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ORIGINAL RESEARCH ARTICLE

Physical health and neurodevelopmental outcome in 7-year-old children whose mothers were at risk of gestational diabetes mellitus: a follow-up of a randomized controlled trial

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Abstract

Introduction: Children born to mothers with gestational diabetes mellitus (GDM) are at risk of metabolic disturbances such as diabetes mellitus and overweight. However, few have examined the outcome of children whose mothers were at risk of GDM. The aim of the study was to investigate how mothers' risk of developing GDM affects physical health and neurodevelopment of the children at 7 years of age.

Material and methods: This is a secondary analysis of a follow-up study of a multicenter randomized controlled trial including 855 pregnant women, carried out at St. Olavs Hospital, Trondheim University Hospital, and Stavanger University Hospital in Norway from 2007 to 2009. Risk factors for developing GDM included age >40 years, diabetes in near family, previous child with birthweight ≥4500 g and pre-pregnancy body mass index (BMI) ≥25 kg/m^2. Data on GDM risk factors were available for 750 women, who were divided into a risk group if they had one or more risk factors for developing GDM ($n = 238$) and a no risk ($n = 512$) group. At 7 years of age, 72 children born to mothers in the risk group and 194 children born to mothers in the no risk group participated. The children's height, weight and physical activity were reported by their parents. Neurodevelopmental outcomes were assessed by using the Five-to-Fifteen questionnaire, which includes motor skills, executive functions, perception, memory, language, social skills, and emotional/behavioral problems.

Results: Most women had only one risk factor for GDM, and pre-pregnancy overweight was the most prevalent risk factor. Children of mothers in the risk group had higher birthweight and length. At the 7-year follow-up, they had a higher weight and BMI, and the odds ratio of being overweight was 3.0 (95% confidence interval 1.1–8.3). There was no group difference in the children's physical activity and their neurodevelopmental outcomes were similar.

Abbreviations: BMI, body mass index; CI, confidence interval; FTF, Five-to-Fifteen; GDM, gestational diabetes mellitus; IADSPG, International Association of Diabetes and Pregnancy Study Groups; MoBa, Norwegian Mother and Child Cohort; MVPA, moderate to vigorous physical activity; NICU, neonatal intensive care unit; OR, odds ratio; PA, physical activity; RCT, randomized controlled trial; SD, standard deviation; SES, socioeconomic status; WHO, World Health Organization.

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Conclusions: We found higher BMI and increased risk of overweight in children born to mothers with one or more risk factors for developing GDM. A focus on preventing pre-pregnancy overweight should be encouraged.

KEYWORDS
body mass index, child, diabetes in pregnancy, follow-up, gestational diabetes mellitus, neurodevelopmental outcome, physical activity, randomized controlled trial

1 | INTRODUCTION

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance with the onset or first recognition during pregnancy, is the most common metabolic complication in pregnancy.[1] It may result in short-term consequences for the offspring, such as higher birthweight, increased pre- and perinatal mortality, prematurity, higher risk of cesarean section and perinatal injuries.[2] Long-term effects of GDM in offspring include a higher risk of developing obesity, metabolic syndrome, type 2 diabetes mellitus and cardiovascular disease later in life.[2]

The diagnostic criteria of GDM have been under debate during the last decade. In Norway, GDM is currently diagnosed as fasting blood glucose level ≥5.3 mmol/L or a 2-hour level of blood glucose ≥9.0 mmol/L after a glucose tolerance test.[3] The prevalence is 10.3% but ranges from 10.7% to 16.9% with use of other diagnostic cut-off values.[4] However, there is evidence of adverse pregnancy outcomes even with maternal glucose levels below those used in diagnostics.[5] Although recommendations for screening of GDM vary,[1] there are some well-documented risk factors for GDM, including advanced maternal age, first-degree relatives with history of diabetes, previous GDM, having a previous child with a birthweight ≥4500 g or having a pre-pregnancy body mass index (BMI) ≥25 kg/m^2.[3,6]

Several studies have reported on anthropometric measures in children of mothers diagnosed with GDM. A systematic review and meta-analysis reported that GDM-exposed children had higher BMI than controls at 6–14 years, which was strongly associated with maternal pre-pregnancy BMI.[5] Also, a positive association with measures of child adiposity at 10–14 years across the range of maternal glucose levels during pregnancy has been documented.[7] Among the risk factors for GDM, studies have found pre-pregnancy overweight to be associated with unfavorable body composition in childhood,[8] adolescence[9] and adulthood.[10,11]

Studies have shown associations between GDM and poorer motor skills in infancy[12,13] and childhood,[14] as well as reduced cognitive[14,15] and social skills.[14] However, it is uncertain whether simply being at risk of GDM affects the child's neurodevelopment. In this study, we aimed to examine whether mothers' risk of developing GDM had an impact on the children's physical health and neurodevelopment at 7 years.

Key message

Children born to mothers at risk for gestational diabetes mellitus have higher body mass index and increased risk of overweight at 7 years of age.

2 | MATERIAL AND METHODS

2.1 | Study design

This is a secondary analysis of a prospective follow-up study of a randomized controlled trial (RCT): "Training in pregnancy" (TRIP), that examined whether exercise during pregnancy could prevent GDM.[16] Participants were invited when booking appointments for their routine ultrasound scans during pregnancy at Stavanger University Hospital and St. Olavs Hospital, Trondheim University Hospital, between April 2007 and June 2009. Inclusion criteria were white women ≥18 years with a singleton live fetus. Exclusion criteria were diseases that could interfere with the women's participation, high-risk pregnancies, or living >30-minute drive from the hospitals. Of approximately 12 000 invited, 875 women accepted and 855 participated (Figure 1). The intervention group (n = 429) was offered a 12-week standardized exercise program including moderate- to high-intensity activity ≥3 days per week between weeks 20 and 36 of pregnancy. The intervention included aerobic, strength and balance exercises as recommended by the American College of Obstetricians and Gynecologists and the Norwegian Directorate of Health.[16,17] Training sessions of 60 minutes led by a physiotherapist were offered once a week and the women were encouraged to follow a written 45-minute home exercise program at least twice a week, including 30 minutes of endurance training and 15 minutes of strength and balance exercises. The control group (n = 426) received standard antenatal care. Participating women were examined at baseline (weeks 18–22 of pregnancy), end of intervention (weeks 32–36 of pregnancy), 3 and 18 months after delivery.

Adherence to the intervention protocol, defined as exercise three times a week or more at moderate to high intensity, was 55%.[16] Prevalence of GDM did not differ between the intervention and control group, based on World Health Organization (WHO) criteria used

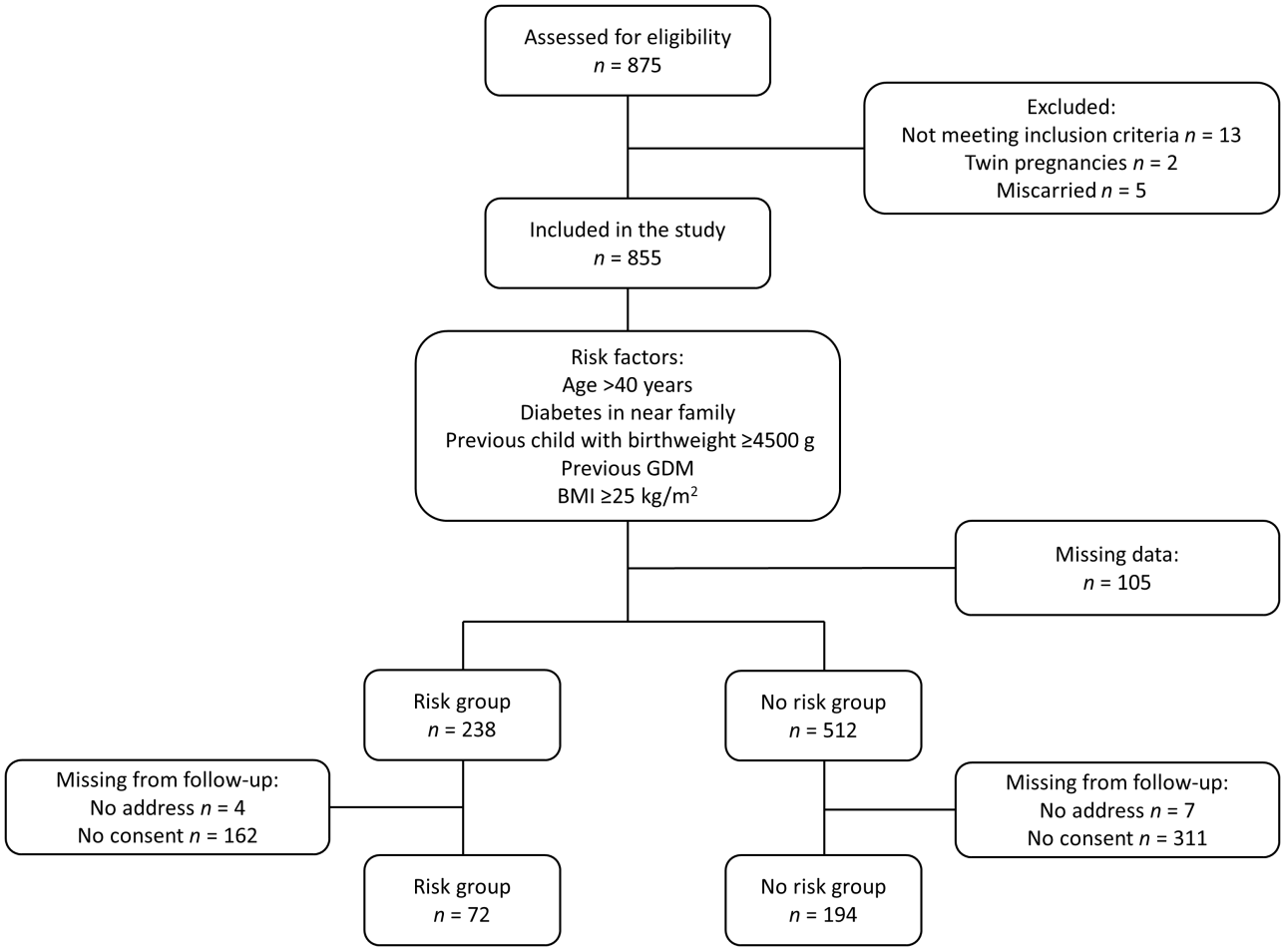

FIGURE 1 Flow of study participants. BMI, body mass index; GDM, gestational diabetes mellitus.

at the time.[16] Secondary analyses examined whether exercise during pregnancy could impact the children's physical health and neurodevelopment. There were no differences between children of mothers in the intervention and the control group in length, weight or head circumference at birth,[16] cognitive, language, motor or daily life functioning at 18 months,[18] neurodevelopmental outcome,[19] BMI or physical activity (PA) at 7 years.[20]

Follow-up data were collected electronically from October 2014 to December 2016 using the software CHECKWARE (CheckWare AS) during the autumn semester of the children's second year of primary school.[19,20] The data were collected by questionnaires on anthropometric measures, general health and diseases of both mother and child as well as neurodevelopment of the children.

2.2 | Exposure variables

Children were divided into a risk group and a no risk group depending on whether their mother had any of the following risk factors for GDM: age >40 years at start of pregnancy, first-degree relatives with history of diabetes, previous child with a birthweight ≥4500 g, previous GDM, or pre-pregnancy BMI ≥25 kg/m^2. Data on risk factors were collected at baseline (n=855), except family history of diabetes which was reported at post-partum follow-up (n=716). Pre-pregnancy BMI (n=848) was based on self-reported weight prior to pregnancy and height measured at baseline.

Data on one or more of the selected GDM risk factors were missing for 143 of 855 women enrolled in the original RCT, of whom 38 women had available information on at least one of the selected GDM risk factors. Thus, 105 women were excluded due to missing data (Figure 1). Of the remaining 740 women, 238 were included in the risk group and 512 in the no risk group. At the 7-year follow-up, information on residence was missing for four children in the risk group and seven children in the no risk group and consent to participate was not obtained for 162 children in the risk and 311 children in the no risk group. In total, 72 (30.3%) children in the risk group and 194 (37.9%) children in the no risk group were assessed at 7 years.

2.3 | Baseline variables

Women's age, weight, height, BMI, parity and sessions of exercise per week were recorded at baseline. We used the Hollingshead Two-Factor Index of Social Position[21] to calculate socioeconomic status

(SES) based on the mother's education and occupation. Information about sex, birthweight, gestational age, length, head circumference, type of delivery and admittance to neonatal intensive care unit (NICU) was retrieved from medical charts after birth.

Fasting plasma glucose and 2-hour plasma glucose were obtained in weeks 32–36 of pregnancy following a standardized 75-g oral glucose tolerance test.[16] In the original RCT, GDM was diagnosed according to the 1999 WHO criteria: fasting glucose level in fasting whole blood ≥6.1 mmol/L, plasma glucose ≥7.0 mmol/L or a 2-hour value ≥7.8 mmol/L.[22] In the present study, we present GDM diagnosed according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria: fasting blood glucose ≥5.1 mmol/L or 2-hour blood glucose ≥8.5 mmol/L.[23]

2.4 | Outcome variables

Questions on children's height, weight, diseases and health problems were developed by the Norwegian Institute of Public Health for the Norwegian Mother and Child Cohort (MoBa) study.[24] We calculated the children's iso-BMI, that is, BMI adjusted for sex and age, using a weight calculator based on Norwegian standards.[25] Childhood overweight was defined as having an iso-BMI ≥25 kg/m^2. Parents reported whether their children had diseases or health problems: rheumatoid arthritis, cancer, diabetes, cerebral palsy, attention-deficit hyperactivity disorder, celiac disease, bone fractures, epilepsy, mental retardation, autistic traits, Asperger's syndrome, chronic fatigue syndrome/myalgic encephalomyelitis, tonsillectomy, ear drainage, other conditions or congenital diseases.[24]

Questions regarding PA were the same as those used and validated in other Norwegian studies.[26–28] To assess whether the child met the recommendation from the Norwegian Directorate of Health to perform ≥1 hour daily moderate to vigorous PA (MVPA),[29] parents reported their child's total (including school, after-school program and leisure time) daily MVPA (<1/≥1 hour).[27] They reported frequency of leisure time MVPA outside school and after-school programs where the child was out of breath or sweaty (never/<once a month/once a week/2–3 times a week/4–6 times a week/every day), weekly leisure time MVPA (none/1 hour/2–3 hours/4–6 hours/≥7 hours)[26,28] and intensity of PA (takes it easy without getting out of breath and/or sweaty/gets out of breath and/or sweaty/gets almost exhausted). Time spent on TV, video, electronic games, DVD or PC outside school (<1/2 hours/1/2–1 hour/2–3 hours a day)[26] and approximate hours of sleep at night on weekdays (≤8/9/10/11 hours/≥12 hours)[24] were also reported.

The Five-to-Fifteen (FTF) questionnaire was used to measure neurodevelopment. It consists of 181 statements about the child's present functioning categorized into the following eight domains: motor skills, executive functions, perception, memory, language, social skills and possible emotional/behavioral problems.[30] Parents are asked to answer each statement by comparing their child with their peers on a three-point scale from 0 (does not apply) to 2 (definitely applies). Higher scores indicate more difficulties and a score ≥90th centile is cut-off for having more difficulties than children their age usually have. The FTF has been found to be reliable and valid as a screening instrument in children.[30–32]

2.5 | Statistical analyses

The IBM SPSS Statistics 27 was used for all analyses. Two-sided *P*-values <0.05 were considered as statistically significant. Group differences were analyzed using chi-square statistics for categorical data, Student's *t*-test for continuous data, Mann–Whitney *U* test for ordinal or continuous data with a non-normal distribution. To assess normality, we visually inspected histograms and Q–Q plots of the residuals. Odds ratio (OR) with 95% confidence interval (CI) was used as an estimate of the relative risk of having an iso-BMI ≥25 kg/m^2 and for having FTF domain scores ≥90th centile, both unadjusted and prespecified adjusted for birthweight, sex, age at follow-up and maternal SES at baseline. In addition, we ran sensitivity analyses excluding preterm children and/or children who had been admitted to the NICU as well as children with reported diseases or health problems, as these factors could potentially influence physical health and neurodevelopment.

2.6 | Ethics statement

The initial RCT was registered in ClinicalTrials.gov (NCT00476567). The follow-up study was conducted in accordance with the Declaration of Helsinki. Both parents and children received written information. Parents gave written consent on behalf of their children. The Regional Committee for Medical and Health Research Ethics in Central Norway approved the follow-up study (REC no. 2014/618, July 7, 2014). Incentives to participate comprised a lottery of an iPad for one participant in each of the three data collection periods.

3 | RESULTS

Baseline characteristics are shown in Table 1. Maternal age, weight and BMI were higher in the risk group than in the no risk group, as these were selection criteria. There were no differences in maternal SES, exercise sessions per week prior to pregnancy, parity or proportion of women randomized to the exercise intervention in each group. Almost four of five women in the risk group had only one risk factor for GDM, and pre-pregnancy BMI ≥25 kg/m^2 was the most prevalent risk factor present in 68.1% of the women in the risk group. The proportion of mothers diagnosed with GDM during pregnancy did not differ significantly between the groups.

Children of mothers in the risk group had higher birthweight and length at birth. There were no group differences in head circumference, sex, type of delivery, prematurity, admittance to the NICU or the child's age at follow-up.

TABLE 1 Baseline characteristics of mothers and children in the risk and no risk group.

	Risk group ($n = 72$)		No risk group ($n = 194$)		
	Mean	(SD)	Mean	(SD)	*P*
Maternal characteristics at baseline					
Age, years	31.7	(4.6)	30.2	(3.5)	0.014
Weight, kg	78.1	(10.7)	66.6	(6.8)	<0.001
Height, cm	168.8	(0.1)	168.7	(0.1)	0.856
BMI, kg/m^2	27.4	(3.5)	23.4	(1.9)	<0.001
SES	3.9	(0.8)	4.1	(0.8)	0.065
Exercise sessions per week	1.7	(1.5)	1.9	(1.4)	0.233
Parity, *n* (%)					
0	34	(47.2)	118	(60.8)	
1	27	(37.5)	58	(29.9)	0.037
2 or more	11	(15.3)	18	(9.3)	
In vitro fertilization, *n* (%)	1	(1.4)	9	(4.7)	0.295
Maternal characteristics in pregnancy					
Randomized to intervention, *n* (%)	42	(58.3)	117	(60.3)	0.770
Systolic BP	110.2	(8.8)	107.9	(8.5)	0.056
Diastolic BP	70.2	(7.5)	67.3	(6.8)	0.001
Fasting glucose[a]	4.4	(0.4)	4.2	(0.3)	<0.001
2-hour oral glucose tolerance test[b]	5.8	(1.3)	5.6	(1.1)	0.209
GDM, *n* (%)	4	(5.8)	6	(3.2)	0.464
Number of GDM risk factors, *n* (%)			-	-	
0			194	(100)	
1	57	(79.2)	-	-	
2	10	(13.9)	-	-	
3	1	(1.4)	-	-	
Missing one or more risk factors	4	(5.6)			
Age >40 years, *n* (%)	5	(6.9)	-	-	
Diabetes in near family, *n* (%)	26	(38.2)	-	-	
Previous child ≥4500 g, *n* (%)	4	(5.6)	-	-	
Previous GDM, *n* (%)	1	(1.4)			
Pre-pregnancy BMI ≥25 kg/m^2, *n* (%)	49	(68.1)	-	-	
Child characteristics at birth					
Gestational age, weeks	40.2	(1.3)	39.9	(1.5)	0.232
Birthweight, g	3708	(573)	3477	(476)	<0.001
Length at birth, cm[c]	50.6	(2.4)	49.8	(2.0)	0.004
Head circumference at birth, cm[d]	35.4	(1.7)	35.0	(1.5)	0.104
Male sex, *n* (%)	37	(51.4)	101	(52.1)	0.922
Older siblings, *n* (%)	38	(52.8)	76	(39.2)	0.046
Vaginal delivery, *n* (%)	59	(81.9)	175	(90.2)	0.066
Prematurity, *n* (%)	2	(2.8)	6	(3.1)	1.000
Admitted to NICU, *n* (%)[e]	1	(1.4)	4	(2.1)	1.000
Child's age at follow-up, years	7.3	(0.3)	7.4	(0.3)	0.203

Note: *P*-values are based on Student's *t*-test for continuous data, Mann–Whitney *U* test for ordinal data (ie SES, exercise sessions per week, parity), and chi-square statistics for dichotomous data.

Abbreviations: BMI, body mass index; BP, blood pressure; GDM, gestational diabetes mellitus (fasting blood glucose ≥5.1 mmol/L or 2-hour blood glucose ≥8.5 mmol/L); SD, standard deviation; SES, socioeconomic status.

[a]Data missing for four mothers in the risk group and four mothers in the no risk group.

[b]Data missing for three mothers in the risk group and four mothers in the no risk group.

[c]Data missing for 10 children in the no risk group.

[d]Data missing for one child in the no risk group.

[e]Data missing for two children in the risk group and three children in the no risk group.

TABLE 2 Parent-reported weight, height and BMI at the 7-year follow-up in the risk and the no risk group.

	Risk group			No risk group				
	n	Mean	(SD)	*n*	Mean	(SD)	Mean difference	(95% CI)
Weight, kg	63	26.8	(5.6)	155	24.7	(3.8)	2.1	(0.8–3.4)
Height, cm	70	128.3	(5.9)	181	126.9	(5.9)	1.4	(−0.2 to 3.1)
BMI	63	16.2	(3.2)	154	15.3	(1.6)	0.9	(0.2–1.5)
Iso-BMI	63	20.2	(3.8)	154	19.1	(2.4)	1.0	(0.2–1.9)

Note: Linear regression model.

Abbreviations: BMI, body mass index; CI, confidence interval; SD, standard deviation.

TABLE 3 Parent-reported physical activity at the 7-year follow-up in the risk and the no risk group.

	Risk group (*n* = 72)		No risk group (*n* = 194)		
	n	(%)	*n*	(%)	*P*
Frequency of MVPA					
Every day	0	0	5	(2.6)	
4–6 times a week	9	(12.5)	30	(15.5)	
2–3 times a week	42	(58.3)	107	(55.2)	0.393
Once a week	19	(26.4)	46	(23.7)	
≤Once a month	2	(2.8)	6	(3.1)	
Hours per week of MVPA					
≥7 hours	2	(2.8)	4	(2.1)	
4–6 hours	9	(12.5)	30	(15.5)	
2–3 hours	36	(50.0)	92	(47.4)	0.995
1 hour	24	(33.3)	60	(30.9)	
None	1	(1.4)	8	(4.1)	
Intensity of PA[a]					
Easy	6	(8.3)	26	(13.5)	
Out of breath	65	(90.3)	158	(81.9)	0.630
Almost exhausted	1	(1.4)	9	(4.7)	
MVPA[b]					
≥1 hour per day	52	(72.2)	114	(59.4)	0.054
Electronical devices					
<1/2 hours a day	5	(7.0)	16	(8.2)	
1/2–1 hour a day	45	(63.4)	136	(70.1)	0.217
2–3 hours a day	21	(29.6)	42	(21.6)	
Hours of sleep					
≥12 hours	0	(0)	3	(1.5)	
11 hours	19	(26.8)	61	(31.4)	
10 hours	42	(59.2)	113	(58.2)	0.168
9 hours	8	(11.3)	15	(7.7)	
≤8 hours	2	(2.8)	2	(1.0)	

Note: *P*-values are based on chi-square statistics for dichotomous data and Mann–Whitney *U* test for ordinal data.

Abbreviations: MVPA, moderate to vigorous PA; PA, physical activity.

[a]Data missing for one child in the no risk group.

[b]Data missing for two children in the no risk group.

3.1 | Body mass index and physical activity

Table 2 shows the children's BMI and PA at the 7-year follow-up. Weight and BMI were higher in the risk group. The OR of being overweight was 3.0 (95% CI 1.1–8.3) in the risk compared with the no risk group (Table S1). The OR did not change when we adjusted for birthweight, sex, age at follow-up or maternal SES (Table S1).

There were no group differences in frequency of MVPA, hours per week of MVPA or intensity of PA, use of electronical devices per day or hours of sleep (Table 3). In all, 72.2% in the risk group and 59.4% in the no risk group met the recommendation of ≥1 hour per day of MVPA.

3.2 | Neurodevelopmental outcome

Table 4 shows the FTF scores in the various domains. There were no group differences in mean scores (Table 4) or in proportion of children with scores ≥90th centile (Table S2). Adjustment for sex, age at follow-up or maternal SES did not change the results (Table S2).

3.3 | Sensitivity analyses

Results were essentially the same when we excluded children born preterm and children admitted to the NICU (3 risk, 8 no risk) and

TABLE 4 Five-to-Fifteen scores in the various domains and subdomains at the 7-year follow-up in the risk and the no risk group.

		Risk group ($n = 72$)		No risk group ($n = 194$)		
	Items	Median	(IQR)	Median	(IQR)	*P*
Motor skills[a]	17	0.12	(0.03–0.24)	0.12	(0.00–0.24)	0.979
Gross motor skills	7	0.00	(0.00–0.14)	0.00	(0.00–0.14)	0.164
Fine motor skills	10	0.10	(0.00–0.30)	0.10	(0.00–0.30)	0.382
Executive functions[b]	25	0.28	(0.08–0.40)	0.20	(0.08–0.44)	0.489
Attention	9	0.33	(0.00–0.56)	0.22	(0.00–0.50)	0.411
Hyperactive/impulsive	9	0.22	(0.00–0.39)	0.11	(0.00–0.44)	0.589
Hypoactive	4	0.00	(0.00–0.25)	0.13	(0.00–0.50)	0.944
Planning and organizing	3	0.00	(0.00–0.33)	0.00	(0.00–0.33)	0.872
Perception[c]	18	0.11	(0.06-0.22)	0.11	(0.00–0.22)	0.987
Relation in space	5	0.00	(0.00–0.20)	0.00	(0.00–0.20)	0.777
Time concepts	4	0.25	(0.00–0.50)	0.25	(0.00–0.75)	0.287
Body perception	5	0.00	(0.00–0.20)	0.00	(0.00–0.20)	0.719
Visual perception	4	0.00	(0.00–0.00)	0.00	(0.00–0.00)	0.097
Memory[d]	11	0.09	(0.00-0.27)	0.09	(0.00–0.27)	0.772
Language[e]	21	0.05	(0.00-0.10)	0.05	(0.00–0.10)	0.640
Comprehension	5	0.00	(0.00–0.20)	0.00	(0.00–0.20)	0.797
Expressive language skills	13	0.00	(0.00–0.08)	0.00	(0.00–0.08)	0.591
Communication	3	0.00	(0.00–0.00)	0.00	(0.00–0.00)	0.798
Social skills[f]	27	0.04	(0.00–0.15)	0.04	(0.00–0.07)	0.164
Emotional/behavioral problems[g]	32	0.05	(0.00–0.13)	0.05	(0.00–0.13)	0.857
Internalizing	11	0.09	(0.00–0.11)	0.00	(0.00–0.09)	0.550
Externalizing	13	0.08	(0.00–0.15)	0.08	(0.00–0.15)	0.660
Obsessive–compulsive	8	0.00	(0.00–0.00)	0.00	(0.00–0.00)	0.407

Note: *P*-values are based on Mann–Whitney *U* test.

Abbreviations: IQR, interquartile range.

[a]Data missing for three children in the risk group and five children in the no risk group.

[b]Data missing for five children in the risk group and eight children in the no risk group.

[c]Data missing for four children in the risk group and eight children in the no risk group.

[d]Data missing for four children in the risk group and five children in the no risk group.

[e]Data missing for four children in the risk group and 10 children in the no risk group.

[f]Data missing for four children in the risk group and seven children in the no risk group.

[g]Data missing for four children in the risk group and six children in the no risk group.

children with diseases or health problems at the 7-year follow-up (14 risk, 38 no risk).

3.4 | Non-respondents

The proportion of non-respondents was 69.7% ($n=166$) in the risk group and 62.1% ($n=318$) in the no risk group ($P=0.264$). There were no significant differences in baseline maternal or child characteristics between non-respondents and respondents in any of the groups (Table S3).

4 | DISCUSSION

In this study, we found that children born to mothers at risk for GDM had higher weight and BMI at 7 years. The higher odds for being overweight remained when we adjusted for birthweight, sex, age at follow-up and maternal SES. Parent-reported PA or neurodevelopmental outcomes did not differ.

The RCT included women who were motivated to participate in an exercise study during pregnancy. This may have introduced a selection bias with healthier participants compared with the general population. Furthermore, external validity is limited to white women and of women living <30 minutes from university hospitals. However, BMI and PA of the participating women were comparable to participants in the MoBa study ($n=34\,508$).[16] Both studies included women within the normal range of BMI who exercised regularly, indicating a representative selection of Norwegian women.[16] Another limitation to the study was the low follow-up rate (35.9%) and missing data on GDM risk factors for 105 women. We do not know why so many parents chose not to participate. A recent meta-analysis demonstrated higher response rates to surveys using monetary incentives instead of a lottery.[33] Also, online surveys have lower response rates than postal surveys.[33] However, follow-up rates were similar in the risk and the no risk group and the respondents did not differ in baseline characteristics from non-respondents. Still, a small sample size may have reduced power to detect differences, and non-significant differences should be interpreted with caution.

The original RCT study used the 1999 WHO criteria,[22] whereas the prevalence of GDM in this study was given according to the updated IADPSG criteria. Further, Norwegian guidelines are somewhat different.[3] However, this study assessed children born to mothers at risk of GDM independent of diagnosis, in line with findings from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, which found risk of adverse pregnancy outcomes even below diagnostic criteria.[5]

We used well-established risk factors for GDM,[3,6] although recommendations for GDM screening vary between countries.[1] In Norway, the current recommendation is that all pregnant women who fulfill one or more of the following criteria are offered an oral glucose tolerance test during weeks 24–28 to diagnose GDM: nulliparous mothers aged >25 years, multiparous women aged >40 years, pre-pregnancy BMI ≥25 kg/m^2, ethnicity from Asia or Africa, previously diagnosed GDM, a previous child with birthweight ≥4500 g, first-degree relatives with history of diabetes and reduced glucose tolerance in non-pregnant state.[3] In the present study, we used maternal age >40 years as a risk factor and we did not differentiate between nulliparous and multiparous women with regard to age.

The 7-year follow-up was based on electronically collected parent-reported data from standardized questionnaires. There is a possibility that these data may be influenced by misinterpretation, exaggeration, social desirability bias or lack of knowledge about their child's weight, PA and neurodevelopment. Height and weight were reported in a questionnaire developed by the Norwegian National Institute of Health for the MoBa study.[24] It has been shown that parents' estimation is less accurate than measurements, although there are no important differences on a group level.[34] Questions regarding PA frequency and duration are shown to be valid and reliable[28] and have been used in other Norwegian studies.[26–28] It has, however, been shown that parents under-report children's PA when compared with accelerometer measurements.[35]

The reliability and validity of the FTF have been examined in other Nordic countries. Inter-rater and test–retest reliability were evaluated in 1350 Swedish children aged 6–14 years and found to be acceptable.[31] FTF has been shown to discriminate between different diagnostic groups in a clinical sample of 155 children aged 5–15 years referred to child and adolescent psychiatry in Denmark.[32] The validity of the FTF in detecting developmental disorders was supported when compared with neuropsychological assessments in a sample of 1291 Finnish children aged 5 years, but parents may report concerns that are not clinically important.[30] Such factors may have influenced the results; however, it is unlikely that they would affect the two groups differently.

We have not found other studies examining outcomes of children born to mothers at risk of GDM based on the risk factors we used. Lowe et al.[7] reported a positive association across the range of maternal glucose levels during pregnancy with measures of child adiposity at 10–14 years. Most of the women in our study did not develop GDM. Pre-pregnancy overweight was the most prevalent risk factor and is the only modifiable risk factor. Our results are consistent with other studies reporting that maternal overweight before pregnancy and weight gain during pregnancy are associated with higher fat mass in children at 6–7 years of age.[8] Three Finnish studies found maternal pre-pregnancy overweight to be an independent risk factor for offspring overweight and abdominal obesity lasting into adolescence[9] and early adulthood.[10,11] Also in Norway, an association between maternal pre-pregnancy obesity and higher BMI in offspring at birth, and thereafter persistently higher BMI at 4–5 years, have been reported.[36] Evidence from both epidemiological and animal studies suggests that programming of childhood and adult obesity can arise from environmental influences occurring in utero through to neonatal life and early childhood.[37] Thus, reducing the prevalence of pre-pregnancy overweight may contribute to easing the societal burden of overweight, even though the mechanisms of overweight are complex.

We did not find any group differences in PA. A national Norwegian study measuring PA in children by accelerometers showed that the proportion of children meeting the recommendation from the Norwegian Directorate of Health for children to perform one or more hours per day of MVPA is declining over time.[29] This may explain the relatively low proportion of children fulfilling the recommendation in our study. However, it could also be that the parents underestimated their children's PA, which has been shown compared with measurements done by accelerometers.[35]

Although some studies have reported poorer neurodevelopmental outcomes in children of GDM mothers,[12,14,15] we have not found studies examining neurodevelopmental outcomes in children born to mothers at risk for GDM. We did not find differences between the risk and no risk group in any of the FTF scores or in the proportion of children having scores ≥90th centile. Indeed, the median FTF domain scores were similar to those in the Swedish normative material.[31] This could be explained by the fact that the majority of the mothers in our study were at low risk and few developed GDM.

Our finding of increased risk of overweight in children born to mothers with risk factors for GDM may have implications for the children's future health. Overweight before puberty is associated with significantly increased risk of mortality and morbidity later in life, especially type 2 diabetes mellitus and cardiovascular disease.[38] Overweight children are also found to be less socially accepted and have fewer friends compared with their non-overweight peers.[39] In addition, obese and overweight children and adolescents are more likely to suffer from psychological comorbidities, such as depression.[40] As we have shown that mother's risk of GDM can impact the weight status of the child, a focus on preventing pre-pregnancy overweight should be encouraged.

5 | CONCLUSION

In this prospective follow-up study of women included in an RCT during pregnancy, we have reported on physical health and neurodevelopment of children born to mothers with one or more risk factors for GDM. Children of mothers in the risk group had higher BMI and increased risk of overweight at 7 years. As we found that the most prevalent risk factor was pre-pregnancy overweight, a focus on preventing it should be encouraged.

AUTHOR CONTRIBUTIONS

ÅJK and SK were involved in data analyses and writing up the work. SNS was involved in the conception, planning and carrying out of the initial RCT and the present follow-up study and reviewed the manuscript. SM and KÅS were involved in the conception and planning of the initial RCT and reviewed the manuscript. KAIE was involved in the conception, planning, carrying out, data cleaning, analyzing and writing up the work in the present follow-up study. All authors read and approved the final article.

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CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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