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Original Article

Pilot trial evaluating maternal docosahexaenoic acid consumption during pregnancy: Decreased postpartum depressive symptomatology

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ABSTRACT

Objective: Docosahexaenoic acid (DHA, 22:6, n-3) is a major structural component of neural tissue critical to neurotransmission and mood regulation. Poor maternal dietary intake coupled with accelerated maternal-fetal transfer of DHA compound risk for maternal deficiency. The objective of this investigation was to determine if maternal DHA supplementation is efficacious in reducing symptoms of postpartum depression.

Methods: This pilot investigation was a randomized, double-blinded, placebo controlled investigation of the role of DHA in preventing risk for postpartum depression. Women were assigned to: i) Placebo (no DHA, corn oil capsule), ii) DHA (300 mg DHA, fish oil capsule). Capsules were consumed from 24 to 40 weeks gestation (1 capsule 5 days/week). Forty-two participants were recruited ($n = 20$, intervention; $n = 22$, placebo). Maternal DHA status and depressive symptoms were followed from 24 to 40 weeks gestation using the Center for Epidemiologic Studies Depression Scale (CES-D) and the Postpartum Depression Screening Scale (PDSS) from 2 weeks to 6 months postpartum.

Results: PDSS total scores were significantly lower ($p = 0.016$; 46.03 ± 2.17, intervention vs. 52.11 ± 2.4, placebo) in the intervention group with less anxiety/insecurity ($p = 0.03$), emotional lability ($p = 0.04$) and loss of self ($p = 0.02$).

Conclusions: Women in the DHA intervention group had fewer symptoms of postpartum depression compared to the placebo group. These results support the notion that the consumption of DHA by pregnant women can be efficacious in preventing depressive symptoms and highlight a need for further larger-scale investigations using the PDSS in tandem with a diagnostic evaluation.

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1. Introduction

Postpartum depression, the most common complication of childbirth, is a major public health problem [1], affecting 13–15% of pregnant women in the U.S. [2]. Further, 25–50% of women diagnosed with postpartum depression have episodic events for up to six months or more [3]. Postpartum depression is a universal phenomenon, affecting women in countries throughout the world [4] and suffered covertly [5]. Because postpartum depression is a term applied to a wide range of postpartum emotional disorders, women may be misdiagnosed. Current DSM-IV-TR guidelines [6] outline that, in addition to depressed mood or loss of interest or pleasure in activities, women need to have three or more other symptoms including insomnia, psychomotor agitation or retardation, fatigue, feelings of worthlessness or excessive or inappropriate guilt, inability to concentrate, or suicidal thoughts. The importance of preventing, diagnosing, and treating postpartum depression is underscored by the findings that postpartum depression has significant adverse effects on children's cognitive and emotional development [7,8]. The evidence for a demonstrated benefit of fish/seafood and n-3 long chain fatty acids (n-3 LCPUFAs) in preventing or decreasing symptomatology of postpartum depression is mixed [9–12]. Given the teratogenic effects of some medications traditionally used to treat depressive disorders, there is the need to explore possible alternative treatments or augmentation to traditional medical treatments for women with depression associated with pregnancy. N-3 LCPUFAs present a possible treatment or adjuvant to treatment for this disorder.

Given the collective evidence we report, the major hypothesis for this investigation was: Women who consume fish oil during pregnancy will have lower postpartum depressive symptomatology measured using the PDSS (total score and individual symptom domains) compared to the placebo group. In the current study we employed the Postpartum Depression Screening Scale (PDSS) to evaluate if pregnant women who consumed fish oil capsules had decreased postpartum depressive symptoms compared to women consuming a placebo.

2. Material and methods

2.1. Research design

This pilot investigation was a double-blind, randomized, control trial, with repeated measures of the primary investigative outcome of maternal postpartum depressive symptomatology at 2 and 6 weeks, and 3 and 6 months postpartum. All participants consumed one capsule (intervention: fish oil with 300 mg docosahexaenoic acid [DHA, 22:6, n-3] per capsule; placebo: corn oil) 5 days weekly. Participants were assigned randomly to either intervention ($n = 20$) or placebo ($n = 22$), and consumed capsules from 24 weeks gestation until delivery. All study procedures were approved by the University of Connecticut and Louisiana State University and in accordance with the Code of Ethics of the World Medical Association.

2.2. Sample/setting

Forty-two maternal-infant dyads completed the investigation. Inclusion criteria were: No other births in the previous two years; ≤20 weeks pregnant; and 18–35 years of age. Women with a self-reported significant medical history were excluded (i.e., currently being treated for depression/psychiatric illness, addiction problems, hyperlipidemia, hypertension, renal disease, liver disease, or diabetes). Recruitment of participants was conducted in collaboration with several Women Infants and Children (WIC) offices and hospitals in New England.

Determination of sample size for a full-scale investigation was based upon a previous investigation comparing rates of postpartum depression with respect to seafood consumption [9]. The sample in this pilot investigation ($n = 42$) is 78% of the minimum calculated to be necessary for a full-scale investigation (effect size based upon a power of 0.8, significance level of 0.05).

All participants were randomized utilizing a coded marble system and assigned to groups by a trained individual who was not a research team member. Packages containing capsules were labeled identically and listed only sequential study

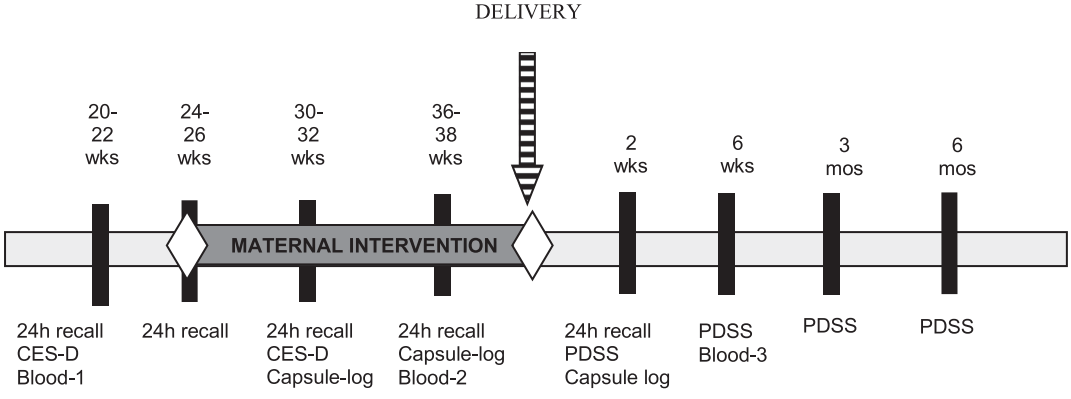

Fig. 1 – Schedule of intervention & sampling. 24 h recall: 24 h dietary recall; CES-D: Center for Epidemiologic Studies Depression Scale; Blood (1–3): Fasting maternal blood draw; Capsule log; PDSS: Postpartum Depression Screening Scale.

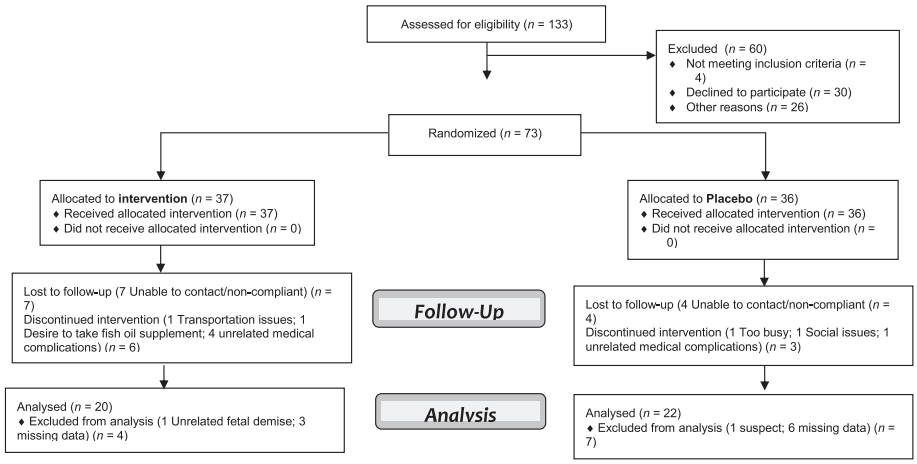

Fig. 2 – CONSORT diagram of trial flow.

identification numbers. A record linking participant names with group assignments was maintained in a secure location away from the researchers to ensure adequate blinding throughout the investigation from recruitment to the completion of data analysis. Identical numbered packages were assembled in advance for use by the research team in enrolling participants. Participants were blinded to group allocation through identical dose and packaging. To monitor protocol compliance, women kept logs of capsule intake (Fig. 1).

2.3. *Measures*

2.3.1. *Blood collection/fatty acid analyses*

Maternal venous blood samples (Fig. 1) were collected into ethylenediaminetetraacetic acid (EDTA)-containing tubes. Maternal RBC fatty acids were determined using methodologies previously reported [13].

2.3.2. *Prenatal/postnatal assessment of maternal depressive symptoms*

The Center for Epidemiologic Studies Depression Scale (CES-D) [14] is a self-report sensitive to emotional state and depressive symptoms in the general population and contains 20 items with a 4 point Likert response: 1 = rarely, 2 = 1–2 days, 3 = 3–4 days, or 4 = 5–7 days in the assessment week (score range 0–60). The CES-D has a test-retest reliability of $r = 0.51–0.67$ and a Cronbach's α of 0.85–0.9 and 64% sensitivity and 94% specificity with a positive predictive value of 33% [15]. The CES-D was administered at baseline and again prior to delivery (Fig. 1).

To evaluate the primary study outcome, postpartum depressive symptomatology, the PDSS [16] was administered four times postpartum: at 2 weeks, 6 weeks, and months 3 and 6 (Fig. 1). The PDSS is a self-report scale consisting of 35 items designed to reflect symptoms over the previous 2-weeks. The response options range from 1 = strongly disagree to 5 = strongly agree (score range 35–175). It consists of seven symptom content scales: Sleeping/Eating Disturbances, Loss of Self, Anxiety/Insecurity, Guilt/Shame, Emotional Lability, Mental Confusion, and Suicidal Thoughts, with high reliability ($\alpha = 0.97$) for the total scale and coefficients ranging from .83 to .94 for the seven symptom subscales [16]. Scores ≥80 indicate a positive screen for postpartum depression and need for a referral for a formal diagnostic evaluation by a trained mental health provider using a Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID) [17]. Beck and Gable [16] reported the PDSS had sensitivity of 94% and specificity of 98% when validated with clinical diagnosis. Mothers diagnosed with postpartum depression during the intervention were referred for follow-up and treatment. Participants with high scores on the suicidal ideation domain were referred immediately to emergency room psychiatric services. To assess consistency in participant response to PDSS items, the PDSS inconsistent responding (INC) index was used, and scores of 4–6 indicate an 85% – 97% (respectively) likelihood of inconsistency [16].

2.4. *Statistical analyses*

Statistical analyses for main effects were conducted using the Statistical Analysis System (SAS) [18] software. Analyses of baseline characteristics included the Student *t*-test for numeric and chi-square tests for categorical variables. The PROC MIXED procedure was used to evaluate the primary outcome measure of change over time among all four of the PDSS assessments and for individual domain scores.

3. Results

Fig. 2 provides the CONSORT diagram outlining the flow of participants from initial contact to final analysis.

The total CES-D score in this investigation had an α coefficient = 0.89 (intervention = 0.90; placebo = 0.90). There were no significant group differences between CES-D scores at baseline, $p = 0.97$ (intervention 14.2 ± 9.5; placebo 14.1 ± 10.7) or at 30–32 wks gestation, $p = 0.24$ (intervention 12.6 ± 8.3; placebo 9.5 ± 8.3). For the total PDSS in this investigation the combined groups had an α coefficient = 0.94 (intervention = 0.93; placebo = 0.94). The mean PDSS INC score for our placebo

group was 0.58 ± 0.97 and for the intervention group 0.82 ± 1.09 (α coefficient = 0.71 for the entire cohort; intervention = 0 .58; placebo = 0.82), which indicated that the PDSS was completed consistently by the sample. There were no significant group differences for any of the baseline characteristics (i.e. age, pre-pregnancy weight, number of live births, income, education, ethnicity, number of people in the household, history of depression, or previous treatment for depression).

The statistical model controlled for maternal CES-D score prior to delivery and PDSS INC index score as they were significantly related to PDSS scores. Additionally, age, dietary DHA outside of intervention, and ethnicity were included as covariates due to evidence that they operate as confounders of the group effect. Using this model, there was a significant group effect ($p = 0.016$), with lower mean PDSS scores in the intervention group across all 4 times evaluating the collective group difference across all time points using the PROC MIXED procedure for repeated measures analysis over time [LS Mean (SEM)]: intervention, 46.03 (2.17); placebo, 52.11 (2.4), Table 1. Women in the intervention group had PDSS scores 6 points lower overall compared to the placebo group (Table 1). Fig. 3 outlines the least square (LS) mean PDSS scores at the 4 individual time-points. Individual LS means were compared individually between groups at 2 weeks and the intervention group PDSS LS mean score was significantly lower compared to the placebo group ($p = 0.0124$). In the entire cohort, 9.5% of participants had a PDSS score ≥80 (1 participant in intervention group, 3 in placebo group).

Using this model, individual domains (Sleeping/Eating Disturbances, Loss of Self, Anxiety/Insecurity, Guilt/Shame, Emotional Lability, Mental Confusion, and Suicidal Thoughts) of the PDSS were compared (Table 1). Anxiety/insecurity, emotional lability, mental confusion, and loss of self were significantly lower in the DHA intervention group compared to the placebo group across the 4 time points (Table 1). RBC DHA (weight%) was significantly higher in the DHA intervention group at 20–22 weeks ($p < 0.01$, DHA = 3.62% (0.83); placebo = 3.0% (0.63)) and 6 weeks postpartum ($p = 0.001$, DHA = 3.72% (0.83); placebo = 2.0% (0.63)).

4. Discussion and conclusion

Lower total PDSS scores in the intervention group compared to the placebo group point to benefit in reducing symptoms of postpartum depression in women consuming supplemental DHA during pregnancy. The clinically and significantly lower mean PDSS score obtained closest to the intervention period, at 2 weeks postpartum in the DHA supplemented group, point to a particular benefit during the early postpartum period. The maternal CES-D score during pregnancy was a significant predictor of elevated postpartum depressive symptoms. This finding highlights the idea that depressed maternal mood during pregnancy is likely to result in more symptoms of depression postpartum. This finding also supports earlier research identifying psychological disturbance during the prenatal period as a significant predictor of postpartum depression [19,20]. Additionally, our finding has clinical implications for routine screening for depression during pregnancy to facilitate early intervention. Higher inconsistency in responding (i.e., INC score) to like PDSS questions was associated with more postpartum depressive symptoms. Mental confusion and emotional lability are associated with postpartum depression and are likely to interfere with consistency in responding [16]. The reported 6-point reduction in PDSS total score underlines that individuals who are either at risk for or actually have elevated symptoms of postpartum depression may experience a moderate benefit, thus highlighting the need for larger-scale investigations. These data demonstrate that women consuming DHA during pregnancy had less maternal anxiety/insecurity, emotional lability and loss of self, compared to the placebo group. Collectively, lower scores in these domains may contribute significantly to maternal feeling of wellness and quality of life during the postpartum period.

Underlying mechanisms to explain depressed mood related to DHA deficiency have been explored. Research in animal models has linked DHA deficiency to alterations in neurotransmission, and evidence points to reduced dopamine

Table 1 – PDSS total and composite scores by group.

	Group	2 Weeks Mean (SD)	6 Weeks Mean (SD)	3 Months Mean (SD)	6 Months Mean (SD)	Repeated Measures LS Mean (SEM)	Repeated measures P-value
PDSS total score	Int.	47.65 (12.96)	47.61 (14.31)	45.28 (12.25)	45.55 (13.50)	[a]46.03 (2.17)	P = 0.016
	Placebo	53.86 (15.25)	47.40 (12.42)	42.63 (9.52)	48.42 (17.18)	[a]52.11 (2.4)	
Disturbances sleep/eating	Int.	8.05 (3.68)	7.39 (4.02)	7.72 (3.68)	6.80 (3.44)	8.1 (0.6)	NS
	Placebo	8.77 (3.31)	7.65 (2.89)	6.22 (1.83)	7.00 (2.67)	9.1 (0.6)	
Anxiety/insecurity	Int.	8.30 (3.56)	7.72 (3.18)	7.00 (2.28)	7.65 (3.70)	[a]7.7 (0.6)	P = 0.03
	Placebo	9.45 (3.54)	7.85 (3.00)	6.56 (2.38)	8.11 (3.51)	[a]9.0 (0.6)	
Emotional lability	Int.	7.35 (2.18)	8.22 (3.62)	7.06 (2.44)	7.20 (3.21)	[a]7.01 (0.6)	P = 0.04
	Placebo	8.86 (3.54)	7.65 (2.32)	6.89 (2.45)	8.16 (4.54)	[a]8.3 (0.7)	
Mental confusion	Int.	6.90 (2.77)	7.61 (4.06)	6.89 (2.91)	7.55 (3.15)	7.1 (0.57)	NS
	Placebo	8.23 (3.64)	7.20 (2.84)	6.39 (2.35)	7.68 (3.53)	8.4 (0.6)	
Loss of self	Int.	6.20 (1.96)	5.67 (1.24)	5.72 (1.32)	5.45 (1.00)	[a]5.5 (0.3)	P = 0.02
	Placebo	7.00 (2.37)	6.10 (1.74)	5.78 (1.56)	6.42 (2.71)	[a]6.4 (0.35)	
Guilt	Int.	5.75 (1.12)	5.83 (1.42)	5.89 (1.94)	5.95 (1.57)	5.4 (0.3)	NS
	Placebo	6.41 (1.47)	5.95 (1.76)	5.39 (0.85)	5.74 (1.37)	5.7 (0.3)	
Suicide	Int.	5.10 (0.31)	5.17 (0.71)	5.00 (0.00)	4.95 (0.22)	5.13 (0.1)	NS
	Placebo	5.14 (0.47)	5.10 (0.31)	5.00 (0.00)	5.47 (1.43)	5.2 (0.1)	

[a] = significant group difference. NS = not significant.

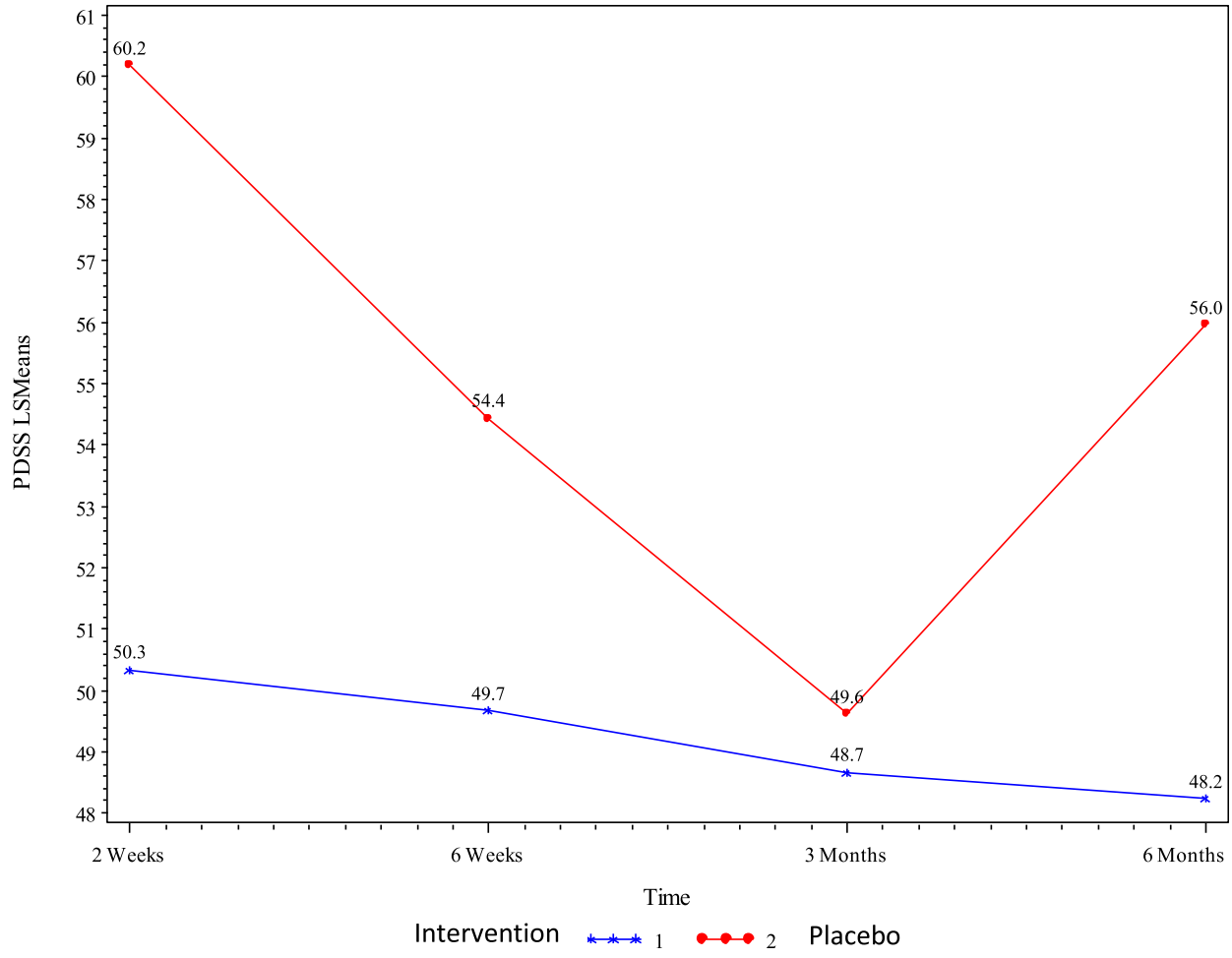

Fig. 3 – PDSS LS mean scores by group at individual time points. ( ) = Standard Deviation.

release [21]. Wood et al. [22] demonstrated in the mouse model that dietary n-3 fatty acids shift endocannabinoids in the brain and that increased dietary DHA results in increased brain and circulating DHA-endocannabinoid species. These impacts of DHA on mood regulation provide a basis for the higher PDSS scores and variability observed in the placebo group with better mood stability and lower PDSS scores in the intervention group.

In the current study the intervention group had higher RBC DHA relative wt% compared to the placebo group. At baseline and in the postpartum period RBC DHA wt% was significantly higher in the intervention group compared to the placebo group without a significant time effect. Our finding of no time effect on a biochemical marker for a moderate supplementation with DHA in women during pregnancy has previously been discussed [13].

Limitations of this pilot investigation include that the majority of the participants recruited were of low socioeconomic status thus limiting generalizability to the general population. Attrition in this investigation was attributed predominately to associated lifestyle and population characteristics. No adverse maternal or infant outcomes were reported associated with this investigation.

In summary, our findings support the efficacy of DHA in decreasing postpartum depressive symptomatology, and these results highlight a need for further larger-scale investigations. Fewer total depressive symptoms, less anxiety/insecurity, less emotional lability and a better sense of self have implications for both maternal and infant well-being and quality of life. Mothers with depressive symptoms are more likely to discontinue breastfeeding [23], display withdrawn or intrusive interaction patterns [24], be less responsive to infants, report more negative emotions relating to care for their infants [25], and be less likely to engage in enrichment activities such as reading, singing and telling stories to infants [26]. Negative mother–infant interactions lead to problematic infant developmental patterns [27]. This interruption in mother–infant interaction negatively impacts toddlers' attachment as well as self-esteem and independence [28]. Our finding offers a contribution toward efforts to increase awareness of the need for further larger-scale investigations focused on DHA in maternal mental health for the general population and as an intervention for high-risk groups. Although our lower postpartum depressive symptomatology with DHA intervention is in contrast to the findings of others [11,29], the use of the Edinburgh Postnatal Depression Scale [30] in those studies

compared to PDSS [16] with its specificity for postpartum symptomatology may be a possible underlying explanation for the dichotomy, and this should be further explored. While our sample was limited in size, our evidence points also to a need for more careful consideration of instrumentation used in the assessment of postpartum depressive symptoms in future investigations.

Author contributions

Lammi-Keefe and Beck conceived the study, designed the trial and obtained research funding. Judge supervised the conduct of the trial and data collection. Judge and McKelvey undertook recruitment of participating centers and patients and managed the data. Judge, Beck, Durham and Lammi-Keefe provided input on statistical analyses in conjunction with the biostatistician Stephen Walsh. Beck and Lammi-Keefe chaired the data oversight committee. Judge drafted the manuscript and all authors contributed substantially to its revision. Judge takes responsibility for the paper as a whole.

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Conflict of interest

No conflicts of interest exist related to this investigation.

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