



Prenatal Maternal Objective and Subjective Stress Exposures and Rapid Infant Weight Gain

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Objectives To evaluate the associations between 3 prenatal stress exposures and rapid infant weight gain.

Study design Participants were 162 maternal–child dyads drawn from a nonrandomized controlled trial evaluating a prenatal intervention for reducing women’s stress and excessive gestational weight gain and subsequent longitudinal observational study of offspring outcomes. Participants were predominantly low-income and racial or ethnic minorities, and mothers were overweight or obese prepregnancy. Primary exposures were objective stress exposures (number of stressful life events) and subjective distress (maternal perceived stress and depressive symptoms) during pregnancy. The primary outcome was rapid infant weight gain from birth to 6 months, assessed via birth records and in-person anthropometry measurements.

Results In total, 28% of the sample (N = 40) met criteria for rapid infant weight gain. In adjusted models, exposure to prenatal stressful life events was associated with increased odds of rapid infant weight gain (OR 1.40, 95% CI 1.07-1.83, $P = .014$). Neither prenatal perceived stress (OR 0.47, 95% CI 0.16-1.37, $P = .17$) nor depressive symptoms (OR 0.89, 95% CI 0.76-1.03, $P = .13$) were significantly associated with rapid infant weight gain.

Conclusions Each additional stressful life event a woman experienced during pregnancy was associated with 40% greater odds of rapid infant weight gain. Future research should evaluate whether prenatal interventions that focus on reducing exposure to stressful events prevent rapid infant weight gain. (*J Pediatr* 2020;222:45-51).

In the US, more than one-quarter of children aged 2-5 years meet criteria for overweight, and nearly 1 in 7 meets criteria for obesity.¹ Obesity rates in this age group increased significantly in 2015-2016.¹ The negative long-term correlates and consequences of child overweight and obesity are well-documented and include coronary heart disease, type 2 diabetes, and hypertension.^{2,3} Efforts to identify early life risk factors for childhood obesity suggest that the rate of weight gain during infancy may play an important role. Rapid infant weight gain predicts childhood obesity⁴ and is associated with determinants of cardiovascular disease and type 2 diabetes, such as greater body fat percentage and central adiposity and reduced insulin sensitivity.⁵ Thus, it is important to identify potentially malleable risk factors of rapid infant weight gain.

Consistent with the developmental origins of health and disease theory,⁶ prenatal exposure to nutritional imbalances or environmental chemicals has been linked to offspring health outcomes,⁷ including obesity.⁸ In addition, there is increasing evidence that maternal prenatal psychological factors, such as stress, may “program” fetal development via maternal–placental–fetal endocrine and immune processes.^{9,10} For example, exposure to a natural disaster during early pregnancy was associated with greater increases in offspring body mass index (BMI) z scores from 2.5 to 4 years,¹¹ and prenatal exposure to subjective psychological distress was associated with greater fat mass index at 10 years.¹²

Our goal was to evaluate the associations between prenatal objective stress exposures (stressful life events) and subjective distress (perceived stress and depressive symptoms) with rapid infant weight gain from birth to 6 months. Based on previous research, we predicted that prenatal maternal stress would be associated with rapid infant weight gain. Previous research suggests that these prenatal exposures may have differential effects on offspring outcomes,^{10,12-14} and the current study provided the unique opportunity to examine all three exposures within one longitudinal study sample. Prenatal stress and depression previously have been linked to low birth weight^{15,16} and low birth weight is associated with catch-up growth.¹⁷ Therefore, to examine the independent contribution of

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BMI Body mass index

prenatal distress, we adjusted for covariates shown or theorized to impact infant growth, such as birth weight.

Methods

Participants had risk factors for child overweight or obesity.^{1,18} They were drawn from a nonrandomized controlled trial evaluating a prenatal mindfulness-based intervention for reducing women's stress and excessive gestational weight gain relative to usual care ([ClinicalTrials.gov NCT01307683](https://clinicaltrials.gov/ct2/show/study/NCT01307683)).^{19,20} Inclusion criteria were (1) English speaking, (2) pregnant 12-24 weeks of gestation (mean 17.19, SD 4.14), (3) age 18-45 years, (4) household income <500% of the federal poverty guidelines (\$91 550 for a family of 3 in 2010), which is lower-income considering that the area from where participants were drawn has one of the highest costs of living in the country,²¹ and (5) self-reported prepregnancy BMI of 25-41 kg/m². Exclusion criteria were (1) medical conditions that might affect gestational weight gain; (2) current meditation practice more than once per week; (3) multiple gestation; (4) currently taking weight-loss drugs, medications for diabetes, antidepressants, antipsychotics, opiate drugs, or corticosteroids; (5) history of gastric bypass surgery; and (6) substance abuse, mental health, or medical condition that would affect metabolism, body composition, or participation in the intervention (eg, diabetes, eating disorder, polycystic ovarian syndrome treated with metformin). Participants with live births were invited to participate in a longitudinal observational study of offspring cardiometabolic risk factors and developmental outcomes.¹⁴

Objective stress exposures during pregnancy were measured via a retrospective interview at 12 months after delivery (mean 11.88 months, SD 5.52). Items were drawn from the Centers for Disease Control and Prevention Pregnancy Risk Assessment Monitoring System,²² and adapted to ask about events that occurred during pregnancy. The 14 events included both acute and chronic stressors. Response options included "yes" and "no." A total continuous score was computed by summing the number of "yes" responses. Event measures are thought to have limited recall bias and be accurate over a span of years.²³

Subjective distress was measured using the 10-item Perceived Stress Scale, which assesses the extent to which situations in the last month were appraised as stressful. A mean score was computed by summing items and dividing by the number of completed items. Greater scores indicate more stress (Cronbach $\alpha = 0.91$). Although depression and stress are unique constructs, they overlap, and it is important to consider their relative potential contributions to rapid infant weight gain. Accordingly, this study included the 9-item Patient Health Questionnaire to evaluate maternal depressive symptom severity. A total score was computed by summing all items. Higher scores indicate more depression (Cronbach $\alpha = 0.83$). Subjective distress measures were collected, on average, in the second trimester at the postintervention

time point (mean 25.76 weeks of gestation, SD 4.55) and at 6 months postpartum.

Birth weight was abstracted from medical records. At 6 months, anthropometric measures were performed by trained individuals in teams of 2; weight was measured using a Seca scale (model 383; Seca, Chino, California) and length was measured using the Infant/Child Height-Length Shorr-Board (Weigh and Measure, LLC, Olney, Maryland). Measures were repeated twice, and a third time if the first 2 measurements were incongruent (eg, weight difference >0.2 kg or length difference >0.5 cm); then, discarding the incongruent measurement, we calculated an average value for use in analysis. Weight measurements were used to derive age- and sex-specific weight according to World Health Organization 2006 growth charts for girls and boys.²⁴ Rapid infant weight gain was defined as a greater than 0.67 increase in weight-for-age z score from birth to 6 months, as in previous research.⁵

Adjusted models included covariates theorized or shown to impact infant growth (ie, poverty, maternal prepregnancy BMI, parity, participation in a mindfulness intervention, gestational weight gain, gestational age at delivery, birth weight, infant ethnicity, infant race, breastfeeding status, and introduction to solid foods before 6 months). To increase our confidence that the effect of prenatal maternal psychological distress was not better accounted for by postnatal psychological distress, we adjusted for depressive symptom severity or perceived stress at 6 months postpartum in models evaluating prenatal depressive symptom severity or perceived stress, respectively.

Statistical Analyses

The distribution of the prenatal stressful life events variable was positively skewed. However, results did not differ substantively when we used a square root transformation. Therefore, analyses reported in this work use the untransformed continuous variable for ease of interpretation. Missing data were evident for several study variables, as is typical in longitudinal research. A nonsignificant Little's missing completely at random test suggested that data were missing completely at random ($\chi^2 = 680$, $P = .996$). We also found a limited number of significant associations between participant characteristics and missingness, suggesting that data were missing at random. Therefore, multiple imputation was warranted. Outcome variables, predictor variables, covariates, and variables related to missingness were included as auxiliary variables in the multiple imputation models,²⁵ and 25 datasets were imputed and combined.²⁶ All data analyses were performed using SPSS, version 25 (IBM Corp, Armonk, New York). Descriptive statistics were used to characterize the sample. Binary logistic regression models were used to evaluate the prospective associations between prenatal maternal psychological factors (ie, prenatal stressful life events, perceived stress, and depressive symptoms) and rapid infant weight gain. Models examined each prenatal maternal psychological factor separately, and a fourth model examined prenatal stressful life events and

perceived stress together to evaluate the effect of prenatal stressful life events over and above perceptions of stress. Findings for unadjusted analyses are presented first, followed by findings for fully adjusted models including all covariates.

Results

A total of 215 pregnant women enrolled in the nonrandomized controlled trial evaluating a prenatal mindfulness-based intervention relative to usual care. Of these, 13 were ineligible to participate in the subsequent longitudinal observational study of offspring cardiometabolic risk factors and developmental outcomes due to study withdrawal, miscarriage or fetal death, or lost-to-follow-up. Of the 202 women who were invited to participate in the subsequent longitudinal observational study, 162 consented to participate. As noted previously, these women did not significantly differ in baseline characteristics from those who did not consent to

participate.¹⁴ Given the documented unique patterns of association between gestational diabetes and our outcomes,²⁷ and our desire to examine psychological influences within normal gestations, 18 offspring of mothers with gestational diabetes were excluded from analyses. Thus, the final analytic sample was 144 dyads. Detailed participant characteristics are presented in **Table I**. Our recruitment strategy has been detailed previously.²⁸

Unadjusted Models

Prenatal stressful life events were associated with increased odds of rapid infant weight gain (OR 1.42, 95% CI 1.15-1.75, $P = .001$). Neither prenatal perceived stress nor depressive symptom severity was significantly associated with odds of rapid infant weight gain (modeled separately: perceived stress OR 0.83, 95% CI 0.48-1.44, $P = .50$; depressive symptom severity OR 0.98, 95% CI 0.90-1.08, $P = .71$). The significant association between prenatal stressful life

Table I. Maternal and infant characteristics

Characteristics	Available N	Imputed mean (SD) or % (n)		
		Full sample	Rapid infant weight gain (n = 40)	No rapid infant weight gain (n = 104)
Maternal characteristics				
Percent of federal poverty level	138	141.39 (135.50)	116.46 (143.17)	151.04 (139.94)
Multiparous	144	54.17% (78)	39.90% (15.96)	59.65% (62.04)*
Prepregnancy BMI	144	30.77 (5.00)	30.74 (5.37)	30.79 (4.92)
Assigned to prenatal mindfulness intervention	144	56.25% (81)	48.30% (19.32)	59.32% (61.68)
Gestational weight gain, pounds	136	31.12 (18.52)	31.48 (20.7)	30.99 (17.81)
Maternal psychological exposures				
Prenatal depressive symptom severity [†]	119	5.65 (4.96)	5.40 (4.60)	5.75 (5.22)
Prenatal perceived stress	124	1.68 (0.74)	1.61 (0.76)	1.70 (0.74)
Count of stressful life events during pregnancy [‡]	134	2.83 (2.16)	3.93 (2.56)	2.39 [§] (1.92)
Postpartum depressive symptom severity [†]	124	4.51 (4.33)	4.97 (4.90)	4.33 (4.26)
Postpartum perceived stress	125	1.52 (0.78)	1.47 (0.75)	1.55 (0.81)
Infant characteristics				
Gestational age at delivery, wk	144	39.61 (1.43)	39.11 (2.09)	39.81* (1.04)
Preterm	144	4.86% (7)	13.30% (5.32)	1.62% (1.68)*
Birth weight, kg	144	3.34 (0.48)	3.09 (0.54)	3.44 [§] (0.42)
Birth weight percentile (WHO)	144	53.37 (26.82)	38.95 (27.24)	58.98 [§] (24.95)
Small for gestational age	144	9.72% (14)	16.40% (6.56)	7.15% (7.44)
Female sex [¶]	144	55.56% (80)	53.40% (21.36)	56.38% (58.64)
Race				
Black or African American		30.56% (44)	32.60% (13.04)	29.77% (30.96)
White		16.67% (24)	10.80% (4.32)	18.92% (19.68)
Multiracial or other, Asian, Native American, Native Hawaiian		52.78% (76)	57.50% (23.00)	50.96% (53.00)
Hispanic ethnicity	144	41.67% (60)	36.40% (14.56)	43.69% (45.44)
Breastfeeding status at 6 mo				
Exclusively breastfeeding		35.94% (51.76)	28.80% (11.52)	38.69% (40.24)
Both breast and formula feeding		16.08% (23.16)	18.40% (7.36)	15.19% (15.80)
Started and stopped breastfeeding		41.17% (59.28)	46.90% (18.76)	38.96% (40.52)
Did not breastfeed		6.81% (9.80)	6.80% (2.72)	6.81% (7.08)
Introduction to solid foods before 6 months	132	38.81% (55.88)	43.40 (17.36)	37.04 (38.52)

WHO, World Health Organization.

*Independent samples t test or χ^2 $P < .05$.

[†]9-item Patient Health Questionnaire scores from 1 to 4 suggest minimal depression, 5 to 9 suggest mild depression, 10 to 14 suggest moderate depression, 15 to 19 suggest moderately severe depression, and 20 to 27 suggest severe depression.

[‡]The list of 14 stressful events included a close family member was sick and hospitalized; participant was separated or divorced from partner; participant was homeless; partner lost a job; participant lost a job; participant argued with partner a lot more than usual; partner said he did not want pregnancy; participant had a lot of bills she couldn't pay; participant was involved in a physical fight; participant was the victim of a crime; participant lost home due to fire, flood, or other disaster; partner went to jail; someone important had a bad problem with drinking or drugs; or someone important to the participant died.

[§] $P < .001$.

[¶]In this sample, boys with rapid infant weight gain weighed an average of 20.01 pounds at 6 months, compared with 18.16 pounds among boys without. Girls with rapid infant weight gain weighed an average of 19.07 pounds at 6 months, compared with 15.99 pounds among girls without.

Table II. Bivariate correlations between the main predictor variables, covariates, and outcome variable

Covariate	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.
1. Count of stressful life events	1.00													
2. Perceived stress	0.21*	1.00												
3. Depressive symptom severity	0.25 [†]	0.61 [‡]	1.00											
4. Assigned to prenatal mindfulness intervention	-0.16	-0.11	-0.25 [†]	1.00										
5. Percent of federal poverty level	-0.25 [†]	-0.02	-0.05	-0.04	1.00									
6. Prepregnancy BMI	0.13	0.03	-0.07	-0.10	-0.13	1.00								
7. Multiparous	-0.09	0.08	-0.002	0.09	-0.09	0.02	1.00							
8. Gestational weight gain (pounds)	-0.01	-0.15	0.05	0.05	-0.01	-0.27*	-0.25 [†]	1.00						
9. Gestational age at delivery, wk	-0.23 [†]	-0.11	-0.11	-0.01	0.23 [†]	0.04	-0.07	0.09	1.00					
10. Birth weight	-0.18*	-0.08	-0.001	0.13	0.11	-0.03	0.03	0.12	0.53	1.00				
11. Hispanic ethnicity	0.14	0.02	0.04	0.09	-0.09	-0.06	-0.04	-0.03	0.03	0.14	1			
12. Perceived stress at 6 mo postpartum	0.09	0.64 [‡]	0.46 [‡]	-0.02	-0.07	0.05	0.09	-0.02	-0.19*	0.05	0.11	1.00		
13. Depressive symptom severity at 6 months postpartum	0.17*	0.58 [‡]	0.59 [‡]	-0.13	-0.15	-0.03	0.14	-0.05	-0.13	0.002	0.03	0.63 [‡]	1.00	
14. Rapid infant weight gain	0.33 [‡]	-0.06	-0.03	-0.11	-0.12	-0.005	-0.18*	0.01	-0.22 [†]	-0.33 [‡]	-0.07	-0.05	0.07	1.00

*Correlation is significant at .05 level.
[†]Correlation is significant at .01 level.
[‡]Correlation is significant at .001 level.

events and rapid infant weight gain remained when adjusting for perceived stress (prenatal stressful life events OR 1.47, 95% CI 1.18-1.84, *P* = .001; prenatal perceived stress OR 0.64, 95% CI 0.34-1.18, *P* = .15). **Table II** shows bivariate correlations.

Of note, prenatal stressful life events, but not prenatal perceived stress or depressive symptom severity, were significantly associated with earlier gestational age at delivery and lower birthweight.

Adjusted Models

Adjusted models included all covariates (herein and **Table III**). Results did not substantively change when adding covariates in adjusted analyses. Prenatal stressful life events were associated with increased odds of rapid infant weight gain (OR 1.40, 95% CI 1.07-1.83, *P* = .014). Neither prenatal perceived stress nor depressive symptom severity was significantly associated with rapid infant weight gain (modeled separately: perceived stress OR 0.47, 95% CI 0.16-1.37, *P* = .17; depressive symptom severity OR 0.89, 95% CI 0.76-1.03, *P* = .13). The significant association between prenatal stressful life events and rapid infant weight gain remained when adjusting for prenatal perceived stress (prenatal stressful life events OR 1.46, 95% CI 1.10-1.94, *P* = .008; perceived stress OR 0.37, 95% CI 0.12-1.15, *P* = .09; **Table III**). Importantly, the association between prenatal stressful life events and rapid infant weight gain remained significant after adjusting for gestational age at delivery and birthweight.

Table III. Adjusted logistic regression model evaluating prenatal stressful live events and perceived stress as predictors of rapid infant weight gain

Predictor	OR	95% CI		<i>P</i> value
		Lower	Upper	
Prenatal perceived stress	0.37	0.12	1.15	.09
Stressful life events	1.46	1.10	1.94	.01
Percent of federal poverty level	1.00	0.99	1.00	.62
Self-reported prepregnancy BMI	0.94	0.85	1.04	.24
Multiparous	2.33	0.85	6.37	.10
Mindfulness group	0.75	0.29	1.96	.56
Gestational weight gain, pounds	0.99	0.96	1.03	.66
Gestational age at delivery, wk	1.05	0.67	1.64	.84
Birth weight, kg	0.13	0.03	0.58	.01
Infant Latino/a	0.43	0.13	1.40	.16
Infant race				
White (reference)	—	—	—	—
Black or African American	1.40	0.26	7.56	.70
Multiracial or other, Asian, Native American, Native Hawaiian	2.62	0.56	12.14	.22
Breastfeeding status				
Exclusively breastfeeding (reference)	—	—	—	—
Both breast- and formula-feeding	1.57	0.37	6.59	.54
Started and stopped breastfeeding	1.13	0.34	3.73	.85
Never breastfed	0.47	0.04	5.15	.53
Introduction to solid foods before 6 mo	1.54	0.53	4.42	.42
6 mo postpartum perceived stress	1.50	0.52	4.28	.45

Discussion

In a sample of predominantly low-income and racial/ethnic minority women and their infants, we found that the number of stressful life events a woman experienced during her pregnancy was associated with increased risk that her infant would experience rapid weight gain from birth to 6 months of age. For each additional stressful life event a woman experienced during her pregnancy, her infant had 40% greater odds of rapid weight gain from birth to 6 months. Prenatal stressful life events are far too common. In a pooled analysis of several states, more than 70% of pregnant women reported one or more stressful life event during pregnancy,²⁹ and prenatal stressful life events are particularly common among low-income women.³⁰

Although not the primary focus of the current investigation, a critical finding is that, consistent with previous

evidence, we found that maternal prenatal stressful life events were associated with lower infant birth weight,³¹⁻³³ and infants with lower birth weight had increased odds of rapid infant weight gain.¹⁷ Of central importance for the current investigation, the association between stressful life events and rapid infant weight gain was statistically significant even after we adjusted for birth weight and gestational age, suggesting that this association was not driven by catch-up growth among infants of low birth weight nor fully mediated by birth weight or gestational age. The current study addresses an important gap by evaluating the association between prenatal stressful life events and infant weight gain.

Neither subjective perceptions of stress nor depressive symptom severity assessed in the second trimester were significantly associated with increased odds of rapid infant weight gain. However, it would be premature to conclude that these initial findings represent a true dissociation in the effect of objective stress vs subjective distress on rapid infant weight gain, particularly as subjective distress was modeled at a single time point. It is well-established that subjective stress and depressive symptoms have adverse consequences for maternal–fetal health more broadly,³⁴ and other work in our laboratory has found maternal perceptions can moderate the role of objective prenatal stressors on offspring health.¹⁴ To this end, many prenatal mental health interventions focus on modifying subjective responses to stressful experiences. Our findings suggest that future research also should evaluate whether prenatal interventions that focus on reducing exposure to stressful events prevent rapid infant weight gain. At a broad level, public health programs designed to prevent homelessness or provide support to pregnant women in need, such as the Temporary Assistance to Needy Families or the Special Supplemental Nutrition Program for Women, Infants, and Children programs, may help reduce risk for rapid infant weight gain.³⁵ At the individual level, some counseling interventions, such as behavioral activation therapy for depression, include intervention components that aim to decrease exposure to negative life events through active problem-solving.^{36,37} Although they have been adapted for perinatal populations, their effects on infant outcomes are unknown. In addition, such interventions are likely to impact only a small proportion of the stressors that were assessed in the objective stressor measure and that socially disadvantaged women face.

This study addresses an important gap in the literature, which has heretofore not examined the association between prenatal maternal psychological factors and rapid infant weight gain. Findings lend further evidence to the hypothesis that maternal prenatal psychological factors can “program” fetal development. Although we were unable to investigate the mechanisms whereby exposure to prenatal stressful life events was associated with increased risk for rapid infant weight gain, a substantial literature points to biological mechanisms for these intergenerational effects. Comprehensive reviews suggest elevated maternal stress can impact maternal hypothalamic–pituitary–adrenocortical axis func-

tion in a manner that affects offspring metabolism and adiposity gain in utero and in early life,³⁸ and research implicates immune and endocrine functioning,⁹ epigenetic marks,³⁹ and placental function⁴⁰ in these processes.⁴¹⁻⁴³ Nonbiological factors, such as such as parental feeding style,⁴⁴⁻⁴⁷ child sedentary behavior,⁴⁸⁻⁵⁰ and child sleep,⁵¹ which can be influenced by experiences of stress, also have been found to associate with child growth⁵² and may play a role in the associations found here.

Participants were predominantly racial and ethnic minorities¹ and the infants were the offspring of mothers who were overweight or obese during pregnancy.¹⁸ However, it is important to note that our sample characteristics are increasingly representative of the US population: approximately two-thirds of adult women are overweight or obese, and nearly one-half begin pregnancy overweight or obese.^{53,54} Second, more than one-half of participants had received a mindfulness intervention. Of note, intervention assignment was not significantly associated with rapid infant weight gain in any of the adjusted analyses. Further, the intervention was not associated with statistically significant reductions in rates of excessive gestational weight gain,²⁰ thus potentially mitigating concerns about its effects on infant weight gain. Finally, rates of exclusive breastfeeding at 6 months are greater than the national average as reported in the Center for Disease Control Breastfeeding Report Card, perhaps reflecting local public health efforts to promote breastfeeding.

A limitation of our study is that depressive symptoms were assessed using a well-validated self-report questionnaire^{55,56} instead of using a clinical diagnostic interview. Exposure to prenatal stressful life events was measured retrospectively at approximately 12 months postpartum and referred broadly to events that occurred during pregnancy. The exact timing of such events is unknown. In contrast, the subjective measures assessed symptoms of stress and depression during the second trimester specifically. Subjective distress measures were not conceptualized specifically as subjective responses to the prenatal stressful life events that were measured by the Pregnancy Risk Assessment Monitoring System. The subjective measures were modeled at a single time point, and it is therefore unknown whether symptoms experienced earlier or later during pregnancy, or experienced chronically over the course of pregnancy, impact risk for rapid infant weight gain. Finally, weight gain in later childhood is also important to assess and may have different maternal and behavioral determinants. Limitations notwithstanding, strengths include the use of 3 distinct measures of prenatal maternal psychological distress which allowed for comparison across constructs and inclusion of a sample at elevated risk of rapid infant weight gain.

In a diverse sample of maternal–infant dyads, we found that exposure to stressful events during pregnancy was associated with increased risk of rapid infant weight gain from birth to 6 months. Although evidence is mixed, previous research suggests that a rapid pace of weight gain during

infancy predicts child obesity and other adverse health and disease outcomes across the life course. Current findings suggest that preventive interventions targeting exposure to prenatal stressful life events may help reduce risk for rapid infant weight gain. ■

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