Original Contribution

Causal Model of the Association of Social Support With Antepartum Depression: A Marginal Structural Modeling Approach

Qiu-Yue Zhong*, Bizu Gelaye, Tyler J. VanderWeele, Sixto E. Sanchez, and Michelle A. Williams

* Correspondence to Dr. Qiu-Yue Zhong, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Room Kresge 502A, Boston, MA 02115 (e-mail: qyzhong@mail.harvard.edu).

We used marginal structural models to evaluate associations of social support with antepartum depression in late pregnancy, if everyone had had high social support both before pregnancy and during early pregnancy, compared with having low social support at one of the 2 time points or low social support at both time points. In 2012–2014, pregnant Peruvian women (n = 3,336) were recruited into a prospective cohort study (at a mean gestational age of 9 weeks). A follow-up interview (n = 2,279) was conducted (at 26–28 weeks of gestation). Number of available support providers and satisfaction with social support were measured using Sarason Social Support Questionnaire–6. Depression was measured using the Edinburgh Postnatal Depression Scale. Low number of support providers at both time points was associated with increased risk of depression (odds ratio = 1.62, 95% confidence interval: 1.12, 2.34). The association for low satisfaction at both time points was marginally significant (odds ratio = 1.41, 95% confidence interval: 0.99, 1.99). Depression risk was not significantly higher for women who reported high social support at one of the 2 time points. Our study reinforces the importance of assessing social support before and during pregnancy and underscores the need for future interventions targeted at increasing the number of support providers to prevent antepartum depression.

antepartum depression; marginal structural models; prenatal interventions; social support

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; MSM, marginal structural model; SSQ-6, Social Support Questionnaire–6; SSQN, Social Support Questionnaire Number Scale; SSQS, Social Support Questionnaire Satisfaction Scale.

Depression is common among women of childbearing age (1) and remains one of the most serious mental health problems faced by women (2). The prevalence of antepartum depression ranges from 10% to 41% in low- and middle-income countries (3, 4). Antepartum depression is associated with many adverse obstetrical outcomes and neonatal outcomes (5); it also places women at high risk for postpartum depression (6).

Although the risk factors for antepartum depression are well-documented, few studies have investigated protective factors. Social support, defined as any process whereby social relationships promote health and well-being (7), is hypothesized to act as a buffer against depression in stressful circumstances or major life transition such as pregnancy (8, 9). The relationship between social support and depression is complex (10, 11). On the one hand, greater social support decreases the risk for depression and depression relapse, and improves treatment outcomes, whereas deficits in social support increase the risk of depression and relapse (10–12). On the other hand, depression may cause strains on interpersonal relationships and negatively affect social support (10, 13). Depressed individuals tend to withdraw from social support, perceive the social support more negatively, and underestimate the level of existing support, which may lead them to receive and perceive low social support (10, 14, 15). Besides, such a negative effect of depression on social support can, in turn, undermine the long-term treatment of depression and increase the risk of relapse (11). Previous studies have shown that low social support was a risk factor for depression during pregnancy and after giving birth and have shown potential benefits of interventions targeted at increasing social support (2, 16–18). However, the majority of prior studies on the association of social support with depression have been cross-sectional, and the causal relationship remains unclear (16, 18–21). Limited longitudinal research has been carried out (2, 22–24), and most such studies have measured social support only once. Understanding the impact of social support at

different time points may have important implications for the prevention and treatment of antepartum depression (22). No study has yet adequately addressed the methodological challenge of the complex, bidirectional relationship between social support and depression. Furthermore, there is relatively little research concerning how social support affects antepartum depression (16, 23) compared with postpartum depression (2, 21, 22, 25–27).

Using data from a prospective cohort study with repeated measures for social support and depression during pregnancy, we applied marginal structural models (MSMs) to assess the time-varying associations of low social support (prior to pregnancy and in early pregnancy) with antepartum depression in late pregnancy. We chose to use MSMs given that depression at early pregnancy was a confounder of the causal association of social support in early pregnancy on antepartum depression in late pregnancy and was affected by social support prior to pregnancy. By fitting MSMs, such temporal ordering was assumed to disentangle the bidirectional relationship between social support and depression. In addition, MSMs can help inform the design of prenatal interventions for clinical practice (28). We aimed to provide the magnitude of the association of social support at 2 different time points on depression at late pregnancy.

METHODS

Participants

Participants in this study were women who received prenatal care at the Instituto Nacional Materno Perinatal and enrolled in the Pregnancy Outcomes, Maternal and Infant Cohort Study. The Pregnancy Outcomes, Maternal and Infant Cohort is a longitudinal study designed to examine social and behavioral maternal risk factors of pregnancy outcomes in Lima, Peru. Eligible participants were pregnant women who were 18–49 years of age and whose offspring were <16 weeks of gestational age at the first prenatal care visit. Participants were interviewed during the first prenatal care visit (interview 1, mean gestational age of 9 weeks) and a follow-up visit (interview 2) during 26–28 weeks of gestational age. Each participant was interviewed, in a private setting, by trained research personnel using a structured questionnaire. All participants provided written informed consent prior to the interview. The institutional review boards of the Instituto Nacional Materno Perinatal, Lima, Peru, and the Harvard T.H. Chan School of Public Health, Office of Human Research Administration, Boston, Massachusetts, approved all procedures used in this study.

The study population for the present analysis is derived from participants who enrolled in the Pregnancy Outcomes, Maternal and Infant Cohort Study between February 2012 and July 2014. During this period, 3,372 participants agreed to participate and completed the initial structured interview (interview 1), 81% of the eligible women approached. At interview 1, 36 participants were excluded because of missing information concerning social support and depression, leaving 3,336 women. Follow-up in-person interviews (interview 2) of 2,292 participants were conducted. Participants who attended interview 1 but not interview 2 ($n = 1,044$) were considered to be "censored." At interview 2, 13 women were excluded due to missing information concerning social support and depression, leaving 2,279 women.

Measures

During the interview 1, participants reported baseline information regarding maternal sociodemographic and lifestyle characteristics, medical and reproductive histories, and experiences of childhood abuse (29) and intimate partner violence (30) before pregnancy. In addition, social support prior (31, 32) to the active pregnancy (any time before pregnancy) and antepartum depression (33) 7 days prior to interview 1 were measured. During the interview 2, social support since becoming pregnant/during early pregnancy and antepartum depression 7 days prior to interview 2 were measured.

Social support consisted of 2 distinct aspects (satisfaction with social support and number of available support providers); it was measured using a Spanish-language version of the 6-item Sarason Social Support Questionnaire–6 (SSQ-6) (31, 32). Participants were asked to indicate how satisfied they were with the overall support received and rate their satisfaction on a Likert scale from 1 (very unsatisfied) to 6 (very satisfied) in the following 6 situations: 1) is dependable when you need help; 2) helps you feel relaxed when you are under pressure; 3) takes care of you regardless of the circumstances; 4) cheers you up when you are feeling down; 5) consoles you when you are upset; and 6) accepts you unconditionally, including both your good and bad points. The Social Support Questionnaire Satisfaction Scale (SSQS) was scored by summing the ratings, ranging from 6 to 36. The Social Support Questionnaire Number Scale (SSQN), the total number of available support providers that participants can count on for help or support in the aforementioned 6 situations, was also calculated. The total SSQN score ranges from 0 to 54. To be compatible with previous studies using the SSQ-6 (32, 34–38), we defined low satisfaction with social support as an SSQS of ≤33 for interview 1 and an SSQS of ≤32 for interview 2 using the median split. The low number of support providers was defined as the SSQN of ≤8 for both interviews 1 and 2. In our population, the SSQ-6 was a reliable measure, with a Cronbach's α of 0.81.

Depression 7 days prior to each interview was measured using the Spanish-language version of the Edinburgh Postnatal Depression Scale (EPDS). The EPDS is a widely used, 10-item screening scale for antepartum and postpartum depression (33). Women were asked to rate how they felt in the previous 7 days. Individual items are totaled to give an overall score ranging from 0 to 30. Prior validation studies suggest a cutoff score of ≥10 for possible depressive disorder (33, 39). The Spanish-language version of the EPDS has been shown to be a reliable and valid scale for antepartum depression screening among Peruvian pregnant women (4).

Models and estimations

MSMs can be used to estimate the causal association of a time-dependent exposure in the presence of time-dependent covariates that are simultaneously confounders and intermediate variables from observational data (40, 41). We fitted 2 sets of MSMs for the 2 distinct aspects of social support (2, 32): low satisfaction with social support and a low number of available support providers. We used the MSMs to account for the potential confounding and intermediary role of depression in early pregnancy (Figure 1): Social support prior to pregnancy (SS_1), measured at interview 1, might be associated with depression at interview 1 (Dep_1), which
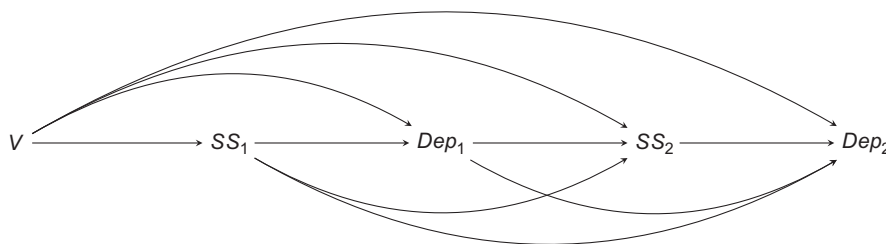
Figure 1. Directed acyclic graph for the association of low social support with antepartum depression at interview 2, Pregnancy Outcomes, Maternal and Infant Cohort Study, Peru, 2012–2014. V represented the time-independent baseline covariates (maternal age, education, race/ethnicity, married/living with partner, difficulty in accessing basic foods, planned pregnancy, parity, childhood abuse, and intimate partner violence prior to pregnancy). SS_1 = 1 if women received low social support prior to index pregnancy, otherwise 0; SS_2 = 1 if women received low social support since becoming pregnant, otherwise 0; Dep_1 = 1 if women were depressed at interview 1, otherwise 0; and Dep_2 = 1 if women were depressed at interview 2, otherwise 0. Dep_1 represented as both confounder and intermediate variable in relation to SS_2.

might, in turn, affect both social support since becoming pregnant (SS_2) and depression at interview 2 (Dep_2) both measured at interview 2.

The models that predicted the expected outcome (Dep_{SS_1,SS_2}) took the form:

$$\text{logit Pr}[Dep_{SS_1,SS_2} = 1|V] = \beta_0 + \beta_1 SS_1 + \beta_2 SS_2 + \beta_3 SS_1 \times SS_2 + \beta_4 V,$$

where Dep_{SS_1,SS_2} was antepartum depression at interview 2 for a woman that would have resulted under the hypothetical joint interventions to set social support at interview 1 and interview 2, possibly contrary to fact, to SS_1 and SS_2, respectively. We evaluated associations of social support with antepartum depression, if all had had high social support at both interviews 1 and 2, compared with having low social support at one of the 2 time points or low social support at both time points. V denoted the baseline covariates including maternal age, education, race/ethnicity, marital status, difficulty in accessing basic foods, planned pregnancy, parity, childhood abuse, and intimate partner violence prior to pregnancy.

Inverse probability weights

MSMs can appropriately control for time-varying confounding and loss to follow-up through inverse-probability-of-treatment and inverse-probability-of-censoring weights and give valid estimates (40, 41).

Inverse-probability-of-treatment weights

We used a stabilized version of inverse-probability-of-treatment weights:

$$SW_A = \frac{pr[SS_1 = 1]}{pr[SS_1 = 1|V]} \times \frac{pr[SS_2 = 1|SS_1, V]}{pr[SS_2 = 1|SS_1, L_1]},$$

given the smaller variance (40, 41), where V represented the aforementioned time-independent baseline covariates, and L_1 included both depression at interview 1 and baseline covariates V. Further details on the distribution of both stabilized and unstabilized

weights are available in the Web Table 1 (available at https://academic.oup.com/aje).

Inverse-probability-of-censoring weights

To adjust for right censoring at interview 2 due to loss to follow-up, we used a similar procedure to estimate the stabilized inverse-probability-of-censoring weights (SW_C), where

$$SW_c = \frac{pr[C_2 = 0|SS_1, V]}{pr[C_2 = 0|SS_1, L_1]}.$$

We defined the censoring indicator as $C_2 = 1$ if a woman was lost to follow-up at interview 2 and $C_2 = 0$ otherwise. We assumed that censoring at interview 2 was random, with the probability of attending interview 2 depending on prior social support, baseline covariates, and depression at interview 1. Further details on the characteristics of women who were lost to follow-up are available in the Web Table 2.

The censoring weights were multiplied by the treatment weights to create a final stabilized weight for each woman.

When fitting MSMs using inverse-probability weights, we made the following 4 assumptions (42): conditional exchangeability (28, 41, 43), positivity, correct specification of models used to estimate weights, and consistency. In addition, we performed a sensitivity analysis for unmeasured confounding to assess the extent to which unmeasured residual confounding would explain away the observed associations (44, 45). Without imposing any assumptions on the unmeasured confounders, we calculated the E-value as a representation of the minimum strength of association that an unmeasured confounder would need to have with the exposure and outcome to nullify an observed exposure-outcome association (*OR*) (44–46). The formula for the E-value is: $E = sqrt(OR) + \sqrt{sqrt(OR) \times (sqrt[OR] - 1)}$ for common outcomes. We assessed model misspecification based on the distribution of stabilized weights (42).

We conducted additional analyses to test the robustness of our results. We fitted multivariate logistic regression models for the associations of social support during early pregnancy on depression in late pregnancy, adjusting for baseline covariates, social support before pregnancy, and depression in early pregnancy. In addition, we modeled the SSQS and SSQN as continuous variables.

All statistical analyses were performed using SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Sociodemographic and reproductive characteristics are provided in Tables 1 and 2. At interview 1, compared with women reporting high satisfaction with social support, women reporting low satisfaction with social support were less likely to have more than 12 years of education, to report the active pregnancy as planned, and to be nulliparous; they also tended to have difficulties in accessing basic foods and to have experienced childhood abuse and intimate partner violence prior to pregnancy (Table 1). Compared with women who reported having a high number of support providers, women who reported having a

Table 1. Characteristics of Women According to Social Support Status Measured by Social Support Satisfaction in the Pregnancy Outcomes, Maternal and Infant Cohort Study, Peru, 2012–2014

Characteristic	Satisfaction With Social Support							
	Before Pregnancy[a]				Since Becoming Pregnant[b]			
	High (n = 1,576)		Low (n = 1,760)		P Value	High (n = 1,058)		Low (n = 1,221)		P Value
	No.	%	No.	%		No.	%	No.	%	
Maternal age, years[c]	28.1 (6.2)		28.3 (6.4)		0.44	27.9 (6.1)		28.4 (6.2)		0.10
Maternal age group, years					0.59					0.42
18–19	86	5.5	86	4.9		52	4.9	58	4.8	
20–29	879	55.8	980	55.7		607	57.4	665	54.5	
30–34	339	21.5	363	20.6		228	21.6	272	22.3	
≥35	272	17.3	331	18.8		171	16.2	226	18.5	
Education, years					<0.0001					0.0008
≤6	60	3.8	85	4.8		35	3.3	59	4.8	
7–12	765	48.5	1,051	59.7		531	50.2	684	56.0	
>12	746	47.3	620	35.2		489	46.2	474	38.8	
Mestizo ethnicity	1,191	75.6	1,318	74.9	0.60	808	76.4	918	75.2	0.48
Married/living with partner	1,277	81.0	1,414	80.3	0.54	863	81.6	986	80.8	0.85
Employed during pregnancy	713	45.2	820	46.6	0.43	474	44.8	569	46.6	0.38
Access to basic foods					0.002					0.004
Hard	739	46.9	919	52.2		490	46.3	639	52.3	
Not very hard	836	53.0	840	47.7		568	53.7	582	47.7	
Planned pregnancy	707	44.9	689	39.1	0.001	478	45.2	482	39.5	0.006
Nulliparous	804	51.0	826	46.9	0.02	548	51.8	583	47.7	0.05
Gestational age at interview 1, weeks[c]	9.1 (3.5)		9.3 (3.5)		0.13	9.5 (3.4)		9.6 (3.5)		0.24
Early pregnancy body mass index[d]										
<18.5	33	2.1	30	1.7	0.84	19	1.8	23	1.9	0.24
18.5–24.9	744	47.2	844	48.0		523	49.4	591	48.4	
25.0–29.9	578	36.7	637	36.2		394	37.2	433	35.5	
≥30.0	204	12.9	226	12.8		112	10.6	163	13.3	
Childhood abuse	1,068	67.8	1,306	74.2	<0.0001	744	70.3	910	74.5	0.02
Lifetime intimate partner violence (physical or sexual)	466	29.6	745	42.4	<0.0001	324	30.6	473	38.8	0.0002
Lifetime abuse										
No abuse	404	25.6	330	18.8	<0.0001	257	24.3	223	18.3	<0.0001
Childhood abuse only	701	44.5	682	38.8		476	45.0	522	42.8	
Intimate partner violence only	104	6.6	124	7.0		57	5.4	88	7.2	
Childhood abuse and intimate partner violence	362	23.0	621	35.3		267	25.2	385	31.5	

[a] Low social support satisfaction before pregnancy was defined as a score of ≤33 on the Social Support Questionnaire Satisfaction Scale (at interview 1).
[b] Low social support satisfaction since becoming pregnant was defined as a score of ≤32 on the Social Support Questionnaire Satisfaction Scale (at interview 2).
[c] Values are expressed as mean (standard deviation).
[d] Weight (kg)/height (m)^2.

Table 2. Characteristics of Women According to Social Support Status Measured by Number of Available Support Providers in the Pregnancy Outcomes, Maternal and Infant Cohort Study, Peru, 2012–2014

Characteristic	Number of Available Support Providers							
	Before Pregnancy[a]				Since Becoming Pregnant[b]			
	High (n = 1,299)		Low (n = 2,037)		P Value	High (n = 996)		Low (n = 1,283)		P Value
	No.	%	No.	%		No.	%	No.	%	
Maternal age, years[c]	27.5 (5.9)		28.6 (6.5)		<0.0001	27.5 (6.0)		28.7 (6.2)		<0.0001
Maternal age group, years					<0.0001					0.0007
18–19	70	5.4	102	5.0		59	5.9	51	4.0	
20–29	783	60.3	1,076	52.8		589	59.1	683	53.2	
30–34	265	20.4	437	21.5		198	19.9	302	23.5	
≥35	181	13.9	422	20.7		150	15.1	247	19.3	
Education, years					<0.0001					<0.0001
≤6		3.0	106	5.2		27	2.7	67	5.2	
7–12	633	48.7	1,183	58.1		492	49.4	723	56.4	
>12	624	48.0	742	36.4		472	47.4	491	38.3	
Mestizo ethnicity	1,035	79.7	1,474	72.4	<0.0001	773	77.6	953	74.3	0.06
Married/living with partner	1,057	81.4	1,634	80.2	0.46	772	77.5	1,077	83.9	0.0001
Employed during pregnancy	580	44.6	953	46.8	0.24	444	44.6	599	46.7	0.33
Access to basic foods					0.002					0.26
Hard	603	46.4	1,055	51.8		480	48.2	649	50.6	
Not very hard	696	53.6	980	48.1		516	51.8	634	49.4	
Planned pregnancy	562	43.3	834	40.9	0.17	436	43.8	524	40.8	0.15
Nulliparous	711	54.7	919	45.1	<0.0001	547	54.9	584	45.5	<0.0001
Gestational age at interview 1, weeks[c]	9.2 (3.5)		9.2 (3.4)		0.97	9.5 (3.5)		9.6 (3.4)		0.70
Early pregnancy body mass index[d]					0.006					0.50
<18.5	30	2.3	33	1.6		18	1.8	24	1.9	
18.5–24.9	661	50.9	927	45.5		503	50.5	611	47.6	
25.0–29.9	436	33.6	779	38.2		356	35.7	471	36.7	
≥30.0	158	12.2	272	13.4		111	11.1	164	12.8	
Childhood abuse	853	65.7	1,521	74.7	<0.0001	688	69.1	966	75.3	0.001
Lifetime intimate partner violence (physical or sexual)	362	27.9	849	41.7	<0.0001	289	29.0	508	39.7	<0.0001
Lifetime abuse					<0.0001					<0.0001
No abuse	363	27.9	371	18.2		249	25.0	231	18.0	
Childhood abuse only	572	44.0	811	39.8		457	45.9	541	42.2	
Intimate partner violence only	83	6.4	145	7.1		59	5.9	86	6.7	
Childhood abuse and intimate partner violence	279	21.5	704	34.6		230	23.1	422	32.9	

[a] Low number of available support providers before pregnancy was defined as a score of ≤8 (at interview 1) on the Social Support Questionnaire Number Scale.

[b] Low number of available support providers since becoming pregnant was defined as a score of ≤8 (at interview 2) on the Social Support Questionnaire Number Scale.

[c] Values are expressed as mean (standard deviation).

[d] Weight (kg)/height (m)[2].

low number of support providers were more likely to be 35 years or older, to have difficulties in accessing basic foods, and to have experienced childhood abuse and intimate partner violence prior to pregnancy; they were less likely to identify themselves as Mestizo, to have received more than 12 years of education, or to be nulliparous (Table 2). At interview 2,

similar patterns of sociodemographic and reproductive characteristics were seen (Tables 1 and 2).

Using marginal structural models (Table 3, Web Tables 3 and 4), compared with women reporting high social support both before and during early pregnancy (reference group), women were at increased risk of depression in late pregnancy if they

Table 3. Associations Between Social Support and Antepartum Depression in Late Pregnancy Using Marginal Structural Models in the Pregnancy Outcomes, Maternal and Infant Cohort Study, Peru, 2012–2014

Social Support (Before Pregnancy)	Social Support (Since Becoming Pregnant)	Marginal Structural Model	
		aOR	95% CI
Satisfaction with social support			
Low[a]	Low[b]	1.41	0.99, 1.99
Low	High	0.88	0.57, 1.35
High	Low	1.43	0.97, 2.10
High	High	1.00	Referent
Number of available support providers			
Low[c]	Low[d]	1.62	1.12, 2.34
Low	High	0.84	0.54, 1.31
High	Low	1.38	0.89, 2.14
High	High	1.00	Referent

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

[a] Low social support satisfaction before pregnancy was defined as a score of ≤33 on the Social Support Questionnaire Satisfaction Scale (at interview 1).

[b] Low social support satisfaction since becoming pregnant was defined as a score of ≤32 on the Social Support Questionnaire Satisfaction Scale (at interview 2).

[c] Low number of available support providers before pregnancy was defined as a score of ≤8 on the Social Support Questionnaire Number Scale.

[d] Low number of available support providers since becoming pregnant was defined as a score of ≤8 on the Social Support Questionnaire Number Scale.

reported, at both time points, low satisfaction with social support (adjusted odds ratio (aOR) = 1.41, 95% confidence interval (CI): 0.99, 1.99) and low number of support providers (aOR = 1.62, 95% CI: 1.12, 2.34). The risk of depression in late pregnancy was not significantly higher among women who reported low social support before pregnancy and high social support during early pregnancy (for low satisfaction, aOR = 0.88, 95% CI: 0.57, 1.35; for low number of support providers, aOR = 0.84, 95% CI: 0.54, 1.31) or high social support before pregnancy but low support during early pregnancy (for low satisfaction, aOR = 1.43,

95% CI: 0.97, 2.10; for low number of support providers, aOR = 1.38, 95% CI: 0.89, 2.14).

Next, we evaluated satisfaction with social support and number of available support providers as continuous variables (Table 4). No statistically significant association was observed between satisfaction with social support and antepartum depression. An increase by 1 available support provider at one of the 2 time points was associated with decreased risk of antepartum depression (prior to pregnancy, aOR = 0.85, 95% CI: 0.73, 0.98; during early pregnancy, aOR = 0.73, 95% CI: 0.63, 0.84). There was a

Table 4. Inverse-Probability-of-Treatment Weighted Estimates of the Causal Association of Social Support (Continuous) on Antepartum Depression at Interview 2, Pregnancy Outcomes, Maternal and Infant Cohort Study, Peru, 2012–2014

Social Support Score	aOR	95% CI
Satisfaction with social support		
Before pregnancy (per 5 units)	1.01	0.52, 1.95
Since becoming pregnant (per 5 units)	0.75	0.36, 1.56
Before pregnancy (per 5 units) × since becoming pregnant (per 5 units)	0.76	0.20, 2.92
Number of available support providers		
Before pregnancy (per 1 unit)	0.85	0.73, 0.98
Since becoming pregnant (per 1 unit)	0.73	0.63, 0.84
Before pregnancy (per 1 unit) × since becoming pregnant (per 1 unit)	0.63	0.49, 0.81

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

37% (aOR = 0.63, 95% CI: 0.49, 0.81) decrease in the risk of antepartum depression for 1-unit increase in available support providers at both time points.

We observed similar estimates from multivariate logistic regression compared with the estimates from the MSMs (Web Table 5). Next, we completed sensitivity analyses to evaluate the extent to which an unmeasured confounder would fully explain away the observed estimates. For example, for the observed estimate of aOR = 1.62 for the low number of support providers before pregnancy and in early pregnancy, an unmeasured confounder associated with both low number of support providers and depression by risk ratios of 2.02-fold each, above and beyond the measured confounders, would explain away the association, but weaker confounding would not. To shift the lower bound of the confidence limit of 1.12 to include the null, an unmeasured confounder that was associated with low number of support providers and depression by risk ratios of 1.39-fold each would suffice, but weaker confounding would not. This association is thus relatively robust to potential unmeasured confounding.

DISCUSSION

In this prospective cohort study, after applying methods that adjusted for potential confounding and the intermediary role of depression during early pregnancy, we found that women with low social support at both (early and late pregnancy) interview time points were at higher risk of depression in late pregnancy. Depression risk was not significantly higher among women who reported high social support at one of the 2 time points. We observed a stronger association with a low number of support providers, compared with low satisfaction with social support, on depression risk.

Consistent with many previous studies (2, 10, 16, 22, 23, 26), we found that low social support was associated with higher risk of depression. One possible mechanism involved in this association is the buffering effect of social support. The buffering hypothesis proposes that social support is related to health only (or primarily) when stressful life events occur (47). This hypothesis predicts that social support will protect individuals from the potentially negative impact of stressful events (47), and thus protect against depression by altering perceptions of negative events; enhancing an individual's self-esteem, self-confidence, and self-efficacy; transferring coping resources; and facilitating changes in health-related behaviors (7, 10, 48).

A larger magnitude of associations between social support during early pregnancy, compared with before pregnancy, with antepartum depression were found in our study. This finding suggested that interventions aimed at increasing social support during early pregnancy might be more influential on depression risk than social support prior to pregnancy. In addition, our results demonstrated a stronger association of the low number of support providers on depression risk in late pregnancy compared with low social support satisfaction. The difference between the number of support providers and satisfaction with social support in relation to depression was also seen in previous studies. For example, significant associations were reported for the number of social support providers during pregnancy with postpartum depression but not the satisfaction with social support during pregnancy (2, 24). As suggested by Sarason et al. (32), the number of support providers, a measure for perceived social support network size, and satisfaction with social support, a measure of the perceived quality of social support, reflected 2 different aspects of perceived social support, and different aspects of social support were associated with different health outcomes (49). Our results suggest benefits of interventions targeted at increasing the number of support providers to prevent antepartum depression (2).

Our results also provide valuable quantitative information on the development of practical interventions. A hypothetical intervention on social support designed to increase by 1 available support provider for one of the 6 situations in the SSQ-6 before pregnancy or during early pregnancy would decrease the risk of depression in late pregnancy. A greater decrease in the risk of depression was seen when the intervention was targeted at increasing available support providers during early pregnancy compared with prior to pregnancy. The available support providers could be friends, family members, or health professionals such as mental health and medical professionals, because pregnancy is a time that women come into frequent contact with healthcare providers. Of note, different sources of social support relationship have different strengths and mechanisms of support for pregnant women (16, 18). For example, in a sample of 156 outpatients with major depression, Clara et al. (50) found that perceived social support provided by family and friends had the strongest association with depression. Future studies illuminating how the source of social support affects the risk of antepartum depression during pregnancy is warranted.

As noted previously, MSMs require several assumptions. For conditional exchangeability, we assumed that measured covariates were sufficient to adjust for both confounding and selection bias due to loss to follow-up. Sensitivity analyses for unmeasured confounding indicated that relatively substantial residual unmeasured confounding was needed to explain away the observed significant associations of early pregnancy social support with depression. With regard to positivity, we concluded that the assumption of positivity was likely to hold in our analysis based on descriptive statistics (Tables 1 and 2) when social support measures were dichotomized. The assumption of correct model specification was likely to hold considering that stabilized weights had a mean of 1 (Web Table 1), a necessary condition for correct model specification (42). We might fail to satisfy the assumptions of consistency. Consistency was not straightforward in our situation (42, 51, 52). It is difficult to intervene on a woman's satisfaction with social support. In addition, a woman could achieve a high number of available support providers through different pathways (53), which could have different implications for the outcome. For our analysis, we defined the high number of available support providers as a summary endpoint of these different pathways.

This study had some limitations. First, there might be a timing overlap between depression measured at interview 1 (Dep_1, in the 7 days prior to interview 1) and social support measured at interview 2 (SS_2, since becoming pregnant). However, interview 1 was conducted during the first prenatal visit, which was unlikely to be a long time after women learned they were pregnant. Therefore, we would not expect a drastic change in social support between pregnancy confirmation and the first prenatal visit. Second, we measured only perceived social support, one of the 3

main aspects of social support (social integration, received support, or perceived support), in this study [10]. Nevertheless, prior research suggested that the perceived level of social support might be more important to an individual's mental health than the objective level of social support [11]. Third, measures of social support might be susceptible to recall bias, especially for social support measured at interview 1, which covered a long time period. Fourth, we defined depressive state using a depression screening instrument, the EPDS, rather than diagnostic interviews completed by psychiatrists.

The strengths of this study included the large sample size of pregnant women, repeated measures of social support and depression, the inclusion of 2 distinct aspects of perceived social support, and the analytical methods accounting for the bidirectional relationship between social support and depression. Furthermore, we adjusted for a wide range of potential confounders, including reproductive and abuse history, using validated questionnaires.

In conclusion, in our prospective study in a cohort of pregnant Peruvian women, we found that consistently low social support before pregnancy and during early pregnancy was associated with increased risk of antepartum depression at late pregnancy, with the associations being stronger in relation to the number of available support providers. Social support during early pregnancy is more influential on the risk of antepartum depression than is social support prior to pregnancy. Assessing social support before and during pregnancy would likely help identify pregnant women vulnerable to depression. The development of interventions targeted at increasing the number of support providers would be beneficial in preventing antepartum depression. Future studies illuminating how different sources of social support affect the risk of depression during pregnancy are warranted.

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