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## Diet, physical activity and mental health status are associated with dysglycaemia in pregnancy: The Healthy Start Study

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### Abstract

**Aims**—Prenatal dysglycaemia is associated with adverse maternal and offspring outcomes. This study examined the association between dysglycaemia and multiple modifiable factors measured during pregnancy.

**Methods**—The Healthy Start Study collected self-reported data on modifiable factors in early and mid-pregnancy (median 17 and 27 weeks gestation, respectively) from 832 women. Women received 1 point for each optimal modifiable factor: diet quality (Healthy Eating Index  $\geq 64$ ), physical activity level (estimated energy expenditure  $\geq 170$  MET-hours/week), and mental health status (Perceived Stress  $<6$  and Edinburgh Postnatal Depression  $<13$ ). Dysglycaemia during pregnancy was defined as an abnormal glucose challenge,  $\geq 1$  abnormal results on an oral glucose tolerance test, or a clinical diagnosis of gestational diabetes. Logistic regression models estimated odds ratios for dysglycaemia as a function of each factor and the total score, adjusted for age, race/ethnicity, pre-pregnant body mass index, history of gestational diabetes, and family history of type 2 diabetes.

**Results**—In individual analyses, only physical activity was significantly associated with a reduced risk of dysglycaemia (adjusted OR 0.67, 95%CI 0.44–1.00). We observed a significant, dose-response association between increasing numbers of optimal factors and odds of dysglycaemia (adjusted  $p=0.01$ ). Compared to having no optimal modifiable factors, having all 3 was associated with a 73% reduced risk of dysglycaemia (adjusted OR 0.27, 95%CI 0.08–0.95).

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#### Conflict of Interest

The authors declare no conflict of interest.

**Conclusions**—An increasing number of positive modifiable factors in pregnancy was associated with a dose-response reduction in risk of dysglycaemia. Our results support the hypothesis that modifiable factors in pregnancy are associated with the risk of prenatal dysglycaemia.

## Introduction

Gestational diabetes (GDM) affects 9% of pregnancies in the United States [1]. GDM and milder glucose intolerance in pregnancy are associated with adverse health outcomes for mother and offspring [1–3]. The Nurses' Health Study reported that 47.5% of GDM cases could be prevented if women maintained a healthy lifestyle before pregnancy with regard to weight, diet, physical activity, and smoking [4]. While dietary habits are relatively stable from preconception through pregnancy [5], physical activity declines [6] and prenatal mental health status may affect prenatal diet and activity [7, 8]. Understanding the degree to which modifiable factors (diet quality, physical activity levels, mental health status) during pregnancy are associated with prenatal dysglycaemia can be useful for developing prevention programs. We examined the association between multiple modifiable factors (diet quality, physical activity levels, mental health status) in early to mid-pregnancy with risk of prenatal dysglycaemia. We hypothesized that women meeting data-derived thresholds for all factors would have significantly a lower risk of dysglycaemia than women not meeting any thresholds.

## Patients and Methods

Participants were from The Healthy Start Study, a pre-birth cohort of 1410 mother-offspring dyads in Colorado, USA. Pregnant women were recruited at the University of Colorado Anschutz Medical Campus obstetric clinic from 2010–2014. Eligibility criteria included age 16 years, <24 weeks gestation, singleton pregnancy, and no history of serious chronic disease (including pre-gestational diabetes), prior stillbirth, or previous delivery <25 weeks gestation. Participants completed research visits in early and mid-pregnancy (median 17 and 27 weeks, respectively). Women were eligible for the present analysis if they completed 1 visit after February 10, 2011 (when the mental health questionnaires were added), completed 1 dietary recall prior to 27 weeks gestation, and had clinical results of GDM screening/diagnosis (n=899). The Healthy Start Study was approved by the Colorado Multiple Institutional Review Board. All participants provided written informed consent.

Modifiable factors were assessed by self-report. Prenatal diet was assessed 1–7 times prior to 27 weeks gestation with Automated Self-Administered 24-hour dietary recalls. We calculated total energy, macro- and micronutrients, and MyPyramid Equivalents with the USDA Food and Nutrition Data System for Research. Recalls with daily energy <450 kilocalories or >5000 kilocalories were excluded (n=35, 1.6% of all recalls). We used the National Cancer Institute mixed-effects model to estimate typical intake, adjusting for pre-pregnancy body mass index (BMI), gravidity, and prenatal smoking [9]. MyPyramid Equivalents were used to calculate the Healthy Eating Index (HEI; scores range 0–100), an indicator of diet quality [10]. Physical activity level (metabolic equivalent task (MET) hours/week) was assessed with the Pregnancy Physical Activity Questionnaire [11]. Perceived stress and depressive symptoms were assessed with the 10-item Perceived Stress Scale

(scores range 0–40) [12] and the Edinburgh Postnatal Depression Scale (scores range 0–30) [13], respectively.

Clinical routine GDM screening occurred at 24–28 weeks (mean 25.7 weeks) with a two-step procedure (50g glucose challenge + 100g oral glucose tolerance test) and results were abstracted from medical records. We classified women as having prenatal dysglycaemia when they had an abnormal glucose challenge, 1 abnormal value on the glucose tolerance test according to Carpenter and Coustan criteria, or a clinical diagnosis of GDM.

Covariate data (age, race/ethnicity, history of GDM, maternal family history of diabetes) were collected via self-report. Pre-pregnant BMI was abstracted from the medical record (91%) or calculated from self-reported data (9%). Weekly rates of gestational weight gain were predicted using mixed models as described previously [14]. Gestational weight gain through 26 weeks was classified according to the 2009 Institute of Medicine guidelines, which recommend a 1.1–4.4 lb gain in the first 13 weeks for all women and BMI-specific weekly rates of gain for the remaining 27 weeks (e.g. 0.4–0.6 lbs/week for BMI  $\geq 30$ ).

### Statistical Analyses

Analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC, USA). We determined the threshold for each modifiable factor using the Youden index [15]. For each predictor, the cut-off for categorization was chosen as the value which maximized the *J* statistic (sensitivity + specificity – 1) from a logistic regression with odds of dysglycaemia as outcome and the specified factor as predictor. Women received one point for each optimal factor: diet quality (HEI  $\geq$  threshold), physical activity level (MET-hours/week  $\geq$  threshold), mental health status (stress  $<$  threshold and depression scores  $<$  13 [the diagnostic threshold for probable depression [13]]).

Odds ratios (OR) and 95% confidence intervals (95%CI) of prenatal dysglycaemia for each individual modifiable factor and the score were assessed with logistic regression in unadjusted and adjusted models. Covariates included age (continuous), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, other), pre-pregnant BMI (continuous), GDM history (yes/no), and maternal family history of diabetes (yes/no). We considered  $p < 0.05$  statistically significant.

### Results

Complete data were available for 832 of 899 eligible participants (4 fetal deaths, 32 missing lifestyle data, 18 missing GDM history, 13 missing diabetes family history). There were no clinically significant differences between the full cohort ( $n=1410$ ), the eligible cohort ( $n=899$ ), and the final analytic cohort ( $n=832$ ) (data not shown). Sample characteristics are presented in Table 1.

The Youden index identified the following factor thresholds: HEI diet quality  $\geq 64$ , physical activity level  $\geq 170$  MET-hours/week, and stress  $< 6$ . In individual analyses, we observed a significantly reduced risk of dysglycaemia for physical activity level (adjusted OR 0.67, 95%CI 0.44–1.00), but not diet quality (adjusted OR 0.71, 95%CI 0.45–1.10) or mental

health status (adjusted OR 0.77, 95%CI 0.46–1.29). For the score, we observed a statistically significant dose-response association with dysglycaemia risk (adjusted  $p$  for trend = 0.01; Fig. 1). Compared to women with a score of 0, women with a score of 3 had a 73% reduced risk of dysglycaemia (adjusted OR 0.27, 95%CI 0.08–0.95). Further adjustment for gestational weight gain through 26 weeks gestation did not substantially change the results.

## Discussion

We found that having multiple positive modifiable factors during pregnancy is associated with a 73% reduced risk of prenatal dysglycaemia in a sample of ethnically-diverse pregnant women. When examined individually, physical activity levels were marginally associated with reduced risk, while diet quality and mental health status were not. However, when examined collectively, the synergistic association of multiple modifiable factors with dysglycaemia was pronounced. Our results were independent of pre-pregnant BMI and not affected by further adjustment for gestational weight gain, suggesting that these modifiable factors in pregnancy may be related to glucose tolerance regardless of maternal weight and weight gain.

Our study is consistent with the Nurses' Health Study, which reported that a healthy pre-pregnancy lifestyle (non-smoker, BMI <25, top 40% of the Alternate HEI diet index, and moderate physical activity 150 min/week) was associated with a reduced risk of GDM by 52% [4]. Results of other observational studies have been mixed [16], potentially because most examined modifiable factors individually rather than collectively. Prenatal intervention trials have had varying degrees of success with diet, physical activity, or combined interventions [17]. The two largest intervention trials (LIMIT [18] and UPBEAT [19]) did not reduce GDM among overweight and/or obese pregnant women despite improvements in diet and physical activity. The smaller DALI Lifestyle Pilot study also observed no difference in fasting glucose at 24–28 weeks in obese women receiving diet, physical activity, or combined interventions [20].

There are several reasons why our results, which suggest that modifiable factors in early-to-mid pregnancy are related to dysglycaemia risk, differ from intervention trials, which have been largely ineffective in preventing dysglycaemia. First, the improvements in diet or physical activity achieved in intervention trials may not have been sufficient to influence glucose tolerance. For example, in the LIMIT trial, mean physical activity was low (<125 MET-hours/week) at baseline and declined in both the intervention and control groups as pregnancy progressed [18]. These activity levels were substantially lower than our data-driven physical activity threshold (170 MET-hours/week), suggesting that even a 6 MET-hour/week treatment effect (equal to 15–20 minutes of walking/day) was insufficient. Second, the timing of interventions may be important. Our results and those from the Nurses' Health Study indicate that pre-pregnancy and early pregnancy lifestyle factors are related to risk of dysglycaemia. However, intervention studies face challenges in recruiting women early in pregnancy, obtaining baseline measurements, and then delivering an intervention quickly enough to produce meaningful changes in behaviors and outcomes by 24–28 weeks gestation. Interventions that begin at the first prenatal appointment, or even prior to conception for high-risk women, may have more potential for success.

Our study is limited by self-reported data, although prospectively-administered and validated questionnaires reduced potential for recall bias. The small sample size prevented examination of GDM separately from dysglycaemia; however, sub-clinical prenatal glucose intolerance is associated with adverse maternal and fetal outcomes [2, 3], and our combined approach suggests that an increasing number of optimal prenatal modifiable factors is related to all degrees of dysglycaemia risk. Study strengths include the diverse sample, prospective data collection, and consideration of multiple modifiable factors and pre-pregnancy characteristics.

In conclusion, we found that women with multiple positive modifiable factors in early-to-mid pregnancy have a significantly reduced risk of prenatal dysglycaemia. Our results support the hypothesis that modifiable factors in early pregnancy are associated with the risk of prenatal dysglycaemia.

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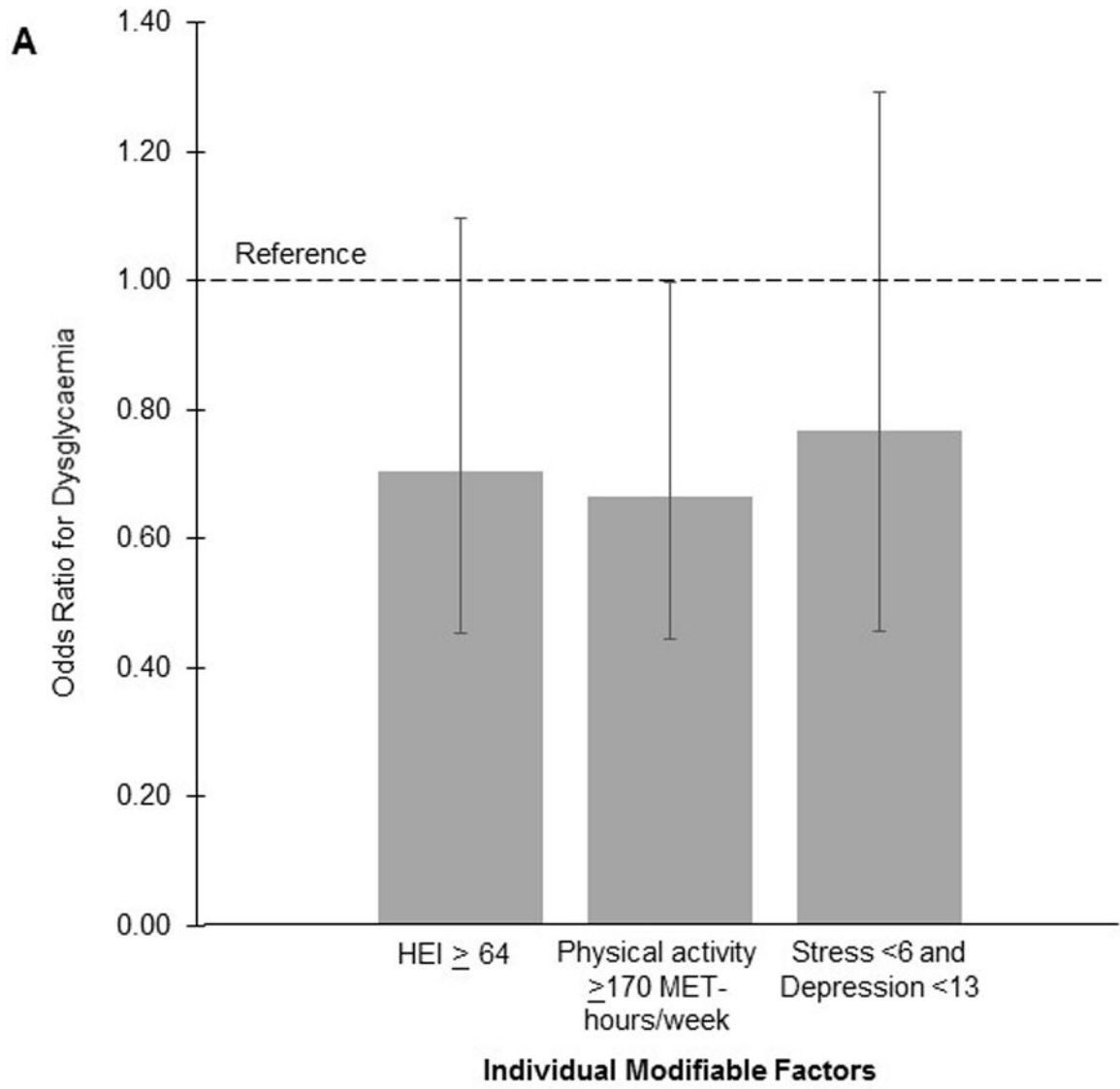
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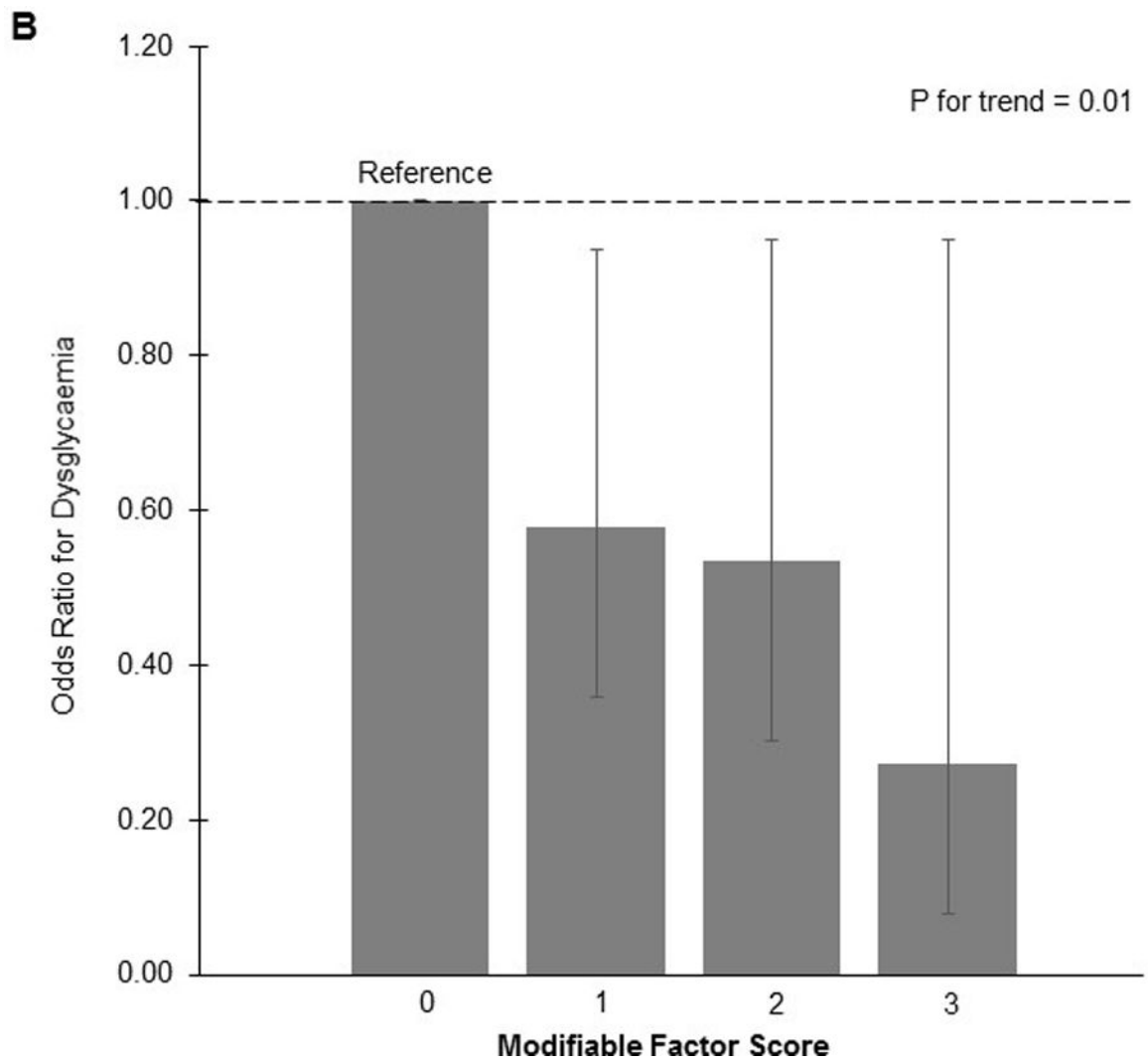
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**Novelty statement**

- We prospectively examined the association between multiple modifiable factors (diet quality, physical activity level, mental health status) in early to mid-pregnancy with risk of prenatal dysglycaemia among 832 women.
- Compared to having no optimal modifiable factors, having any 1 optimal modifiable factor reduced the risk of dysglycaemia by 42% (OR 0.58, 95% CI 0.36–0.94), and having all 3 optimal modifiable factors reduced the risk by 73% (OR 0.27, 95% CI 0.08–0.95).
- Our results support the hypothesis that modifiable factors in pregnancy are associated with the risk of prenatal dysglycaemia.







**Fig. 1.** Odds of prenatal dysglycaemia according to individual modifiable factors (A) and total score (B) in early to mid-pregnancy

**Table 1**

## Sample characteristics

	Normal n=713	Dysglycaemia* n=119	p-value
Age (years)	28.0 (6.1)	29.5 (5.8)	0.01
Pre-pregnancy BMI (kg/m <sup>2</sup> )	25.5 (6.2)	27.6 (7.0)	0.003
Race (n)			
Non-Hispanic White	403 (57%)	55 (46%)	0.05
Hispanic	170 (24%)	39 (33%)	
Black	100 (14%)	14 (12%)	
Other	40 (6%)	11 (9%)	
History of GDM (n)	10 (1%)	8 (7%)	0.0002
Family history of T2DM (n)	67 (9%)	22 (18%)	0.003
Education (n)			
Less than 12th grade	92 (13%)	18 (15%)	0.82
High school degree or GED	120 (17%)	19 (16%)	
Some college or associate's degree	168 (24%)	30 (25%)	
Four years of college (BA, BS)	170 (24%)	23 (19%)	
Graduate degree (Master's, PhD)	163 (23%)	29 (24%)	
Employment (n)			
Full-time student	67 (9%)	13 (11%)	0.70
Part-time student	46 (6%)	5 (4%)	
Currently employed	405 (57%)	76 (64%)	0.20
Household income (n)			
< \$40,000	200 (28%)	40 (34%)	0.26
\$40,000 – \$70,000	121 (17%)	24 (20%)	
> \$70,000	136 (19%)	16 (13%)	
Missing or don't know	256 (36%)	37 (31%)	
Gravidity (n)	1.3 (1.5)	1.4 (1.5)	0.45
Smoking in pregnancy (n)	52 (7%)	7 (6%)	0.58
Gestational weight gain (kg) †	7.4 (4.0)	6.2 (4.2)	0.01
Inadequate (n)	130 (18%)	35 (29%)	0.01
Adequate (n)	203 (28%)	33 (28%)	
Excessive (n)	380 (53%)	51 (43%)	
Lifestyle factors (n)			
HEI 64	300 (42%)	41 (34%)	0.11
Physical activity 170 MET-hours/week	375 (53%)	51 (43%)	0.05
Stress <6 and Depression <13	167 (23%)	21 (18%)	0.14
Lifestyle score (n)			
0	142 (20%)	38 (32%)	0.02
1	343 (48%)	52 (44%)	
2	185 (26%)	26 (22%)	
3	43 (6%)	3 (3%)	

Values are mean (SD) or n (%). P-values determined with t-tests for continuous variables and the Cochran-Mantel-Haenszel test for categorical variables. BMI; body mass index; GDM, gestational diabetes; T2DM, type 2 diabetes mellitus; HEI, Healthy Eating Index; MET, metabolic equivalent of task; Stress, Perceived Stress Scale; Depression, Edinburgh Postnatal Depression Scale.

\* Dysglycaemia defined as abnormal glucose screen, 1 abnormal value on the 100g oral glucose tolerance test, or a clinical diagnosis of gestational diabetes.

† Classified according to the 2009 Institute of Medicine recommendations through 26 weeks gestation.

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