MONASH University

Obesity and (In)fertility

Ben W Mol

Disclosures

Payed consultant for ObsEva, Merck, Guerbet

Received honarium for lectures (Japanese Perinatal Society, CFAS, 2016 World Life Science Conference)

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I have no financial interest in the material presented

Content

- Fertility and obesity
- Lifestyle intervention
- IVF and obesity
- David barker and the Hungerwinter study
- Bariatric surgery

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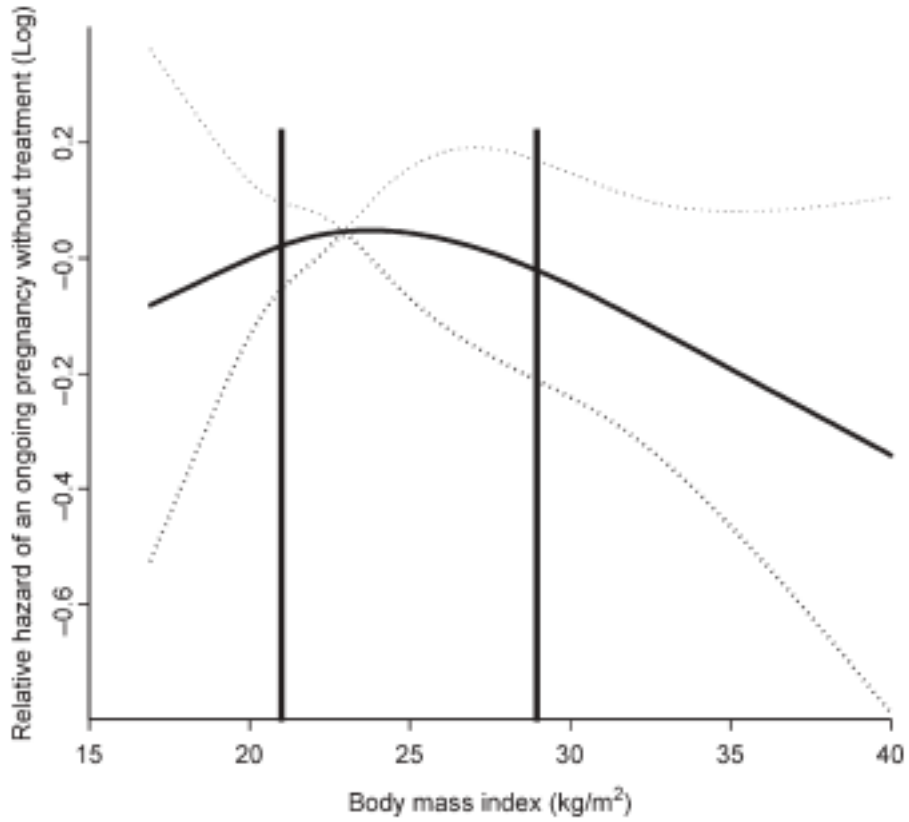
Obesity affects spontaneous pregnancy chances in subfertile, ovulatory women

Jan Willem van der Steeg[1,2,4,8], Pieternel Steures[1,2,4], Marinus J.C. Eijkemans[1], J. Dik F. Habbema[1], Peter G.A. Hompes[4], Jan M. Burggraaff[5], G. Jur E. Oosterhuis[6], Patrick M.M. Bossuyt[3], Fulco van der Veen[2] and Ben W.J. Mol[2,7]



Incidence of complications following ART in overweight versus normal weight women

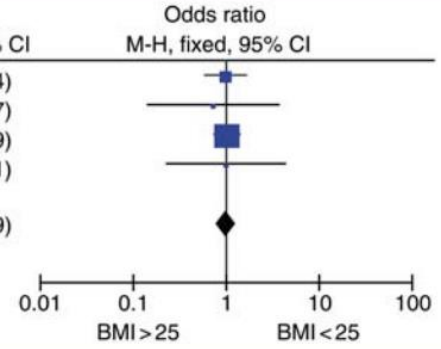
Study	ART	*n*	Per	Complication rate in overweight[a] versus normal weight women								
				OHSS			Multiple pregnancy			Ectopic pregnancy		
				Incidence %		OR (95% CI)	Incidence % (p/p)		OR (95% CI)	Incidence % (p/p)		OR (95% CI)
				BMI > 25	BMI < 25		BMI > 25	BMI < 25		BMI > 25	BMI < 25	
Luke *et al.* (2011)	IVF	451 63	ET	NA	NA	NA	32	32	1.0 (0.9 to 1.1)	NA	NA	NA
Farhi *et al.* (2010)	IVF	233	Woman	2.7	3.8	0.7 (0.1 to 3.7)	NA	NA	NA	NA	NA	NA
Sathya *et al.* (2010)	IVF	308	Woman	NA	NA	NA	32	26	1.3 (0.6 to 3.1)	6.7	2.6	2.7 (0.3 to 22.7)
Zhang *et al.* (2010)	IVF/ICSI	2628	Woman	NA	NA	NA	NA	NA	NA	4.5	3.8	1.2 (0.5 to 2.9)
Maheshwari *et al.* (2009a)	IVF	1756	Woman	10.3	10.2	1.0 (0.7 to 1.4)	18	21	0.9 (0.6 to 1.3)	NA	NA	NA
Sneed *et al.* (2008)	IVF/ICSI	1273	Woman	NA	NA	NA	NA	NA	NA	1.7	3.0	0.6 (0.2 to 1.8)
Matalliotakis *et al.* (2008)	IVF/ICSI	278	Woman	NA	NA	NA	28[b]	27[b]	1.1 (0.5 to 2.1)[b]	1.1[b]	1.2[b]	1.0 (0.06 to 15.5)[b]
Esinler *et al.* (2008)	ICSI	775	ET	0.8	1.0	0.9 (0.2 to 3.0)	47	52	0.8 (0.6 to 1.2)	NA	NA	NA
Dokras *et al.* (2006)	IVF/ICSI	1291	Woman	4.8	4.8	1.0 (0.6 to 1.6)	28	31	0.9 (0.6 to 1.2)	NA	NA	NA
Van Swieten *et al.* (2005)[c]	IVF/ICSI	162	Woman	4.9	5.0	1.0 (0.2 to 4.3)	NA	NA	NA	NA	NA	NA
Spandorfer *et al.* (2004)	IVF/ICSI	828	Cycle	NA	NA	NA	36[d]	52[d]	0.5 (0.3 to 0.8)[d]	NA	NA	NA
Fedorcsak *et al.* (2004)	IVF/ICSI	2660	Woman	NA	NA	NA	NA	NA	NA	0.5	1.7	0.3 (0.03 to 2.0)
Wittemer *et al.* (2000)	IVF/ICSI	325	Cycle	NA	NA	NA	NA	NA	NA	15.0	5.0	3.4 (0.6 to 18.2)
Lashen *et al.* (1999)[c]	IVF	228	Woman	2.6[e]	5.3[e]	0.5 (0.1 to 2.4)	NA	NA	NA	NA	NA	NA

OHSS for overweight and normal weight women

Study or subgroup	BMI > 25 Events	Total	BMI < 25 Events	Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
Dokras *et al.* (2006)	29	610	33	683	25.9	0.98 (0.59, 1.64)
Farhi *et al.* (2011)	2	73	6	160	3.2	0.72 (0.14, 3.67)
Maheshwari *et al.* (2009a,b)	75	725	105	1031	67.8	1.02 (0.74, 1.39)
Van Swieten *et al.* (2005)	3	61	5	101	3.1	0.99 (0.23, 4.31)
Total (95% CI)		1469		1975	100.0	1.00 (0.77, 1.29)
Total events	109		149			

Heterogeneity: $\chi^2 = 0.17$, df = 3 ($P = 0.98$); $I^2 = 0\%$

Test for overall effect: $Z = 0.01$ ($P = 0.99$)

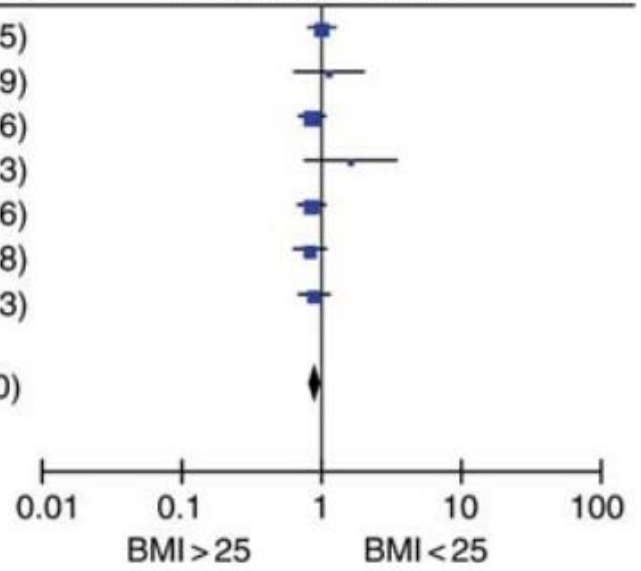


Live birth rate for overweight and normal weight women

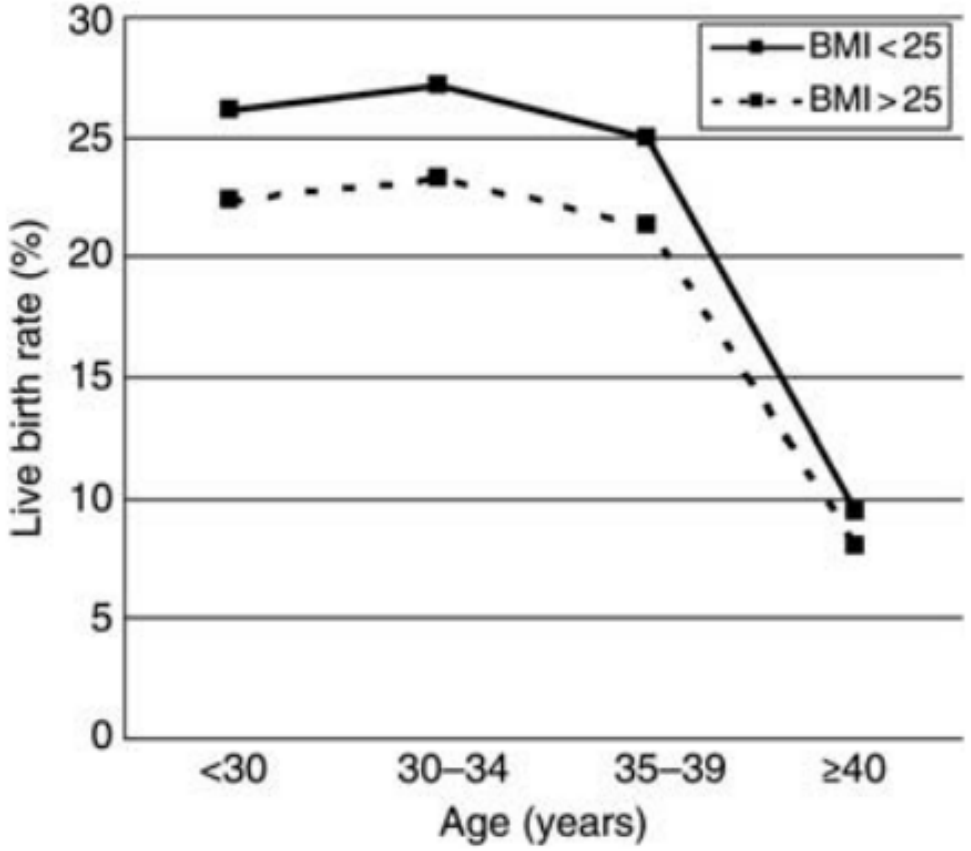
Study or subgroup	BMI > 25 Events	Total	BMI < 25 Events	Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
Dokras *et al.* (2006)	254	609	284	682	19.3	1.00 (0.80, 1.25)
Farhi *et al.* (2010)	30	73	61	160	2.8	1.13 (0.64, 1.99)
Fedorcsak *et al.* (2004)	143	745	416	1915	23.3	0.86 (0.69, 1.06)
Hill *et al.* (2011)	26	59	19	58	1.3	1.62 (0.76, 3.43)
Maheshwari *et al.* (2009a,b)	166	725	267	1031	21.1	0.85 (0.68, 1.06)
Sneed *et al.* (2008)	134	632	157	641	15.2	0.83 (0.64, 1.08)
Zhang *et al.* (2010)	97	406	582	2222	17.0	0.88 (0.69, 1.13)
Total (95% CI)		3249		6709	100.0	0.90 (0.82, 1.00)
Total events	850		1786			

Heterogeneity: $\chi^2 = 4.74$, df = 6 ($P = 0.58$); $I^2 = 0\%$

Test for overall effect: $Z = 2.02$ ($P = 0.04$)



Live birth rate for overweight and normal weight women



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of a Lifestyle Program in Obese Infertile Women

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Henk Groen, M.D., Ph.D., Jan M. Burggraaff, M.D.,
Walter K.H. Kuchenbecker, M.D., Ph.D., Denise A.M. Perquin, M.D., Ph.D.,
Carolien A.M. Koks, M.D., Ph.D., Ron van Golde, M.D., Ph.D.,
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Yvonne M. van Kasteren, M.D., Ph.D., Annemiek W. Nap, M.D., Ph.D.,
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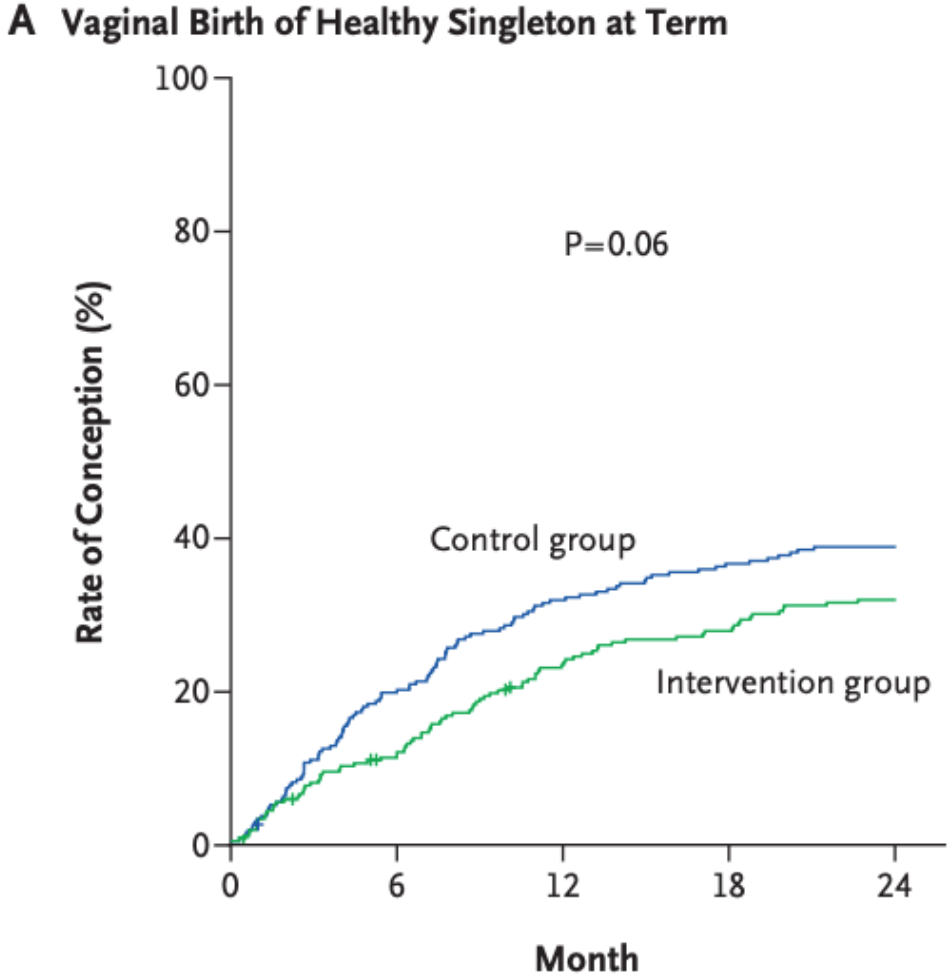
Ed T.C.M. Gondrie, M.D., Jan P. de Bruin, M.D., Ph.D., J. Marko Sikkema, M.D.,
Mathieu H.G. de Greef, Ph.D., Nancy C.W. ter Bogt, Ph.D.,
Jolande A. Land, M.D., Ph.D., Ben W.J. Mol, M.D., Ph.D.,
and Annemieke Hoek, M.D., Ph.D.

Table 2. Pregnancy Outcomes within 24 Months after Randomization, According to Trial Group.*

Outcome	Intervention Group (N=280)	Control Group (N=284)	Rate Ratio (95% CI)
Fetal or neonatal outcomes			
Primary outcome: vaginal birth of healthy singleton at term — no. (%)	76 (27.1)	100 (35.2)	0.77 (0.60 to 0.99)
Live birth — no. (%)	123 (43.9)	153 (53.9)	0.82 (0.69 to 0.97)
Ongoing pregnancy — no. (%)	150 (53.6)	167 (58.8)	0.91 (0.79 to 1.05)
Clinical pregnancy — no. (%)	175 (62.5)	186 (65.5)	0.95 (0.84 to 1.08)
Ectopic pregnancy — no. (%)†	4 (1.4)	7 (2.5)	0.58 (0.17 to 1.96)
Miscarriage — no. (%)	41 (14.6)	27 (9.5)	1.54 (0.98 to 2.43)



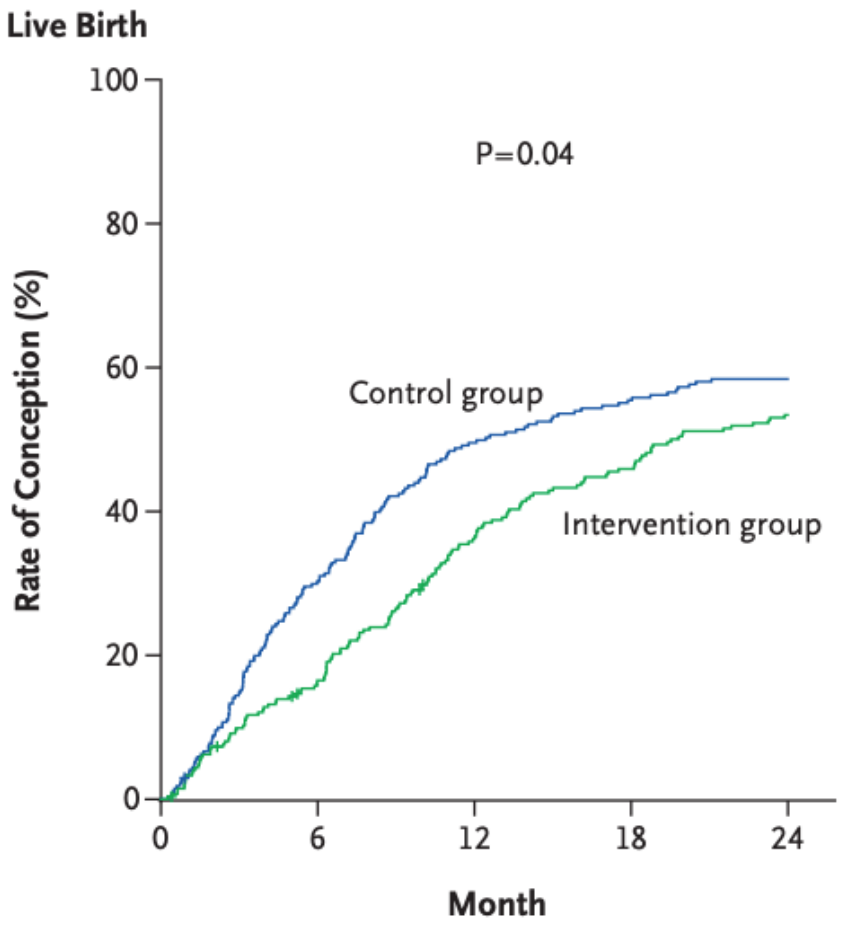


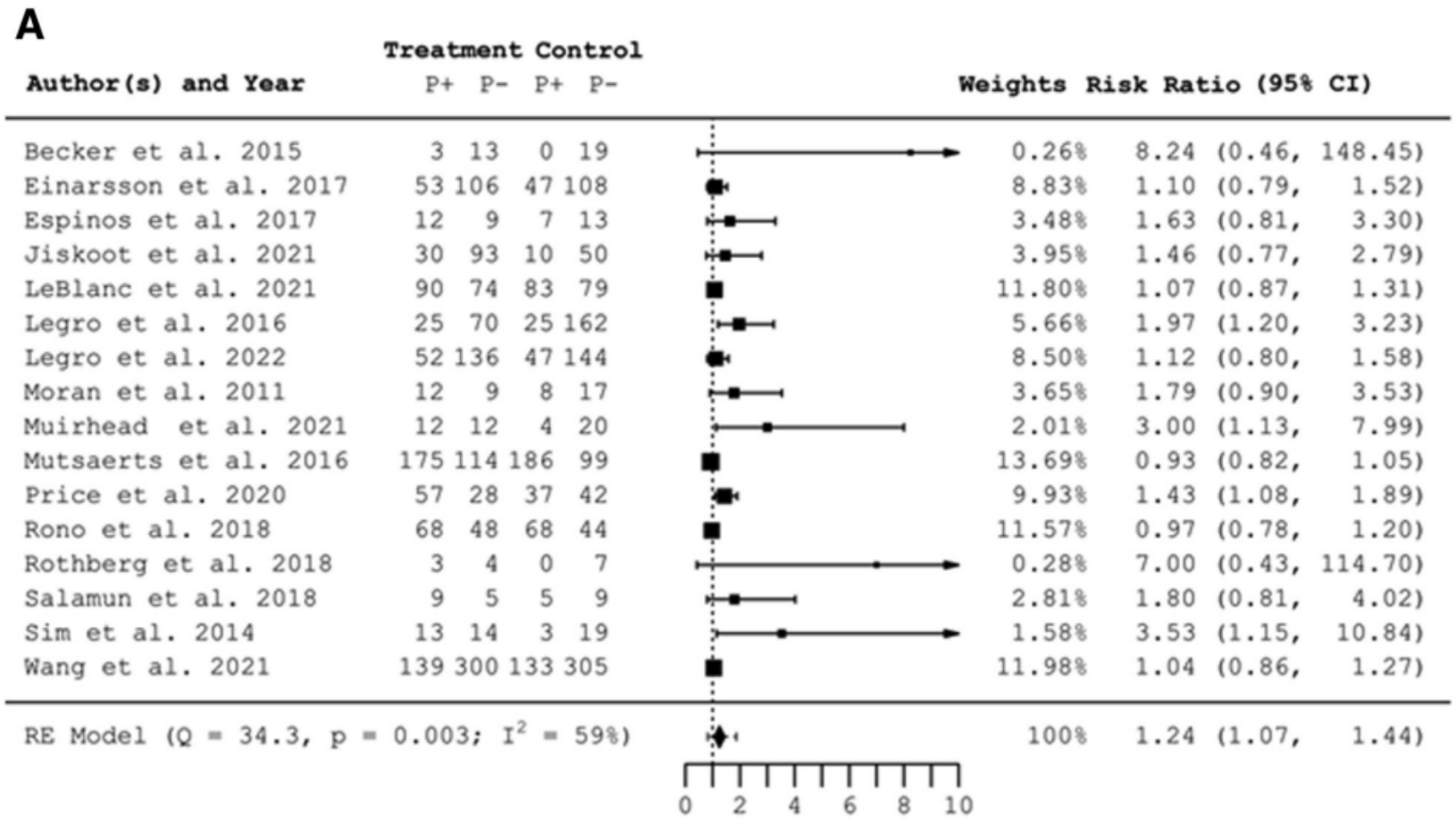
Table S2. Pregnancy outcome and mode of conception in both groups including pregnancies ending beyond 24 months of randomization

Outcome	Intervention (N=280)	Control (N=284)	RR (95 CI)
Pregnancies			
Vaginal birth of healthy singleton at term	90 (32.1)	111 (39.1)	0.82 (0.65 to 1.02)
Live birth	149 (53.2)	165 (58.1)	0.91 (0.79 to 1.05)
Ongoing pregnancy	154 (55.0)	167 (58.8)	0.94 (0.81 to 1.08)
Clinical pregnancy	179 (63.9)	188 (66.2)	0.96 (0.85 to 1.08)
Ectopic pregnancy	4 (1.4)	7 (2.5)	0.58 (0.17 to 2.0)
Miscarriage	41 (14.6)	27 (9.5)	1.54 (0.98 to 2.4)
Multiple gestation	7 (2.5)	9 (3.2)	0.79 (0.30 to 2.1)
Twins	6 (2.1)	9 (3.2)	0.68 (0.24 to 1.9)
Triplets	1 (0.36)	0	NA
Mode of conception leading to ongoing pregnancy			
Natural	74 (26.4)	46 (16.2)	1.6 (1.2 to 2.3)
Ovulation induction	36 (12.9)	64 (22.5)	0.57 (0.39 to 0.83)
Intrauterine insemination	22 (7.9)	25 (8.8)	0.89 (0.52 to 1.5)
IVF/ICSI**	22 (7.9)	32 (11.3)	0.70 (0.42 to 1.2)

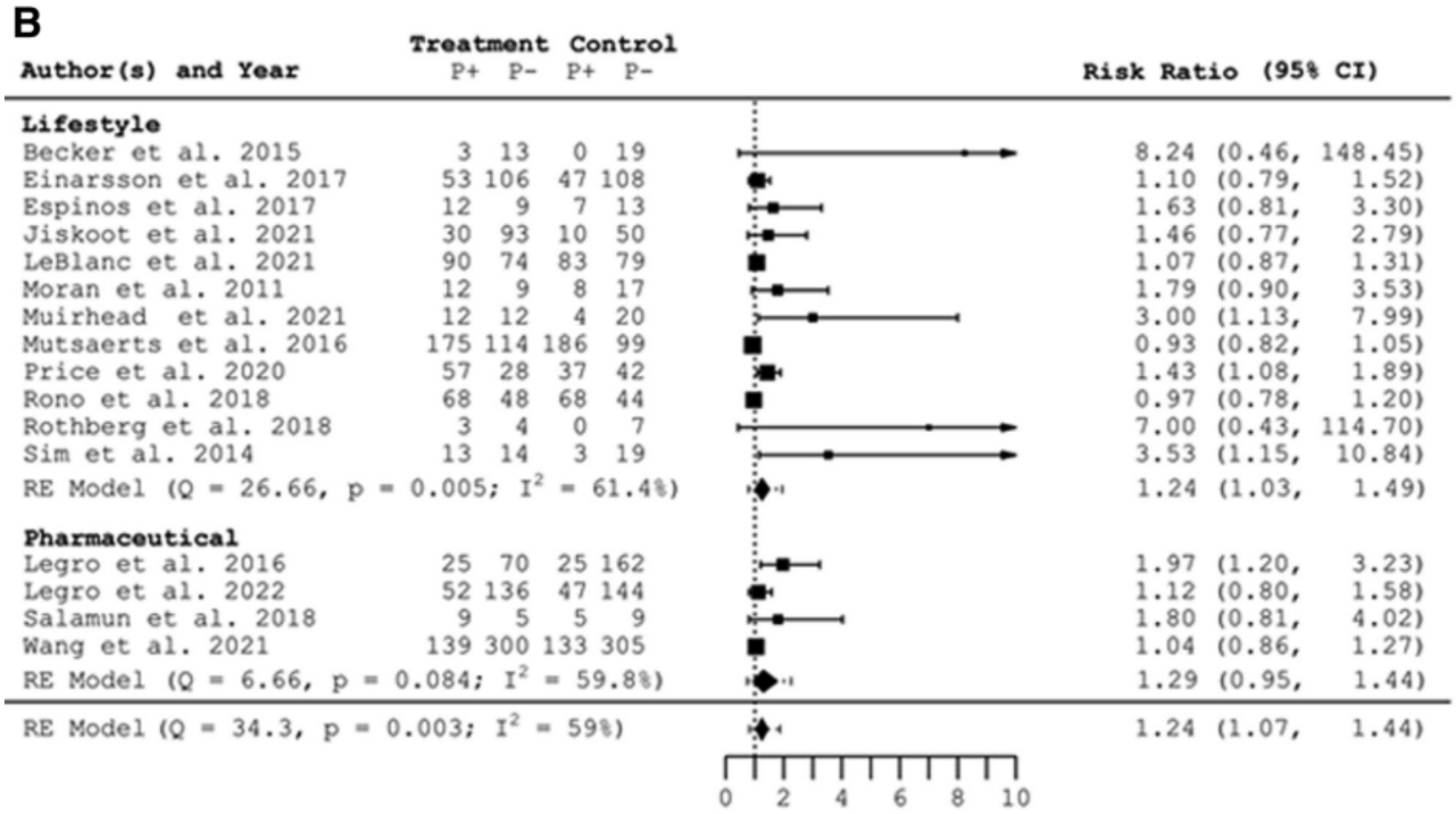
Effectiveness of preconception weight loss interventions on fertility in women: a systematic review and meta-analysis

Ann E. Caldwell, Ph.D.,[a] Anna M. Gorczyca, Ph.D.,[b] Andrew P. Bradford, Ph.D.,[c] Jacinda M. Nicklas, M.D., M.P.H.,[d] Robert N. Montgomery, Ph.D.,[e] Heather Smyth, Ph.D.,[f] Shannon Pretzel, B.A.,[g] Thy Nguyen, B.A.,[g] Kristen DeSanto, M.S.,[h] Celia Ernstrom, B.S.,[g] and Nanette Santoro, M.D.[c]

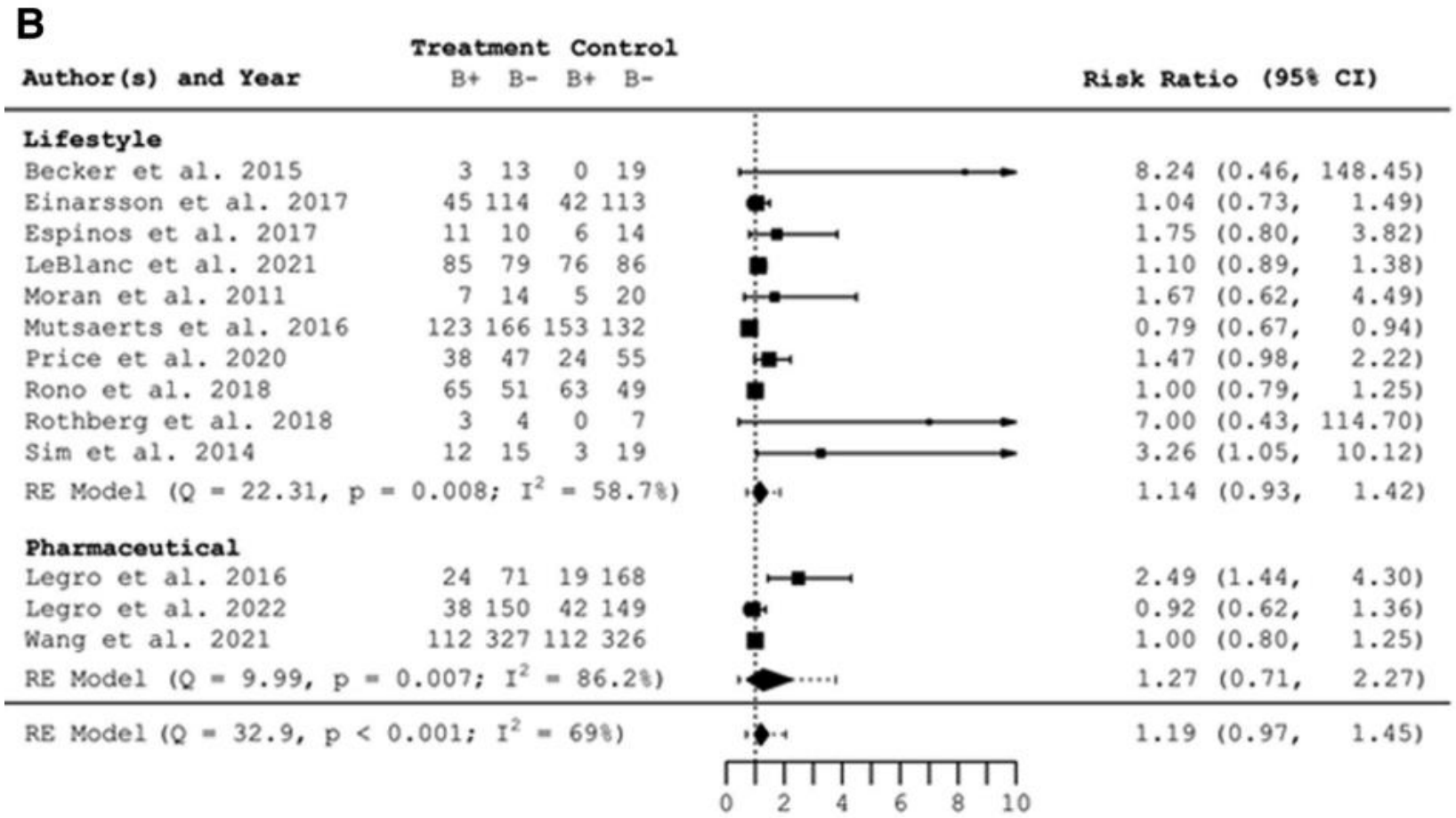
Impact of treatment on pregnancy by study



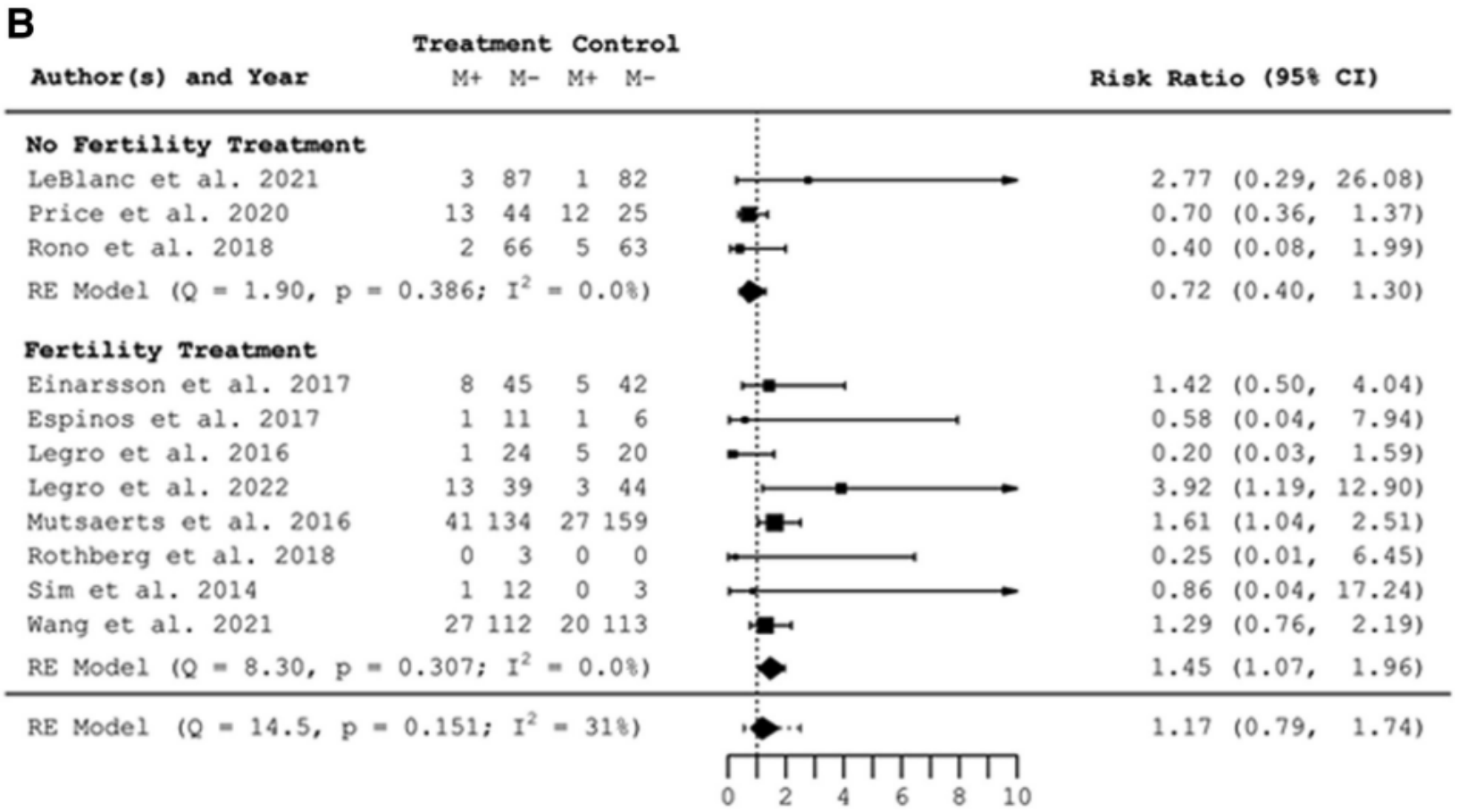
Impact of treatment on pregnancy by by intervention type



Impact of treatment on live birth by intervention type



Impact of treatment on miscarriage by intervention type



Open access Protocol

BMJ Open

Dietary and/or physical activity interventions in women with overweight or obesity prior to fertility treatment: protocol for a systematic review and individual participant data meta-analysis

Emily Evans-Hoeker,[1,2] Zheng Wang ,[3] Henk Groen ,[4] Astrid E P Cantineau,[3] Ann Thurin-Kjellberg,[5,6] Christina Bergh,[5,6] Joop S E Laven,[7] Alexandra Dietz de Loos,[7] Geranne Jiskoot,[7] Jean-Patrice Baillargeon ,[8] Stefano Palomba ,[9] Kyra Sim,[10] Lisa J Moran,[11] Juan J Espinós,[12] Trine Moholdt ,[13,14] Amy E Rothberg ,[15,16] Donna Shoupe,[17] Annemieke Hoek ,[3] Richard S Legro,[18] Ben W Mol ,[19,20] Rui Wang ,[19] On behalf of the Venus-IPD Collaboration

Human Reproduction Open, pp. 1–4, 2017
doi:10.1093/hropen/hox009

human reproduction open

DEBATE

It is not justified to reject fertility treatment based on obesity

Aafke Koning[1,*], Ben Willem Mol[2], and Wybo Dondorp[3]

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David Barker

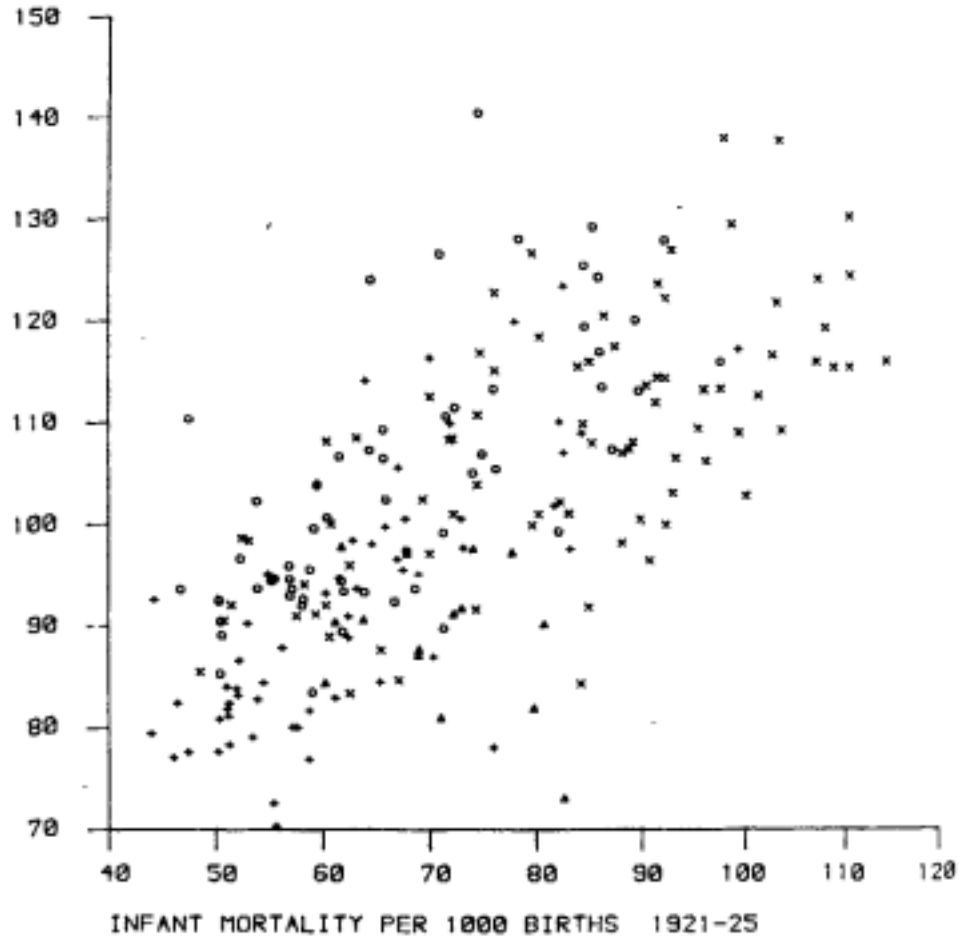
THE LANCET, MAY 10, 1986

Epidemiology

INFANT MORTALITY, CHILDHOOD NUTRITION, AND ISCHAEMIC HEART DISEASE IN ENGLAND AND WALES

D. J. P. BARKER C. OSMOND

MRC Environmental Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton SO9 4XY

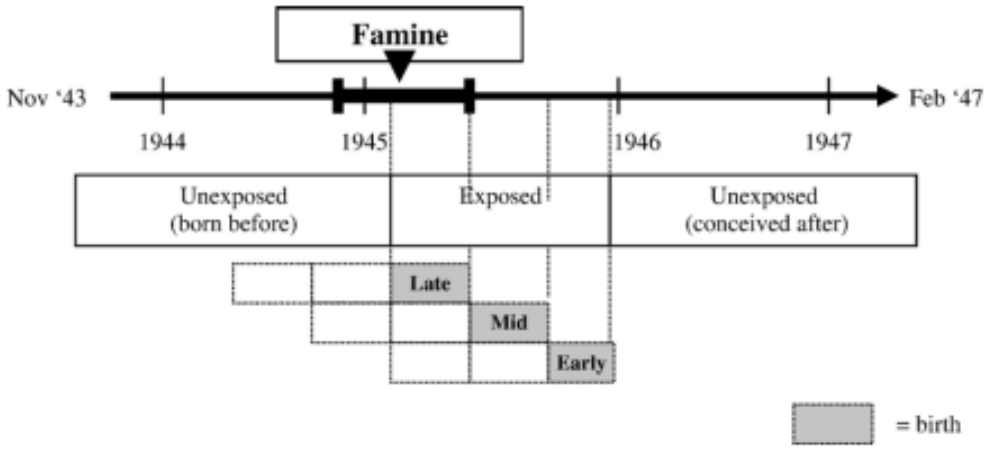


SMRs for ischaemic heart disease in 1968-78 at ages 35-74, men and infant mortality per 1000 births in 1921 - 25 in the 212 areas of England and Wales.

Glucose tolerance in adults after prenatal exposure to famine

A C J Ravelli, J H P van der Meulen, R P J Michels, C Osmond, D J P Barker, C N Hales, O P Bleker

Prenatal exposure to famine, especially during late gestation, is linked to decreased glucose tolerance in adults.



The Dutch famine birth cohort: famine exposure and birth in relation to the timing of the Dutch famine.

Exposure to famine		
In **late** gestation	In **mid** gestation	In **early** gestation
Glucose intolerance	Glucose intolerance	Glucose intolerance
	Microalbuminuria	Atherogenic lipid profile
	Obstructive airways disease	Altered blood coagulation
		Obesity (women only)
		Stress sensitivity
		Coronary heart disease
		Breast cancer

Long-term consequences of exposure to famine according to timing during gestation.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Outcomes of Pregnancy after Bariatric Surgery

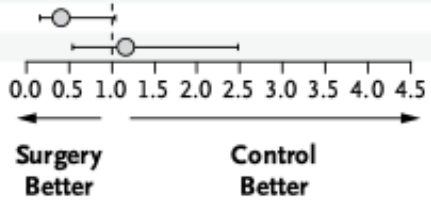
Kari Johansson, Ph.D., Sven Cnattingius, M.D., Ph.D., Ingmar Näslund, M.D., Ph.D., Nathalie Roos, M.D., Ph.D., Ylva Trolle Lagerros, M.D., Ph.D., Fredrik Granath, Ph.D., Olof Stephansson, M.D., Ph.D., and Martin Neovius, Ph.D.

Table 2. Gestational Diabetes and Perinatal Outcomes among Women with and Those without a History of Bariatric Surgery.

Variable	Bariatric-Surgery Group (N=596)	Matched Control Group (N=2356)	Risk Difference	Odds Ratio (95% CI)*	P Value
	no./total no. (%)		*percentage points (95% CI)*		
Gestational diabetes†					
Total	11/578 (1.9)	157/2294 (6.8)	−4.9 (−6.5 to −3.4)	0.25 (0.13 to 0.47)	<0.001
Insulin-treated	4/578 (0.7)	83/2294 (3.6)	−2.9 (−3.9 to −1.9)	0.17 (0.06 to 0.49)	<0.001
Large-for-gestational-age infant‡	51/590 (8.6)	523/2336 (22.4)	−13.8 (−16.6 to −11.0)	0.33 (0.24 to 0.44)	<0.001
Macrosomia‡	7/590 (1.2)	221/2336 (9.5)	−8.3 (−9.7 to −6.8)	0.11 (0.05 to 0.24)	<0.001
Small-for-gestational-age infant‡	92/590 (15.6)	178/2336 (7.6)	8.0 (4.8 to 11.1)	2.20 (1.64 to 2.95)	<0.001
Low-birth-weight infant‡	40/590 (6.8)	105/2336 (4.5)	2.3 (0.1 to 4.5)	1.34 (0.88 to 2.04)	0.17
Preterm birth§	59/590 (10.0)	176/2344 (7.5)	2.5 (−0.2 to 5.1)	1.28 (0.92 to 1.78)	0.15
Stillbirth¶	6/596 (1.0)	12/2356 (0.5)	0.5 (−0.4 to 1.3)	1.89 (0.59 to 6.05)	0.28
Neonatal death <28 days after live birth§	4/590 (0.7)	5/2344 (0.2)	0.5 (−0.2 to 1.2)	2.93 (0.57 to 15.14)	0.20
Stillbirth or neonatal death	10/596 (1.7)	17/2356 (0.7)	1.0 (−0.1 to 2.0)	2.39 (0.98 to 5.85)	0.06
Major congenital malformations§					
Total	14/590 (2.4)	83/2344 (3.5)	−1.2 (−2.6 to 0.3)	0.72 (0.40 to 1.29)	0.27
Excluding chromosomal abnormalities§	12/590 (2.0)	79/2344 (3.4)	−1.3 (−2.7 to 0.0)	0.63 (0.34 to 1.18)	0.16

B Years from Surgery to Delivery

Subgroup and Years	Bariatric-Surgery Cohort (no. of cases/total no. (%))	Control Cohort (no. of cases/total no. (%))	P Value
Gestational diabetes			0.18
<1.8	7/292 (2.4)	70/1148 (6.1)	
≥1.8	4/286 (1.4)	87/1146 (7.6)	
LGA			0.41
<1.8	30/296 (10.1)	276/1168 (23.6)	
≥1.8	21/294 (7.1)	247/1168 (21.1)	
SGA			0.02
<1.8	40/296 (13.5)	100/1168 (8.6)	
≥1.8	52/294 (17.7)	78/1168 (6.7)	
Preterm birth			0.77
<1.8	28/296 (9.5)	86/1173 (7.3)	
≥1.8	31/294 (10.5)	90/1171 (7.7)	
Malformations			0.10
<1.8	5/296 (1.7)	48/1173 (4.1)	
≥1.8	9/294 (3.1)	35/1171 (3.0)	



C Decrease in BMI Units

Subgroup and BMI Units	Bariatric-Surgery Cohort (no. of cases/total no. (%))	Control Cohort (no. of cases/total no. (%))	P Value
Gestational diabetes			0.67
<12.9	4/253 (1.6)	71/1141 (6.2)	
≥12.9	7/306 (2.3)	80/1088 (7.4)	
LGA			<0.001
<12.9	37/263 (14.1)	226/1157 (19.5)	
≥12.9	12/309 (3.9)	276/1112 (24.8)	
SGA			0.52
<12.9	40/263 (15.2)	88/1157 (7.6)	
≥12.9	52/309 (16.8)	87/1112 (7.8)	
Preterm birth			0.04
<12.9	20/263 (7.6)	94/1163 (8.1)	
≥12.9	37/309 (12.0)	74/1114 (6.6)	
Malformations			0.08
<12.9	3/263 (1.1)	44/1163 (3.8)	
≥12.9	10/309 (3.2)	35/1114 (3.1)	

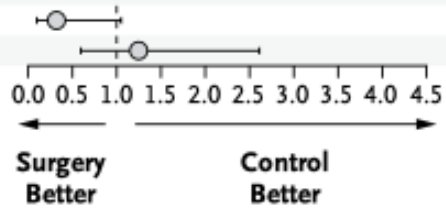


Figure. Major Birth Defects in Infants Born to Women With Gastric Bypass Surgery and Matched Controls

	Total No.		Events, No. (%)			
	After Gastric Bypass	Matched Controls	After Gastric Bypass	Matched Controls	Risk Ratio (95% CI)	*P* Value
Primary analysis						
Any major birth defect	2921	30573	98 (3.4)	1510 (4.9)	0.67 (0.52-0.87)	.002
Sensitivity analysis						
Excluding chromosomal abnormalities	2916	30516	93 (3.2)	1470 (4.8)	0.66 (0.51-0.85)	.001
First birth after surgery	2436	20045	75 (3.1)	1058 (5.3)	0.58 (0.44-0.77)	<.001
Excluding coarsened exact matching weights >20	2587	30463	85 (3.3)	1387 (4.6)	0.72 (0.56-0.91)	.007