Article

Common pregnancy complications and risk of childhood obesity - influence of maternal obesity: An individual participant data meta-analysis

Bernadeta Patro Golab[1,2,3], Susana Santos[1,2], Ellis Voerman[1,2], Henrique Barros[4,5], Anna Bergström[6,7], Marie-Aline Charles[8,9], Leda Chatzi[10,11,12], Cécile Chevrier[13], George P. Chrousos[14], Eva Corpeleijn[15], Nathalie Costet[13], Sarah Crozier[16], Graham Devereux[17], Merete Eggesbø[18], Sandra Ekström[6], Maria Pia Fantini[19], Sara Farchi[20], Francesco Forastiere[20], Vagelis Georgiu[11], Keith M. Godfrey[16,21], Davide Gori[19], Wojciech Hanke[22], Irva Hertz-Picciotto[23], Barbara Heude[8,9], Daniel Hryhorczuk[24], Hazel Inskip[16,21], Jesus Ibarluzea[25,26,27,28], Louise C. Kenny[29,30], Leanne K. Küpers[15,31,32], Hanna Lagström[33], Irina Lehmann[34], Virissa Lenters[18], Sabrina Llop[28,35], Per Magnus[36], Renata Majewska[37], Johanna Mäkelä[38], Yannis Manios[39], Fionnuala M. McAuliffe[40], Sheila W. McDonald[41], John Mehegan[42], Monique Mommers[43], Camilla S. Morgen[44,45], George Moschonis[46], Deirdre Murray[29,47], Carol Ní Chaoimh[29,48], Ellen A. Nøhr[49], Anne-Marie Nybo Andersen[45], Emily Oken[50], Adriëtte J.J.M. Oostvogels[51], Agnieszka Pac[37], Eleni Papadopoulou[52], Costanza Pizzi[53], Kinga Polanska[22], Daniela Porta[20], Lorenzo Richiardi[53], Sheryl L. Rifas-Shiman[50], Franca Rusconi[54], Ana C. Santos[4,5], Henriette A. Smit[55], Thorkild I.A. Sørensen[45,56], Marie Standl[57], Camilla Stoltenberg[58,59], Jordi Sunyer[28,60,61], Michelle Taylor[31, 32], Elisabeth Thiering[57,62], Carel Thijs[43], Maties Torrent[63], Suzanne C. Tough[41,64], Tomas Trnovec[65], Steve Turner[66], Lenie van Rossem[55], Andrea von Berg[67], Martine Vrijheid[28,60,61],Tanja Vrijkotte[51], Jane West[68], John Wright[68], Oleksandr Zvinchuk[69], Debbie A. Lawlor[31,32], Vincent W.V. Jaddoe*[1,2,70], Romy Gaillard*[1,2]

** Authors contributed equally*

[1] The Generation R Study Group, Erasmus MC, University Medical Center, Rotterdam, the Netherlands.

[2] Department of Pediatrics, Erasmus MC, University Medical Center, Rotterdam, the Netherlands.

[3] Department of Pediatrics, Medical University of Warsaw, Warsaw, Poland.

[4] EPIUnit - Instituto de Saúde Pública, Universidade do Porto, Rua das Taipas, nº 135, 4050-600 Porto, Portugal. 7 Department of Public Health and Forensic Sciences and Medical Education, Unit of Clinical Epidemiology, Predictive Medicine and Public Health, University of Porto Medical School, Porto, Portugal.

[5] Department of Public Health and Forensic Sciences and Medical Education, Unit of Clinical Epidemiology, Predictive Medicine and Public Health, University of Porto Medical School, Porto, Portugal.

[6] Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.

[7] Centre for Occupational and Environmental Medicine, Stockholm County Council, Stockholm, Sweden.

[8] INSERM, UMR1153 Epidemiology and Biostatistics Sorbonne Paris Cité Center (CRESS), ORCHAD Team, Paris, France.

[9] Paris Descartes University, Paris, France.

[10] Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.
[11] Department of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Greece.
[12] Department of Genetics and Cell Biology, Maastricht University, the Netherlands.
[13] Inserm UMR 1085, Irset - Research Institute for Environmental and Occupational Health, F-35000 RENNES, France.
[14] First Department of Pediatrics, Athens University Medical School, Aghia Sophia "Children's Hospital, National and Kapodistrian University of Athens, Athens, Greece.
[15] Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
[16] MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK.
[17] Liverpool School of Tropical Medicine, Liverpool, UK.
[18] Department of Exposure and Environmental Epidemiology, Norwegian Institute of Public Health, Oslo, Norway.
[19] The Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy.
[20] Department of Epidemiology, Lazio Regional Health Service, Rome, Italy.
[21] NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK.
[22] Department of Environmental Epidemiology, Nofer Institute of Occupational Medicine, Lodz, Poland.
[23] Department of Public Health Sciences, School of Medicine, University of California Davis, Davis, California 95616, USA.
[24] Center for Global Health, University of Illinois College of Medicine, Chicago, IL, USA.
[25] Subdirección de Salud Pública Gipuzkoa, San Sebastián, Spain.
[26] Instituto de Investigación Sanitaria BIODONOSTIA, San Sebastián, Spain.
[27] School of Psychology-University of the Basque Country, San Sebastián, Spain.
[28] CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain.
[29] Irish Centre for Fetal and Neonatal Translational Research, Cork University Maternity Hospital, University College Cork, Cork, Ireland.
[30] Department of Obstetrics and Gynaecology, Cork University Maternity Hospital, Cork, Ireland.
[31] MRC Integrative Epidemiology Unit at the University of Bristol, Oakfield House, Oakfield Grove, Bristol, BS8 2BN, UK.
[32] Population Health Science, Bristol Medical School, University of Bristol, Bristol BS8 2BN, UK.
[33] Department of Public Health, University of Turku, Turku, Finland.
[34] Department of Environmental Immunology/Core Facility Studies, Helmholtz Centre for Environmental Research – UFZ, Leipzig, Germany.
[35] Epidemiology and Environmental Health Joint Research Unit, FISABIO (Foundation for the Promotion of Health and Biomedical Research in the Valencian Region), Valencia, Spain.
[36] Division of Health Data and Digitalization, Norwegian Institute of Public Health, Oslo, Norway.
[37] Department of Epidemiology, Chair of Epidemiology and Preventive Medicine, Jagiellonian University Medical College, Krakow, Poland.
[38] Turku Centre for Biotechnology, University of Turku and Abo Akademi University, Turku, Finland.
[39] Department of Nutrition and Dietetics, School of Health Science and Education, Harokopio University, Athens, Greece.
[40] UCD Perinatal Research Centre, Obstetrics & Gynaecology, School of Medicine, University College Dublin, National Maternity Hospital, Dublin, Ireland.

[41] Department of Pediatrics, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada.
[42] UCD Perinatal Research Centre, School of Public Health and Physiotherapy and Sports Science, University College Dublin, Dublin, Ireland.
[43] Department of Epidemiology, Care and Public Health Research Institute, Maastricht University, Maastricht, The Netherlands.
[44] National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark.
[45] Department of Public Health, Section of Epidemiology, University of Copenhagen, Øster Farimagsgade 5, 1014, Copenhagen, Denmark.
[46] Department of Rehabilitation, Nutrition and Sport; La Trobe University, Australia
[47] Paediatrics & Child Health, University College Cork, Cork, Ireland.
[48] Cork Centre for Vitamin D and Nutrition Research, School of Food and Nutritional Sciences, University College Cork, Cork, Ireland.
[49] Research Unit for Gynaecology and Obstetrics, Institute for Clinical Research, University of Southern Denmark, Denmark.
[50] Department of Population Medicine, Harvard Medical School, Harvard Pilgrim Health Care Institute, Boston, MA, USA.
[51] Department of Public Health, Amsterdam Public Health Research Institute, Academic Medical Center, Amsterdam, The Netherlands.
[52] Department of Environmental Exposures and Epidemiology, Domain of Infection Control and Environmental Health, Norwegian Institute of Public Health, Lovisenberggata 8, 0477 Oslo, Norway
[53] Department of Medical Sciences, University of Turin, Turin, Italy.
[54] Unit of Epidemiology "Anna Meyer", Children's University Hospital, Florence, Italy.
[55] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.
[56] Novo Nordisk Foundation Center for Basic Metabolic Research, Section of Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.
[57] Institute of Epidemiology I, Helmholtz Zentrum München-German Research Center for Environmental Health, Neuherberg, Germany.
[58] Norwegian Institute of Public Health, Oslo, Norway.
[59] Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway.
[60] ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain.
[61] Universitat Pompeu Fabra (UPF), Barcelona, Spain.
[62] Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University Munich, Munich, Germany.
[63] Ib-salut, Area de Salut de Menorca, Palma, Spain.
[64] Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada.
[65] Department of Environmental Medicine, Slovak Medical University, Bratislava 833 03, Slovak Republic.
[66] Child Health, Royal Aberdeen Children's Hospital, Aberdeen, UK.
[67] Research Institute, Department of Pediatrics, Marien-Hospital Wesel, Wesel, Germany.
[68] Bradford Institute for Health Research, Bradford Royal Infirmary, Bradford, UK.
[69] Department of Medical and Social Problems of Family Health, Institute of Pediatrics, Obstetrics and Gynecology, Kyiv, Ukraine.

[70] Department of Epidemiology, Erasmus MC, University Medical Center, Rotterdam, the Netherlands.

Address correspondence to: Romy Gaillard, MD, PhD. The Generation R Study Group (Na29-15). Erasmus MC, University Medical Center, PO Box 2040, 3000 CA Rotterdam, The Netherlands (r.gaillard@erasmusmc.nl). Phone: +31 (0) 10 7043405, Fax: +31 (0) 10 7044645

Word count of the abstract: 244; Word count of the text: 2907

Tables: 1; Figures: 3; Supplemental files: 1

RESEARCH IN CONTEXT

Evidence before this study

Gestational diabetes and gestational hypertensive disorders are common pregnancy complications associated with increased risks of perinatal mortality and morbidity, and seem to influence the risk of obesity in the offspring. Maternal obesity is a major risk factor for common pregnancy complications, and is also associated with an increased risk of obesity in the offspring. It is not clear whether gestational diabetes and gestational hypertensive disorders affect the risk of offspring obesity independently of the risk conferred by maternal obesity.

Added value of this study

We performed an individual participant data meta-analysis of 160757 mother-offspring pairs from 34 prospective European or North-American contemporary pregnancy/birth cohorts. We observed that children born to mothers with gestational diabetes and gestational hypertension had a higher BMI and higher risk of being overweight throughout childhood. Pre-eclampsia was associated with a lower BMI in early-childhood. All associations were largely explained by maternal pre/early-pregnancy BMI.

Implications of all the available evidence

Lowering maternal risk of gestational diabetes, gestational hypertension and pre-eclampsia, though important in relation to maternal and fetal pregnancy outcomes, is unlikely to have a direct impact on offspring obesity. Preventive strategies for reducing childhood obesity should not focus on these pregnancy complications.

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SUMMARY

Background: Gestational diabetes and gestational hypertensive disorders are associated with offspring obesity. The role of maternal adiposity in these associations remains unclear.

Methods: In this individual participant data meta-analysis of 160757 mother-offspring pairs from 34 prospective European or North-American pregnancy/birth cohorts, we assessed the associations of gestational diabetes, gestational hypertension and pre-eclampsia with childhood BMI and the risk of overweight and obesity throughout childhood. We explored to which extent any association was explained by maternal pre/early-pregnancy BMI.

Findings: Gestational diabetes was associated with a higher risk of overweight throughout childhood (Odds Ratio (OR) 1·59 (95% Confidence Intervals (CI) 1·36, 1·86); OR 1·41 (95% CI 1·26, 1·57); OR 1·32 (95% CI 0·99, 1·78) for early-, mid- and late-childhood, respectively) when compared to uncomplicated pregnancies. These associations attenuated towards the null following adjustment for maternal BMI. Likewise, gestational hypertension was associated with a higher risk of overweight throughout childhood, with the strongest association in late-childhood (OR 1·49 (95% CI 1·30, 1·70)), when compared to uncomplicated pregnancies. Additional adjustment for maternal BMI partly explained these associations. Pre-eclampsia was associated with a lower BMI in early-childhood only (difference in BMI-SDS - 0.05 SDS (95% CI - 0·09, - 0·01)), when compared to uncomplicated pregnancies. This association strengthened upon additional adjustment for maternal BMI.

Interpretation: Our results suggest that lowering maternal risk of gestational diabetes and hypertensive disorders is unlikely to have a direct impact on offspring obesity.

Funding: Funding sources for participating cohorts were declared as an acknowledgment.

INTRODUCTION

Gestational diabetes and gestational hypertensive disorders are common pregnancy complications with high global prevalences.[1,2] These complications are major risk factors for maternal and fetal morbidity and mortality, and seem to be associated with obesity in offspring.[1-6] Both fetal exposure to hyperglycemia due to gestational diabetes or altered utero-placental perfusion due to gestational hypertension and pre-eclampsia affect fetal nutrient supply.[7,8] Alterations in the fetal supply line may influence fetal development, and trigger developmental adaptations in adipose tissue, neuroendocrine and metabolic function, which could predispose offspring to adiposity in later life.[9]

Maternal obesity is a risk factor for gestational diabetes and gestational hypertensive disorders, and is also associated with an increased risk of obesity in offspring.[10] Thus far, it is not clear whether gestational diabetes and gestational hypertensive disorders affect the risk of offspring obesity independently of the risk conferred by maternal obesity. Previous studies have shown that diabetes during pregnancy is associated with an increased risk of offspring obesity and higher fat mass levels, independent of maternal socio-demographic and lifestyle characteristics.[11-17] Inconsistent findings were reported for the specific role of maternal obesity in these associations. Prospective cohort studies have assessed the relations of gestational hypertensive disorders with offspring blood pressure, but only few have also assessed the relation with offspring adiposity.[18,19] A UK study reported that children of women who had either gestational hypertension or pre-eclampsia had higher risk of obesity at 9 years, whereas an Australian study found similar associations only in term born young adults of mothers with gestational hypertension, but not with pre-eclampsia.[18,19]

Using individual participant data (IPD) from 160757 mother-offspring pairs, we assessed the strength and consistency of the associations of maternal gestational diabetes, gestational hypertension and pre-eclampsia with the risks of offspring overweight and obesity throughout childhood. We also explored whether any observed association was independent of maternal pre-/early-pregnancy BMI.

METHODS

Inclusion criteria and participating cohorts

We used data from an existing international collaboration on maternal obesity and childhood outcomes. Pregnancy and birth cohort studies were eligible for inclusion in this international collaboration if they were able to provide IPD on mothers with singleton live-born children born from 1989 onwards, and had information available on maternal pre/early-pregnancy BMI and birth weight and/or one measure of childhood BMI. We identified 50 potentially eligible cohorts from Europe, North America and Oceania from the existing collaborations or databases concerned with childhood health (EarlyNutrition Project, CHICOS Project, www.birthcohorts.net; last accessed July 2014). We invited all cohorts to participate, and 38 agreed and provided data on 274174 singleton births. For this study, we only included cohorts that were able to provide IPD on maternal gestational diabetes, gestational hypertension or pre-eclampsia, and childhood BMI measured at least once between age 2 and 17·9 years. This resulted in 160757 mothers-offspring pairs available for analyses. Details on study selection process are provided in Supplemental Figure S1. Anonymized datasets were stored on a single central secured data server with access for the main analysts (BPG, SS). All studies were approved by their local institutional review boards/ ethics committees.

Gestational diabetes, hypertensive disorders and pre/early-pregnancy BMI

Information on gestational diabetes, gestational hypertension, pre-eclampsia and maternal BMI was obtained from medical records, through research assessments or was self-reported (cohort-specific information is shown in Supplemental Table S1). Where possible we used maternal pre-pregnancy BMI (<18·5, 18·5 - <25, 25 - <30, ≥30 kg/m^2). Five cohorts (including 6,513 participants) did not have information about pre-pregnancy BMI but obtained BMI in early pregnancy (all assessed before or at 20 weeks of gestation).

Childhood BMI

Data on childhood weight and height were mostly obtained through direct research assessments, with a small number of studies abstracting information about weight and height, or BMI, from medical records, report by parents/caregivers or self-reported (cohort-specific information is provided in Supplemental Table S1). We grouped BMI based on the age of children at assessment into 3 periods: early-childhood (2·0 – 4·9 years), mid-childhood (5·0 – 9·9 years), and late-childhood (10·0-17·9 years of age). If studies had multiple repeated measurements within the same age period, we used data collected at the oldest age. We calculated sex- and age-adjusted standard deviation scores (SDS) of childhood BMI using WHO reference growth charts (Growth Analyzer 4·0, Dutch Growth Research Foundation).[20-23]
Childhood underweight, normal weight, overweight and obesity were defined based on the age- and sex-specific WHO criteria.[20,21]

Covariates

Information on covariates was mostly obtained by questionnaires (cohort-specific information is shown in Supplemental Table S1 and S2). As potential confounders other than maternal pre-pregnancy BMI, we considered maternal age (<25·0 years, 25-29·9 years, 30-34·9 years, ≥35·0 years), educational level (low, medium, high), ethnicity (European/White, non-European/non-White), parity (nulliparous, multiparous), smoking during pregnancy (yes, no), and offspring's sex. We did not adjusted the primary analyses for offspring birth weight and gestational age at delivery, as these birth characteristics are likely to be mediators on the causal pathway and adjustment might introduce bias.[24]

Statistical analysis

We applied multilevel mixed effects models, taking into account clustering of participants within cohorts, to analyze simultaneously IPD from all cohorts.[25] Our models were defined assuming a random intercept at cohort level, which allowed for differences in the intercepts between cohorts. First, we used multilevel linear mixed effects models to examine the associations of gestational diabetes, gestational hypertension

or pre-eclampsia with BMI SDS in early-, mid-, and late-childhood. Second, we used multilevel binary logistic mixed effects models to examine the associations of these pregnancy complications with the risk of childhood underweight, overweight and obesity in the same age windows. Participants exposed to either gestational hypertension or pre-eclampsia were compared to those with none of these conditions, irrespective of their gestational diabetes status. Similarly, those exposed to gestational diabetes were compared to those with no gestational diabetes, irrespective of whether or not they had gestational hypertension or pre-eclampsia. For all analyses, we constructed an unadjusted model (Basic model), a model adjusted for offspring's sex, maternal age, educational level, ethnicity, parity and smoking during pregnancy (Lifestyle characteristics model), and a model additionally adjusted for maternal pre/early-pregnancy BMI (Maternal BMI model). For the associations of pregnancy complications with the risk of childhood underweight, only the basic model was applied due to insufficient sample size. We tested potential interactions between each pregnancy complication and (i) offspring´s sex and (ii) maternal BMI, in their associations with childhood BMI. Since no consistent significant interactions were observed, no further stratified analyses were performed. The amount of missing data on covariates varied between cohorts (percentage missings per cohort given in Supplemental Table S2). To prevent exclusion of non-complete cases, we used missing values in these covariates as an additional group. We did not include information for a cohort for a specific categorical covariate, if information for this variable was available for less than 50% of the cohort sample. As sensitivity analysis, we performed a 2-stage random effects meta-analysis and examined whether there was evidence of heterogeneity between cohorts using the I^2.[25] Analyses were undertaken using the Statistical Package of Social Sciences version 21.0 for Windows (SPSS Inc, Chicago, IL, USA) and Review Manager ((RevMan) Version [5.3.5]. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) software.

RESULTS

Subject characteristics

The characteristics of the participants per cohort are presented in Table 1. Out of a total of 160757 mothers, 2618 (1·7%) had gestational diabetes, 9755 (6·5%) had gestational hypertension, and 4836 (3·3%) had pre-eclampsia. 30927 (19·7%) of the mothers were overweight and 12467 (7·9%) obese. Among offspring 5606 (6·6%), 24254 (20·1%) and 3699 (21·3 %) were overweight or obese in early-, mid-, and late-childhood, respectively. Cohort-specific information on childhood age at assessment and BMI is shown in Supplemental Table S4.

Gestational diabetes and childhood body mass index

Figure 1A shows that in the basic and lifestyle characteristics models, gestational diabetes was associated with a higher offspring BMI throughout childhood (difference in BMI-SDS from the lifestyle characteristics models: 0·11 SDS (95% Confidence Intervals (CI) 0·06, 0·16); 0·21 SDS (95% CI 0·16, 0·26); 0·08 SDS (95% CI -0·04, 0·21) in early-, mid- and late-childhood, respectively), as compared to uncomplicated pregnancies. After additional adjustment for maternal BMI, these associations fully attenuated towards the null. Similarly, gestational diabetes was associated with increased risks of overweight and obesity throughout childhood in the basic and lifestyle characteristics models, with the strongest association in early-childhood (OR 1·59 (95% Confidence Intervals (CI) 1·36, 1·86) (Figure 1B). Adjustment for maternal BMI largely attenuated the effect estimates towards the null. Only the association of gestational diabetes with the risk of early childhood overweight and obesity remained significant (OR 1·35 (95% CI 1·15; 1·58)). Gestational diabetes tended to be associated with a lower risk of underweight throughout childhood in basic model. We were not able to examine adjustment for maternal BMI due to small numbers (Supplemental Table S4). Additional adjustment for gestational hypertension and pre-eclampsia did not affect the observed associations of gestational diabetes with childhood outcomes (data not shown).

Gestational hypertensive disorders and childhood body mass index

Figure 2A shows that, as compared to uncomplicated pregnancies, gestational hypertension was associated with a higher BMI throughout childhood in the basic and lifestyle characteristics models (differences in BMI-SDS in lifestyle characteristics model: 0·07 SDS (95% CI 0·03, 0·11); 0·13 SDS (95% CI 0·10, 0·17); 0·20 SDS (95% CI 0·14, 0·27) in early-, mid- and late-childhood, respectively). These associations were partly explained by maternal BMI (difference in BMI-SDS: 0·01 SDS (95% CI -0·03, 0·06); 0·04 SDS (95% CI 0·01, 0·07); 0·07 SDS (95% CI 0·01, 0·13) in early-, mid- and late-childhood, respectively). Gestational hypertension was also associated with higher risks of overweight and obesity throughout childhood. The strongest association was observed for late-childhood (OR 1·49 (95% CI 1·30, 1·70)). Additional adjustment for maternal BMI largely attenuated these associations (Figure 2B). In the basic model, gestational hypertension was associated with a lower risk of childhood underweight at all ages (Supplemental Table S4).

Pre-eclampsia was associated with a lower BMI in early-childhood in both the basic and lifestyle characteristics models (difference in BMI-SDS in lifestyle characteristics model: - 0.05 SDS (95% CI -0·09, - 0·01)) (Figure 3A). This inverse association strengthened upon additional adjustment for maternal BMI. In contrast, we observed a positive association of pre-eclampsia with BMI in mid- and late-childhood in the basic and lifestyle characteristics models (differences in BMI-SDS in lifestyle characteristics model: 0·10 SDS (95% CI 0·06, 0·13); 0·16 SDS (95% CI 0·03, 0·30) in mid- and late-childhood, respectively). These associations fully attenuated after additional adjustment for maternal BMI. The associations of pre-eclampsia with overweight and obesity in mid- and late-childhood also fully attenuated after adjustment for maternal BMI (Figure 3B). In the basic model pre-eclampsia was associated with a higher risk of underweight in early-childhood only (Supplemental Table S4). We were unable to further explore adjustment for maternal BM because of small numbers. Similar associations between both gestational hypertension and pre-eclampsia with childhood outcomes were observed for all models when additionally adjusted for gestational diabetes (data not shown).

2-stage meta-analyses as sensitivity analyses

Analyses performed with 2-stage meta-analyses were consistent with those obtained from our main (1-stage) meta-analyses (Supplemental Figures S2-10). We did not observe substantial heterogeneity between the cohorts (I^2 range 0 to 40%, with 6 out of the 9 meta-analyses having I^2 <25%; Supplemental Figures S2-10).

DISCUSSION

Results from our IPD analysis of 160757 mothers and children from 18 different countries from Europe and North America, demonstrated that children born to mothers with gestational diabetes and gestational hypertension had a higher BMI and higher risk of being overweight or obese throughout childhood, whereas pre-eclampsia was associated with a lower BMI in early-childhood. These associations were largely explained by maternal pre/early-pregnancy BMI.

Interpretation of main findings

Gestational diabetes, gestational hypertension and pre-eclampsia affect substantial numbers of pregnancies and are associated with a wide range of adverse maternal and fetal pregnancy outcomes.[1-3] Gestational diabetes may lead to fetal overnutrition as a result of maternal hyperglycemia during pregnancy.[7] Gestational hypertension and pre-eclampsia are related to placental dysfunction, which may lead to impaired fetal nutrient supply.[8,26] Both conditions may subsequently induce permanent changes in offspring body composition, neuroendocrine systems and metabolic functions, which predispose offspring to an increased risk of obesity in later life.[9] Our aim was to explore if gestational diabetes and gestational hypertensive disorders affect the risk of offspring obesity independently of the risk conferred by maternal obesity. Disentangling the independent role of these maternal pregnancy complications on childhood obesity risk is important for development of future childhood obesity prevention strategies.

Results from two systematic reviews of 12 and 9 published cohort studies suggested that maternal diabetes during pregnancy was associated with a higher offspring BMI . These associations were no

longer present in single studies that adjusted for maternal pre-pregnancy BMI.[6,27] Recently, several prospective observational studies reported inconsistent findings for the association of gestational diabetes with offspring BMI after adjustment for maternal BMI.[11-17,28-30] An older prospective cohort study of 280866 Swedish men recruited from 1973 to 1988, suggested that diabetes during pregnancy, including gestational diabetes and pre-existing diabetes, was associated with a higher BMI at the age of 18 years. This association was independent of maternal BMI.[17] In contrast, we observed that children of mothers with gestational diabetes had a higher BMI throughout childhood, but this association was largely explained by maternal pre/early-pregnancy BMI. This different finding might be explained by differences in study populations as our IPD included contemporary cohorts only with newer screening and treatment strategies, and mainly included offspring measurements at younger ages. We observed the strongest association of gestational diabetes with offspring obesity in early-childhood. This may be explained by tracking of birth size.[31].[32] Consistent with our findings, treatment of mild gestational diabetes was found to be beneficial for neonatal outcomes, but did not influence offspring obesity risk at age 5-10 years in a multicenter randomized controlled trial.[33] Using the diagnosis of gestational diabetes may insufficiently reflect glycemic status during pregnancy. Maternal glucose levels below current diagnostic criteria of diabetes, are linearly and positively associated with adverse perinatal outcomes.[31,34] However, several studies showed that maternal glucose levels during pregnancy were not associated with offspring BMI in early childhood, after adjustment for maternal BMI.[35,36] Thus, our findings strongly suggest that the association of gestational diabetes with higher BMI in the offspring is largely explained by maternal BMI.

Few studies have examined the association of gestational hypertensive disorders with childhood adiposity. Data from a UK prospective cohort study of 6343 mother-offspring pairs found a positive association of gestational hypertension with childhood adiposity at age 9, which attenuated after adjustment for parental BMI.[18] This study also found inverse associations of pre-eclampsia with offspring lean mass and adiposity at age 9 after adjustment for parental BMI.[18] In contrast, an Australian cohort study of 1151 mother-offspring pairs born at term showed that offspring of mothers with gestational hypertension had higher BMI and risk of overweight and obesity at 20 years, independently of maternal

BMI.[19] No association of pre-eclampsia with offspring BMI was present.[19] In the current study, we observed that gestational hypertension was associated with a higher BMI and risk of overweight throughout childhood, but this association was also largely explained by maternal BMI. Pre-eclampsia was associated with a lower BMI in early-childhood, and this inverse association was stronger after adjustment for maternal BMI. In later childhood, no associations independent of maternal BMI were present. This might be explained by tracking of lower birth size into early-childhood among children of mothers with pre-eclampsia due to placental dysfunction and fetal growth restriction.[37] Further studies aiming at detailed assessment of maternal blood pressure and placental vascular function, which provides details on the severity of the disease, may provide more insight into the effects of pre-eclampsia on childhood adiposity development.

Our observations that the associations of gestational diabetes and gestational hypertensive disorders with offspring obesity largely dependent on maternal BMI are important from an etiological and preventive perspective. Interventions to reduce the risk of pregnancy complications or improve the effectiveness of their treatment may be important in relation to a range of problems for the mother and child, but they are unlikely to influence directly the development of obesity in offspring.

Strengths and limitations

Major strengths of our study are the large sample of contemporary populations reflecting current diagnosis and treatment policies and the use individual participant data from a wide selection of existing studies to reduce the risk of publication bias. We were able to adjust for a range of relevant confounding factors, with a particular focus on maternal pre-pregnancy BMI. We are aware that our study cannot overcome potential limitations of individual studies in terms of their design and conduct, differences in measurements and definitions of exposure and outcome data, variation in missing data and loss to follow up. .Especially, the prevalence of gestational diabetes in our sample was relatively low and varied substantially between cohorts, which might suggest underascertainment of this condition. However, our 2-stage meta-analysis suggested low heterogeneity between studies. We have no information on how any

of the pregnancy complications were treated. Effective treatment that reduced circulating glucose and blood pressure during pregnancy may lead to weaker associations of these conditions with offspring obesity. However, this reflects contemporary clinical practice. Finally, due to the observational design, residual confounding cannot be excluded.

Conclusions

The associations of gestational diabetes, gestational hypertension and pre-eclampsia with childhood obesity are largely explained by maternal pre/early-pregnancy BMI. Interventions focused on prevention or treatment of these pregnancy complications, though important for other maternal and fetal pregnancy outcomes, are unlikely to have a direct impact on offspring BMI.

AUTHOR CONTRIBUTIONS

Bernadeta Patro Golab and Susana Santos had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Bernadeta Patro Golab, Susana Santos, Vincent W.V. Jaddoe, Romy Gaillard

Analysis and interpretation of data: Bernadeta Patro Golab, Susana Santos, Vincent W.V. Jaddoe, Romy Gaillard

Drafting of the manuscript: Bernadeta Patro Golab, Susana Santos, Debbie Lawlor, Vincent W.V. Jaddoe, Romy Gaillard

Critical revision of the manuscript for important intellectual content: All authors

ACKNOWLEDGMENTS (PER COHORT)

ABCD

The authors especially thank all participating mothers and their children, and are grateful to all obstetric care providers in Amsterdam for their contribution to the data collection of the ABCD-study.

ALSPAC

The authors are extremely grateful to all the families who took part in this study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses.

AOB/F

The authors acknowledge the contribution and support of All Our Families participants and team.

BAMSE

The authors thank all the children and their parents for participating in the BAMSE cohort and the nurses and other staff members working in the BAMSE project.

BIB

The authors thank the children and parents for their enthusiasm and commitment. The authors are grateful to all participants, health professionals and researchers who have made Born in Bradford happen. The authors are particularly grateful to John Corkett and Hanan Ahmed, all the school nurse teams in Bradford and to Jonnie Dance and Becky Harrop at Bradford District Metropolitan Council for their support for this study.

DNBC

The authors thank all the families for participating in the Danish National Birth Cohort.

EDEN

The authors thank the EDEN mother-child cohort study group, whose members are: I. Annesi-Maesano, J.Y. Bernard, J. Botton, M.A. Charles, P. Dargent-Molina, B. de Lauzon-Guillain, P. Ducimetière, M. de Agostini, B. Foliguet, A. Forhan, X. Fritel, A. Germa, V. Goua, R. Hankard, B. Heude, M. Kaminski, B. Larroque†, N. Lelong, J. Lepeule, G. Magnin, L. Marchand, C. Nabet, F Pierre, R. Slama, M.J. Saurel-Cubizolles, M. Schweitzer, O. Thiebaugeorges.

FCOU

The authors wish to acknowledge the University of Illinois at Chicago School of Public Health's Louise Hamilton Kyiv Data Management Center for their assistance in the data management for FCOU study.

GASPII

The authors acknowledge the families involved in the study.

GECKO Drenthe

The authors are grateful to the families who took part in the GECKO Drenthe study, the midwives, gyneacologists, nurses and GPs for their help for recruitment and measurement of participants, and the whole team from the GECKO Drenthe study.

Generation R

The authors gratefully acknowledge the contribution of general practitioners, hospitals, midwives, and pharmacies in Rotterdam.

Generation XXI

The authors gratefully acknowledge the families enrolled in Generation XXI for their kindness, all members of the research team for their enthusiasm and perseverance and the participating hospitals and their staff for their help and support.

GENESIS

The authors thank the Genesis research group which was comprised from Evdokia Oikonomou, Vivian Detopoulou, Christine Kortsalioudaki, Margarita Bartsota, Thodoris Liarigkovinos and Christos Vassilopoulos.

GINIplus

The authors thank all the families for their participation in the GINIplus study. Furthermore, the authors thank all members of the GINIplus Study Group for their excellent work. The GINIplus Study group consists of the following: Institute of Epidemiology I, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg (Heinrich J, Brüske I, Schulz H, Flexeder C, Zeller C, Standl M, Schnappinger M, Ferland M, Thiering E, Tiesler C); Department of Pediatrics, Marien-Hospital, Wesel (Berdel D, von Berg A); Ludwig-Maximilians-University of Munich, Dr von Hauner

Children's Hospital (Koletzko S); Child and Adolescent Medicine, University Hospital rechts der Isar of the Technical University Munich (Bauer CP, Hoffmann U); IUF- Environmental Health Research Institute, Düsseldorf (Schikowski T, Link E, Klümper C, Krämer U, Sugiri D).

HUMIS

The authors thank the mothers who participated in the study and the Norwegian Research Council for their continuous support through several grants.

INMA-Valencia

The authors would particularly like to thank all the participants for their generous collaboration.

INMA-Gipuzkoa

The authors thank the children and parents who participated to the INMA-Gipuzkoa study.

INMA-Menorca

The authors thank all the participants for their generous collaboration. The authors are grateful to Mireia Garcia, Maria Victoria Estraña, Maria Victoria Iturriaga, Cristina Capo and Josep LLuch for their assistance in contacting the families and administering the questionnaires.

KOALA

The authors thank the children and parents who participated to the KOALA study.

Krakow Cohort

The authors acknowledge Jagiellnonian University Medical College in Krakow and Columbia University in New York. Principal investigator: Prof. FP Perera; co-investigator: Prof. W Jedrychowski.

LISAplus

The authors thank all the families for their participation in the LISAplus study. Furthermore, the authors thank all members of the LISAplus Study Group for their excellent work. The LISAplus Study group consists of the following: Helmholtz Zentrum München, German Research Center for Environmental Health, Institute of Epidemiology I, Munich (Heinrich J, Schnappinger M, Brüske I, Ferland M, Schulz H, Zeller C, Standl M, Thiering E, Tiesler C, Flexeder C); Department of Pediatrics, Municipal Hospital "St. Georg", Leipzig (Borte M, Diez U, Dorn C, Braun E); Marien Hospital Wesel, Department of

Pediatrics, Wesel (von Berg A, Berdel D, Stiers G, Maas B); Pediatric Practice, Bad Honnef (Schaaf B); Helmholtz Centre of Environmental Research – UFZ, Department of Environmental Immunology/Core Facility Studies, Leipzig (Lehmann I, Bauer M, Röder S, Schilde M, Nowak M, Herberth G , Müller J); Technical University Munich, Department of Pediatrics, Munich (Hoffmann U, Paschke M, Marra S); Clinical Research Group Molecular Dermatology, Department of Dermatology and Allergy, Technische Universität München (TUM), Munich (Ollert M, J. Grosch).

MoBa

The authors are grateful to all the participating families in Norway who take part in this on-going cohort study.

NINFEA

The authors thank all families participating in the NINFEA cohort.

PÉLAGIE

The authors thank the gynecologists, obstetricians, ultrasonographers, midwives, pediatricians, and families who participated in the study.

Piccolipiù

The authors acknowledge the Piccolipiù Working Group and the families involved in the study.

Project Viva

The authors thank the Project Viva mothers, children and families for their ongoing participation.

REPRO_PL

The authors would particularly like to thank all the cohort participants for their collaboration.

RHEA

The authors would particularly like to thank all the cohort participants for their generous collaboration.

ROLO The authors are grateful to the families and healthcare staff who partake in ROLO and ROLO kids.

SCOPE BASELINE

The authors are grateful to the families and healthcare staff who kindly gave their time to the study.

Slovak PCB study

The authors thank the Slovak PCB study participants for their ongoing cooperation.

STEPS

The authors are grateful to all the families who took part in STEPS study.

SWS

The authors are grateful to the women of Southampton who gave their time to take part in the Southampton Women's Survey and to the research nurses and other staff who collected and processed the data.

CONFLICT OF INTEREST DISCLOSURES

Keith M. Godfrey has received reimbursement for speaking at conferences sponsored by companies selling nutritional products, and is part of an academic consortium that has received research funding from Abbott Nutrition, Nestec and Danone. Debbie A. Lawlor has received support from Roche Diagnostics and Medtronic in relation to biomarker research that is not related to the research presented in this paper. Andrea von Berg has received reimbursement for speaking at symposia sponsored by Nestlé and Mead Johnson, who partly financially supported the 15 yrs follow-up examination of the GINIplus study. The rest of the authors reported no conflicts of interest.

FUNDING/SUPPORT (PER COHORT)

ABCD

This work was supported by the Netherlands Organization for Health Research and Development (ZonMw) (TOP grant, 40-00812-98-11010).

ALSPAC

The UK Medical Research Council and Wellcome (Grant ref: 102215/2/13/2) and the University of Bristol provide core support for ALSPAC. This study has received support from the US National Institute of Health (R01 DK10324) and European Research Council under the European Union's Seventh

Framework Programme (FP7/2007-2013) / ERC grant agreement no 669545. DA Lawlor works in a unit that receives UK MRC funding (MC_UU_12013/5) and is an NIHR senior investigator (NF-SI-0611-10196).

AOB/F

All Our Families is funded through Alberta Innovates Interdisciplinary Team Grant #200700595, the Alberta Children's Hospital Foundation, and the Max Bell Foundation.

BAMSE

The Swedish Research Council, The Swedish Heart and Lung Foundation, The Swedish Research Council for Working Life and Social Welfare, the Swedish Asthma and Allergy Association Research Foundation, The Swedish Research Council Formas, Stockholm County Council, and the European Commission's Seventh Framework 29 Program MeDALL under grant agreement No. 261357.

BIB

BiB receives core infrastructure funding from the Wellcome Trust (WT101597MA) and a joint grant from the UK Medical Research Council (MRC) and Economic and Social Science Research Council (ESRC) (MR/N024397/1). This study has received support from the British Heart Foundation (CS/16/4/32482), US National Institute of Health (R01 DK10324) and European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013) / ERC grant agreement no 669545. J West is funded by a UK Medical Research Council (MRC) Population Health Scientist Postdoctoral Award (MR/K021656/1). DA Lawlor works in a unit that receives UK MRC funding (MC_UU_12013/5) and is an NIHR senior investigator (NF-SI-0611-10196).

Co.N.ER

No funding reported.

DNBC

The Danish National Research Foundation has established the Danish Epidemiology Science Centre that initiated and created the Danish National Birth Cohort. The cohort is furthermore a result of a major grant from this foundation. Additional support for the Danish National Birth Cohort is obtained from the

Pharmacy Foundation, the Egmont Foundation, the March of Dimes Birth Defects Foundation, the Augustinus Foundation, and the Health Foundation. The DNBC 7-year follow-up is supported by the Lundbeck Foundation (195/04) and the Danish Medical Research Council (SSVF 0646). The 11-year follow-up was funded by the Danish Independent Research Council, the Lundbeck Foundation and a strategic grant from Department of Public Health, University of Copenhagen.

EDEN

The EDEN study was supported by: Foundation for medical research (FRM), National Agency for Research (ANR), National Institute for Research in Public health (IRESP: TGIR cohorte santé 2008 program), French Ministry of Health (DGS), French Ministry of Research, INSERM Bone and Joint Diseases National Research (PRO-A) and Human Nutrition National Research Programs, Paris-Sud University, Nestlé, French National Institute for Population Health Surveillance (InVS), French National Institute for Health Education (INPES), the European Union FP7 programmes (FP7/2007-2013, HELIX, ESCAPE, ENRIECO, Medall projects), Diabetes National Research Program (through a collaboration with the French Association of Diabetic Patients (AFD)), French Agency for Environmental Health Safety (now ANSES), Mutuelle Générale de l'Education Nationale a complementary health insurance (MGEN), French national agency for food security, French speaking association for the study of diabetes and metabolism (ALFEDIAM).**FCOU**

FCOU study is supported by the U.S. National Institutes of Health Fogarty International Center, US NIEHS, US CDC, US EPA, and National Academy of Medical Sciences of Ukraine.

GASPII

Ministry of Health.

GECKO Drenthe

The GECKO Drenthe birth cohort was funded by an unrestricted grant of Hutchison Whampoa Ld, Hong Kong and supported by the University of Groningen , Well Baby Clinic Foundation Icare, Noordlease, Paediatric Association Of The Netherlands and Youth Health Care Drenthe.

Generation R

The general design of the Generation R Study is made possible by financial support from the Erasmus MC, University Medical Center, Rotterdam, Erasmus University Rotterdam, Netherlands Organization for Health Research and Development (ZonMw), Netherlands Organisation for Scientific Research (NWO), Ministry of Health, Welfare and Sport and Ministry of Youth and Families. Research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition under grant agreement n°289346, the European Union's Horizon 2020 research and innovation programme under grant agreement No 633595 (DynaHEALTH) and the European Union's Horizon 2020 research and innovation programme under grant agreement 733206 (LifeCycle Project). Bernadeta Patro Golab received a research training fellowship grant from the Nestle Nutrition Institute. Romy Gaillard received funding from the Dutch Heart Foundation (grant number 2017T013) and the Dutch Diabetes Foundation (grant number 2017.81.002). Vincent Jaddoe received grants from the Netherlands Organization for Health Research and Development (VIDI 016.136.361) and the European Research Council (Consolidator Grant, ERC-2014-CoG-648916).

Generation XXI

Generation XXI was funded by Programa Operacional de Saúde – Saúde XXI, Quadro Comunitário de Apoio III and Administração Regional de Saúde Norte (Regional Department of Ministry of Health). This study was funded by FEDER through the Operational Programme Competitiveness and Internationalization and national funding from the Foundation for Science and Technology – FCT (Portuguese Ministry of Science, Technology and Higher Education) (POCI-01- 0145-FEDER-016837), under the project "PathMOB.: Risco cardiometabólico na infância: desde o início da vida ao fim da infância" (Ref. FCT PTDC/DTP-EPI/3306/2014) and the Unidade de Investigação em Epidemiologia - Instituto de Saúde Pública da Universidade do Porto (EPIUnit) (POCI-01-0145-FEDER-006862; Ref. UID/DTP/04750/2013). AC Santos holds a FCT Investigator contract IF/01060/2015.

GENESIS

The study was supported by a research grant from Friesland Foods Hellas.

GINIplus

The GINIplus study was mainly supported for the first 3 years of the Federal Ministry for Education, Science, Research and Technology (interventional arm) and Helmholtz Zentrum Munich (former GSF) (observational arm). The 4 year, 6 year, 10 year and 15 year follow-up examinations of the GINIplus study were covered from the respective budgets of the 5 study centres (Helmholtz Zentrum Munich (former GSF), Research Institute at Marien-Hospital Wesel, LMU Munich, TU Munich and from 6 years onwards also from IUF - Leibniz Research-Institute for Environmental Medicine at the University of Düsseldorf) and a grant from the Federal Ministry for Environment (IUF Düsseldorf, FKZ 20462296). Further, the 15 year follow-up examination of the GINIplus study was supported by the Commission of the European Communities, the 7th Framework Program: MeDALL project, and as well by the companies Mead Johnson and Nestlé.

HUMIS

European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreements Early Nutrition n° 289346 and by funds from the Norwegian Research Council's MILPAAHEL programme, project No.213148.

INMA-Sabadell

This study was funded by grants from the Instituto de Salud Carlos III (Red INMA G03/176) and the Generalitat de Catalunya-CIRIT (1999SGR 00241).

INMA-Valencia

This study was funded by Grants from UE (FP7-ENV-2011 cod 282957 and HEALTH.2010.2.4.5-1), Spain: ISCIII (G03/176; FIS-FEDER: PI09/02647, PI11/01007, PI11/02591, PI11/02038, PI13/1944, PI13/2032, PI14/00891, PI14/01687, and PI16/1288; Miguel Servet-FEDER CP11/00178, CP15/00025, and CPII16/00051), and Generalitat Valenciana: FISABIO (UGP 15-230, UGP-15-244, and UGP-15-249).

INMA-Gipuzkoa

This study was funded by grants from the Instituto de Salud Carlos III (FISFIS PI06/0867, FIS-PS09/0009) 0867,Red INMA G03/176) and the Departamento de Salud del Gobierno Vasco (2005111093 and 2009111069) and the Provincial Government of Guipúzcoa (DFG06/004 and FG08/001).

INMA-Menorca

This study was funded by grants from the Instituto de Salud Carlos III (Red INMA G03/176).

KOALA

Royal Friesland Foods (Leeuwarden); Triodos Foundation (Zeist); Phoenix Foundation; Raphaël Foundation; Iona Foundation; Foundation for the Advancement of Heilpedagogie (all in the Netherlands).

Krakow Cohort

The study received funding from a NIEHS R01 grants entitled: "Vulnerability of the Fetus/Infant to PAH, PM2.5 and ETS" and "Developmental effects of early-life exposure to airborne PAH" (R01ES010165 and R01ES015282) and from The Lundin Foundation, The John and Wendy Neu Family Foundation, The Gladys and Roland Harriman Foundation and an Anonymous Foundation.

LISAplus

The LISAplus study was mainly supported by grants from the Federal Ministry for Education, Science, Research and Technology and in addition from Helmholtz Zentrum Munich (former GSF), Helmholtz Centre for Environmental Research - UFZ, Leipzig, Research Institute at Marien-Hospital Wesel, Pediatric Practice, Bad Honnef for the first 2 years. The 4 year, 6 year, 10 year and 15 year follow-up examinations of the LISAplus study were covered from the respective budgets of the involved partners (Helmholtz Zentrum Munich (former GSF), Helmholtz Centre for Environmental Research - UFZ, Leipzig, Research Institute at Marien-Hospital Wesel, Pediatric Practice, Bad Honnef, IUF – Leibniz-Research Institute for Environmental Medicine at the University of Düsseldorf) and in addition by a grant from the Federal Ministry for Environment (IUF Düsseldorf, FKZ 20462296). Further, the 15 year follow-up examination of the LISAplus study was supported by the Commission of the European Communities, the 7th Framework Program: MeDALL project.

MoBa

The Norwegian Mother and Child Cohort Study is supported by the Norwegian Ministry of Health and Care Services and the Ministry of Education and Research, NIH/NIEHS (contract no N01-ES-75558), NIH/NINDS (grant no.1 UO1 NS 047537-01 and grant no.2 UO1 NS 047537-06A1).

NINFEA

The NINFEA cohort was partially funded by the Compagnia San Paolo Fundation and by the Piedmont Region.

PÉLAGIE

The Pélagie cohort was supported by the French National Research Agency (ANR-2010-PRSP-007), and the French Research Institute for Public Health (AMC11004NSA-DGS).

PIAMA

The PIAMA study was supported by the Netherlands Organization for Health Research and Development; The Netherlands Organization for Scientific Research; The Netherlands Asthma Fund; The Netherlands Ministry of Spatial Planning, Housing, and the Environment; and The Netherlands Ministry of Health, Welfare, and Sport.

Piccolipiù

The Piccolipiù project was financially supported by the Italian National Center for Disease Prevention and Control (CCM grants years 2010 and 2014) and by the Italian Ministry of Health (art 12 and 12 bis D.lgs 502/92).

Project Viva

National Institutes of Health (R01 HD034568, UG3OD023286).

REPRO_PL

National Science Centre, Poland, under the grant DEC-2014/15/B/NZ7/00998, FP7 HEALS Grant N° 603946 and the Ministry of Science and Higher Education under grant agreement no. 3068/7.PR/2014/2.

RHEA

The "Rhea" project was financially supported by European projects (EU FP6-2003-Food-3-NewGeneris, EU FP6. STREP Hiwate, EU FP7 ENV.2007.1.2.2.2. Project No 211250 Escape, EU FP7-2008-ENV-

1.2.1.4 Envirogenomarkers, EU FP7-HEALTH-2009- single stage CHICOS, EU FP7 ENV.2008.1.2.1.6. Proposal No 226285 ENRIECO, EU- FP7- HEALTH-2012 Proposal No 308333 HELIX) and the Greek Ministry of Health (Program of Prevention of obesity and neurodevelopmental disorders in preschool children, in Heraklion district, Crete, Greece: 2011-2014; "Rhea Plus": Primary Prevention Program of Environmental Risk Factors for Reproductive Health, and Child Health: 2012-15).

ROLO

ROLO is supported by the Health Research Board Ireland, the Health Research Centre for Health and Diet Research, and the European Union's Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition under grant agreement no. 289346.

SCOPE BASELINE The SCOPE Ireland study was funded by the Irish Health Research Board. The Cork BASELINE Birth Cohort Study was funded by the National Children's Research Centre, Dublin, Ireland. SCOPE Ireland was funded by the Health Research Board, Ireland (CSA 2007/2). The BASELINE cohort was supported by the National Children's Research Centre, Dublin, Ireland, and the Food Standards Agency of the United Kingdom (grant no. TO7060). SCOPE and BASELINE are supported by INFANT, an SFI funded Research Centre (grant no 12/RC/2272).

SEATON

The ten year follow up of this cohort was funded by the Medical Research Council (grant 80219), the recruitment and follow up at one, two and five years was funded by Asthma UK (grants 00/011, 02/017).

Slovak PCB study

Support was provided by U.S. National Institutes of Health grants R01 CA096525, R03 TW007152, P30 ES001247, and K12 ES019852.

STEPS

This study was supported by the University of Turku, Abo Akademi University, the Turku University Hospital, and the City of Turku, as well as by the Academy of Finland (grants 121569 and 123571), the Juho Vainio Foundation, the Yrjö Jahnsson Foundation, the Turku.

SWS

The SWS is supported by grants from the Medical Research Council, National Institute for Health Research Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton National Health Service Foundation Trust, and the European Union's Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition (grant 289346). Study participants were drawn from a cohort study funded by the Medical Research Council and the Dunhill Medical Trust.

ROLE OF THE FUNDER/SPONSOR

FCOU

Investigators from the U.S. National Institute of Environmental Health Scientists (NIEHS) were involved in the design of the birth outcomes phase of the FCOU study.

The other cohorts declared that the funding agencies had no role in the design and conduct of the study; collection, management, analysis and interpretation of data; preparation, review, approval of manuscript; or decision to submit manuscript for publication.

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Table 1. Characteristics of the participating pregnancy and birth cohorts (n=160757)[a,b]

Cohort name, number of participants, birth years (country)	Gestational diabetes	Gestational hypertension	Pre-eclampsia	Early childhood (2·0-4·9y)		Mid childhood (5·0-9·9y)		Late childhood (10·0-17·9y)	
				Body mass index (SDS)	Overweight and obesity	Body mass index (SDS)	Overweight and obesity	Body mass index (SDS)	Overweight and obesity
ABCD, n=5512, 2003-2004 (The Netherlands)	120 (2·2)	1045 (19·0)	233 (4·2)	0·3 (-1·5, 2·4)	213 (4·5)	0·1 (-1·7, 2·4)	768 (17·1)	NA	NA
ALSPAC, n=9041, 1991-1992 (United Kingdom)	77 (0·9)	1282 (14·5)	170 (1·9)	0·6 (-1·0, 2·5)	77 (6·5)	0·2 (-1·6, 2·7)	2113 (26·4)	0·2 (-1·9, 2·5)	2063 (26·4)
AOB/F, n=1672, 2008-2010 (Canada)	71 (4·2)	118 (7·1)	104 (6·2)	0·2 (-2·3, 2·7)	96 (5·7)	NA	NA	NA	NA
BAMSE, n=3329, 1994-1996 (Sweden)	56 (1·7)	NA	55 (1·7)	0·6 (-0·9, 2·5)	187 (6·5)	0·5 (-1·2, 2·6)	799 (31·2)	0·1 (-1·7, 2·0)	425 (16·9)
BIB, n=983, 2007-2010 (United Kingdom)	100 (10·2)	51 (5·3)	13 (1·4)	0·5 (-1·4, 2·6)	74 (7·5)	NA	NA	NA	NA
Co.N.ER, n=528, 2004-2005 (Italy)	14 (2·7)	20 (3·8)	12 (2·3)	0·3 (-2·3, 2·9)	47 (9·7)	0·7 (-1·3, 2·9)	102 (35·5)	NA	NA
DNBC, n=40349, 1996-2002 (Denmark)	273 (0·7)	1878 (4·7)	1380 (3·4)	NA	NA	0 (-1·9, 2·1)	6304 (15·6)	NA	NA
EDEN, n=1361, 2003-2005 (France)	92 (6·8)	67 (4·9)	30 (2·2)	0·3 (-1·4, 2·0)	27 (2·2)	0 (-1·5, 2·0)	147 (12·9)	NA	NA
FCOU, n=2332, 1993-1996 (Ukraine)	5 (0·2)	367 (15·7)	148 (6·3)	0·5 (-1·9, 3·1)	140 (10·6)	0 (-2·0, 2·0)	124 (12·6)	-0·1 (-2·0, 1·8)	75 (8·9)
GASPII, n=570, 2003-2004 (Italy)	25 (4·4)	28 (4·9)	5 (0·9)	0·7 (-1·1, 2·9)	52 (9·7)	0·7 (-1·4, 2·7)	172 (37·1)	NA	NA
GECKO Drenthe, n=2119, 2006-2007 (The Netherlands)	72 (3·4)	209 (11·0)	46 (2·4)	NA	NA	0·4 (-1·2, 2·4)	465 (21·9)	NA	NA
GENESIS, n=2143, 2003-2004 (Greece)	30 (1·4)	NA	NA	0·8 (-1·2, 3·6)	297 (14·6)	1·0 (-1·5, 3·9)	45 (42·1)	NA	NA
GENERATION R, n=7550, 2002-2006 (The Netherlands)	80 (1·1)	274 (4·0)	149 (2·3)	0·3 (-1·5, 2·5)	220 (5·1)	0·3 (-1·5, 2·7)	1849 (27·4)	0·4 (-1·5, 2·6)	160 (30·0)
GENERATION XXI, n=5921, 2005-2006 (Portugal)	390 (6·6)	135 (2·3)	90 (1·5)	0·5 (-1·3, 3·1)	485 (10·4)	0·6 (-1·4, 3·2)	2015 (38·0)	NA	NA
GINIplus, n=2313, 1995-1998 (Germany)	61 (2·6)	NA	NA	0·1 (-1·7, 2·0)	53 (2·4)	0 (-1·8, 1·9)	227 (10·6)	0 (-1·9, 2·1)	365 (16·0)

Table 1. Characteristics of the participating pregnancy and birth cohorts (n=160757)[a] (continued)

Cohort name, number of participants, birth years (country)	Gestational diabetes	Gestational hypertension	Pre-eclampsia	Early childhood (2·0-4·9 y)		Mid childhood (5·0-9·9y)		Late childhood (10·0-17·9y)	
				Body mass index (SDS)	Overweight and obesity	Body mass index (SDS)	Overweight and obesity	Body mass index (SDS)	Overweight and obesity
HUMIS, n=970, 2003-2008 (Norway)	5 (0·5)	37 (3·8)	70 (7·2)	0·3 (-1·8, 2·4)	53 (6·0)	0·0 (-2·0, 2·3)	63 (17·6)	NA	NA
INMA, n=1933, 1997-2008 (Spain)	191 (11·3)	58 (3·0)	4 (0·9)	0·5 (-1·2, 2·8)	143 (8·2)	0·6 (-1·4, 3·3)	503 (37·6)	0·3 (-1·6, 2·5)	79 (25·3)
KOALA, n=2061, 2000-2002 (The Netherlands)	21 (1·0)	72 (3·5)	26 (1·3)	-0·1 (-2·0, 1·9)	17 (1·7)	-0·2 (-2·2, 1·8)	199 (11·3)	-0·2 (-2·1, 2·2)	19 (18·1)
Krakow Cohort, n=424, 2000-2003 (Poland)	18 (4·2)	19 (4·5)	0 (0·0)	0 (-2·2, 2·3)	11 (4·1)	0·2 (-1·8, 2·6)	90 (26·5)	NA	NA
LISAplus, n=1584, 1997-1999 (Germany)	58 (3·7)	NA	NA	0 (-1·7, 1·9)	33 (2·3)	-0·1 (-1·8, 1·8)	140 (9·9)	0 (1·8, 2·1)	236 (15·2)
MoBa, n=55008, 1999-2009 (Norway)	418 (0·8)	3131 (5·7)	2023 (3·7)	0·4 (-1·8, 2·5)	2456 (6·1)	0·1 (-2·0, 2·3)	6793 (19·5)	NA	NA
NINFEA[b], n=1726, 2005-2010 (Italy)	132 (7·7)	136 (7·9)	44 (2·6)	0·1 (-2·3, 2·5)	86 (5·1)	0 (-2·2, 2·4)	90 (21·2)	NA	NA
PÉLAGIE, n=738, 2002-2005 (France)	21 (2·8)	24 (3·3)	8 (1·1)	0·1 (-1·8, 1·9)	15 (2·0)	NA	NA	NA	NA
PIAMA, n=1815, 1996-1997 (The Netherlands)	19 (1·0)	179 (9·9)	46 (2·5)	0·7 (-1·2, 2·5)	78 (8·9)	0·1 (-1·6, 2·4)	325 (20·0)	-0·2 (-1·7, 1·8)	77 (10·0)
Piccolipiù, n=687, 2011-2015 (Italy)	69 (10·1)	24 (3·5)	6 (0·9)	0·3 (-2·1, 2·5)	40 (5·8)	NA	NA	NA	NA
Project Viva, n=1389, 1999-2002 (United States)	64 (4·7)	85 (6·3)	46 (3·4)	0·7 (-1·0, 2·7)	87 (7·1)	0·4 (-1·4, 3·0)	328 (30·8)	0·4 (-1·5, 3·7)	8 (25·8)
REPRO_PL, n=291, 2007-2011 (Poland)	13 (4·5)	17 (5·8)	0 (0·0)	0·3 (-2·2, 2·5)	19 (6·9)	0·6 (-1·5, 3·6)	19 (38·8)	NA	NA
RHEA, n=740, 2007-2008 (Greece)	60 (8·8)	35 (5·2)	5 (0·7)	0·6 (-1·1, 3·6)	91 (12·3)	NA	NA	NA	NA
ROLO, n=283, 2007-2011 (Ireland)	10 (3·5)	NA	NA	0·2 (-1·7, 2·6)	19 (6·7)	NA	NA	NA	NA
SCOPE BASELINE, n=1046, 2008-2011 (Ireland)	NA	129 (12·3)	35 (3·3)	0·6 (-1·0, 2·3)	62 (5·9)	NA	NA	NA	NA

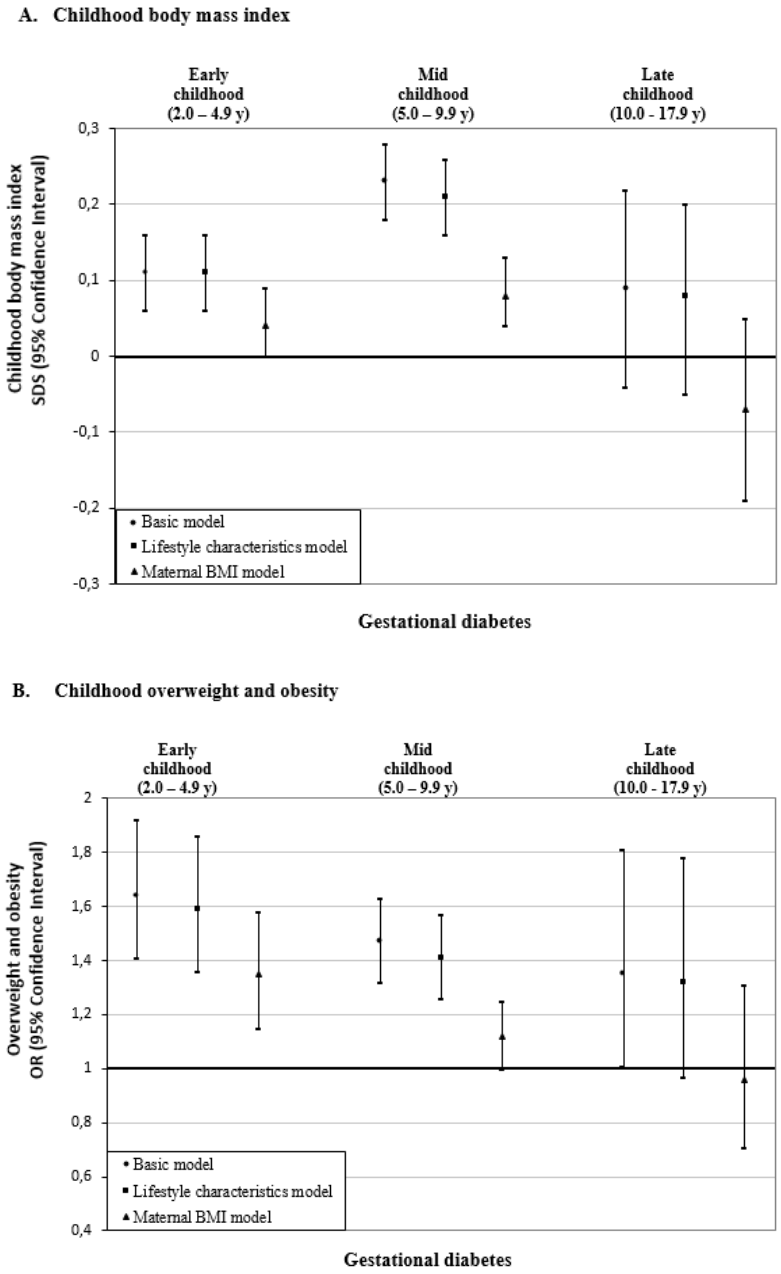
Table 1. Characteristics of the participating pregnancy and birth cohorts (n=160757)[a] (continued)

Cohort name, number of participants, birth years (country)	Gestational diabetes	Gestational hypertension	Pre-eclampsia	Early childhood (2·0-4·9 y)		Mid childhood (5·0-9·9y)		Late childhood (10·0-17·9y)	
				Body mass index (SDS)	Overweight and obesity	Body mass index (SDS)	Overweight and obesity	Body mass index (SDS)	Overweight and obesity
SEATON, n=872, 1998-1999 (United Kingdom)	NA	119 (13·9)	16 (2·1)	0·7 (-0·9, 2·7)	36 (8·1)	0·6 (-1·1, 2·8)	55 (19·8)	0·4 (-1·6, 2·6)	192 (32·9)
Slovak PCB study, n=524, 2002-2004 (Slovakia)	3 (0·6)	54 (12·4)	NA	1·9 (-2·4, 5·3)	222 (48·2)	0·3 (-1·7, 3·3)	123 (31·0)	NA	NA
STEPS, n=297, 2008-2010 (Finland)	20 (6·7)	NA	NA	0·5 (-1·2, 2·2)	13 (4·4)	NA	NA	NA	NA
SWS, n=2646, 1998-2007 (United Kingdom)	30 (1·1)	162 (6·1)	72 (2·7)	0·5 (-1·3, 2·6)	157 (6·2)	0·2 (-1·5, 2·5)	396 (22·0)	NA	NA

[a]Values are expressed as medians (95% range) or numbers of subjects (valid %). NA, not available.

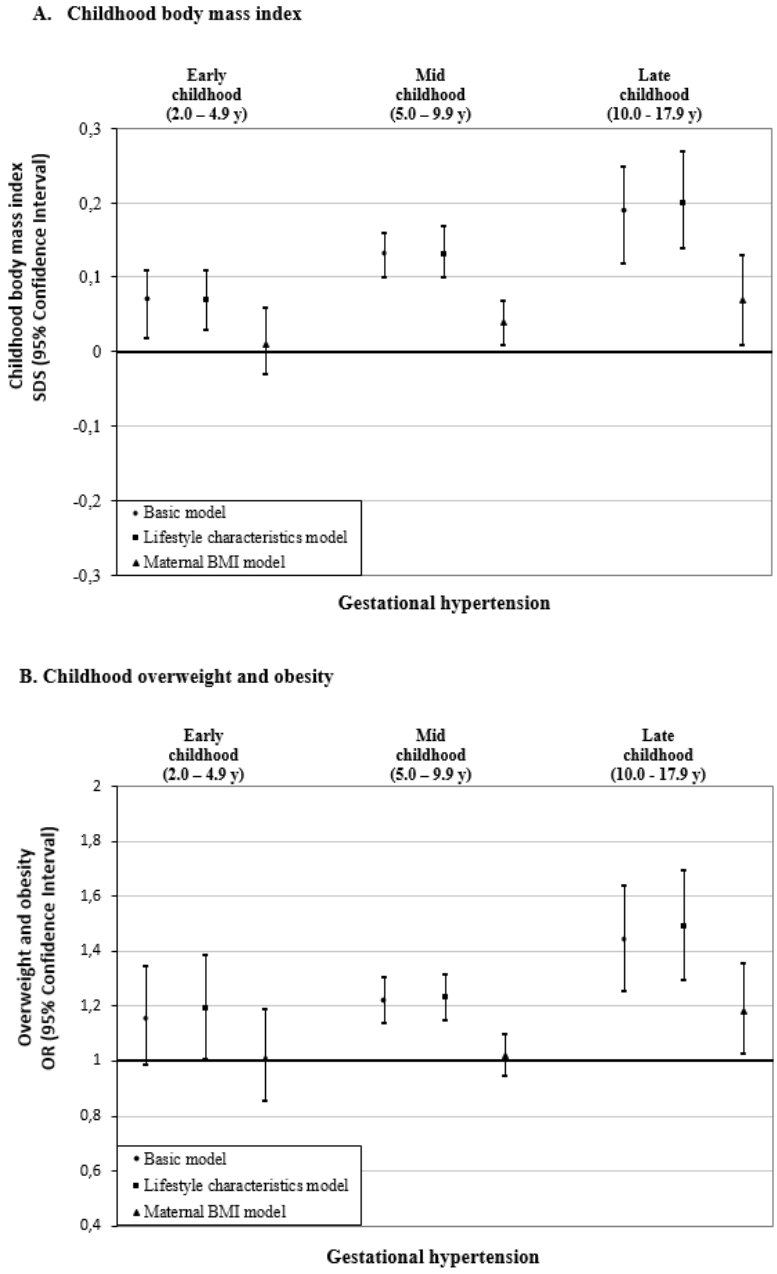
[b] Subset of participants with follow-up completed at 4 years of child's age by the time of data transfer (March 2015).

Figure 1. Associations of gestational diabetes with offspring BMI outcomes in early, mid, and late childhood.[a]



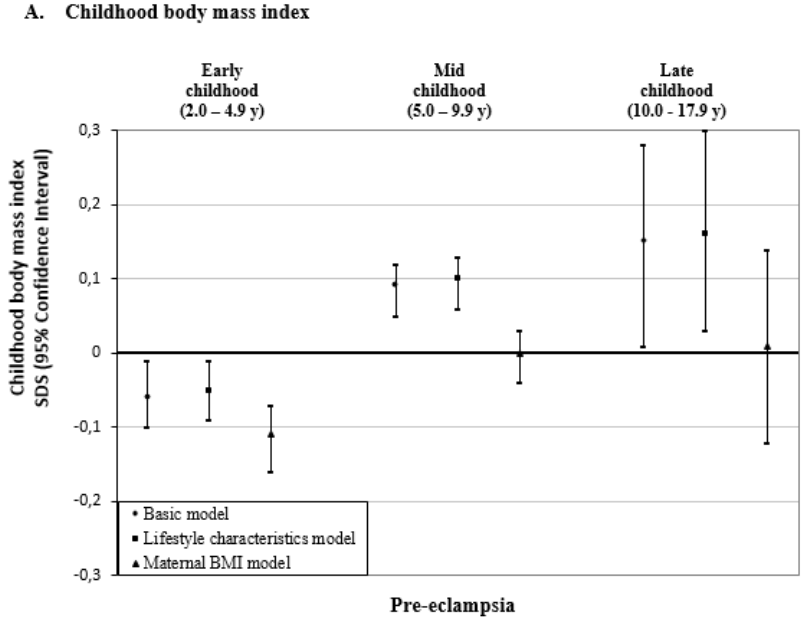
[a]Values are regression coefficients (95% confidence intervals) from multilevel linear mixed effects models and odds ratios (95% confidence intervals) from multilevel binary logistic models that reflect differences in early childhood (2·0 to 4·9 years), mid childhood (5·0 to 9·9 years) and late childhood (10·0 to 17·9 years) BMI SDS and risk of overweight and obesity, respectively, for children born to mothers with gestational diabetes, as compared with the reference group (children born to mothers with an uncomplicated pregnancy). Lifestyle characteristics models are adjusted for offspring's sex, maternal age, educational level, ethnicity, parity, and smoking during pregnancy. Maternal BMI models are additionally adjusted for maternal pre/early-pregnancy BMI.

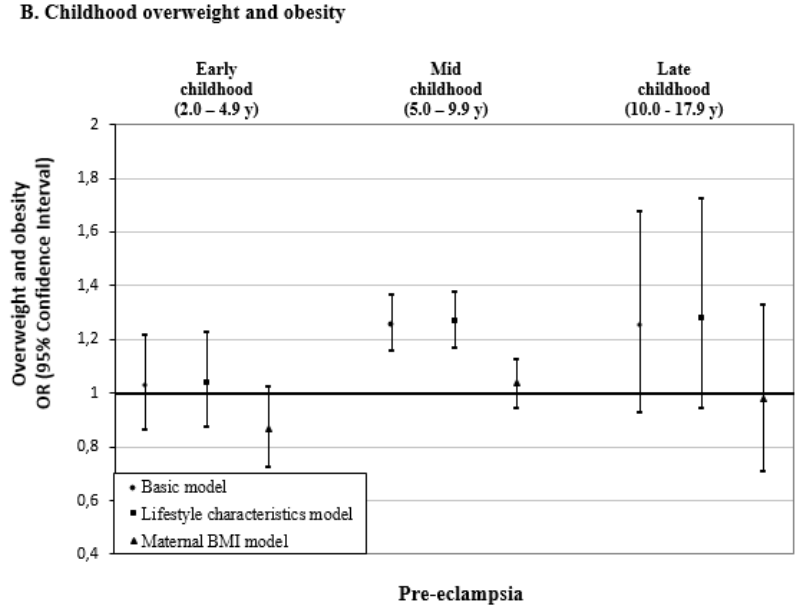
Figure 2. Associations of gestational hypertension with offspring BMI outcomes in early, mid, and late childhood.[a]



[a]Values are regression coefficients (95% confidence intervals) from multilevel linear mixed effects models and odds ratios (95% confidence intervals) from multilevel binary logistic models that reflect differences in early childhood (2·0 to 4·9 years), mid childhood (5·0 to 9·9 years) and late childhood (10·0 to 17·9 years) BMI SDS and risk of overweight and obesity, respectively, for children born to mothers with gestational hypertension, as compared with the reference group (children born to mothers with an uncomplicated pregnancy). Lifestyle characteristics models are adjusted for offspring's sex, maternal age, educational level, ethnicity, parity, and smoking during pregnancy. Maternal BMI models are additionally adjusted for maternal pre/early-pregnancy BMI.

Figure 3. Associations of pre-eclampsia with offspring BMI outcomes in early, mid, and late childhood.[a]





[a]Values are regression coefficients (95% confidence intervals) from multilevel linear mixed effects models and odds ratios (95% confidence intervals) from multilevel binary logistic models that reflect differences in early childhood (2·0 to 4·9 years), mid childhood (5·0 to 9·9 years) and late childhood (10·0 to 17·9 years) BMI SDS and risk of overweight and obesity, respectively, for children born to mothers with pre-eclampsia, as compared with the reference group (children born to mothers with an uncomplicated pregnancy). Lifestyle characteristics models are adjusted for offspring's sex, maternal age, educational level, ethnicity, parity, and smoking during pregnancy. Maternal BMI models are additionally adjusted for maternal pre/early-pregnancy BMI.