Is pediatric obesity a risk factor for cardiovascular disease?

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What is the aim of this talk?

- To discuss the methodological challenges associated with testing whether pediatric obesity (PO) is a risk factor for cardiovascular disease (CVD)

What is PO?

- “Body mass index in children (ages 2-12) and adolescents (ages 13-18) that is grossly above the recommended cut-off for a specific age and sex”
  - Year introduced: 2014
    http://www.ncbi.nlm.nih.gov/mesh/68063766

Are all CVD-related outcomes created equal?

- Hard outcomes, e.g. coronary heart disease
- Surrogate outcomes, e.g. carotid intima media thickness (cIMT)

Are there systematic reviews on PO and CVD?

- "Pediatric Obesity"[Mesh] AND "Cardiovascular Diseases"[Mesh] AND systematic[sb]
  - 5 references (Sep 29, 2015)
    - As expected…

Are there systematic reviews on PO and CVD?

- "Body mass index"[Mesh] AND "Child"[Mesh] AND "Cardiovascular Diseases"[Mesh] AND systematic[sb]
  - 18 references (Sep 29, 2015)

- "Body mass index"[Mesh] AND "Adolescent"[Mesh] AND "Cardiovascular Diseases"[Mesh] AND systematic[sb]
  - 37 references (Sep 29, 2015)

- …

How is the PO-CVD association studied?

- Is PO associated with childhood CVD?
- Is PO associated with adult CVD?

How is the PO-CVD association studied?

- *Is PO associated with childhood CVD?*
- Is PO associated with adult CVD?

Is PO associated with childhood CVD?

- Cross-sectional (prevalence estimates and “risk” factors)
- Cohort studies (incidence and risk factors)
  - Problem: CVD takes a long time to develop

Is PO associated with childhood CVD?

Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis

BMJ 2012;345:e4759 doi: 10.1136/bmj.e4759 (Published 25 September 2012)

Claire Friedemann *DPhil student*, Carl Heneghan *reader in evidence based medicine*, Kamal Mahtani *NIHR academic clinical lecturer*, Matthew Thompson *general practitioner and senior clinical scientist*, Rafael Perera *head of statistics*, Alison M Ward *director of postgraduate studies*

Is PO associated with childhood CVD?

What is already known on this topic

Increased weight is associated with raised risk of an abnormal blood pressure and lipid profile, and could contribute to early changes in risk parameters for cardiovascular disease in children

The magnitude of the association between weight and these risk parameters among children in different categories body mass index has not been systematically established

What this study adds

Compared with normal weight children, obese children (body mass index ≥30) have raised systolic and diastolic blood pressure by 7.49 mm Hg and 4.45 mm Hg, respectively, and increased concentrations of total cholesterol by 0.15 mmol/L

All parameters measured had similar increases, showing a gradient effect with lesser increases in overweight children compared with normal weight children

Being overweight or obese in childhood may have a larger effect on risk parameters for cardiovascular disease and on future health than previously thought. Existing definitions of "normal" levels of risk parameters should be re-examined to take into account the child's weight and the age when changes in cardiovascular disease risk parameters begin should be established

Is PO associated with childhood CVD?

Weight Gain in Infancy and Vascular Risk Factors in Later Childhood

AUTHORS: Michael R. Skilton, PhD,[a,b] Guy B. Marks, PhD,[c] Julian G. Ayer, PhD,[b] Frances L. Garden, MBiostat,[b,c,d] Sarah P. Garnett, PhD,[b,e,f] Jason A. Harmer, MBBS,[b] Stephen R. Leeder, PhD,[b,d,g] Brett G. Toelle, PhD,[c] Karen Webb, PhD,[h] Louise A. Baur, PhD,[b,d,e] and David S. Celermajer, PhD[b]

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WHAT'S KNOWN ON THIS SUBJECT: Excessive weight gain over the first 18 months of life may have consequences for later body size. However, the relationship of weight gain in this period to atherogenic risk factors in later childhood is not well characterized.

WHAT THIS STUDY ADDS: Early postnatal weight gain from birth to 18 months is independently associated with childhood overweight and obesity, excess central adiposity, and greater arterial wall thickness at age 8 years.

PEDIATRICS Volume 131, Number 6, June 2013

Is PO associated with childhood CVD?

TABLE 3 Multivariable Model of Height-Adjusted Weight Gain From 0 to 18 Months and Cardiovascular Risk Factors at 8 Years of Age

	BMI *z* score	*P*	SBP (mm Hg)	*P*	Carotid IMT (mm)	*P*
Age (years)	0.37 (−0.29 to 1.04)	.27	3.3 (−1.6 to 8.1)	.18	−0.00 (−0.06 to 0.05)	.91
Female gender	0.13 (−0.06 to 0.32)	.19	1.2 (−0.2 to 2.6)	.08	−0.00 (−0.02 to 0.01)	.71
Randomization						
Omega-3	0.03 (−0.16 to 0.21)	.79	0.2 (−1.2 to 1.5)	.78	0.01 (−0.01 to 0.02)	.42
Dust mite reduction	−0.08 (−0.27 to 0.10)	.38	0.3 (−1.0 to 1.7)	.61	0.00 (−0.01 to 0.02)	.87
Maternal education						
≤10 years of school	Referent	—	Referent	—	Referent	—
11–12 years of school	−0.12 (−0.40 to 0.16)	.39	0.7 (−3.8 to 5.2)	.77	−0.00 (−0.03 to 0.02)	.76
Tertiary education	−0.01 (−0.22 to 0.21)	.95	0.7 (−3.6 to 5.0)	.74	−0.02 (−0.03 to 0.00)	.09
Height-adjusted weight gain from 0 to 18 mo (kg)	0.416 (0.327 to 0.506)	<.001	1.24 (0.59 to 1.88)	<.001	0.012 (0.004 to 0.019)	.002

Values are unstandardized β-regression coefficients (95% CI) from a single multivariable model incorporating all variables; $N = 395$. Results shown are increase in BMI *z* score, SBP, or carotid IMT per kilogram increase in height-adjusted weight gain from 0 to 18 months.

How is the PO-CVD association studied?

- Is PO associated with childhood CVD?
- *Is PO associated with adult CVD?*

Is PO associated with adult CVD?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 6, 2007 VOL. 357 NO. 23

Childhood Body-Mass Index and the Risk of Coronary Heart Disease in Adulthood

Jennifer L. Baker, Ph.D., Lina W. Olsen, Ph.D., and Thorkild I.A. Sørensen, M.D., Dr.Med.Sci.

Is PO associated with adult CVD?

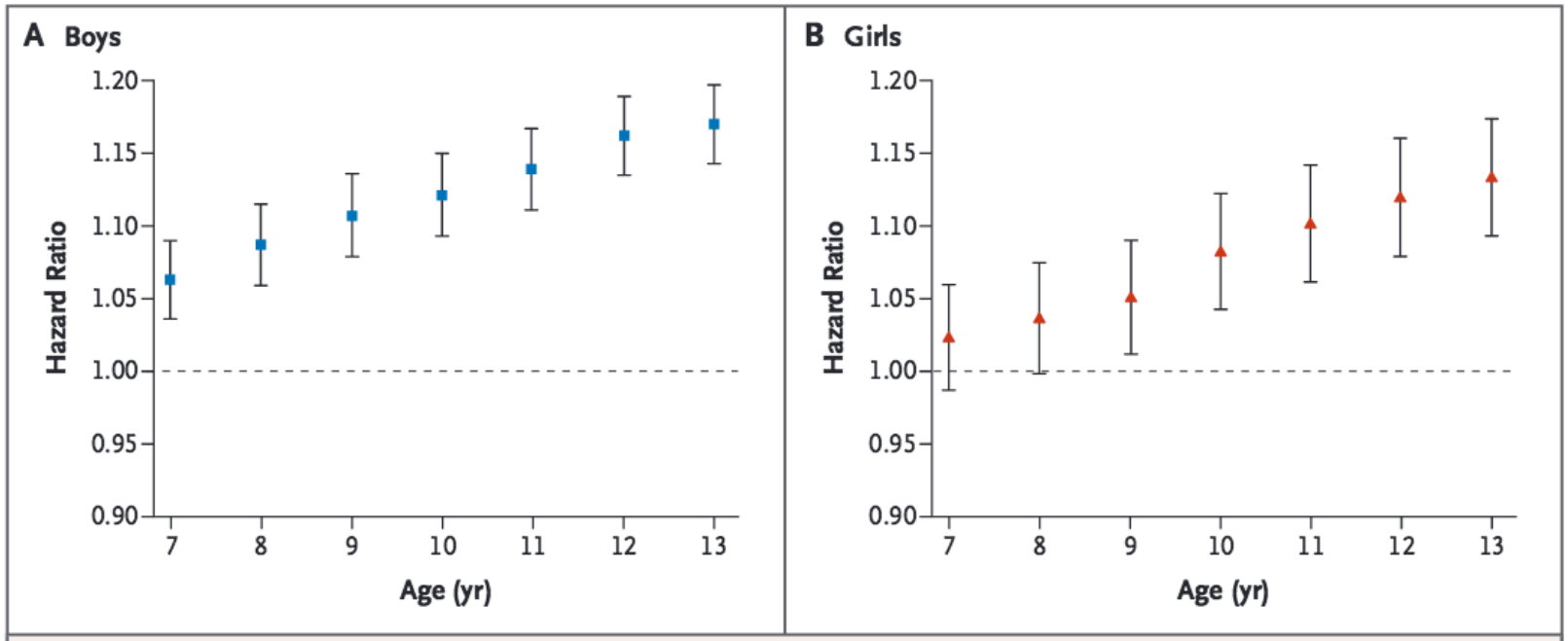

Figure 1. Body-Mass Index (BMI) in Childhood and the Risk of Coronary Heart Disease (CHD) in Adulthood.

The graphs depict the association between childhood BMI and the risk of having a CHD event (nonfatal or fatal) in adulthood. Hazard ratios and 95% confidence intervals are given for a 1-unit increase in BMI z score at each age from 7 to 13 years. The data are from 139,857 boys (Panel A) and 136,978 girls (Panel B) in the Copenhagen School Health Records Cohort. The associations were linear within each age, since trend tests resulted in the rejection of the alternative of nonlinearity modeled as a restricted cubic spline with five knots (all P values >0.15).

Is PO associated with adult CVD?

The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review

M. H. Park[1], C. Falconer[1], R. M. Viner[2] and S. Kinra[1]

obesity reviews (2012) **13**, 985–1000

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Received 14 March 2012; revised 23 May 2012; accepted 23 May 2012

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Summary

The objective of this study was to evaluate the evidence on whether childhood obesity is a risk factor for adult disease, independent of adult body mass index (BMI). Ovid MEDLINE (1948–May 2011), EMBASE (1980–2011 week 18) and the Cochrane Library (1990–2011) were searched for published studies of BMI from directly measured weight and height in childhood (2–19 years) and disease outcomes in adulthood. Data were synthesized in a narrative fashion. Thirty-nine studies (*n* 181–1.1 million) were included in the review. There was evidence for associations between childhood BMI and type 2 diabetes, hypertension and coronary heart disease. Few studies examined associations independent of adult BMI; these showed that effect sizes were attenuated after adjustment for adult BMI in standard regression analyses. Although there is a consistent body of evidence for associations between childhood BMI and cardiovascular outcomes, there is a lack of evidence for effects independent of adult BMI. Studies have attempted to examine independent effects using standard adjustment for adult BMI, which is subject to over-adjustment and problems with interpretation. Studies that use more robust designs and analytical techniques are needed to establish whether childhood obesity is an independent risk factor for adult disease.

Is PO associated with adult CVD?

International Journal of Obesity (2010) 34, 18–28
 0307-0565/10 $32.00
www.nature.com/ijo

PEDIATRIC REVIEW

Childhood obesity and adult cardiovascular disease risk: a systematic review

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Background: Although the relationship between adult obesity and cardiovascular disease (CVD) has been shown, the relationship with childhood obesity remains unclear. Given the evidence of tracking of body mass index (BMI) from childhood to adulthood, this systematic review investigated the independent relationship between childhood BMI and adult CVD risk.
Objective: To investigate the association between childhood BMI and adult CVD risk, and whether the associations observed are independent of adult BMI.
Design: Electronic databases were searched from inception until July 2008 for studies investigating the association between childhood BMI and adult CVD risk. Two investigators independently reviewed studies for eligibility according to inclusion/exclusion criteria, extracted the data and assessed study quality using the Newcastle–Ottawa Scale.
Results: Positive associations between childhood BMI and adult blood pressure or carotid intima-media thickness were generally attenuated once adjusted for adult BMI. Associations between childhood BMI and CVD morbidity/mortality had not been adjusted and do not provide evidence of an independent relationship. Negative associations between childhood BMI and blood pressure were observed in several adjusted data sets.
Conclusions: Little evidence was found to suggest that childhood obesity is an independent risk factor for CVD risk. Instead, the data suggest that relationships observed are dependent on the tracking of BMI from childhood to adulthood. Importantly, evidence suggests that risk of raised blood pressure is highest in those who are at the lower end of the BMI scale in childhood and overweight in adulthood. The findings challenge the widely accepted view that the presence of childhood obesity is an independent risk factor for CVD and that this period should be a priority for public health intervention. Although interventions during childhood may be important in prevention of adult obesity, it is important to avoid the potential for negative consequences when the timing coincides with critical stages of neurological, behavioural and physical development.
International Journal of Obesity (2010) **34**, 18–28; doi:10.1038/ijo.2009.61; published online 12 May 2009

What is “tracking”?

obesity reviews

doi: 10.1111/j.1467-789X.2008.00475.x

obesity reviews (2008) **9**, 474–488

Tracking of childhood overweight into adulthood: a systematic review of the literature

A. S. Singh[1], C. Mulder[1], J. W. R. Twisk[2,3], W. van Mechelen[1] and M. J. M. Chinapaw[1]

What is “tracking”?

- “The likelihood of persistence of overweight into adulthood is moderate for overweight and obese youth”

- “However, predictive values varied considerably”

Conclusions

- There are many methodological challenges associated with testing whether childhood obesity is a risk factor for cardiovascular disease (CVD)

- Addressing the effect of adult BMI should be a central issue of future research on the PO-CVD association

Thank you!

Backup slides

What is a risk factor?

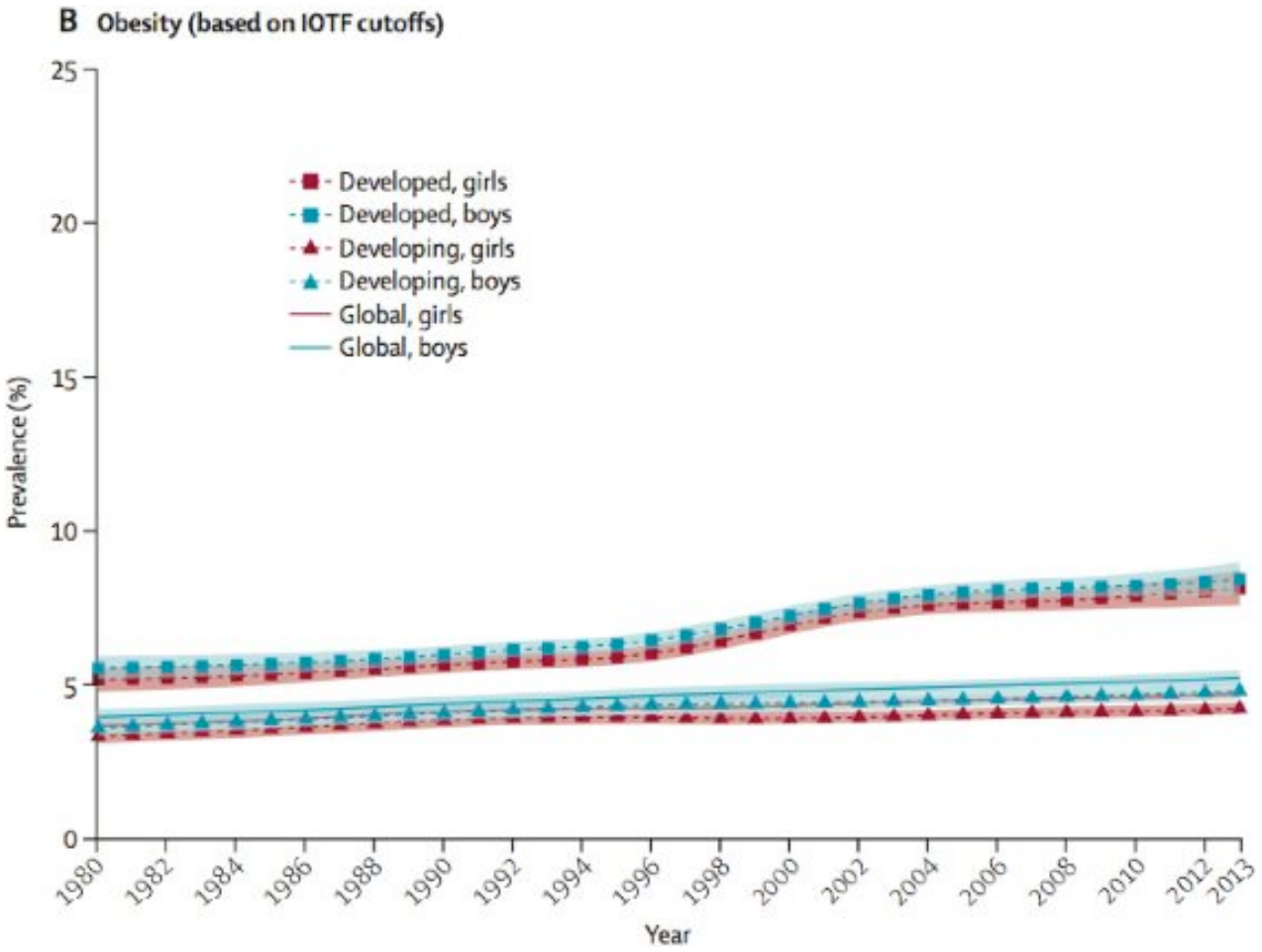
- “An aspect of personal behavior or lifestyle, environmental exposure, or inborn or inherited characteristic, which, on the basis of epidemiologic evidence, is known to be associated with a health-related condition considered important to prevent”
  - Year introduced: 1988
    http://www.ncbi.nlm.nih.gov/mesh/68012307

How common is PO?

Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013

Lancet 2014; 384: 766–81

How common is PO?



Is obesity a risk factor for death and disability?

Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

*GBD 2013 Risk Factors Collaborators**

www.thelancet.com **Published online September 11, 2015 http://dx.doi.org/10.1016/S0140-6736(15)00128-2**

Is obesity a risk factor for death and disability?

	1990 deaths (in thousands)	2013 deaths (in thousands)	Median percent change deaths	Median percent change of age-standardised deaths PAF	1990 DALYs (in thousands)	2013 DALYs (in thousands)	Median percent change DALYs	Median percent change of age-standardised DALYs PAF
(Continued from previous page)								
Low physical activity	**1489 (1257 to 1741)**	**2182 (1858 to 2555)**	**46·5% (40·9 to 52·9)**	**6·4% (4·0 to 9·2)**	**31247 (26556 to 36521)**	**45143 (38328 to 52671)**	**44·3% (37·2 to 52·8)**	**13·6% (9·4 to 18·3)**
Metabolic risks	**10398 (9811 to 11003)**	**15723 (14719 to 16767)**	**51·2% (46·2 to 57·0)**	**10·6% (8·8 to 12·6)**	**250957 (233711 to 267582)**	**373817 (343978 to 403889)**	**48·9% (43·1 to 54·9)**	**18·4% (15·3 to 21·7)**
High fasting plasma glucose	**2444 (2101 to 2853)**	**4014 (3499 to 4641)**	**64·4% (56·3 to 73·4)**	**21·8% (17·4 to 26·8)**	**68903 (60506 to 78071)**	**116893 (101592 to 133368)**	**69·6% (60·9 to 78·7)**	**37·0% (31·6 to 42·6)**
High total cholesterol	2204 (1574 to 3126)	2830 (1966 to 4053)	28·0% (19·9 to 37·4)	−7·4% (−11·3 to −2·5)	49289 (38075 to 63764)	62715 (49244 to 80986)	26·9% (19·8 to 36·3)	−0·6% (−5·7 to 5·7)
High systolic blood pressure	6949 (6182 to 7665)	10364 (9178 to 11544)	49·1% (43·2 to 55·2)	8·8% (6·4 to 11·2)	143434 (130053 to 156023)	208129 (188307 to 227509)	45·1% (38·7 to 52·1)	14·1% (10·0 to 18·4)
High body-mass index	2724 (2263 to 3187)	4444 (3716 to 5169)	63·2% (57·8 to 69·5)	22·2% (19·0 to 25·4)	78310 (65436 to 92006)	134048 (112420 to 156787)	71·3% (64·4 to 78·0)	36·3% (32·3 to 40·1)
Low bone mineral density	176 (164 to 198)	334 (285 to 361)	92·1% (62·8 to 104·0)	35·4% (15·4 to 44·6)	10903 (8958 to 13231)	14249 (11658 to 17500)	30·6% (20·9 to 40·7)	−1·8% (−9·4 to 6·9)
Low glomerular filtration rate	1310 (1176 to 1480)	2164 (1960 to 2387)	65·6% (54·5 to 74·5)	18·9% (11·1 to 24·8)	34159 (30499 to 38394)	51906 (46246 to 57573)	52·0% (43·5 to 59·3)	25·5% (18·4 to 31·3)

DALYs=disability-adjusted life-years. PAF=population attributable fraction.

***Table 3*: Global, all-age, all-cause deaths, and DALYs for both sexes combined attributable to each risk factor in 1990 and 2013 with 95% uncertainty intervals**