

Racial Disparities in Mental Health Outcomes Among Women With Early Pregnancy Loss

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OBJECTIVE: To explore the relationship between race and depression symptoms among participants in an early pregnancy loss clinical trial.

METHODS: We performed a planned secondary analysis of a randomized trial by comparing treatments for medical management of early pregnancy loss. We hypothesized that Black participants would have higher odds of risk for major depression (measured with the CES-D [Center for Epidemiological Studies-Depression] scale) 30 days after early pregnancy loss treatment when compared with non-Black participants. We analyzed the data as a cohort, with the primary exposure being race and secondary exposure being high adverse childhood experience scores (measured with the Adverse Childhood Experience scale). Our primary outcome was risk for major depression

(score of 21 or higher on the CES-D scale) 30 days after early pregnancy loss treatment.

RESULTS: Three hundred participants diagnosed with a nonviable intrauterine pregnancy from 5 to 12 weeks of gestation were randomized as part of the original trial from May 2014 to April 2017. Of 275 respondents included in this analysis, 120 [44%] self-identified as Black and 155 [56%] self-identified as non-Black. After early pregnancy loss treatment, 65 [24%] participants were at risk for major depression. Black participants had an increased risk for major depression (57%) after early pregnancy loss treatment compared with non-Black participants (43%; odds ratio [OR] 2.02; 95% CI 1.15–3.55). After adjustment for risk for baseline depression, adverse childhood experience score, and parity, the odds of risk for major depression 30 days after pregnancy loss treatment remained higher for Black participants when compared with non-Black participants (OR 2.02; 95% CI 1.15–3.55; adjusted OR 2.48; 95% CI 1.28–4.81).

CONCLUSION: Overall, approximately one quarter of women who experience an early pregnancy loss are at an increased risk for major depression 30 days after treatment. This risk is about twice as high for Black women compared with non-Black women. There is a need for appropriate mental health resources for women undergoing early pregnancy loss care.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, NCT02012491.

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Approximately one in four women will experience a pregnancy loss in her lifetime.^{1,2} After a pregnancy loss, many women will experience psychological sequelae, including higher levels of depression, anxiety, and posttraumatic stress disorder compared with women who experienced no pregnancy complications, and these effects can persist up to 9 months after the loss.^{3–7}

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Maternal morbidity and mortality rates persistently highlight racial disparities in the United States, regardless of socioeconomic or educational status,^{8–10} and Black women specifically experience pregnancy loss at higher rates than other racial or ethnic groups.¹¹ Black women are more likely to experience higher rates of perinatal depression when compared with other racial groups in the United States.^{9,12–16} Other variables, such as stress and adverse childhood experiences, may mediate some of these associations, because they are also more prevalent among Black people when compared with other racial groups.^{17–23} Higher adverse childhood experience scores are associated with a greater likelihood of pregnancy loss, preterm birth, and perinatal depression,^{24–26} but the relationship between race, adverse childhood experience, and pregnancy-related morbidity has only recently been explored.^{24,27}

We sought to characterize the relationship between race, adverse childhood experience, and adverse mental health outcomes around the time of pregnancy loss treatment. Based on data showing higher rates of pregnancy loss,¹¹ perinatal depression, and perceived stress²³ in Black women,^{16,28} we hypothesized that the odds of having risk for major depression or high perceived stress 30 days after miscarriage treatment would be higher in Black participants when compared with non-Black participants.

METHODS

We performed a planned secondary data analysis of data collected during a clinical trial of medical management of early pregnancy loss from May 2014 to April 2017.²⁹ The primary results of the trial have been previously reported.²⁹ In brief, we enrolled 300 participants in a multicenter, randomized, pragmatic clinical trial to compare the effectiveness of combination treatment (mifepristone 200 mg orally followed 24 hours later by misoprostol 800 micrograms vaginally) to usual treatment (misoprostol 800 micrograms vaginally). The trial included participants aged 18 years and older who were diagnosed with a nonviable intrauterine pregnancy (anembryonic gestation or embryonic or fetal death) between 5 and 12 completed weeks of gestation. Participants were recruited at University of Pennsylvania, University of California, Davis, and Albert Einstein College of Medicine. The primary outcome for the trial was complete expulsion of the gestational sac by the first follow-up visit without further intervention over the 30-day study period. Validated psychometric measures included the CES-D (Center for Epidemiological Studies-Depression) scale, Perceived Stress Scale,

and Adverse Childhood Experience scale. The adverse childhood experience scale was collected at baseline, and the CES-D and Perceived Stress scales were collected at baseline and at 30 days after randomization. The institutional review boards from each of the study sites approved this trial (ClinicalTrials.gov NCT02012491).

The CES-D scale is the most widely studied and highly validated depression scale that was created to identify depression in the general population.^{30,31} The 20 items assess frequency of symptoms experienced during the prior week and comprise six scales that reflect the major dimensions of depression (depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance). Published studies report that a cutoff score of 16 or greater identifies individuals at risk for clinical depression with good sensitivity and specificity.^{30,32} In our study, CES-D scores were placed into three categories: scores of less than 16 were defined as no clinical significance, scores between 16 and 20 were defined as likely mild–moderate depression, and scores of 21 or greater were defined as likely major depression. Although there are limited studies reporting on the appropriate threshold for screening for and detection of likely major depression,³³ we chose the cut-off of a score of 21 or greater to increase the specificity of our analysis.³⁴

The Perceived Stress Scale is a validated scale and the most widely used psychological instrument for measuring the perception of stress.^{35,36} The items query respondents about how unpredictable, uncontrollable, and overloaded they found their lives during the previous month. Because the Perceived Stress Scale is not a diagnostic instrument, there are no published threshold values. However, based on published normative data from large samples in the United States,³⁶ we used the following definitions for our study population: low perceived stress (score of 0–13), moderate perceived stress (score of 14–26), and high perceived stress (score of 27–40).

The Adverse Childhood Experience scale is a validated scale that assesses three types of adverse childhood experiences: abuse, neglect, and household dysfunction.³⁷ Because the questions examine events from birth to age 18 years, responses should not change over time.³⁸ Thus, we only collected these data at baseline. Before analysis, we dichotomized adverse childhood experience scores into “high” (two or more options endorsed) or “low” (fewer than two options endorsed) scores. This definition is based on multiple studies displaying significant health effects

in adulthood (eg, smoking, depressed mood, sexually transmitted infections, suicide attempt, substance abuse) in participants reporting an adverse childhood experience score of 2 or more.^{38–40}

Participants who completed the CES-D and Perceived Stress scales at 30 days after treatment were included in our data analyses. We did not perform a sample size calculation for this planned analysis. Baseline characteristics were summarized and compared between Black participants and non-Black participants using the Pearson χ^2 test for categorical variables or *t* test for continuous variables. The primary outcome was risk for major depression 30 days after medical management of miscarriage, considered to be a score of 21 or higher on the CES-D scale. The secondary outcome was high perceived stress 30 days after medical management of miscarriage.

We performed two multivariable logistic regression analyses, one with the dependent variable of risk for major depression at 30 days and one with the dependent variable of high perceived stress at 30 days. The main exposure was patient race, dichotomized as Black or non-Black. Based on the association between adverse childhood experience scores and risk for major depression,^{40,41} as well as perceived stress,^{42,43} we included adverse childhood experience as a secondary exposure. Reported high adverse childhood experience scores, defined as an adverse childhood experience score of 2 or more on the Adverse Childhood Experience scale similar to previously published studies, were used.^{29–31} Using backwards selection, additional covariates were considered for our model if they had a significance level ($P < .2$) or were possibly related to the outcome based on biological plausibility. Unadjusted odds ratios (ORs), adjusted odds ratios (aORs), and 95% CIs were reported for all regression models.

Initial analyses showed a significant association between adverse childhood experience score and both race and our posttreatment outcomes. Therefore, to further examine the association between Black race and posttreatment outcomes (risk for major depression and high perceived stress) we tested an interaction term for effect modification by adverse childhood experience score.

All data were analyzed using STATA 15.1 statistical software. A two-sided $P < .05$ was considered statistically significant for all statistical tests.

RESULTS

Of the 300 participants enrolled in the primary study, 275 [92%] completed 30-day surveys. Of the 275 respondents included in this analysis, 266 [97%] completed the baseline CES-D and 268 [97%] completed the baseline Perceived Stress Scale surveys. In

our cohort, 120 [44%] participants self-identified as Black, and 155 [56%] self-identified as non-Black. Of the non-Black participants, 72 [26%] identified as Hispanic, 20 [7%] identified as Asian, and 36 [13%] identified as other. The category “other” was a formal category in the database of the original clinical trial.

All sociodemographic, pregnancy history, and baseline psychosocial and stress-related variables are shown in Table 1. Black participants were overall younger, of a lower education level, and more likely to have public insurance when compared with non-Black participants. Reproductive factors that were associated with being of Black race included having at least one living child, having a history of a previous induced abortion, and reporting that their current pregnancy was unplanned.

Of the 275 participants, 65 [24%] had a posttreatment CES-D score of 21 or more, corresponding to an increased risk for major depression. More Black women experienced a higher risk for major depression when compared with non-Black women 30 days after treatment (37 [57%] vs 28 [43%]; OR 2.02; 95% CI 1.15–3.55 Table 2). Baseline major depressive symptoms occurred in more than a quarter of participants (72/266 [27%]) and were associated with an increased risk for posttreatment major depression compared with those without such a history (34/63 [54%]; OR 9.47; 95% CI 4.47–20.1, Table 2). Black participants and non-Black participants reported similar levels of risk for baseline major depression scores (30 [27%] vs 42 [27%]; $P = .53$, Table 1). After adjusting for parity, baseline depression, and adverse childhood experience score, the association between being of Black race and the risk for major depression 30 days after treatment persisted (aOR 2.48; 95% CI 1.28–4.81). Few respondents reported having baseline high perceived stress (16 [6%]). Black participants, compared with non-Black participants, reported similar baseline (10 [9%] vs 6 [4%]; $P = .06$) and 30-day (OR 1.67; 95% CI 0.64–4.37; aOR 1.09; 95% CI 0.36–3.26, Table 3) high perceived stress scores.

Nearly half of respondents reported experiencing at least two adverse childhood experiences (126 [46%]). Women with high adverse childhood experience scores (two or more adverse childhood experiences reported) were younger (mean [SD] age, 29.2 [5.8] vs 31.6 [6.1] years; $P = .009$) and less likely to have completed post-high school education (45% vs 69%; OR 0.55, 95% CI 0.24–1.27). High adverse childhood experience scores were more common among Black participants (64/120 [53%]) than non-Black participants (62/155 [40%]); OR 1.71, 95% CI 1.06–2.77, Table 1). An adverse childhood experience score of 0, indicating no adverse childhood

Table 1. Baseline Characteristics of Participants

Characteristic	Non-Black* (n=155)	Black (n=120)	P [†]
Age (y)	32.1±5.3	28.5±6.4	<.001
Education			<.001
Some grade school or high school	10 (6)	16 (13)	
High school diploma or high school equivalency certificate	30 (19)	59 (49)	
Some college or post-high school education	115 (74)	45 (38)	
Medical insurance			<.001
None	6 (4)	13 (11)	
Medicaid or Medicare	51 (33)	83 (69)	
Private	98 (63)	24 (20)	
Gravidity			.002
1	50 (32)	17 (14)	
2	32 (21)	26 (22)	
3 or more	73 (47)	77 (64)	
Parity			<.001
0	76 (49)	33 (28)	
1 or more	79 (51)	87 (72)	
Gestational age (wk)			.089
Less than 7	63 (41)	36 (30)	
7 0/7–8 6/7	72 (46)	59 (49)	
9 0/7–12 6/7	20 (12)	25 (21)	
Previous miscarriage			.143
Yes	61 (39)	37 (31)	
No	94 (61)	83 (69)	
Previous induced abortion			<0.001
Yes	36 (23)	52 (43)	
No	119 (77)	68 (57)	
Planned pregnancy			<.001
Yes	103 (66)	45 (37)	
No	52 (34)	75 (63)	
Adverse childhood experience score			.028
High (2 or more)	62 (40)	64 (53)	
Baseline CES-D score [‡]			.528
Likely not depressed	83 (54)	56 (50)	
Likely mild-moderate depression	28 (18)	27 (24)	
Likely major depression	42 (27)	30 (27)	
Baseline perceived stress score [§]			.058
Low stress	68 (44)	37 (32)	
Moderate stress	79 (52)	68 (59)	
High stress	6 (4)	10 (9)	
Treatment method			.744
Mifepristone pretreatment	78 (50)	58 (52)	
Misoprostol alone	77 (50)	62 (48)	

Data are mean±SD or n (%) unless otherwise specified.

CES-D, Center for Epidemiological Studies-Depression.

* Self-identify as Hispanic, Asian, or "other."

[†] P values determined by χ^2 test or *t* test.

[‡] Missing data from nine participants.

[§] Missing data from seven participants.

experiences, was more common among non-Black women (58 [67%]) vs Black women (29 [33%]). The distribution of frequencies of adverse childhood experience scores for Black women compared with non-Black women can be seen in Figure 1. Individual adverse childhood experience categories differed by race (Table 4). Black participants more frequently reported a history of exposure to parental separation or divorce

(77 [64%] vs 58 [37%]; $P<.001$) and household criminal behavior (29 [24%] vs 13 [8%]; $P<.001$) compared with non-Black participants. In bivariate analyses, high adverse childhood experience scores were associated with both posttreatment major depression (OR 2.51; 95% CI 1.41–4.46, Table 2) and posttreatment high perceived stress (OR 4.53; 95% CI 1.45–14.1, Table 3). After adjusting for race, baseline depression, and parity,

Table 2. Association Between Race and Risk for Major Depression 30 Days After Medical Management of Early Pregnancy Loss

	n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Race			
Non-Black [†]	28 (43)	1 (ref)	1 (ref)
Black	37 (57)	2.02 (1.15–3.55)	2.48 (1.28–4.81)
Parity			
0	29 (45)	1 (ref)	1 (ref)
1 or more	36 (55)	0.76 (0.43–1.34)	0.55 (0.29–1.07)
Baseline depression [‡]			
None	12 (19)	1 (ref)	1 (ref)
Mild–moderate	17 (27)	4.73 (2.08–10.8)	4.26 (1.83–9.92)
Major	34 (54)	9.47 (4.47–20.1)	9.26 (4.24–20.2)
Adverse childhood experience score			
Low	24 (37)	1 (ref)	1 (ref)
High	41 (63)	2.51 (1.42–4.46)	1.71 (0.89–3.27)

OR, odds ratio; ref, reference.

* Adjusted for parity, baseline depression, and adverse childhood experience score.

[†] Self-identify as Hispanic, Asian, or “other.”

[‡] Missing data from two participants.

the relationship between high adverse childhood experience scores and posttreatment major depression was no longer statistically significant (aOR 1.71; 95% CI 0.89–3.27, Table 2); high adverse childhood experience scores remained associated with posttreatment high perceived stress (aOR 3.90; 95% CI 1.08–14.0). A test for effect modification by adverse childhood experience score on the association of race and posttreatment depression ($P=.72$) or posttreatment high perceived stress ($P=.94$) was not statistically significant.

DISCUSSION

An elevated risk for major depression occurs in about one in four women 30 days after treatment for early pregnancy loss, and our findings support the hypothesis that Black women who are undergoing early pregnancy loss treatment are about twice as likely to experience risk for major depression compared with non-Black women,

even after adjusting for risk for baseline depression and exposure to adverse childhood experiences.

In our study, being of Black race was not significantly associated with high perceived stress after early pregnancy loss treatment, likely owing to low statistical power, because only a small number of participants reported high levels of perceived stress. However, the risk for depression and stress were found to be linked in our cohort, which is consistent with previous studies demonstrating a strong association between depression and stress.^{41,42} Depressed people often have a decreased tolerance for stress and perceive more stress compared with nondepressed individuals.⁴³ Although it would have been interesting to further explore the relationship between stress and risk for depression among our early pregnancy loss population, baseline CES-D and Perceived Stress Scale scores were found to be highly correlated and, therefore, were not included in our multivariable models.

Table 3. Association Between Race and High Perceived Stress 30 Days After Medical Management of Early Pregnancy Loss

	n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Race			
Non-Black [†]	8 (44)	1 (ref)	1 (ref)
Black	10 (56)	1.67 (0.64–4.37)	1.09 (0.36–3.26)
Baseline stress		1.23 (1.13–1.33)	1.22 (1.12–1.33)
Adverse childhood experience score			
Low	4 (22)	1 (ref)	1 (ref)
High	14 (78)	4.53 (1.45–14.1)	3.90 (1.08–14.0)

OR, odds ratio; ref, reference.

* Adjusted for baseline stress and adverse childhood experience score.

[†] Self-identify as Hispanic, Asian, or “other.”

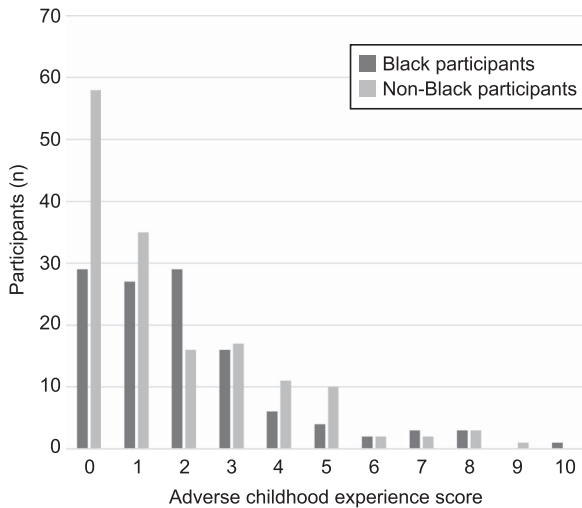


Fig. 1. Frequency of total adverse childhood experience score by race.

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Being of Black race was associated with higher odds of risk for posttreatment major depression, after accounting for adverse childhood experience score. However, similar to prior studies,^{17–20,44–48} we found that high adverse childhood experience scores were associated both with being of Black race and with the risk for major depression. Therefore, adverse childhood experiences potentially play a role in the pathway to an increased risk for major depression after early pregnancy loss management. Potentially owing to a lack of statistical power, we found that adverse childhood experience was not an effect modifier. Adverse childhood experience was also not a mediator, but it demonstrated positive confounding of the association between being of

Black race and the risk for posttreatment major depression in our study. Others have also demonstrated a complex relationship between adverse childhood experiences, race, and poor overall health. Being of Black race has been shown to be associated with an increased risk for depression, attributed partially to higher levels of stressful life events and overall chronic stress.⁴⁹

Our study has several strengths. The clinical trial setting was an advantage as it provided us with an opportunity to elicit 30-day outcomes in a racially diverse population with a high response rate and minimal missing data. Additionally, the racial and geographic diversity of the population improves the generalizability of our study.

Our findings should also be interpreted within the context of limitations. This study is a secondary analysis of a randomized controlled trial and the prevalence of childhood adversity and the risk for major depression may be different in individuals who chose to participate in research from the clinical population. Another limitation of our study is the use of the original Adverse Childhood Experience survey. This conventional scale, may not capture the totality of adversities faced by a poor or Black population.³⁸ An expanded adverse childhood experience scale includes questions on experiencing racism, living in an unsafe neighborhood, and witnessing violence was created to capture sources of adversity in urban populations.⁵⁰ The Philadelphia Adverse Childhood Experience Study,⁵¹ which examined conventional and expanded adverse childhood experience responses in a population that was 44% African American, found that Black women were eight times more likely to report having witnessed violence. A recent study examining the relationship between

Table 4. Prevalence of Adverse Childhood Experiences by Race

Category of Childhood Exposure	Total (N=275)	Non-Black* (n=155)	Black (n=120)	P [†]
Abuse				
Psychological	47 (17)	28 (18)	19 (16)	.626
Physical	38 (14)	22 (14)	16 (13)	.838
Sexual	35 (13)	18 (12)	17 (14)	.529
Household dysfunction				
Substance abuse	60 (22)	35 (23)	25 (21)	.728
Mental illness	50 (18)	36 (23)	14 (12)	.014
Mother treated violently	33 (12)	19 (12)	14 (12)	.881
Parental separation or divorce	135 (49)	58 (37)	77 (64)	<.001
Criminal behavior in household	42 (15)	13 (8)	29 (24)	<.001
Neglect				
Emotional	52 (19)	27 (17)	25 (21)	.473
Physical	23 (8)	15 (10)	8 (7)	.371

* Self-identify as Hispanic, Asian, or "other."

† P values determined by χ^2 test.

childhood exposure to racism and environmental trauma, found that the expanded risk categories are associated with perinatal mental illness.²⁶ Therefore, the adverse childhood experience scores obtained in our study may not truly reflect the trauma that our patient population experiences. This limitation may partially explain the lack of adverse childhood experience scores' effect on the relationship between Black race and risk for posttreatment depression.

Given the high incidence of early pregnancy loss, attention to improved subsequent health outcomes has a public health effect. Mental illness has been identified as a risk factor for maternal morbidity and mortality.⁵² One in four women were found to be at increased risk for major depression 30 days after treatment for early pregnancy loss, and our study identifies Black women experiencing an early pregnancy loss as a high-risk population. Because depression is a medical condition that responds to treatment, identification of those at risk is essential. These findings should be not be used to stigmatize Black women; instead it is important to consider the complex systemic factors, such as structural racism, that are the root causes of disparate health outcomes. Appropriate mental health resources and intervention programs are needed for women experiencing an early pregnancy loss. This will require a structurally and culturally competent workforce to meet the needs of high-risk populations.

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Authors' Data Sharing Statement

Will individual participant data be available (including data dictionaries)? *No*.

What data in particular will be shared? *Not available*.

What other documents will be available? *Not available*.

When will data be available (start and end dates)? *Not applicable*.

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? *Not applicable*.

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