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# Evidence Based Management of Gestational Diabetes

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## Gestational Diabetes Trends. Sheffield 2005-8

2005	2006	2007	2008
100	198	189	244*

\* Rate 34/1000 births



- Diagnosis of GDM
- Adverse outcomes of GDM
- Treatment options
- Screening for GDM



# Diagnosis of GDM

# GDM: Traditional Diagnostic Criteria

WHO Criteria: 75g glucose load

Fasting Plasma Glucose  $>6.9$  or 2h  $>7.7$   
mmol/l

ADA Criteria: 100g glucose load

Fasting 5.3 1h 10.0 2h 8.6 3h 7.8mmol/l

- Two or more values to be met or exceeded



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## Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group\*

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ABSTRACT

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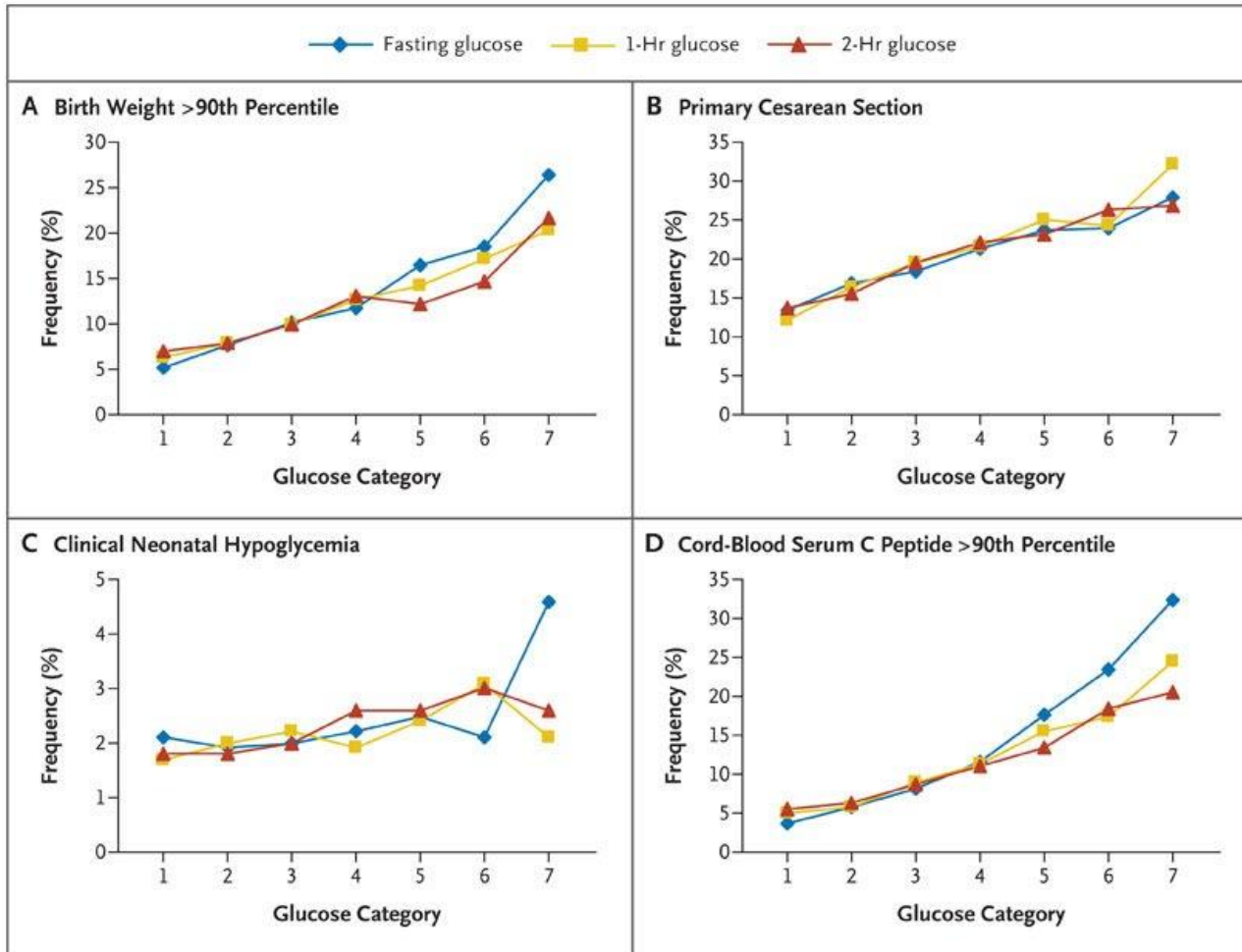


## HAPO: Glucose Categories (mmol/l)

	1	2	3	4	5	6	7
Fasting n	<4.2 4035	-4.4 7501	-4.7 6168	-4.9 2741	-5.2 1883	-5.5 672	>5.5 217
1 hour n	<5.8 3721	-7.3 6806	-8.6 5483	-9.5 2378	-10.7 1601	-11.7 560	>11.7 183
2 hour n	<5.0 4043	-6.0 7503	-6.9 6164	-7.7 2744	-8.7 1884	-9.8 672	>9.8 217



## Frequency of Primary Outcomes across the Glucose Categories



# HAPO Study Consensus on revised diagnostic criteria.

- Risk factor positive; if FPG  $>7.0$ mmol/l, or random glucose above 11.1mmol/l, or  
HB A1c  $>6.5\%$  consider as likely overt diabetes and treat accordingly.
- Or if universal blood testing : 75g load
- Fasting plasma glucose  $>5.1$ mmol/l
- And/or 1hr level  $>10.0$ mmol/l
- And/or 2hr level  $> 8.5$ mmol/l



# Adverse outcomes of GDM



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## Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes

Caroline A. Crowther, F.R.A.N.Z.C.O.G., Janet E. Hiller, Ph.D., John R. Moss, F.C.H.S.E.,  
Andrew J. McPhee, F.R.A.C.P., William S. Jeffries, F.R.A.C.P., and Jeffrey S. Robinson, F.R.A.N.Z.C.O.G.,  
for the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group\*



# Australian Carbohydrate Intolerance Study in Pregnant Women: (ACHOIS)

Double blind trial to determine whether treatment of GDM reduces risk of perinatal complications

75g OGTT: WHO Criteria

Crowther et al (2005)



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes

Mark B. Landon, M.D., Catherine Y. Spong, M.D., Elizabeth Thom, Ph.D.,  
Marshall W. Carpenter, M.D., Susan M. Ramin, M.D., Brian Casey, M.D.,  
Ronald J. Wapner, M.D., Michael W. Varner, M.D., Dwight J. Rouse, M.D.,  
John M. Thorp, Jr., M.D., Anthony Sciscione, D.O., Patrick Catalano, M.D.,  
Margaret Harper, M.D., George Saade, M.D., Kristine Y. Lain, M.D.,  
Yoram Sorokin, M.D., Alan M. Peaceman, M.D., Jorge E. Tolosa, M.D., M.S.C.E.,  
and Garland B. Anderson, M.D., for the Eunice Kennedy Shriver National  
Institute of Child Health and Human Development Maternal–Fetal  
Medicine Units Network\*



# Maternal-fetal Medicine Units Network Trial

Randomised double blind trial to determine  
if treatment of mild GDM (100g OGTT,  
Fasting Glucose <5.0 mmol/l) improves  
perinatal outcomes

Landon et al(2009)



## MUN Trial and ACHOIS Trial: Double Blind design.

In both studies a large group of women with normal GTT were assigned “not GDM”, as well as those women with GDM randomised to ‘no treatment’

Therefore women with GDM randomised to ‘no treatment’ in the Trials could not be identified, by clinicians.



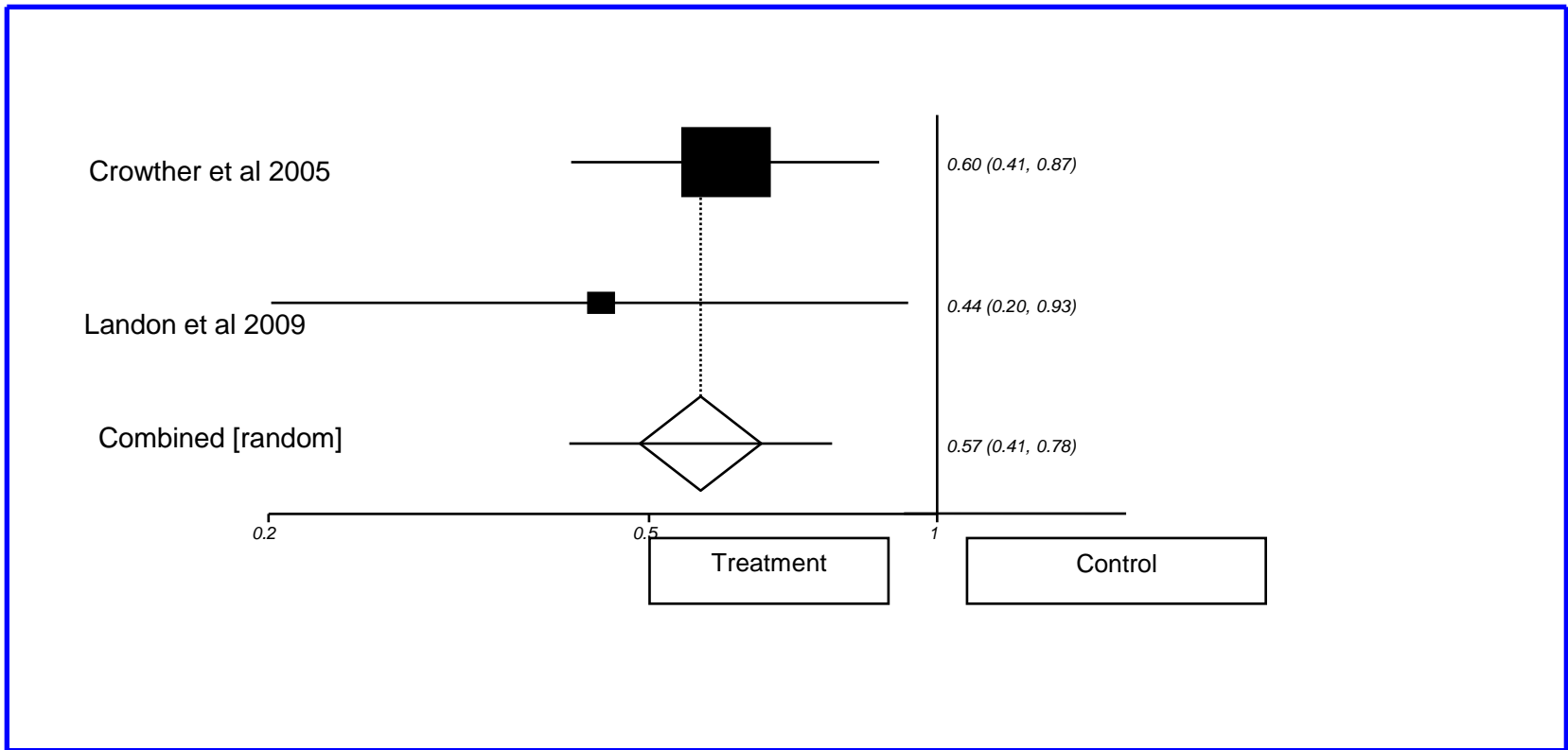
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- Preliminary Meta-analysis of Crowther and Landon Trials

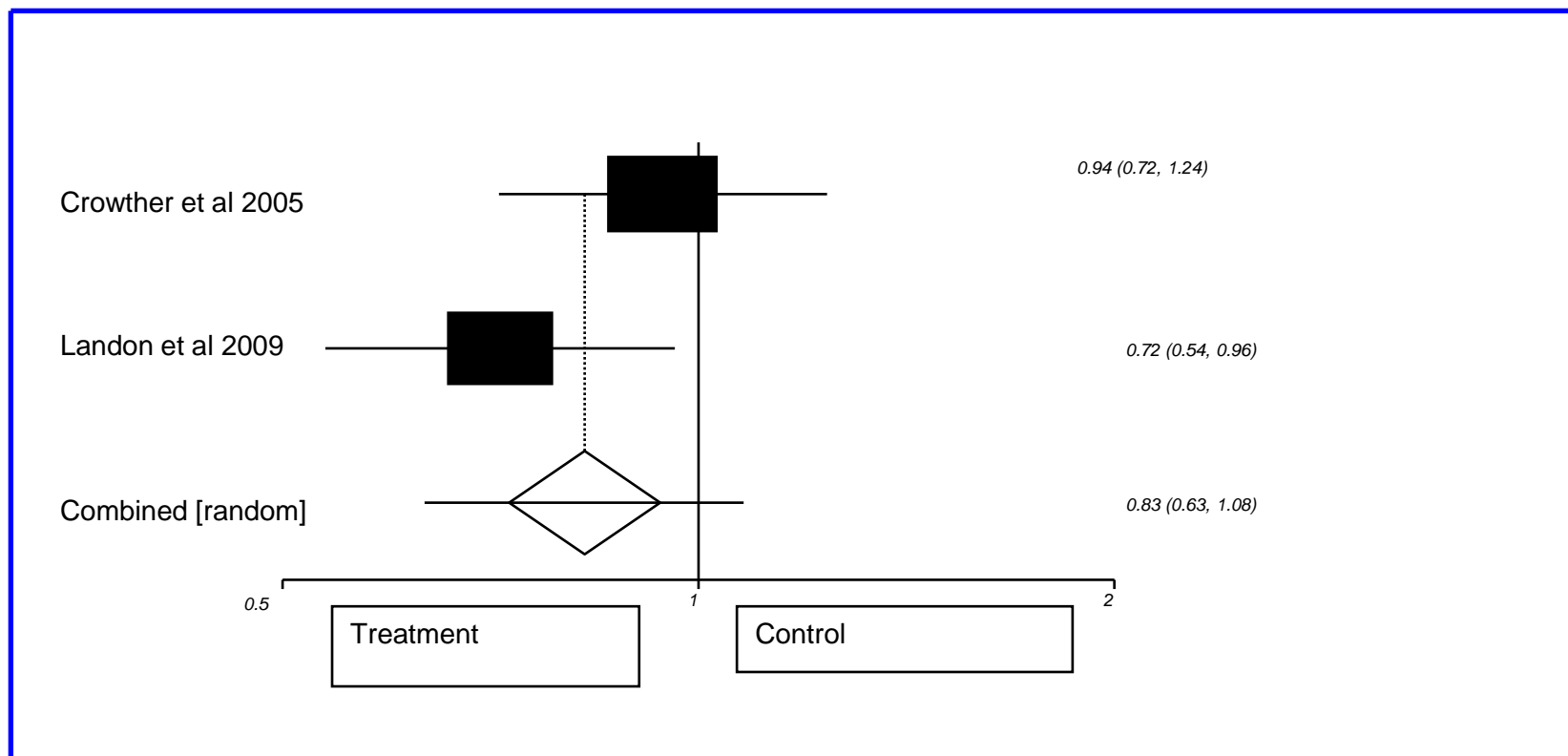
Ola et al.(Unpublished)



# Pre eclampsia

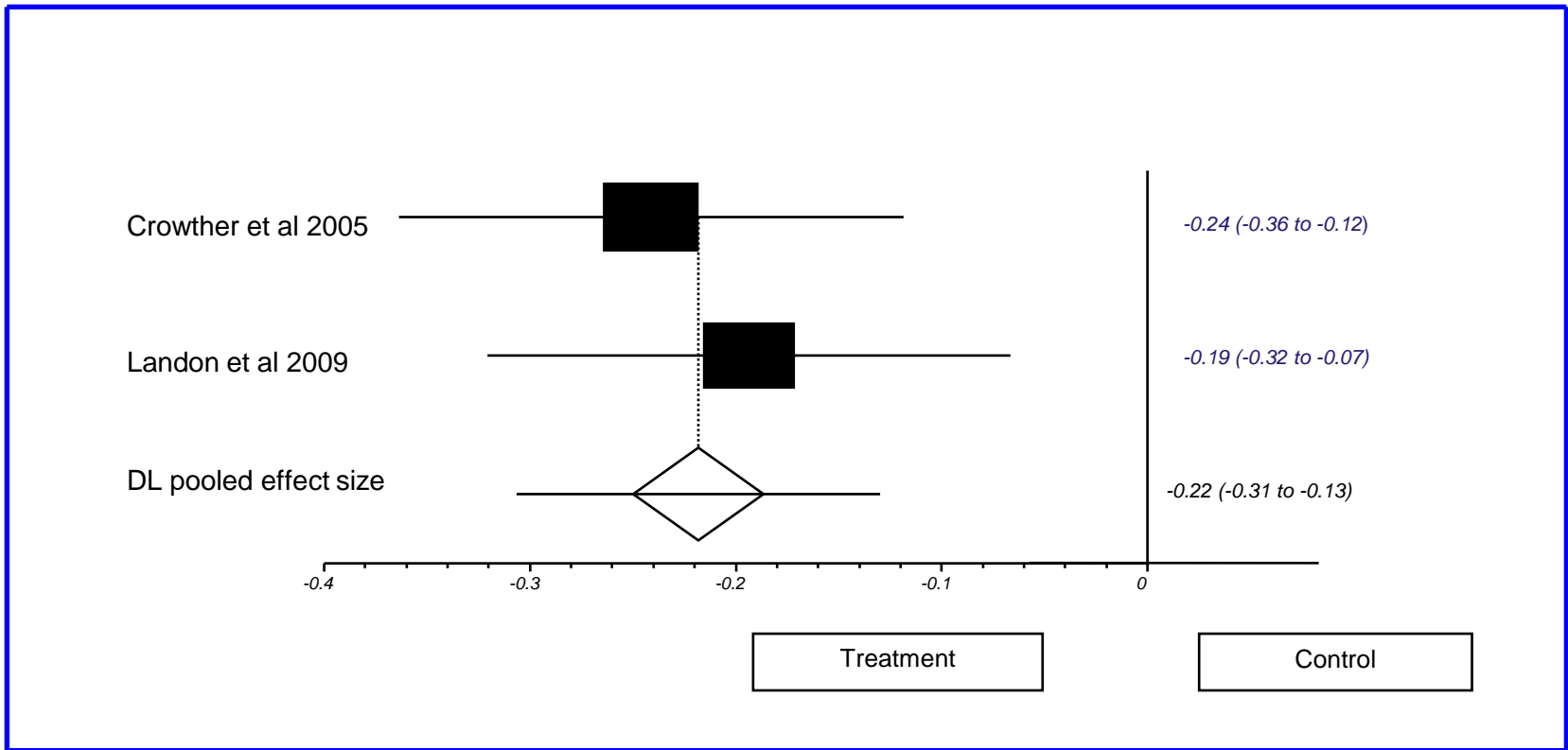


## Caesarean section



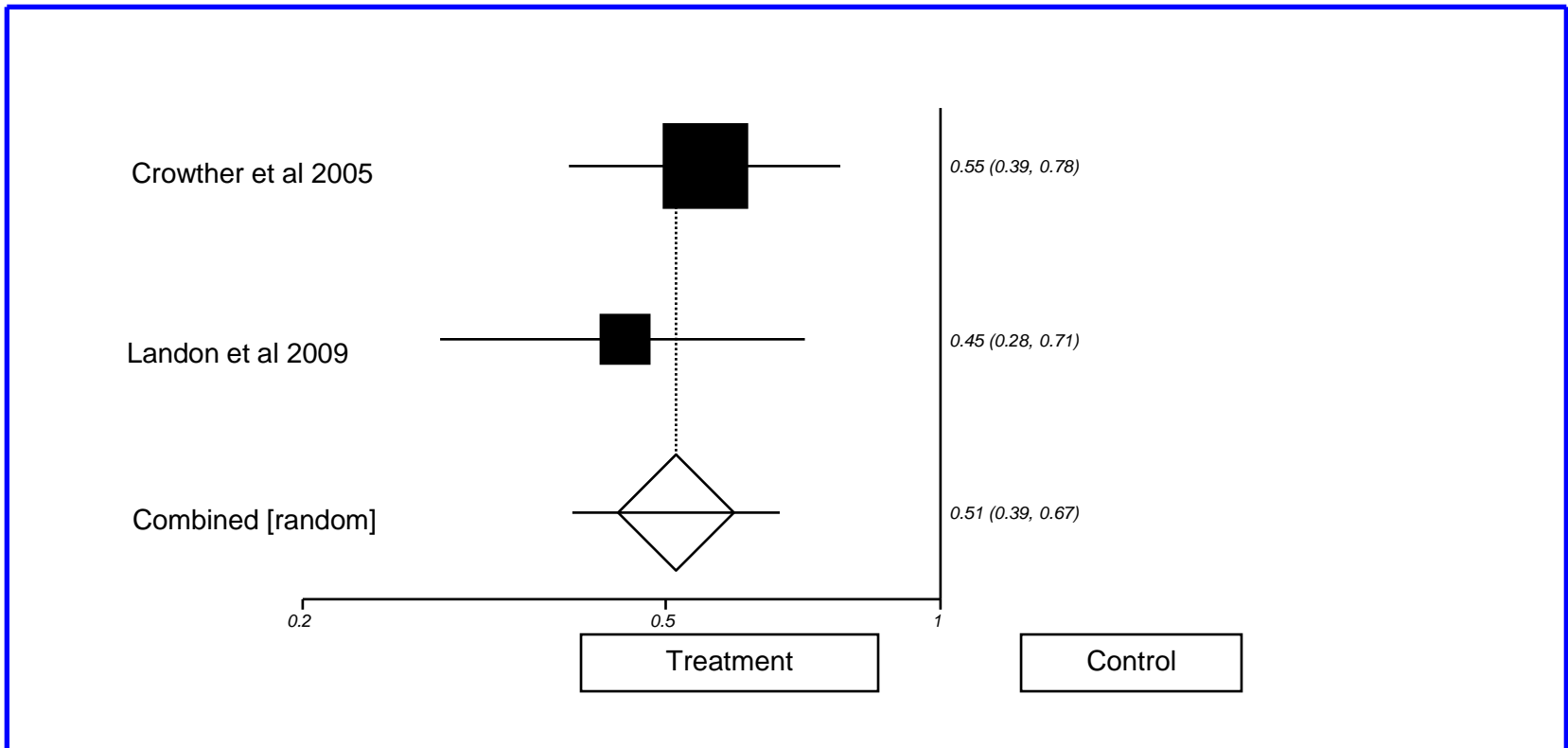


# Birth weight



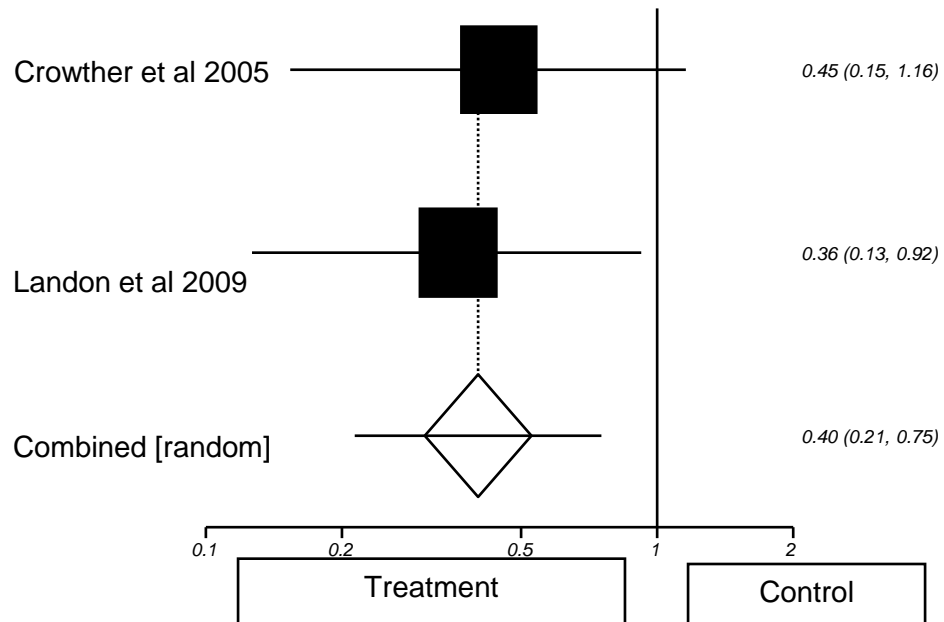


# Large for gestational age



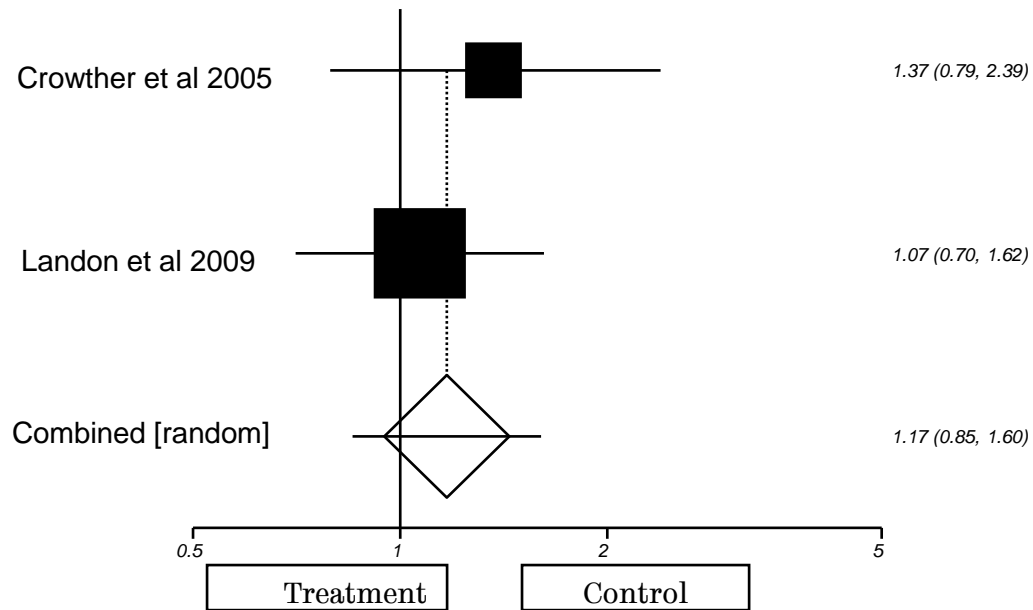


# Shoulder dystocia





# Neonatal hypoglycaemia





# Treatment options



# Standard management of GDM

- Diet
- Blood glucose self-monitoring
- Supplementary insulin
- Oral hypoglycaemic agents (OHA)

FATBURGER

BANITZA



# Gestational Diabetes; can a low glycemic index diet reduce the need for insulin? A randomised trial.

- 63 women randomised to low GI diet or conventional High Fibre diet.
- Low GI 9/31 (29%) required insulin.
- High Fibre 19/32 (59%) required insulin
- (P= 0.023)

(Moses et al 2009)

# Effect of Low GI diet during Pregnancy on Obstetric Outcomes

	Low GI diet n= 32	High GI diet n=30	p
Birth Wt (g)	3408 ± 78	3644 ± 90	0.05
Head circumference (cm)	34.6 ± 0.25	35.1 ± 0.25	0.13
Length (cm)	50.8 ± 0.3	51.1 ± 0.4	0.64
B wt centile	48 ± 5	69 ± 5	0.005
LGA (%)	3.1	33.3	0.001
SGA (%)	9.4	6.7	0.69



# Pre-prandial vs Post-prandial BG monitoring in Insulin treated GDM

RCT 66 women with GDM by ADA Criteria : Diagnosed before 30 weeks.

Pre-prandial Group : Insulin adjusted to keep fasting glucose 3.3 - 5.0 mmol/L  
and pre-prandial 3.3 – 5.9 mmol/L

Post-prandial Group: Insulin adjusted to keep fasting glucose 3.3 - 5.0 mmol/L  
and 1hr post prandial < 7.8 mmol/L

## Pre-prandial vs Post-prandial BG monitoring in GDM

	Pre-prandial n=33	Post-prandial n=33	p
Target control met	86.0 ± 4.1%	88.0 ± 5.2%	
Insulin dose U/day	76.8 ± 21.4	100.4 ± 29.5	0.003
Final HbA <sub>1c</sub>	8.1 ± 2.2 %	6.5 ± 1.4%	0.006

de Veciana et al 1995

# Pre-prandial vs Post-prandial BG monitoring in GDM

## Neonatal outcomes

	Pre-prandial n=33	Post-prandial n=33	RR (95% CI)	p
Birth Wt	3848 ± 434	3469 ± 668		0.01
LGA	14 (42%)	4 (12%)	3.5 (1.3-9.5)	0.01
SGA	0	1 (3%)		ns
Shoulder dystocia	6 (18%)	1 (3%)	6.0 (0.8-47.1)	ns
Hypoglycaemia (<1.6mmol/L)	7 (21%)	1 (3%)	7.0 (0.9-53.8)	ns



# Historical concerns for OHA agents

- Teratogenicity
- Inadequate control of postprandial glucose levels
- Neonatal hypoglycaemia



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ORIGINAL ARTICLE

# Metformin versus Insulin for the Treatment of Gestational Diabetes

Janet A. Rowan, M.B., Ch.B., William M. Hague, M.D., Wanzhen Gao, Ph.D.,  
Malcolm R. Battin, M.B., Ch.B., and M. Peter Moore, M.B., Ch.B.,  
for the MiG Trial Investigators\*

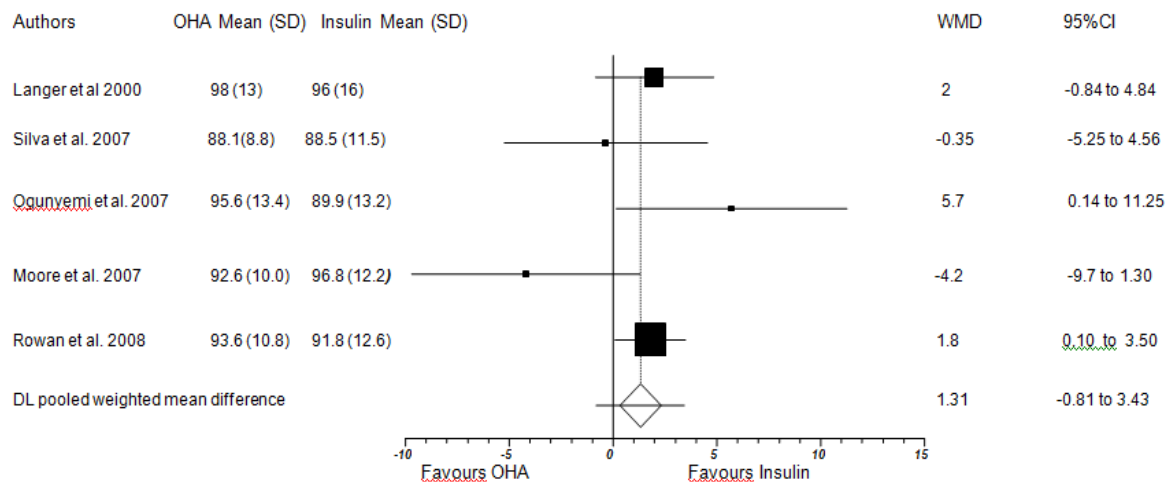


# Meta-analysis of RCTs comparing insulin with Oral Hypoglycaemic Agents in GDM

- Glycaemic control
- Maternal outcomes
- Perinatal outcomes

Dhulkotia et al (Am J Obstet Gynecol 2010)

## Fasting glycaemic control



Chi-square (for  $wmd+$ ) = 5.42 (df = 1) P = 0.02

Q ("combinability" for  $wmd+$ ) = 7.09 (df = 4) P = 0.13

DerSimonian-Laird chi-square = 1.47 (df = 1) P = 0.23

Figure 2. Effects of oral hypoglycemic agents (OHA) versus Insulin on fasting glycaemic control

## Postprandial glycaemia

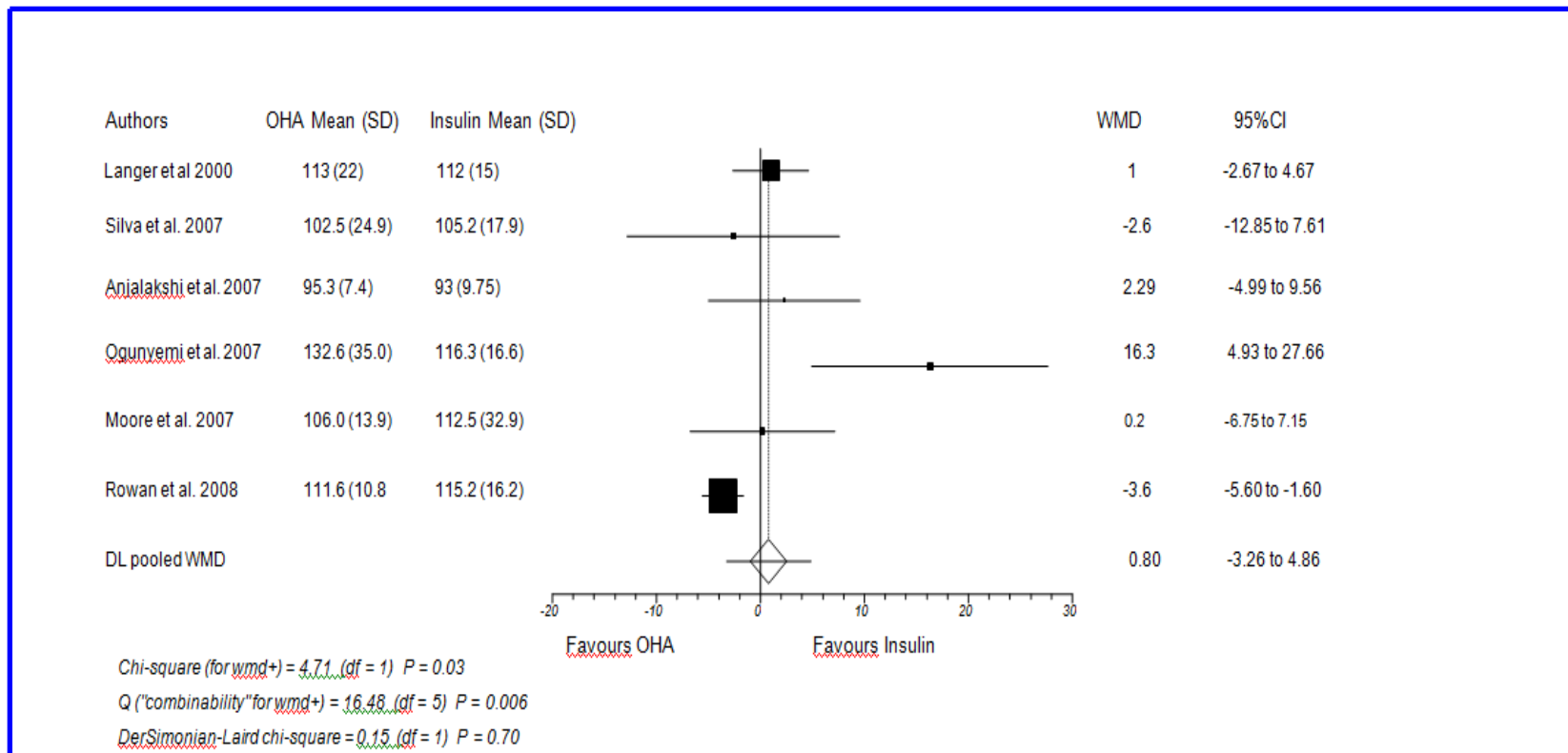
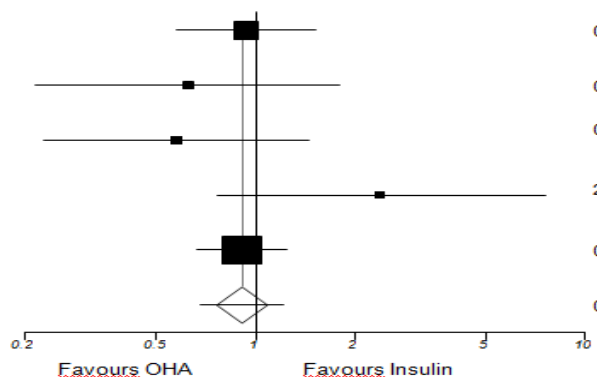


Figure 3. Effects of oral hypoglycemic agents (OHA) versus Insulin on post-prandial glycaemic control



# Caesarean section rate

Author	OHA (n/N)	Insulin (n/N)	Odds ratio (95% CI)
Langer et al 2000	46/201	49/203	0.93 (0.57, 1.52)
Silva et al. 2007	14/32	20/36	0.62 (0.21, 1.80)
Ogunyemi et al. 2007	18/43	25/43	0.58 (0.23, 1.45)
Moore et al. 2007	17/32	10/31	2.38 (0.76, 7.55)
Rowan et al. 2008	131/363	142/370	0.91 (0.66, 1.24)
Combined [random]	226/671	246/683	0.91 (0.68, 1.22)



Heterogeneity test (Cochran Q) = 5.12 (df = 4), P = 0.28  
DerSimonian-Laird Chi<sup>2</sup> = 0.43 (df = 1), P = 0.51

Figure 7. Effects of oral hypoglycemic agents (OHA) versus Insulin on caesarean section rates

## Birth weight

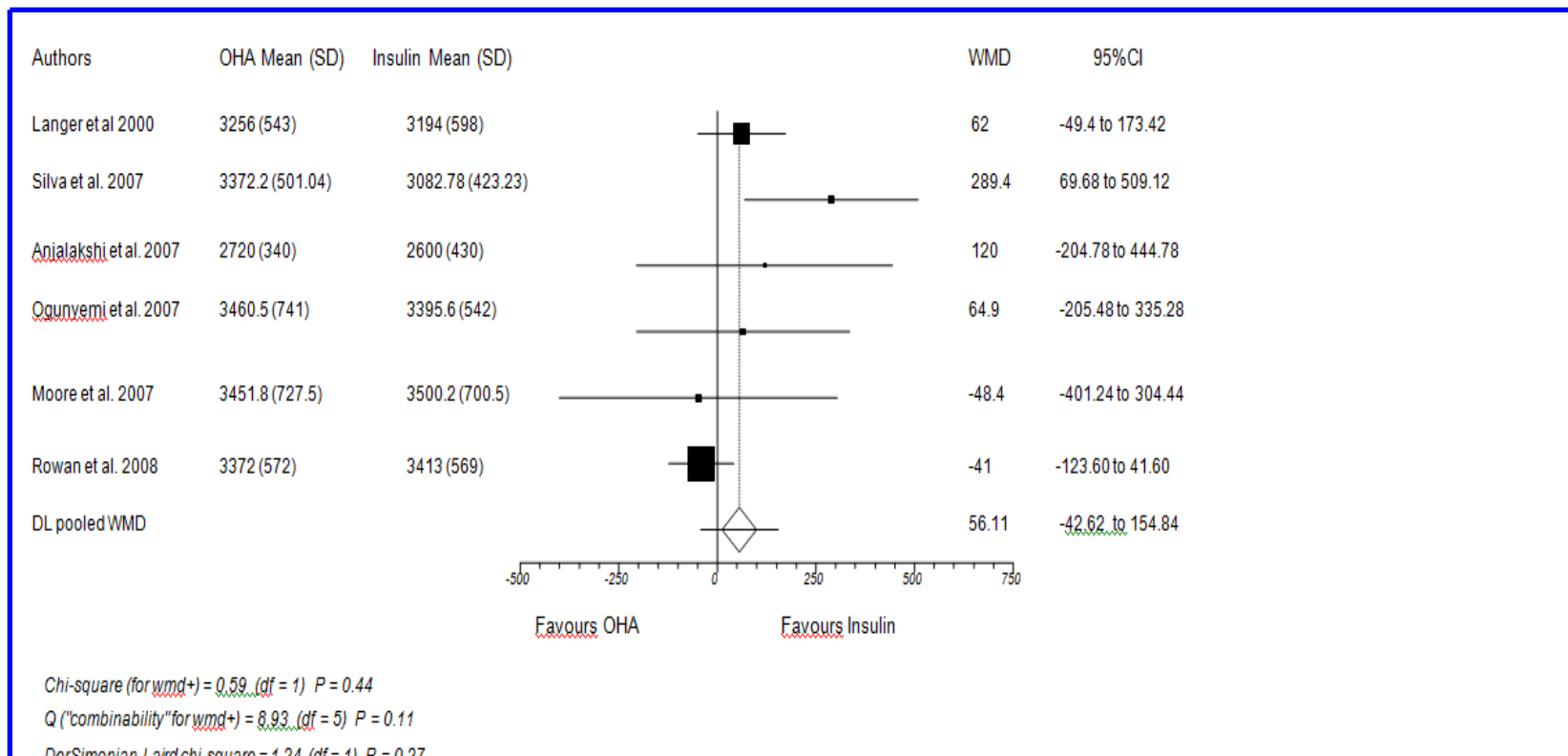


Figure 5. Effects of oral hypoglycemic agents (OHA) versus Insulin on neonatal birth weight

## Large for gestational age

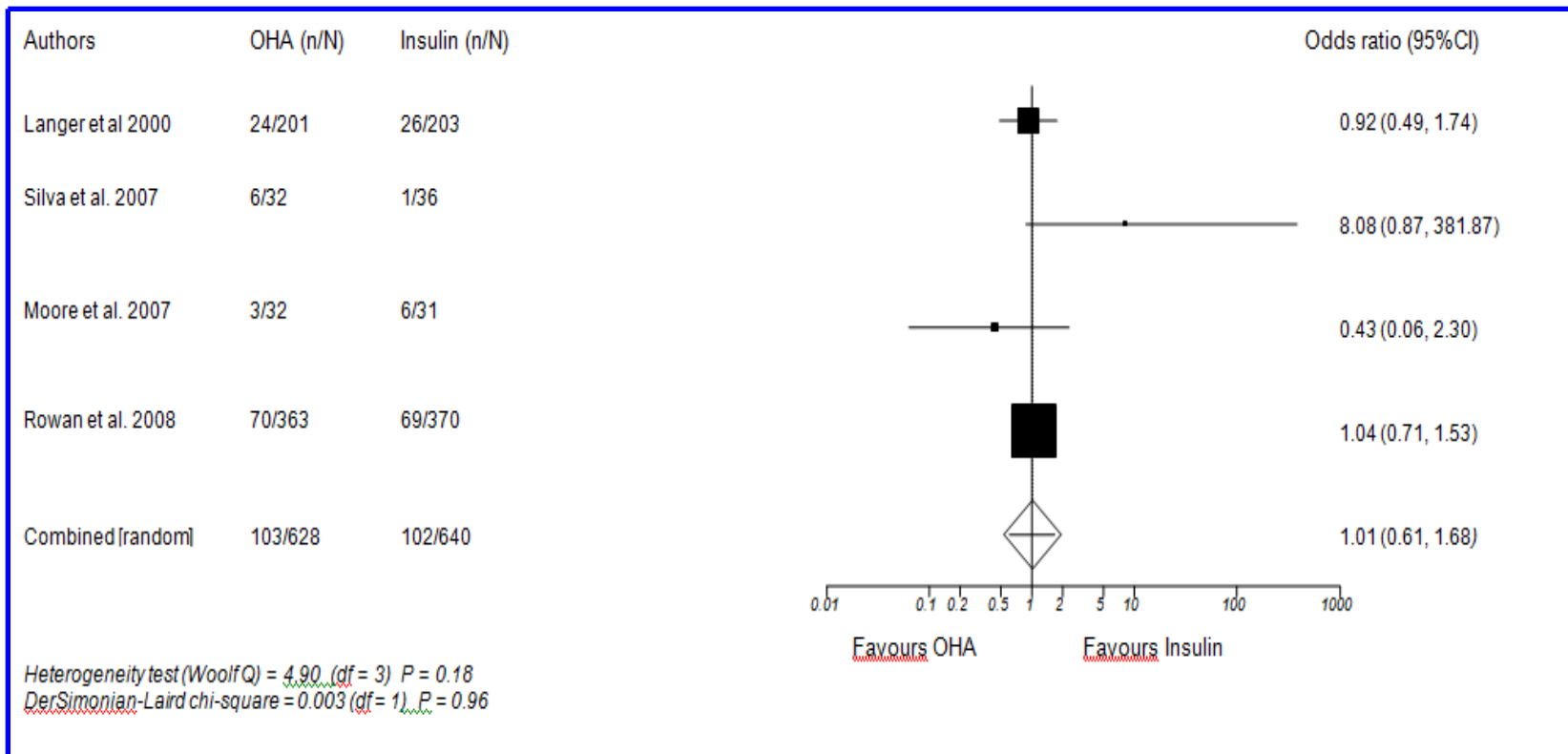


Figure 6. Effects of oral hypoglycemic agents (OHA) versus Insulin on LGA babies



# Neonatal hypoglycaemia

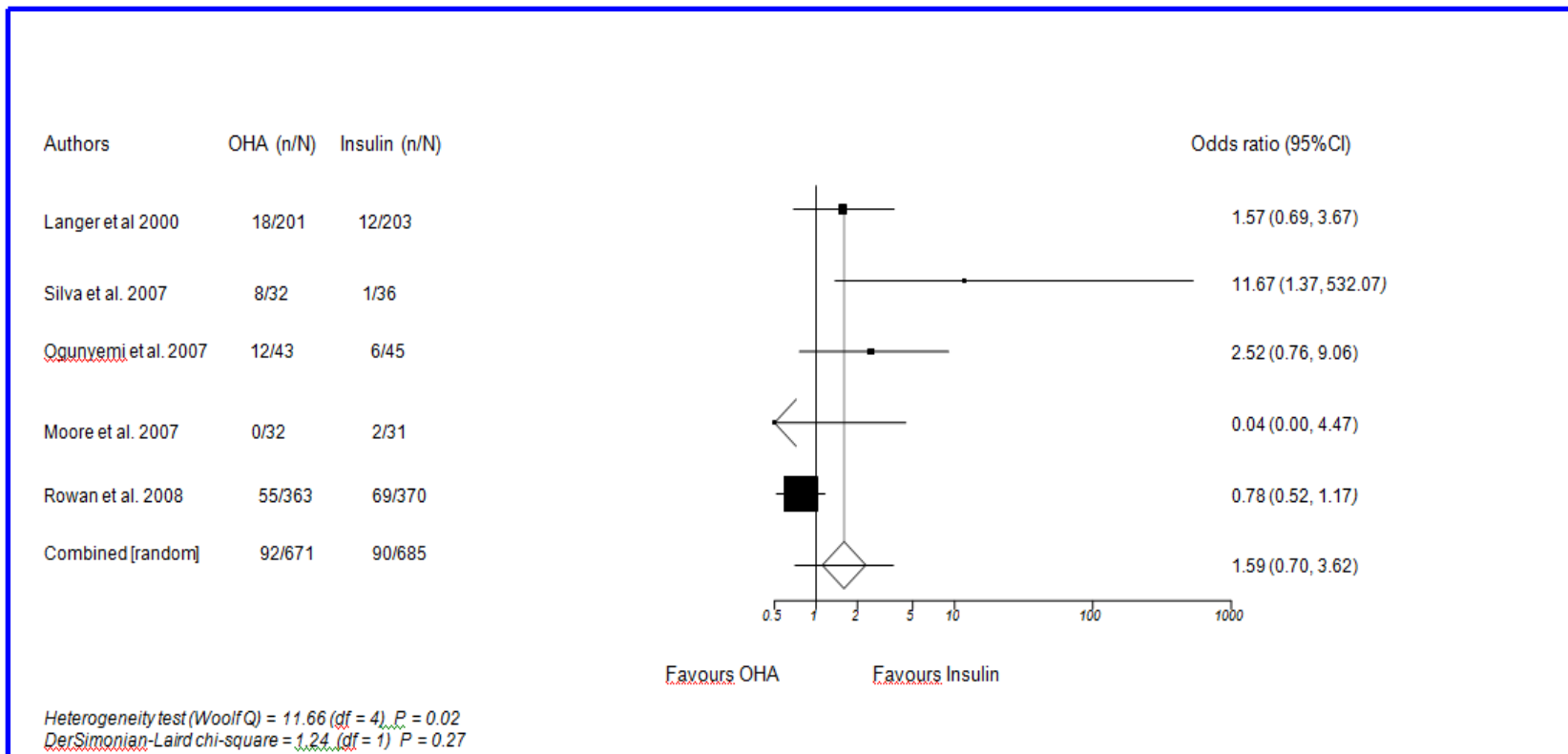


Figure 4. Effects of oral hypoglycemic agents (OHA) versus Insulin on neonatal hypoglycemia.....Dhulkotia et al.

# Metformin compared with Glyburide in GDM: a Randomised Controlled Trial

(Moore et al 2010)

<b>Outcomes</b>	<b>Glyburide (n=74)</b>	<b>Metformin (n = 75)</b>	<b>p</b>
Birthweight	3.33 Kg	3.10 Kg	0.02
>4.0 Kg	4	1	ns
Neonatal Hypoglycaemia	1	2	ns
Shoulder Dystocia	1	0	ns
CS delivery	2	11	0.02

# Metformin compared with Glyburide in GDM: a Randomised Controlled Trial

(Moore et al 2010)

	<b>Glyburide (n = 74)</b>	<b>Metformin (n = 75)</b>	<b>p</b>
Required Insulin	12 (16.2%)	26 (34.7%)	0.01



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## MiG Study Secondary Outcomes

	Metformin Group n = 363	Insulin Group n = 370	p
Maternal Weight (from enrolment to 6 weeks post- partum)	-8.1 ± 5.1 Kg	-6.9 ± 5.3 Kg	0.006



# Conclusions

- Metformin and glyburide should therefore be considered as credible and safe alternatives to Insulin
- In overweight women Metformin should be preferred to Glyburide.



# Screening for GDM

# Estimated Sensitivity and Specificity of Screening Tests for GDM

(Round, 2010, submitted, in revision)

	<b>Sens</b>	<b>Spec</b>
Fasting Plasma Glucose	0.84	0.78
Random Blood Glucose	0.48	0.97
Glucose Challenge Test	0.80	0.43
OGTT (Reference Test)	1.00	1.00

# Screening for GDM: cost utility of different screening strategies based on a woman's individual risk of disease

(Round et al: 2010, submitted, in revision)

<b>GDM risk</b>	
0 – 1.0%	No screening/treatment strategy is cost effective
1.0 -4.2%	Fasting Plasma Glucose and OGTT
>4.2%	Universal GTT





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## Percentage of LGA in infants according to Quintiles of Daily Carbohydrate Intake in GDM

	<173g	173-186	186-211	211-243	>243
LGA	5 (37%)	2 (12%)	4 (25%)	0 (0%)	0 (0%)
SGA	0 (0%)	0 (0%)	2 (13%)	0 (0%)	1 (6%)

# Pre-prandial vs Post-prandial BG monitoring

## Maternal outcomes

	Pre prandial	Post prandial	p
	n = 33	n = 33	
Pre eclampsia	2 (6%)	2 (6%)	ns
GA at delivery (weeks)	37.6 ± 3.8	37.9 ± 1.4	ns
CS	13 (39%)	8 (24%)	ns
3° Tear	8(24%)	3 (9%)	ns



# Screening for GDM by Risk Factors

( Helton 1997)

Obesity, FH Diabetes, Previous pregnancy failure,  
Previous macrosomia.

Sensitivity 69%

Specificity 68%

PPV 5%

(High risk ethnic minority groups)