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Priming of the Obesity Risk by Smoking in Pregnancy

Prof. Rüdiger von Kries

Institute for Social Pediatrics





Maternal smoking in Pregnancy and childhood obesity

- An unexpected observation.
- Becoming almost convinced about causality.
- Becoming less convinced.
- Where are we now - and how to understand more.



Breast feeding and obesity: cross sectional study

Rüdiger von Kries, Berthold Koletzko, Thorsten Sauerwald, Erika von Mutius, Dietmar Barnert,
Veit Grunert, Hubertus von Voss

BMJ VOLUME 319 17 JULY 1999 www.bmj.com



...higher levels of parental education (>10 years), premature birth and low birth weight were inversely associated with being overweight or obese, whereas **maternal smoking during pregnancy** and the child having his or her own bedroom were positively correlated.



Eur J Pediatr (2002) 161: 445–448
DOI 10.1007/s00431-002-0983-z

ORIGINAL PAPER

André Michael Toschke · Berthold Koletzko
William Slikker Jr · Monika Hermann
Rüdiger von Kries

Childhood obesity is associated with maternal smoking in pregnancy

Maternal smoking ^a	Overweight (BMI > 90th percentile)	Obesity (BMI > 97th percentile)
Never smoked (<i>n</i> = 5,919)	9.1 (8.3–9.8)	2.8 (2.4–3.2)
Smoked		
Before pregnancy or before and after pregnancy but not throughout pregnancy (<i>n</i> = 1,542)	14.1 (12.4–15.9)	4.5 (3.6–5.7)
Throughout pregnancy (<i>n</i> = 660)	15.6 (12.9–18.6)	6.2 (4.5–8.3)
After pregnancy only (<i>n</i> = 244)	7.4 (4.4–11.4)	1.6 (0.4–4.1)

^aThe information was considered as inconclusive if maternal smoking was ticked as “yes” in one category but not as “yes” or “no” in the other categories (*n* = 400). Hence these were children whose mothers had smoked at some time but we do not know whether they only smoked during that stated period



Period of smoking	BMI > 90th percentile		BMI > 97th percentile	
	Crude OR	Adjusted OR ^a	Crude OR	Adjusted OR ^a
Smoking before pregnancy or before and after pregnancy but not throughout pregnancy (<i>n</i> = 1,542)	1.64 (1.39–1.94)	1.63 (1.37–1.94)	1.67 (1.26–2.22)	1.74 (1.29–2.34)
Throughout pregnancy (<i>n</i> = 660)	1.85 (1.47–2.33)	1.58 (1.23–2.04)	2.32 (1.63–3.30)	1.92 (1.29–2.86)
After pregnancy (<i>n</i> = 244)	0.80 (0.49–1.30)	0.80 (0.48–1.32)	0.59 (0.22–1.59)	0.63 (0.23–1.73)

^aORs adjusted for breast-feeding, parental education, low birth weight and prematurity



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Maternal Smoking during Pregnancy and Childhood Obesity

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Received for publication January 4, 2002; accepted for publication June 4, 2002.



TABLE 4. Adjusted odds ratios (final logistic regression model) for being overweight or being obese, Bavaria, Germany, 1999–2000

Potential risk factors	Being overweight*		Being obese†	
	Odds ratio	95% CI‡	Odds ratio	95% CI
Maternal smoking during pregnancy	1.43	1.07, 1.90	2.06	1.31, 3.23
High level of parental education (≥ 10 years)§	0.70	0.55, 0.89	0.68	0.45, 1.03
Body mass index of either parent of ≥ 30 kg/m ²	2.70	2.09, 3.49	4.55	3.07, 6.74
Birth weight above the 90th percentile	2.12	1.52, 3.46	2.23	1.27, 3.90
Watching television or playing video games (Game Boy®) more than 1 hour daily§	1.39	1.11, 1.74	1.86	1.22, 2.79
Any breastfeeding§	0.84	0.66, 1.06	0.91	0.60, 1.38
Eating snacks while watching television, never/ever§	1.52	1.18, 1.97	1.35	0.84, 2.15



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Early Intrauterine Exposure to Tobacco-inhaled Products and Obesity

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Received for publication March 7, 2003; accepted for publication June 3, 2003.

TABLE 3. Crude and adjusted odds ratios* for maternal smoking early in pregnancy only vs. throughout pregnancy, Bavaria, Germany, 2001–2002†

	Maternal smoking in early pregnancy				Maternal smoking throughout pregnancy			
	Overweight		Obesity		Overweight		Obesity	
	Odds ratio	95% CI‡	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Maternal smoking in early pregnancy (unadjusted)	1.66	1.27, 2.18	2.41	1.49, 3.91	1.85	1.38, 2.47	3.23	2.00, 5.21
Adjusted for								
Breastfeeding§	1.59	1.21, 2.09	2.22	1.37, 3.61	1.62	1.20, 2.19	2.49	1.50, 4.11
+ educational level	1.56	1.19, 2.06	2.16	1.33, 3.52	1.50	1.10, 2.03	2.14	1.29, 3.55
+ parental obesity	1.58	1.20, 2.09	2.17	1.32, 3.56	1.47	1.08, 2.01	2.09	1.24, 3.51
+ watching television, playing electronic games occasionally, physical activity, high infant weight gain	1.52	1.14, 2.01	2.22	1.33, 3.69	1.23	0.89, 1.70	1.70	1.02, 2.87



REVIEW

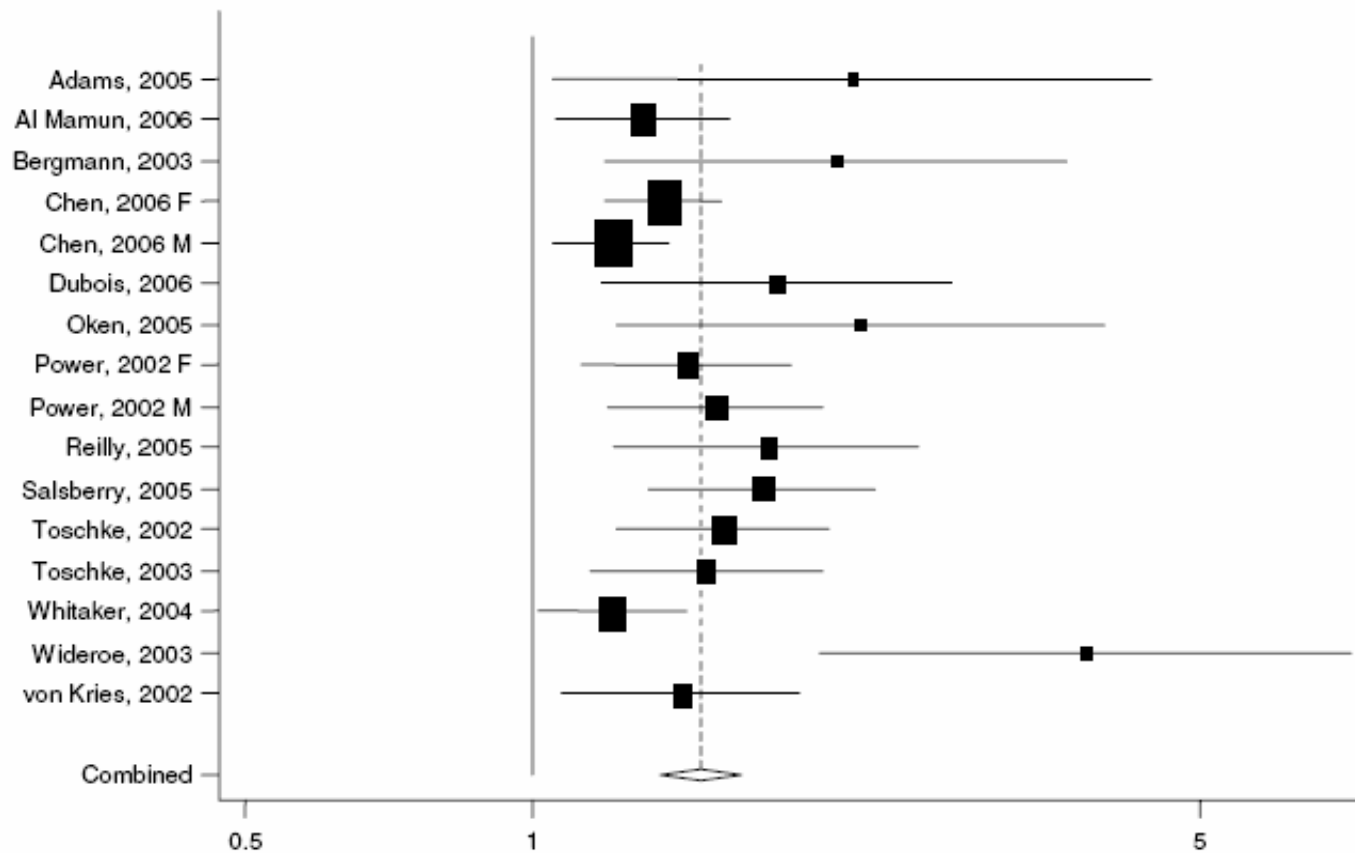
Maternal smoking during pregnancy and child overweight: systematic review and meta-analysis

E Oken¹, EB Levitan² and MW Gillman^{1,3}

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OR for smoking during pregnancy and childhood overweight





Association smoking during pregnancy and childhood obesity = causal association?

Strength of Association ✓

Temporality ✓

Consistency ✓

Theoretical Plausibility?

Specificity in the causes - no

Dose Response Relationship +-

Experimental Evidence ✓

Analogy?



Diabetologia (2005) 48: 2661–2666
DOI 10.1007/s00125-005-0022-5

ARTICLE

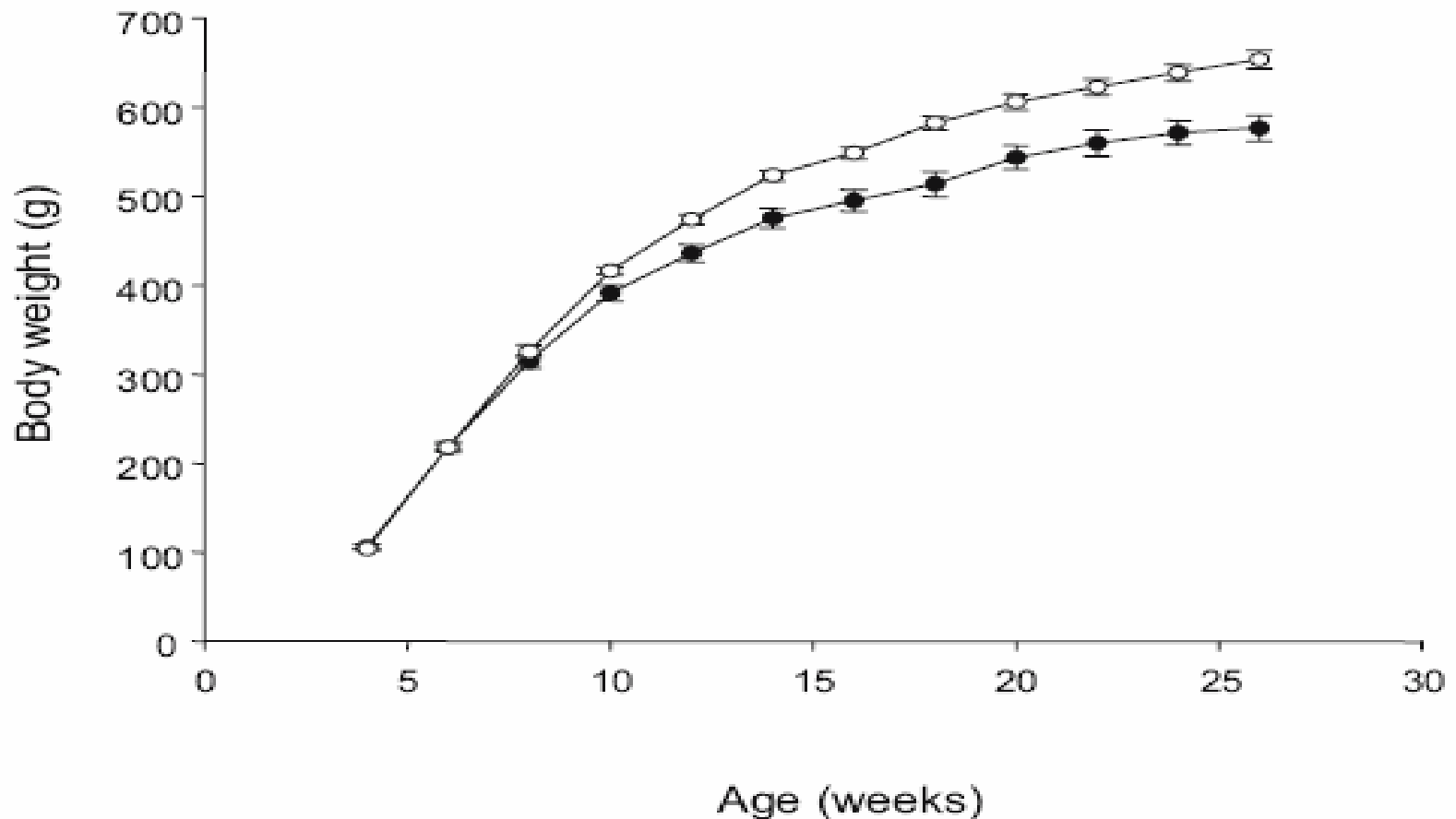
A. C. Holloway · G. E. Lim · J. J. Petrik · W. G. Foster ·
K. M. Morrison · H. C. Gerstein

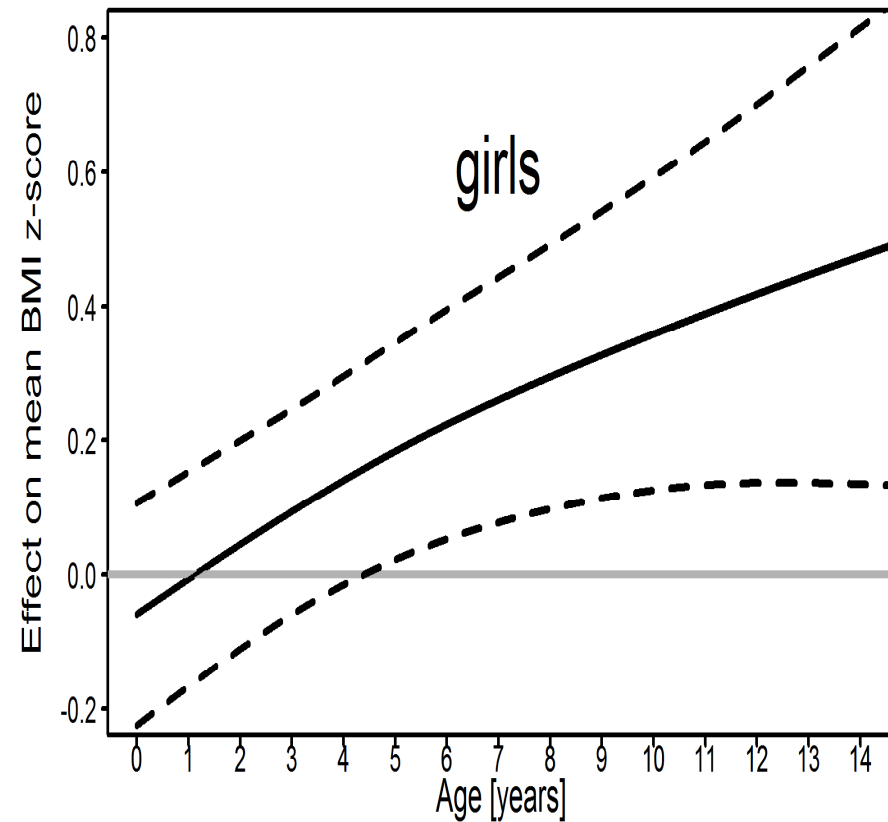
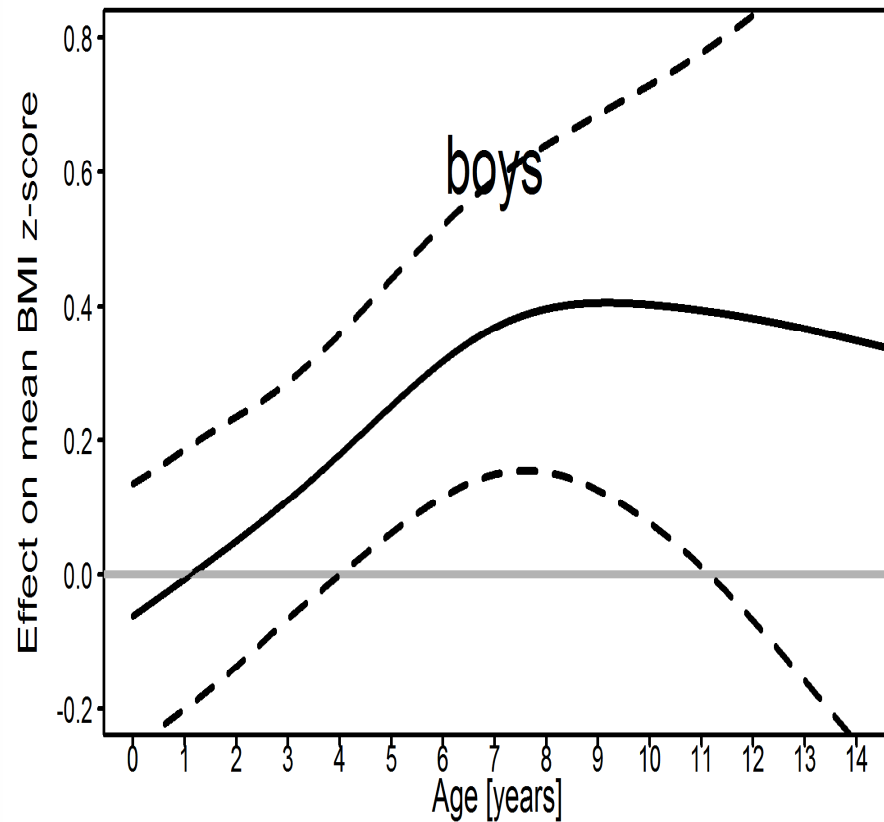
Fetal and neonatal exposure to nicotine in Wistar rats results in increased beta cell apoptosis at birth and postnatal endocrine and metabolic changes associated with type 2 diabetes

Received: 5 May 2005 / Accepted: 18 July 2005 / Published online: 4 November 2005
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open circle: 1 mg nicotine daily in pregnancy
closed circle: no nicotine





Age-varying effect of maternal smoking during pregnancy (black lines) compared to non-smoking mothers during pregnancy (grey horizontal line at zero) .



Association smoking during pregnancy and childhood obesity - valid?

Chance - very unlikely

Temporality ✓

Bias – not likely

Confounding - possible

Pediatric Original Article

International Journal of Obesity (29 May 2013) | doi:10.1038/ijo.2013.101
.....

Parental smoking during pregnancy and risk of overweight and obesity in the daughter

H R Harris, W C Willett and K B Michels

ORs of overweight by maternal smoking during pregnancy with multiple adjustment including paternal smoking

	Maternal Smoking					P _{trend}
	No smoking during pregnancy	Quit smoking during pregnancy	Smoked throughout pregnancy			
			1-14 cigarettes/day	15-24 cigarettes/day	25+ cigarettes/day	
Adjusted for paternal smoking ³	1.00 (ref)	1.00 (0.88-1.14)	1.07 (0.99-1.16)	1.17 (1.05-1.29)	1.32 (1.04-1.67)	<0.001

ORs of overweight by paternal smoking during pregnancy with multiple adjustment including maternal smoking

	Paternal Smoking				P _{trend}
	No smoking during pregnancy	1-14 cigarettes/day	15-24 cigarettes/day	25+ cigarettes/day	
Adjusted for maternal smoking ³	1.00 (ref)	1.09 (1.02-1.17)	1.12 (1.04-1.20)	1.17 (1.06-1.28)	<0.001



BMC Public Health



Research article

Open Access

Potential determinants of obesity among children and adolescents in Germany: results from the cross-sectional KiGGS study

Christina Kleiser*¹, Angelika Schaffrath Rosario¹, Gert BM Mensink¹,
Reinhild Prinz-Langenohl² and Bärbel-Maria Kurth¹

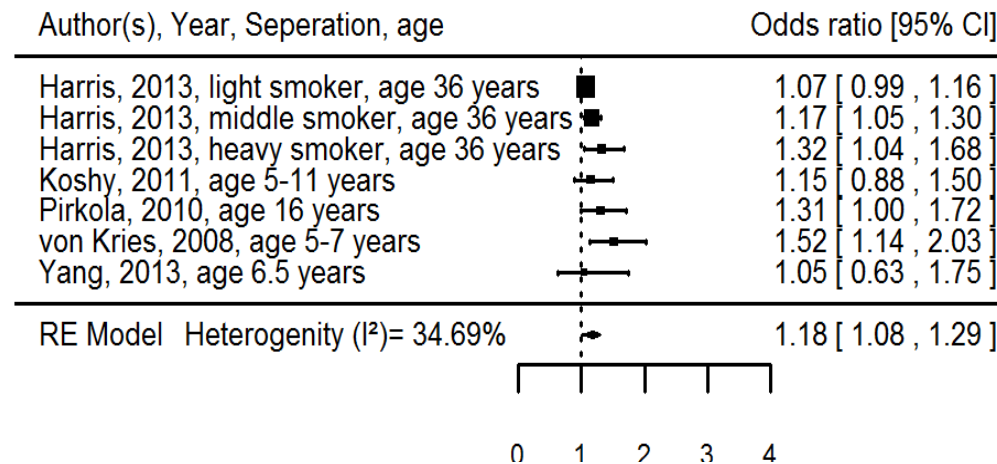
ORs for childhood obesity by maternal smoking during and paternal smoking at interview mutually adjusted

	Odds ratio	95%-CI	p
Parental smoking (at time of interview)			
Mother and/or father	1.30	(1.0–1.7)	0.0601
None	ref.	-	
Maternal smoking during pregnancy			
Yes	1.37	(1.0–1.8)	0.0267
No	ref.	-	



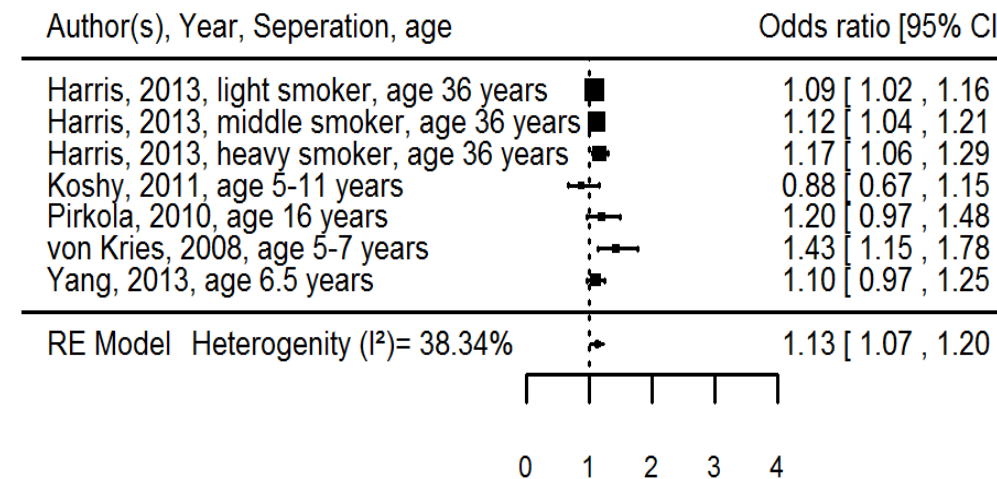
ORs for childhood
overweight by
maternal smoking
during pregnancy
adjusted for
paternal smoking

Overweight - maternal smoking during pregnancy



ORs for childhood
overweight by
paternal smoking
adjusted for
maternal smoking
during pregnancy

Overweight - anytime paternal smoking



	Cotinin (ng/mg) hair:	
	mean	± standard deviation
Mothers		
active smoker	6.3	4.0
passive smoker	0.9	0.3
unexposed	0.3	0.06
Newborns		
smoking mothers	2.8	0.8
passive smoker	0.6	0.15
unexposed	0.26	0.04

Eliopoulos et al. (1994): Hair concentrations of nicotine and cotinine in women and their newborn infants, J. Am. Med. Assoc., 271, 621.



- In case of a linear dose response relation similar strengths of the effect would not be plausible
- Are both maternal smoking in pregnancy and paternal smoking a surrogate for an unmeasured confounder: family condition?
- The best means to address this issue is a sibling study: one exposed to maternal smoking in pregnancy the other one not.



THEME: PERINATAL EPIDEMIOLOGY

Familial factors confound the association between maternal smoking during pregnancy and young adult offspring overweight

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Maternal smoking in first and second born son and the risk of overweight in siblings

Maternal smoking during pregnancy		First son				
		Total <i>N</i>	Overweight <i>n</i>	BMI mean	Crude OR (95% CI)	Adjusted ^d OR (95% CI)
1st	2nd					
No	No ^b	6190	979	22.42	1.00	1.00
Yes	No	524	96	22.91	1.19 (0.95–1.51)	1.19 (0.87–1.63)
No	Yes	228	46	23.09	1.34 (0.97–1.87)	1.15 (0.75–1.78)
Yes	Yes	1499	366	23.44	1.72 (1.50–1.97)	1.65 (1.35–2.01)

Maternal smoking in first and second born son and the risk of overweight in siblings

Maternal smoking during pregnancy		Second son				
		Total <i>N</i>	Overweight <i>n</i>	BMI mean	Crude OR (95% CI)	Adjusted ^d OR (95% CI)
1st	2nd					
No	No ^b	6190	1078	22.51	1.00	1.00
Yes	No	524	113	22.88	1.30 (1.05–1.62)	1.20 (0.88–1.65)
No	Yes	228	51	23.32	1.37 (0.99–1.88)	0.96 (0.58–1.57)
Yes	Yes	1499	400	23.48	1.72 (1.51–1.97)	1.71 (1.39–2.09)



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Original Contribution

Maternal Smoking during Pregnancy and Children's Cognitive and Physical Development: A Causal Risk Factor?

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	Level of maternal smoking during pregnancy (cigarettes/day)						χ^2 or F (3 df)	p value
	1-9		10-19		≥ 20			
	OR* or β †	95% CI*	OR or β	95% CI	OR or β	95% CI		
Overweight**								
Full sample, adjusted	0.99, 1.33	1.35	1.15, 1.58	1.17	1.02, 1.34	15.0	0.002	
Siblings, adjusted	1.11, 2.17	1.61	1.15, 2.26	1.35	1.00, 1.82	11.1	0.011	
Siblings, fixed effects	1.30, 6.49	2.47	1.00, 6.10	2.55	1.01, 6.44	7.2	0.066	

OR for any maternal smoking vs. none: 2.73 [95% CI: 1.30,5.71]

Unfortunately not consistent!



Body mass index#

Full sample, adjusted

Siblings, adjusted

Siblings, fixed effects

	Level of maternal smoking during pregnancy (cigarettes/day)						χ^2 or F (3 df)	p value
	1-9		10-19		≥ 20			
	OR* or β †	95% CI*	OR or β	95% CI	OR or β	95% CI		
Full sample, adjusted	0.08	0.01, 0.14	0.20	0.13, 0.27	0.19	0.13, 0.25	49.8	<0.001
Siblings, adjusted	0.11	-0.02, 0.23	0.22	0.08, 0.35	0.24	0.12, 0.36	19.7	<0.001
Siblings, fixed effects	0.11	-0.08, 0.31	0.14	-0.09, 0.38	0.17	-0.07, 0.42	0.8	0.523

+

OR for any maternal smoking vs. none: 1.46 [95% CI: 0.83,2.58] in all siblings from 10 complete data sets generated by multiple imputation

Where are we now?

- Confused: more doubt than conviction as to a causal effect of maternal smoking in pregnancy on childhood overweight and obesity.
- If the association of maternal and paternal smoking were caused by exposure to smoke products - there should definitely be no linear dose response.
- A non-linear dose-effect pointing to a threshold effect would be compatible with a genuine effect for a low dose exposure to smoke products.



Causality or another fallacy in epidemiology?

- Next step: individual patient data meta-analysis (IPD) on the dose-effect associations of maternal smoking in pregnancy and childhood obesity



Could avoidance of smoking have a major impact of the prevalence of overweight?

Attributable Risks for Childhood Overweight: Evidence for Limited Effectiveness of Prevention

Sandra Plachta-Danielzik, Britta Kehden, Beate Landsberg, Angelika Schaffrath Rosario, Bärbel-Maria Kurth, Christiane Arnold, Christine Graf, Sabrina Hense, Wolfgang Ahrens and Manfred James Müller

Pediatrics 2012;130:e865; originally published online September 3, 2012;
DOI: 10.1542/peds.2011-3296

2.7 % (2.4–2.9) of the risk for overweight in German children was explained by maternal smoking in pregnancy



Avoidance of maternal smoking in pregnancy: A powerful lever in obesity prevention?

- The association may be causal or not.
- Even if the association were causal:
- The potential impact on obesity prevention will be small.



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