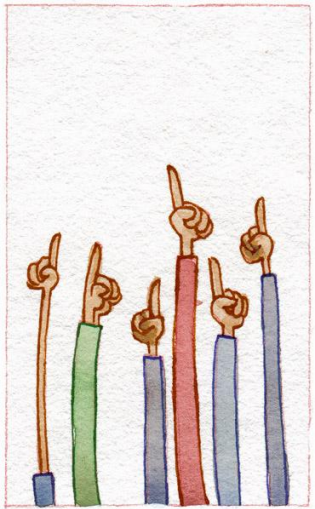

Table 1: Threshold Values for Diagnosis of GDM or Overt Diabetes Mellitus in Pregnancy

A. To diagnose GDM and cumulative proportion of HAPO cohort equaling or exceeding those thresholds			
Glucose Measure	**Glucose Concentration Threshold+**		**Percent ≥ Threshold**
	mmol/l	**mg/dl**	**Cumulative**
FPG	**5.1**	**92**	**8.3**
1-hr PG	**10.0**	**180**	**14.0**
2-hr PG	**8.5**	**153**	**16.1***

B. To diagnose overt diabetes mellitus in pregnancy	
Measure of Glycemia	Consensus Threshold
Fasting plasma glucose[1]	**≥ 7.0 mmol/l (126 mg/dl)**
HbA1c[1]	**≥ 6.5% (DCCT/UKPDS standardized)**
Random plasma glucose (RPG)	**> 11.1 mmol/l (200 mg/dl) + confirmation[2]**

Table 2. Strategy for the detection and diagnosis of hyperglycemic disorders in pregnancy[1]

First Prenatal Visit
Measure fasting plasma glucose, HbA1c or random plasma glucose on all or only "high risk" women[2]
• If results indicate overt diabetes as per Table 1-B
○ Treatment and follow-up as for pre-existing diabetes
• If results not diagnostic of overt diabetes
○ and fasting plasma glucose ≥ 5.1 mmol/l (92 mg/dl) but < 7.0 mmol/l (126 mg/dl), diagnose as GDM
○ and fasting plasma glucose < 5.1 mmol/l (92 mg/dl) test for GDM between 24 – 28 weeks gestation with a 75 gm OGTT[3]
24 – 28 weeks Gestation: Diagnosis of GDM
Two hour 75 gm OGTT: Perform after overnight fast on all women not previously found to have overt diabetes or GDM during testing earlier in this pregnancy
• **Overt DM if fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl)**
• **GDM if 1 or more values > thresholds indicated in Table 1-A**
• **Normal if all values on OGTT < thresholds indicated in Table 1-A**

BMJ

RESEARCH

Effects of treatment in women with gestational diabetes mellitus: systematic review and meta-analysis

Karl Horvath, project manager EBM review center,[1] head of outpatient facility diabetes and metabolism,[2] Klaus Koch, project manager,[3] Klaus Jeitler, scientific assistant,[1] Eva Matyas, scientific assistant,[1] Ralf Bender, head of department of medical biometry,[3] Hilda Bastian, head of department of health information,[3] Stefan Lange, deputy director,[3] Andrea Siebenhofer, professor for chronic care and health services research,[4] project manager[1]

BMJ. 2010 Apr 1;340:c1395

Table 1 | Characteristics of studies included in pool A: specific treatment for gestational diabetes mellitus versus usual care. All studies took place in hospital outpatient facilities

	No	Diagnosis	Intervention	Mean (SD) age (years)	Mean (SD) gestation at study entry (weeks)	Mean (SD) BMI	Ethnicity (%)
Bonomo 2005[17] (Italy)		C&C, 1 pt					
Intervention	150	2 steps: risk factors present, positive on 50 g glucose challenge*; negative on 100 g oral glucose tolerance test†	Diet	31 (5)	NA	23 (4)	All white
Control	150		Usual care	31 (5)	NA	23 (5)	All white
Crowther 2005[18-20] (Australia)		WHO					
Intervention	490	2 steps: risk factors present or positive result on 50 g glucose challenge*; positive result on 75 g oral glucose tolerance test§	Diet/insulin	31 (5)	29 (28-30)‡	27 (23-31)‡	White 73, Asian 19, other 9
Control	510		Usual care	30 (6)	29 (28-30)‡	26 (23-31)‡	White 78, Asian 14, other 8
Landon 2009[21] (USA)		C&C					
Intervention	485	2 steps: positive on 50 g glucose challenge, positive on 100 g oral glucose tolerance test¶	Diet/insulin	29 (6)	29 (2)	30 (5)	White 25, Latin-American 58, Afro-American 12, Asian 5, other 1
Control	473		Usual care	29 (6)	29 (2)	30 (5)	White 25, Latin-American 56, Afro-American 11, Asian 6, other 2
Langer 1989[22] (USA)		NDDG					
Intervention	63	2 steps: positive on 50 g glucose challenge**, positive on 100 g oral glucose tolerance test††	Diet/insulin	31 (5)	31 (3)	NA‡‡	White 36, Latin-American 33, Afro-American 30
Control	63		Usual care	28 (6)	31 (3)	NA‡‡	White 33, Latin-American 33, Afro-American 33
O'Sullivan 1966[23] (USA)		O'Sullivan					
Intervention	307	2 steps: risk factors present or positive on 50 g glucose challenge**, positive on 100 g oral glucose tolerance test¶¶	Diet and insulin	30 (NA)	NA	NA	NA
Control	308		Usual care	31 (NA)	NA	NA	NA

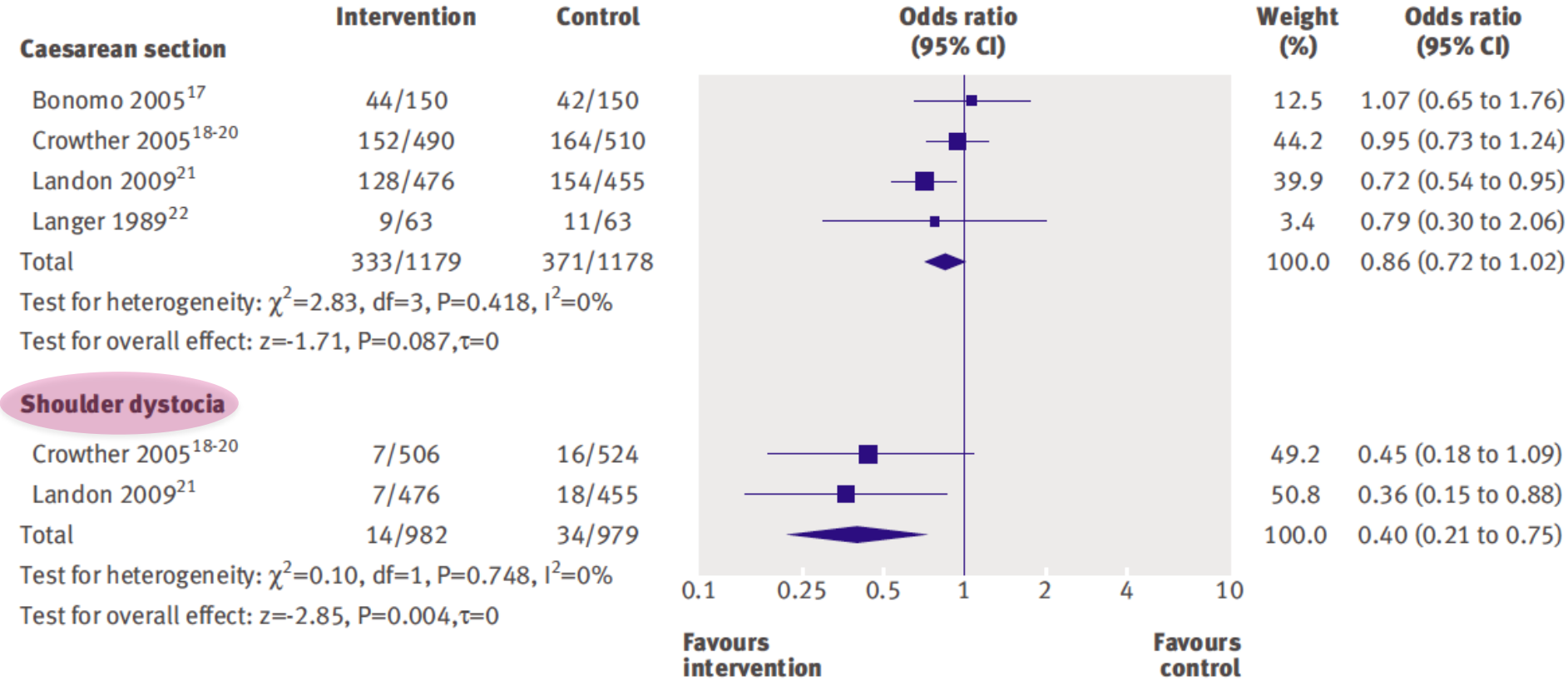

Fig 2 | Maternal outcomes in pool A (DerSimonian and Laird random effects model)

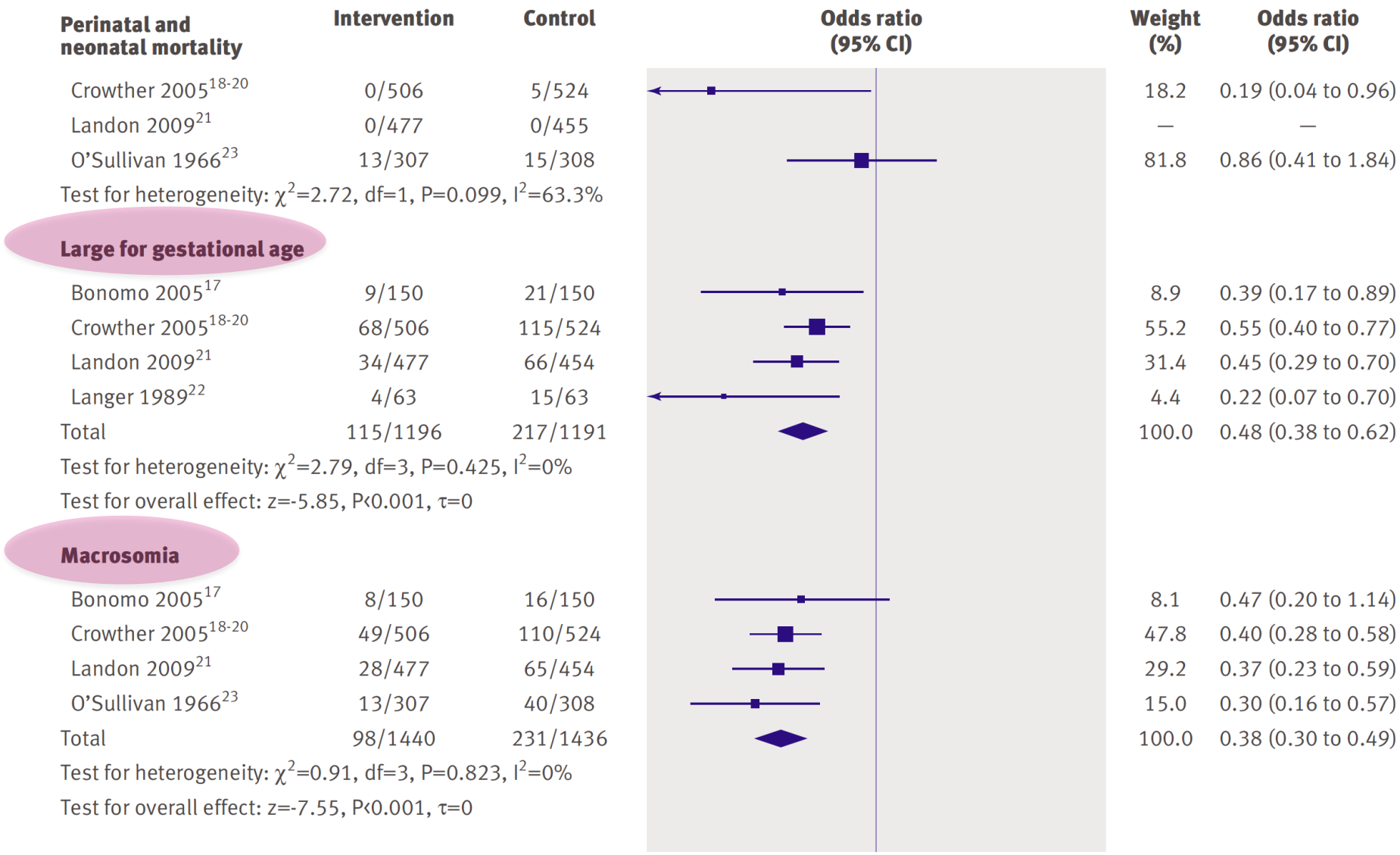

Fig 3 | Neonatal outcomes in pool A (DerSimonian and Laird random effects model, except for perinatal and neonatal morality and birth trauma, which use Peto fixed effects model)

Table 1 | Characteristics of studies included in pool A: specific treatment for gestational diabetes mellitus versus usual care. All studies took place in hospital outpatient facilities

	No	Diagnosis	Intervention	Mean (SD) age (years)	Mean (SD) gestation at study entry (weeks)	Mean (SD) BMI	Ethnicity (%)
Bonomo 2005[17] (Italy)		C&C, 1 pt					
Intervention	150	2 steps: risk factors present, positive on 50 g glucose challenge*; negative on 100 g oral glucose tolerance test†	Diet	31 (5)	NA	23 (4)	All white
Control	150		Usual care	31 (5)	NA	23 (5)	All white
Crowther 2005[18-20] (Australia)		WHO					
Intervention	490	2 steps: risk factors present or positive result on 50 g glucose challenge*; positive result on 75 g oral glucose tolerance test§	Diet/insulin	31 (5)	29 (28-30)‡	27 (23-31)‡	White 73, Asian 19, other 9
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Landon 2009[21] (USA)		C&C					
Intervention	485	2 steps: positive on 50 g glucose challenge, positive on 100 g oral glucose tolerance test¶	Diet/insulin	29 (6)	29 (2)	30 (5)	White 25, Latin-American 58, Afro-American 12, Asian 5, other 1
Control	473		Usual care	29 (6)	29 (2)	30 (5)	White 25, Latin-American 56, Afro-American 11, Asian 6, other 2
Langer 1989[22] (USA)		NDDG					
Intervention	63	2 steps: positive on 50 g glucose challenge**, positive on 100 g oral glucose tolerance test††	Diet/insulin	31 (5)	31 (3)	NA‡‡	White 36, Latin-American 33, Afro-American 30
Control	63		Usual care	28 (6)	31 (3)	NA‡‡	White 33, Latin-American 33, Afro-American 33
O'Sullivan 1966[23] (USA)		O'Sullivan					
Intervention	307	2 steps: risk factors present or positive on 50 g glucose challenge**, positive on 100 g oral glucose tolerance test¶¶	Diet and insulin	30 (NA)	NA	NA	NA
Control	308		Usual care	31 (NA)	NA	NA	NA

Faltaria una diapo d’indicar que s’han d’adaptar els criteris de tra

Conclusions Treatment for gestational diabetes, consisting of treatment to lower blood glucose concentration alone or with special obstetric care, seems to lower the risk for some perinatal complications. Decisions regarding treatment should take into account that the evidence of benefit is derived from trials for which women were selected with a two step strategy (glucose challenge test/screening for risk factors and oral glucose tolerance test).

Reproducibility of DM diagnosis (WHO 1999 criteria) in women

- 696 women with previous GDM undergoing an OGTT at a median of 6.2 years after delivery

Albareda M. Acta Diabetol. 2004;41:14-7

Table 2 Glucose tolerance at the second evaluation in 35 women diagnosed with diabetes mellitus (DM) after gestational diabetes mellitus. Results are stratified according to the abnormality at the first evaluation

	Second test, number of women							
	No DM			DM				
First test	NGT	IFG	IGT	OGTT	Symptoms + random PG	Drug treatment for DM	Confirmation, n (%)	
FPG ≥7 mmol/l + 2-h PG <11.1 mmol/l (n=12)	2	6	0	3	1	0	4	(33)
FPG <7 mmol/l + 2-h PG ≥11.1 mmol/l (n=10)	1	0	5	2	0	2	4	(40)[a]
FPG ≥7 mmol/l + 2-h PG ≥11.1 mmol/l (n=10)	0	0	0	3	2	5	10	(100)[b,c,d]
Symptoms of hyperglycemia + random PG (n=3)	0	0	0	0	0	3	3	(100)
Total	3	6	5	8	3	10	21	(60)

- **How reliable is the fifty-gram, one-hour glucose screening test?**

  Sacks DA. Am J Obstet Gynecol. 1989 Sep;161(3):642-5

  … the 1h glucose Sc test is moderately reproducible. Reliance should not be placed on a single N test result, particularly among patients with RF

- **Reproducibility of the oral glucose tolerance test in pregnancy**

  Harlass FE. Am J Obstet Gynecol. 1991 Feb;164(2):564-8

  … overall, the reproducibility of the oral glucose tolerance test was 78% (50 of 64)

- **Reproducibility of the oral glucose tolerance test in pregnant women**

  Catalano PM. Am J Obstet Gynecol. 1993 Oct;169(4):

  .... The OGTT was not reproducible for diagnosis in 2
  38) of pregnant women

The impact of potential new dx criteria on the prevalence of GDM in Australia

Moses RG. Med J Aust 2011;194(7):338-40

revalenc

- 1/3 of births are in private centers
- ADIPS:

  75 g, 2h

  basal >= 5,5 mmol/l and/or

  2h >= 8,0 mmol/l

	ADIPS	IADPSG
Hospital	8.6%	9.1%
Private center	10.5%	16.2%
Overall	9.6%	13.0%
	18% non Identified by IADPSG	39% non identified by ADIPS

Atlantic DIP: the prevalence and outcomes of GDM using new diagnostic criteria

O'Sullivan EP. Diabetologia 2011;54(7):1670-5

revalenc

- 5500 women (44%)
- 92.9% caucasian
- IMC 26.9
- 24-28 wks
- OGTT 75 g
- 2006-2009
- WHO criteria:
  - 9.4%
  - 17.9% Ins

	N	GDM	IADPSG only
Prevalencia		0.5 overt 12.4	3
Insulin Tx		If WHO +	0
PIH	7.5	13.8*	15.0*
Preeclampsia	4	6.3*	7.1*
Hydramnios	0.8	3.4*	ns
Cesarean S	24.9	37.2*	35.2*
Preterm birth	4.8	7.1*	ns
LGA	16.2	22.6*	26.8*
SGA	4.4	5.8	ns
NICU	9.1	26*	16.5*
NN hypo	0.6	2.4*	ns
Distress	1.8	3.6*	ns

Assessing the incidence of GDM and NN outcomes using the IADPSG guidelines in comparison with the CC criteria in a Belgian general hospital

Oriot P. Acta Clin Belg 2014;69:8-11

utcomes in GD

- Belgium, retrospective before-after study
- 2009-2011, N =1424, 2-step CC criteria, 8% GDM
- 4/2011-12/2012, N=1206, 1-step IADPSG criteria, 23% GDM

Among women with GDM

- Insulin Tx 34.2 vs 34.7%, ns
- GA 38.2 vs 38.15, ns
- LGA 11.2 vs .8%, ns
- CS 27 vs 25.%, NS

The effect of adopting the IADPSG screening guidelines on the risk profile and outcomes of the GDM population

March MI. J Matern Fetal Neonatal Med 2016;29:1141-5

utcomes in GD

- USA
- 2010: 2 step, NDDG, 131 diagnosis
- 2011: 1 step, IADPSG, 104 diagnosis

- The 1 step group
  - was diagnosed with GDM one week earlier [26.0 vs 27]
  - had significantly higher WG per week [0.67 vs 0.56 pounds/week]
  - similar perinatal outcomes

Perinatal outcomes after adopting 1- versus 2-step approach to diagnosing GDM

Ogunleye OK. J Matern Fetal Neonatal Med. 2017;30:186-190

tcomes in GD

- **Switzerland, retrospective before-after study**
- **Before: 2011-2012, ACOG 2-step, N=471; 5.5% GDM**
- **After: 2012-2013, IADPSG 1-step, N= 332; 15.96% GDM**

Table 3. Comparison of maternal and neonatal outcomes*.

	Odds ratio†	Confidence interval	*p* values
Total $n = 79$‡	(Ref. 2-step)		
Maternal outcome			
SVD	1.84	0.71, 4.76	0.21
Prim C/section	1.06	0.35, 3.19	0.92
Preeclampsia	0.69	0.18, 2.69	0.59
Chronic hypertension	0.59	0.23, 1.56	0.29
Neonatal outcome			
Macrosomia (>4000g)	0.48	0.06, 3.62	0.48
Low 5-min Apgar (<7)	0.96	0.08, 11.11	0.98
Respiratory distress syndrome	0.38	0.12, 1.25	0.11
Neonatal hypoglycemia	0.66	0.12, 1.08	0.07
Hyperbilirubinemia/phototherapy	0.66	0.17, 2.57	0.55
NICU$^{\alpha}$ admission	0.48	0.16, 1.43	0.19

Diagnostic protocol for GDM (IADPSG): influence on the occurrence of GDM and MGH and on the perinatal outcomes

Sirimarco MP. Diabetol Metab Syndr. 2017 Jan 3;9:2

utcomes in GD

- Brazil, retrospective before-after study
- Before: ADA 2010 criteria + glycemic profile
- After: ADA 2011 + glycemic profile: 85% increase in GDM, 17.3% MGH

Table 4 Perinatal outcomes in the ND, mild gestational hyperglycemia (MGH), and gestational diabetes mellitus (GDM) groups stratified according to diagnostic protocol

	ND (N = 199)			MGH (N = 89)			GDM (N = 194)		
	OLD	NEW	*p*	OLD	NEW	*p*	OLD	NEW	*p*
NB-LGA	0 (0, 0)	9 (8, 0)	*0.0196*	6 (4, 15)	7 (14, 0)	1.0000	6 (8)	14 (1, 11)	0.8006
Macrossomia	3 (4, 4)	5 (4, 4)	1.0000	6 (4, 15)	7 (14, 0)	1.0000	5 (3, 7)	13 (3, 10)	0.6747
First C-section	25 (25, 5)	43 (38, 1)	0.2409	8 (5, 20)	16 (32, 0)	0.3316	16 (5, 23)	30 (8, 23)	1.0000
Length of hospital stay (days)									
1–3	64 (76, 6)	87 (77, 0)	0.8003	29 (74,4)	41 (82, 0)	0.5404	50 (73,5)	96 (76,2)	0.8138
4–7	14 (1, 11)	22 (5, 19)	0.6942	10 (25,6)	8 (16, 0)	0.3911	14 (6, 20)	25 (8, 19)	1.0000
>7	8 (2, 12)	4 (3, 5)	0.1642	0 (0, 0)	1 (2, 0)	1.0000	4 (5, 9)	5 (4, 0)	0.8049
Total	86	113		39	50		68	126	

- Convenience sample, stratified perinatal outcome: similar

Introduction of IADPSG criteria for the Sc & Dx of GDM results in improved pregnancy outcomes at a lower cost in a large cohort of pregnant women: the St. Carlos GDM Study

Duran A. Diabetes Care. 2014 Sep;37(9):2442-50

lation outcomes, before-

≠ in smoking

- Spain, before-after study
- ↑ GDM
  - 10.6% CC, N = 1750 vs, vs 35.5% IADPSG, N = 1526
  - At 24-28 weeks 2 step GCT + CC criteria vs 1 step IADPSG criteria

- Improvement in pregnancy outcomes
  - ↓ in the rate of gestational hypertension (4.1 to 3.5%: -14.6%, P < 0.021)
  - ↓ prematurity (6.4 to 5.7%: -10.9%, P < 0.039)
  - ↓ cesarean section (25.4 to 19.7%: -23.9%, P < 0.002)
  - ↓ small for gestational age (7.7 to 7.1%: -6.5%, P < 0.042)
  - ↓ large for gestational age (4.6 to 3.7%: -20%, P < 0.004)
  - ↓ Apgar 1-min score <7 (3.8 to 3.5%: -9%, P < 0.015)
  - ↓ admission to neonatal intensive care unit (8.2 to 6.2%: -24.4%, P < 0.001)

GDM Screening: The IADPSG Compared With Carpenter-Coustan Screening

Feldman RK. Obstet Gynecol 2016;127:10-7

lation outcomes, before- **≠ in glyburide use**

- **USA, before-after study**
- **17% dx in the CC group**

  N=2972, 1st T RF Sc + universal 2 step GCT + CC criteria at 24-28 wks
- **27% in the IADPSG group**

  N=3094, 1st T A1c + universal 1 step IADPSG at 24-28 weeks

No improvement in pregnancy outcomes

- **No differences in LGA: 10% CC, 9% IADPSG**

⑩ **↑ primary CS delivery rate: 16% CC vs 20% IADPSG**

⑩ **↑ NICU admission: 4% CC vs 5% IADPSG (ns after adjustment)**

⑩ **↑ PE: 3% CC vs 4% IADPSG (ns after adjustment)**

Diagnosis of more GDM lead to better pregnancy outcomes: Comparing the IADPSG and CC criteria

Wu ET. J Diabetes Investig 2016; 7:121-6

lation outcomes, before- ≠ in chronic HT & WG

- Taiwan, before-after study, 2011
- 2 step CC criteria, N = 888 women, 2.59%
- 1 step IADPSG criteria, N =952 women, 13.44%

- Improvement in pregnancy outcomes
  - ↓ GA at dx (27 vs 30.5 weeks)
  - ↓ BW (3,065 vs 3,128 g)
  - ↓ primary CS (adjusted OR 0.79)
  - ↓ adverse fetal otucome (adjusted OR 0.79)

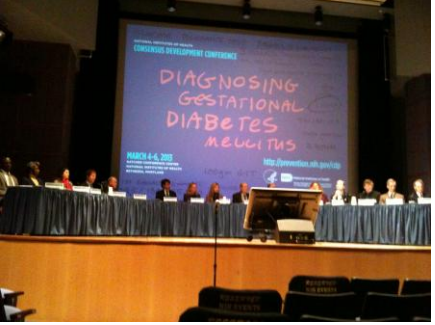
    LGA, jaundice, NICU, trauma, NN hypo, fetal death

When are RCT unnecessary? Picking signal from noise

Glasziou P. BMJ. 2007 Feb 17;334(7589):349-51

Some historical examples of treatments with dramatic effects

- Insulin for diabetes[w1]
- Blood transfusion for severe haemorrhagic shock[w2]
- Sulphanilimide for puerperal sepsis[w3]
- Streptomycin for tuberculous meningitis[w4]
- Defibrillation for ventricular fibrillation[w5]
- Closed reduction and splinting for fracture of long bones with displacement
- Salicin for acute rheumatism[w6]
- Neostigmine for myasthenia gravis[w7]
- Tracheostomy for tracheal obstruction[w8]
- Suturing for repairing large wounds
- Drainage for pain associated with abscesses
- Pressure or suturing for arresting haemorrhage
- Ether for anaesthesia
- One way valve or underwater seal drainage for pneumothorax and haemothorax[w9]
- Phototherapy for skin tuberculosis[w10]
- Combination chemotherapy with cisplatin, vinblastine, and bleomycin for disseminated testicular cancer



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- **Based on the above considerations, the panel believes that there are benefits from standardization within the United States and between the United States and the world with regard to the diagnostic approach to GDM.**

- **Nevertheless, at present, the panel believes that there is not sufficient evidence to adopt a one-step approach, such as that proposed by the IADPSG. The panel is particularly concerned about the adoption of new criteria that would increase the prevalence of GDM, and the corresponding costs and interventions, without clear demonstration of improvements in the most clinically important health and patient-centered outcomes. Thus, the panel recommends that the two-step approach be continued.**

- **However, given the potential benefits of a one-step approach, resolution of the uncertainties associated with its use would warrant reconsideration of this conclusion.**

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Now Available for Public Comment: Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Trials

Randomizing Two Gestational Diabetes Screening Methods in a Diverse HMO

This study is enrolling participants by invitation only.

Sponsor:
Kaiser Permanente

Collaborator:
Eunice Kennedy Shriver N

Information provided by (R
Kaiser Permanente

ClinicalTrials.gov Identifier:
NCT02266758

First received: May 22, 2014
Last updated: October 21, 2014

Full Text View | Tal

Purpose

This project randomizes two
their babies (over 35,000 tota
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ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Now Available for Public Comment: Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Tr

Gestational Diabetes Diagnostic Methods (GD2M)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified December 2014 by University of Pittsburgh

Sponsor:
University of Pittsburgh

Information provided by (Responsible Party):
University of Pittsburgh

ClinicalTrials.gov Identifier:
NCT02309138

First received: November 25, 2014
Last updated: December 2, 2014
Last verified: December 2014
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

This is a single site blinded RCT of 920 pregnant women with singleton gestation designed to compare the Carpenter-Coustan and IADP
for diagnosing gestational diabetes. Maternal metabolic profiles and infant growth will be assessed at randomization and at one year pos

Critical evaluation of IADPSG implementation studies
Take home messages

- Continuous association of HiP & pregnancy outcome
- Tx of GDM (2-step protocol) improves outcome vs routine care
- IADPSG implementation protocols
  - lead to ↑ prevalence
  - identify women at ↑ risk
  - information on outcomes at population level
    - before-after studies: limited & varied
    - RCTs: unavailable
- We need more information!
  - Real life before-after studies
  - RCTs