THE LANCET Psychiatry

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Postpartum Depression: Action Towards Causes and Treatment (PACT) Consortium. Heterogeneity of postpartum depression: a latent class analysis. *Lancet Psychiatry* 2014; published online Dec 22. http://dx.doi.org/10.1016/S2215-0366(14)00055-8.

PACT Supplement Table 1

Study Site Locations, Collaborators, Design and Records Submitted

Country	Institution	Collaborators	Study Designs Submitted	Records Submitted
Australia	U of Melbourne	Buist, A., Bilszta, J. *	Prospective	Single
France	Univ of Paris	Apter, G., Devouche, E.	Prospective	Repeated
Sweden	Karolinska	Magnusson, P., Lichtenstein, P.	Retrospective	Single
The Netherlands	Erasmus	Bergink, V.	Prospective	Single
The Netherlands	VU University Medical Center	Penninx, B.	Retrospective	Single
The Netherlands	Erasmus MC	Roza, S.	Prospective	Single
UK	Cardiff	Jones, I.	Retrospective	Repeated
USA	Cornell	Altemus, M.	Retrospective	Single
USA	U Mass	Deligiannidis, K.	Prospective	Single
USA	U Penn	Epperson, N.C., Kim, D.	Prospective	Single
USA	Medical U of South Carolina	Guille, C.	Prospective	Single
USA	UNC	Meltzer-Brody, S., Sullivan, P.F., Rubinow, D. *	Prospective	Repeated
USA	Iowa	O'Hara, M., Stuart, S., Brock, R. L. *	Mixed	Repeated
USA	Hopkins	Payne, J.	Prospective	Single
USA	U of Rochester	Robertson-Blackmore, E.	Prospective	Repeated
USA	NIH/NIMH	Schmidt, P., Martinez, P. *	Mixed	Single
USA	Brown	Sharkey, K.	Prospective	Repeated
USA	U of Arkansas/Emory	Stowe, Z., Newport, J.	Prospective	Repeated
USA	Northwestern (Pittsburgh)	Wisner, K., Heather, E., Dills, J.L., Sit, D. *	Prospective	Repeated
USA	UNC	Putnam, K.T. Biostatistician		
Denmark	Aarhus University	Munk-Olsen, T. Epidemiologist		
* Data submitted included study participants across multiple cohorts				

PACT Supplement Table 2

Enrollment Period, Recruitment Setting, Assessment Measures, PPD Criteria and Past Psychiatric History across Sites

Country	Site PI	Time of Study Enrollment	Recruitment Setting	Depression Asssessment Measure	Structured Clinial Interview	Site Criteria for PPD Dx	Past Psychiatic History of MDE or Anxiety
Australia	Buist, A	prior and during PPD	MBU	HAM-D	SCID	DSM-IV for major depression	yes - self-report
France	Apter, G	prior, during and after PPD	Multiple	EPDS (French validated)	MADRS (French validated)	EPDS > 11	yes - interview and self-report
Sweden	Magnusson, P	after PPD	Swedish Twin Community	EPDS (Swedish)	CIDI	EPDS definition	yes self report
The Netherlands	Bergink, V	during and after PPD	Psychiatric clinic	EPDS (Dutch), Hamilton	SCID	EPDS > 13	yes I nterview and self report
The Netherlands	Penninx, B	prior, during and after PPD	Psychiatric clinic, community, multiple	L-EPDS[1] (Dutch)	CIDI	EPDS > 12	yes - interview and self-report - CIDI
The Netherlands	Rosa, S	prior to PPD	Comminity	L-EPDS[1] (Dutch)	None	EPDS > 12	no
UK	Jones, I	after PPD	Multiple	Site specific diagnostic instrument	SCAN	DSM IV	yes- SCAN, Clinical interview
USA	Altemus, M	during and after PPD	Psychiatric clinic	N/A	None	DSM	yes - clinical interview x
USA	Deligiannidis, K	prior to PPD	obstetric clinic	EPDS (English); quick inventory depressive symptoms self report (QIDS-SR)	SCID/MINI	used diagnostic interview	yes-clinical interview and self-report
USA	Epperson, N	prior to PPD	Obstetric clinic, Community, Advertised	EPDS (English)	CDIS (mood module)	EPDS ≥ 10	yes - self-report
USA	Guille, C	prior to PPD	Obstetric clinic	EPDS (English)	None	EPDS ≥ 10	yes- self report
USA	Meltzer-Brody, S	prior, during and after PPD	Multiple,Psychiatric clinic, Obstetric Clinic, Community, Advertized	EPDS (English) - all, PHQ some	SCID/MINI	EPDS > 12	yes - interview and self-report
USA	O'Hara, M	prior and during PPD	Multiple	EPDS (English), PHQ, Hamilton	SCID	SCID diagnosis	yes - clinical interview
USA	Payne, J	prior to PPD	Multiple	EPDS (English), IDS-SR, MADRS	SCID	DSM-IV major depressive episode & clearly began postpartum	yes - interview and self-report
USA	Robertson-Blackmore, E	prior to PPD	Obstetric clinic	EPDS (English)	SCID (mood module)	Narrow definition SCID diagnosis of major, minor or depression NOS at 6 weeks postpartum, Broader within 6 months.	yes - interview and self-report
USA	Schmidt, P	during and after PPD	Multiple, Advertized	EPDS (English), CES-D, BDI, Hamilton	SCID	SCID diagnosis	yes - clinical interview
USA	Sharkey, K	prior to PPD	Psychiatric clinic, Obstetric Clinic, Community, Advertised, Multiple	Hamilton, Inventory of Depressive Symptomotology,also measuring manic symptoms with the Highs questionnaire and the Bech-Rafelson interview	SCID, at 16 weeks also the LIFE	HAM-D > 13, IDS-SR>25	yes - interview and self-report
USA	Stowe, Z	prior to PPD	Multiple, Clinic sample	EPDS (English) - on 40%, BDI, Hamilton	SCID (mood module), SCID lifetime		yes - interview and self-report
USA	Wisner, K	prior and during PPD	Multiple	EPDS (English), SIGHADS, Hamilton	SCID	SIGHADS score of >/=18, HRSD >/= 15	yes - clinical interview
[1]The EPDS-Lifetime: assessment of lifetime prevalence and risk factors for perinatal depression in a large cohort of depressed women.							
Meltzer-Brody S, Boschloo L, Jones I, Sullivan PF, Penninx BW. Arch Womens Ment Health. 2013 Dec;16(6):465-73. doi: 10.1007/s00737-013-0372-9. Epub 2013 Aug 1. PMID:23904137							

PACT Phenotypic Site Survey

After signing the memo of understanding a survey was distributed to each site to learn what types of studies and variables were available for submission. The survey was developed by the PACT Phenotype Committee comprised of PIs from 9 sites. The survey included questions about recruitment, depression assessment measures and timing, the types of structured clinical interview used, criteria for PPD diagnosis, availability of psychiatric and medication histories, pregnancy and obstetric complications and if biological samples were collected. These data were synthesized to create the data codebook questions.

PACT Codebook

The Phenotype Committee next created a listing of variables and questions areas to collect the available data from PACT sites. The questions were divided into nine sections. The nine sections corresponded with nine electronic excel templates for data submission. Each site sent in de-identified data that corresponded with the PACT Codebook question item. Many sites did not have existent data for all the variables requested.

The PACT codebook contained nine sections with a total of 122 questions that collected de-identified subject information on the following: 1) site identification, study design, case definition and assessment period; 2) demographic information; 3) obstetric, delivery, breast feeding and offspring history/parity; 4) perinatal depression episode status (PND), PND history, family history of psychiatric illness/mood disorders and PND, and trauma history; 5) EPDS score/items; 6) SCID or SCAN mood module individual items; 7) SCID interview summary items; 8) HAM-D items; and 9) medication and treatment history.

Section 1 was site identification, study design and case definition. Data were coded as prospective or retrospective as well as single or repeated time assessments submitted. Section 2 collected de-identified demographic information that included the age of mom at first assessment submitted, marital status, race/ethnicity, education of mom, form of health care insurance, low income status, employment of mom during pregnancy as well as during the postpartum period and the Global Assessment Functioning Score. Section 3 was the Obstetric, Delivery, Breast Feeding and Off Spring History that included collection of gestation weeks at delivery, gravidity, parity for living, nonliving and miscarriages, if the pregnancy was planned, were assisted reproductive technology options used, smoking during pregnancy, alcohol during pregnancy, antiemetic or opiates medicines, gestational onset, hypertension, maternal obesity (BMI GE 30) pre-eclampsia,, gestational onset diabetes, high risk pregnancy due to maternal medical condition, fetal stress, postpartum hemorrhage, premature rupture of membranes (PROM), type of delivery (vaginal, caesarean or unknown). Breastfeeding, birth defect (major), low birth weight, number of delivery births, hospital care (nursery mom/NICU/unknown). Section 4 coded for the Perinatal Depression Episode (PND), PND History, Family History and Trauma History items that included PPD onset timing and previous history, family history of PPD or other DSM diagnoses, childhood sexual, physical or other trauma. The PPD onset was based on patient reports and time of assessment in the parent study. The phenotype committee defined PPD onset timing levels and each site selected the appropriate timing onset category from the defined choices listed in the codebook to describe their study. The information submitted by each site was derived from patient report and timing of assessments in the parent study. Section 5 coded for the 10 EPDS individual items and total score. Section 6 coded the SCID Mood Module individual items. Section 7 coded the SCID Diagnosis Summary items. Section 8 coded the Hamilton Depression Rating total score. Section 9 coded Medication and Treatment History items that included antenatal and postpartum usage of any anti-depressant, anti-anxiety/hypnotics, anti-psychotics, PPD psychotherapy or a PPD psychiatric admission.

Latent Class Analyses (LCA)

Data analyses of the aggregated PACT records were conducted for a 2 tier analysis plan. LCA is a useful tool to identify mutually exclusive classes based on profiles of multiple variables. Subjects within both tiers were unique subjects with a post birth rating. There was overlap of the subjects between tiers and missing data were largely due to the fact the measure was not originally collected in the parent study. There were a total of 2537 subjects that were included in both Tier 1 and Tier 2 LCAs. In Tier 1, 39% of the subjects were part of Tier 2. In Tier 2, 57% of subjects were included in Tier 1. For cases having multiple ratings submitted, the most severe depression rating was selected. In this paper, Tier 1 LCA utilized complete (no missing data) EPDS records. Class membership was assigned based on the 10 EPDS questions with follow up validation analyses on categorical phenotypic variables detailed below. Given that inclusion criteria was singularly determined by having a complete EPDS rating, many of the cases did not collect data on the validation variables. Tier 1 validation analyses used the EPDS 10 question class assigned membership to quantify additional phenotypic values and percentages for the EPDS total, EPDS anxiety subscale, pregnancy and obstetric complications, psychiatric history of major depression or anxiety data available. Chi-square statistics tested the significance of the latent class for each validation variable and are found in Table 3. Tier 2 LCA analyses were conducted to examine a wider range of clinical data about severity and to include sites not submitting the 10 question EPDS item scores. Tier 2 analyses were restricted to cases meeting a strict case definition of PPD. The EPDS total score and anxiety subscale were indicator variables not the individual EPDS items.

Using Mplus 7.2 mixture model methods, ordinal, categorical and continuous were subjected to LCA. Given the wide range of studies aggregated the data were not imputed. Mplus estimated the model parameters individually prior to using the full information by maximum likelihood. Both Tiers utilized the step up LCA procedure meaning that the initial models were run having a single class and the number of classes were increased stepwise if the model converged and The Vuong-Lo-Mendell-Rubin likelihood ratio supported additional classes. The assumption of conditional independence addresses the correlations among observed variables in the model and deviation is assessed by examination of bivariate residuals of the indicator variables. Examination of entropy, BIC, AIC**,** and bivariate residuals along with the clinical meaningfulness of the classes were used for final model section. Sensitivity/specificity analyses were conducted to assess if the class memberships held through forward inclusion of each of the indicator variables separately. The results held up across the multiple iterations. The model estimation terminated normally in both Tiers. Mplus analyses report if the model estimation terminated normally as part of the default output. Terminated normally can be defined as the final estimates outputted being not affected by problems that arose in LCA that include: 1) the residual covariance matrix contained a negative residual variance, 2) a correlation greater than one was reported among indicator variables, or 3) that local dependencies among the variables existed. A Mplus message that the model estimation did not terminate normally noting the above warnings indicates that additional TECH reports are needed to track down what influences the indicator variables are having on the model estimation for accurate results. Mplus Mixture model and other model syntax are located online along with a very informative FAQ detailing syntax and modeling questions. http://www.statmodel.com/examples/

LCA Categorical Variables Definitions

For Tier 1 validation and Tier 2 LCA analyses the following categorical variables were created and utilized. Measures were selected for commonality among sites and clinical importance recommended by the Phenotype Committee. PPD status for inclusion in Tier 2 LCA2 were unique subjects having either an EPDS total minimum score of 10 or a minimum Hamilton 17 item score of 8 or a clinical interview that quantified depression severity. Minor depression was defined as having an EPDS total score 10-11 or Hamilton score of 8-17. Major depression was defined as an EPDS total score of at least 12 and Hamilton score equaling 18 or higher. EPDS total score was included in the Tier 2 model to include sites that only provided an EPDS total score and not the ten individual item scores. OB Complications included endorsement of any one of the five items for fetal stress, postpartum hemorrhage, PROM, delivery type, low birth weight. Pregnancy Complications included endorsement of any one of the five items for

gestational hypertension, maternal obesity, pre-eclampsia, gestation diabetes and high risk pregnancy status. Birth Defects included endorsement of a birth defect. Gravidity was converted to a binary yes/no variable. Anxiety diagnoses included endorsement of any one or more of the following DSM-IV lifetime diagnoses: GAD, Panic, Agoraphobia, PTSD, Social Phobia, Specific Phobia, Anxiety NOS, and Obsessive Compulsive. Mood diagnoses included endorsement of any one or more of the following DSM-IV lifetime diagnoses: PPD, Major Depressive Disorder, Depression NOS and Dysthymia. Co-Morbidity for Depression and Anxiety disorders included endorsement of one or more mood and one or more anxiety diagnoses.

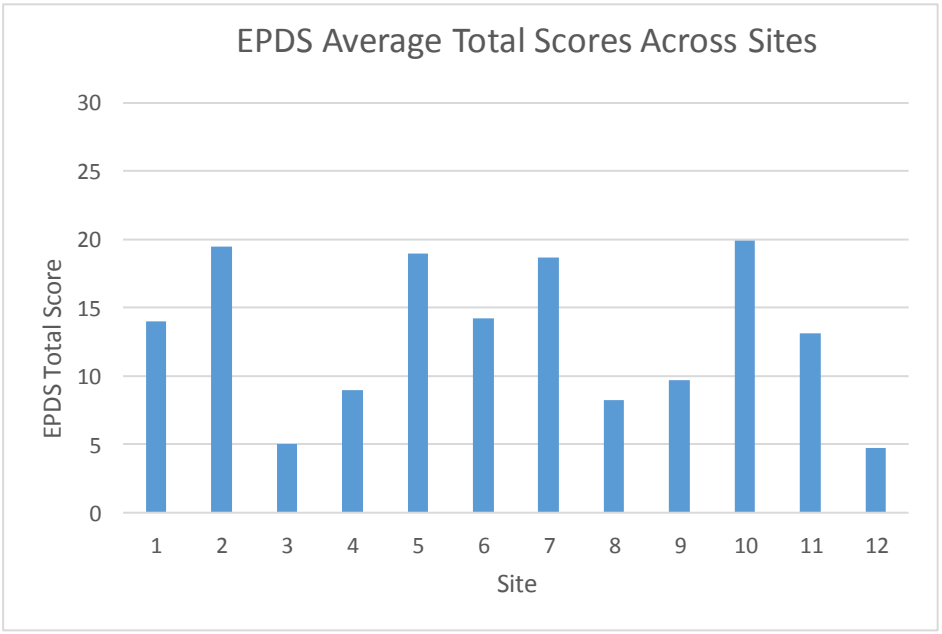
Demographic Characteristics Among LCA2 Latent Classes

Demographic Variables N=4245		Class 1 N=759 18%	Class 2 N=2099 49%	Class 3 N=1387 33%	Chi_Sq
Race	% white	73.2	81.6	81.4	x^2_4= 29.9 p<.0001
	% AA	19.9	13.8	12.0	
	% other	6.9	4.6	6.6	
Education	% HS or less	48.2	61.4	32.1	x^2_4= 253.3 p<.0001
	% college	34.3	29.2	43.3	
	% prof/grad	17.5	9.4	24.6	
Martial status	% married/cohab	82.4	78.0	80.6	x^2_2= 6.9 p=0.03
	% single/alone	17.6	22.0	19.4	
Low Income proxy	% no	78.2	73.3	48.0	x^2_2= 26.2 p<.0001
-gov/state assistance	% yes	21.8	26.7	52.0	
Design	prospective	71.9	51.2	70.8	x^2_2= 173.1 p<.0001
	retrospective	28.1	48.8	29.2	

Demographic Characteristics for PACT Sample

PACT Unique Subjejcts Demographic Variables		N=17912
Race	% white	78.3
	% AA	15.7
	% other	6.0
Education	% HS or less	56.1
	% college	28.4
	% prof/grad	15.5
Martial status	% married/cohab	83.2
	% single/alone	16.8
Low Income proxy	% no	86.6
-gov/state assistance	% yes	13.4
Design	prospective	46.5
	retrospective	53.4

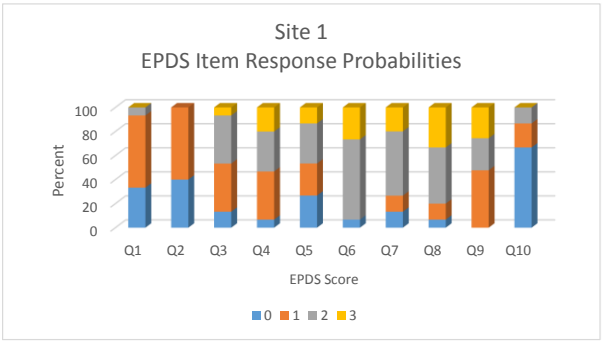
Tier 1 LCA1 EPDS Total Scores by Site

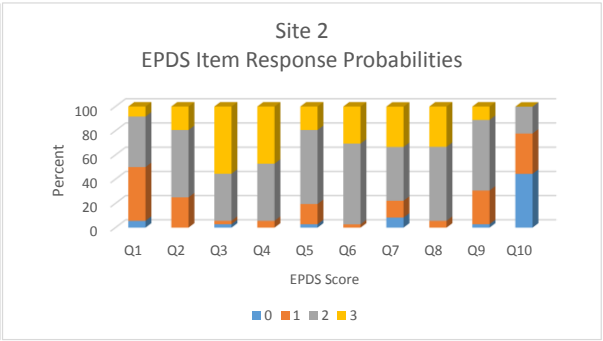


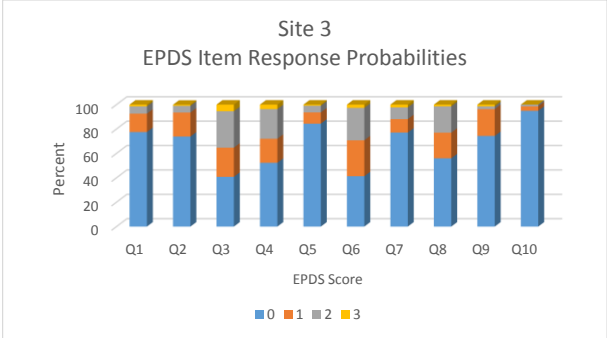
Tier 1 LCA1 EPDS Item Response Probabilities by Site

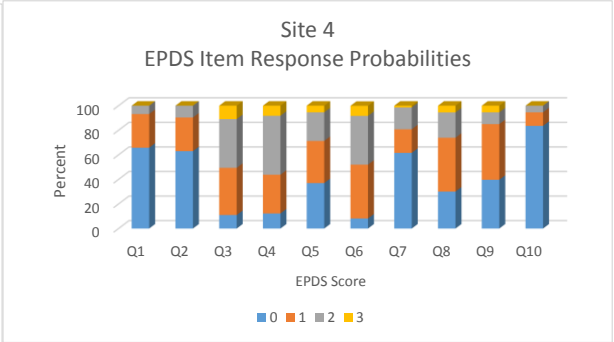
EPDS Item Response Probabilities By Site

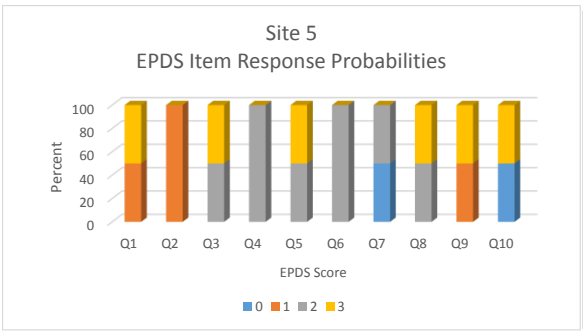
Tier 1 EPDS Item Response Probabilities by Site

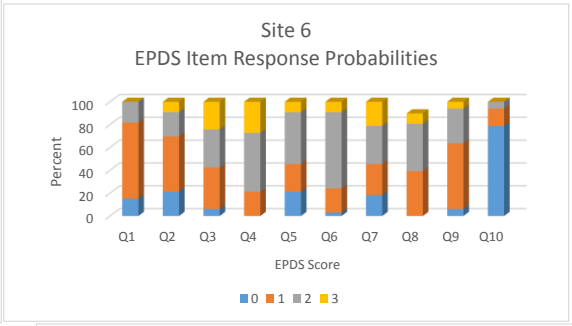


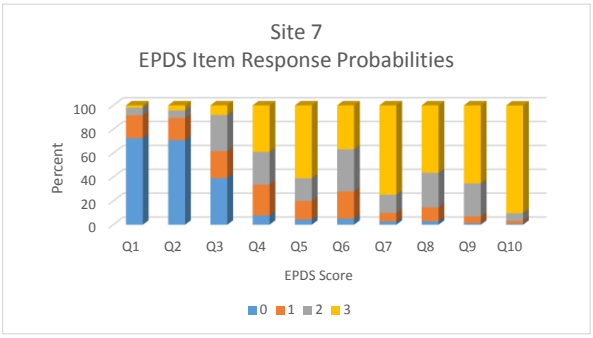


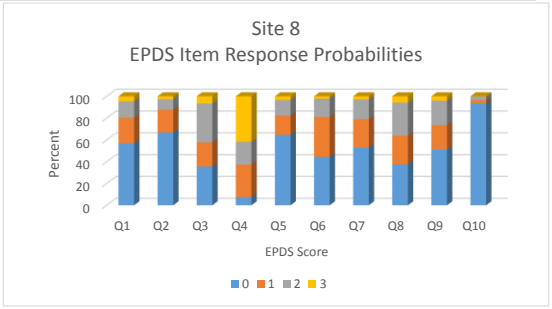


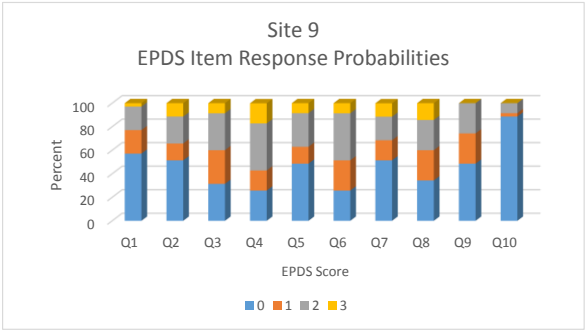


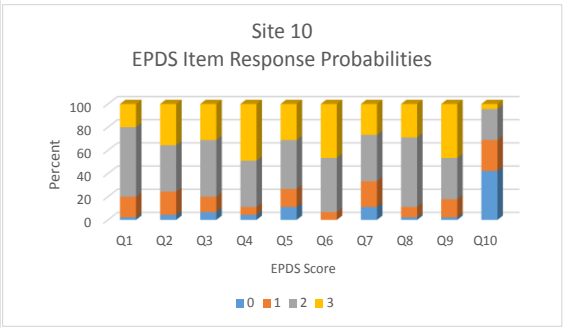


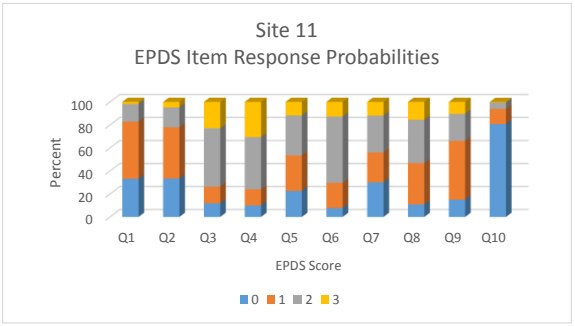


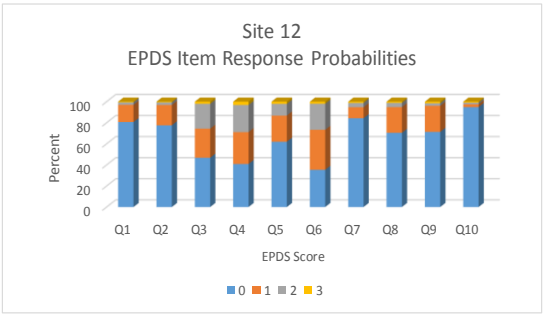




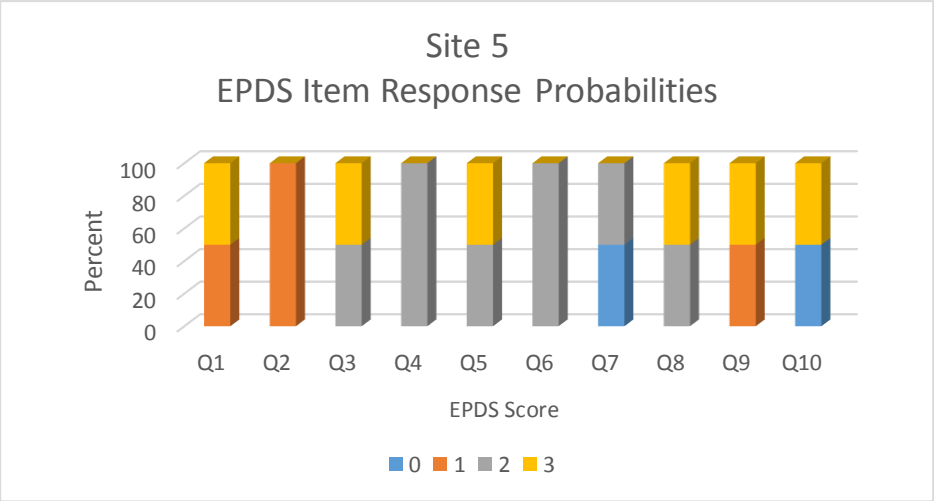


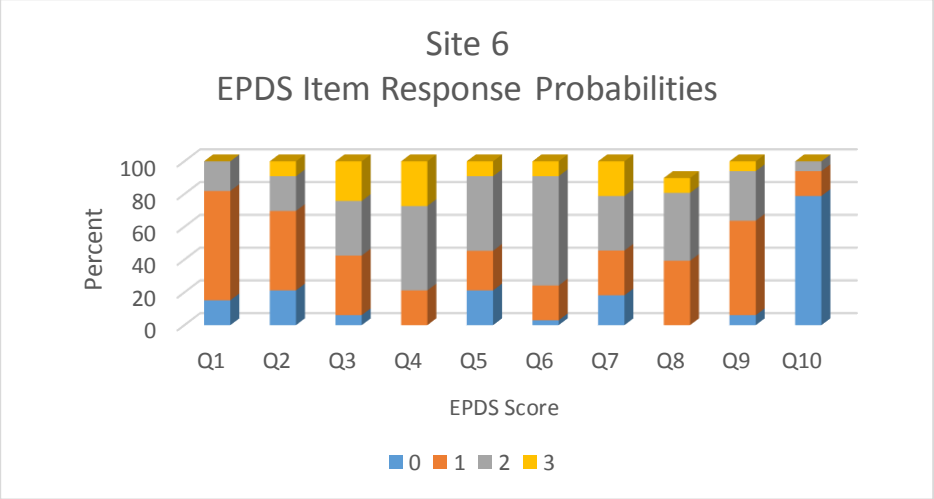


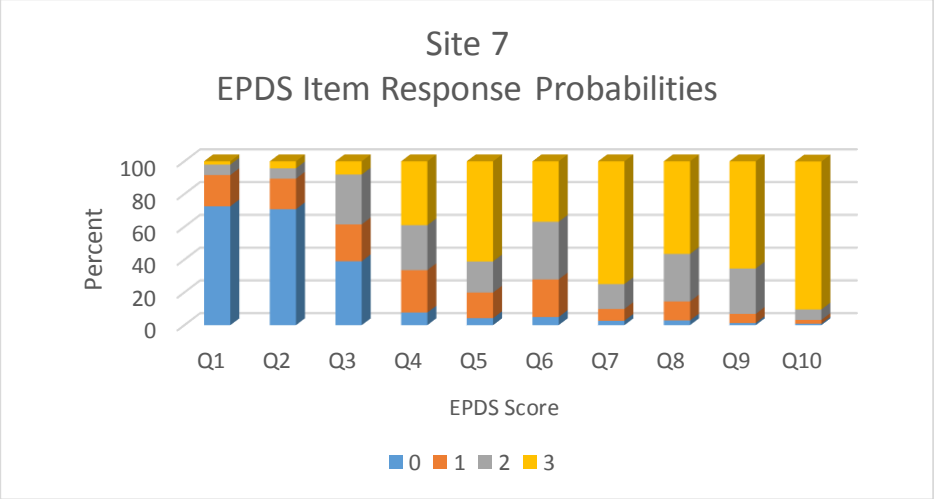


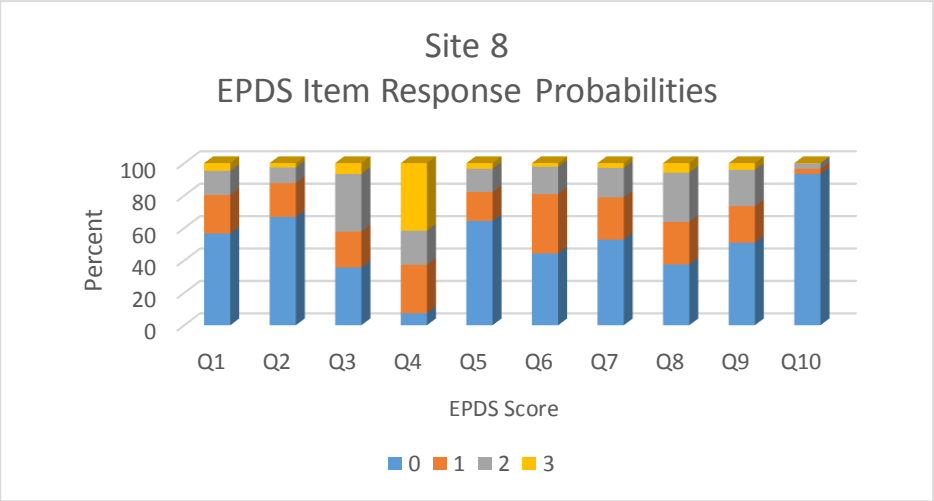


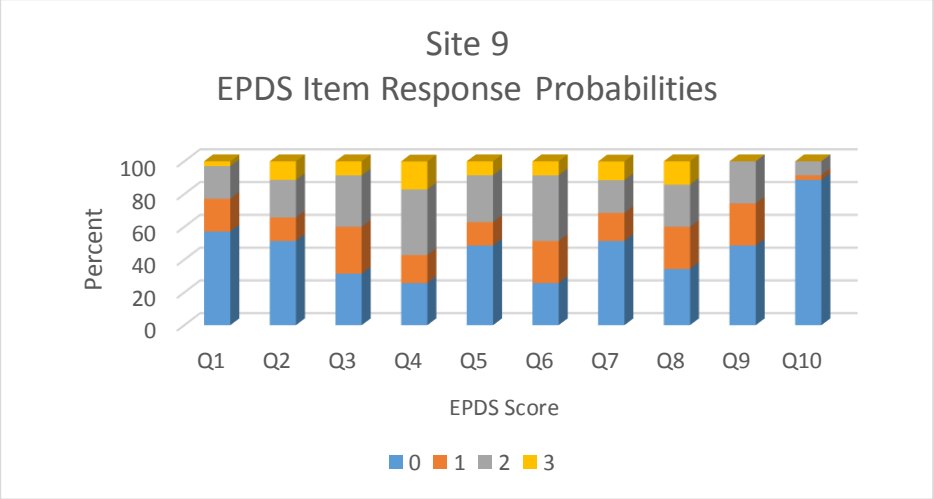
Note: The sample sizes are not consistent across sites

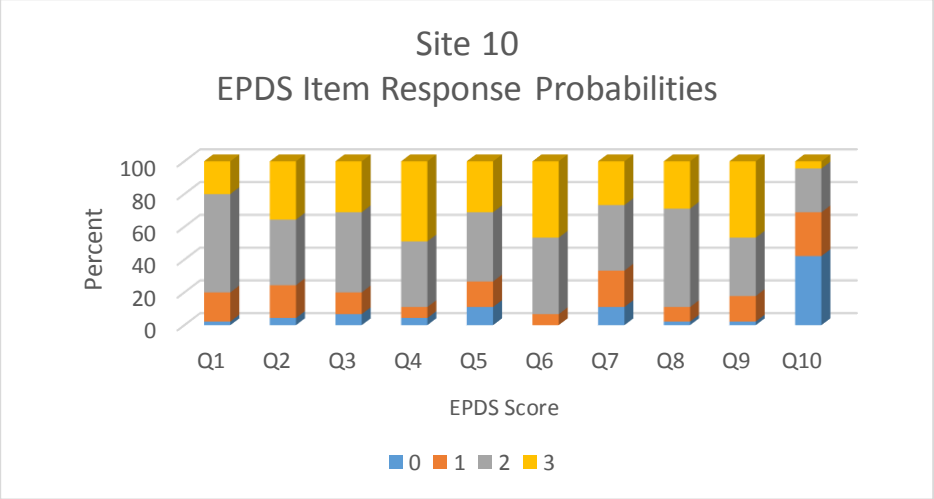

Site 5
EPDS Item Response Probabilities
Percent
100
80
60
40
20
0
Q1 Q2 Q3 Q4 Q5 Q6 Q7 Q8 Q9 Q10
EPDS Score
0 1 2 3

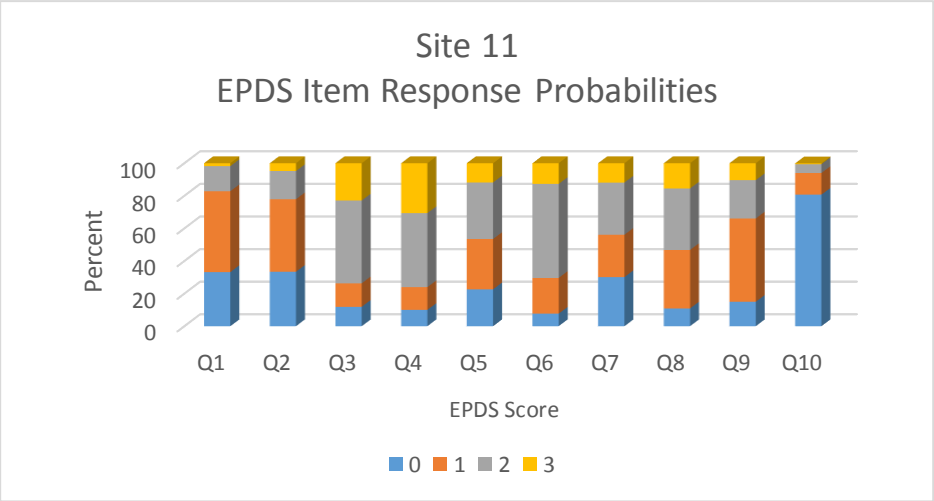

Site 6
EPDS Item Response Probabilities
Percent
100
80
60
40
20
0
Q1 Q2 Q3 Q4 Q5 Q6 Q7 Q8 Q9 Q10
EPDS Score
0 1 2 3

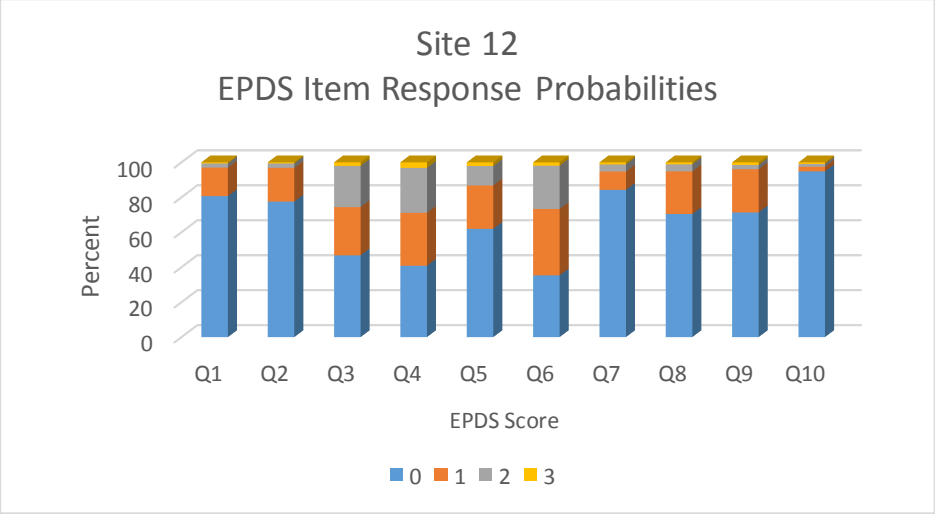

Site 7
EPDS Item Response Probabilities
Percent
100
80
60
40
20
0
Q1 Q2 Q3 Q4 Q5 Q6 Q7 Q8 Q9 Q10
EPDS Score
0 1 2 3


Site 8
EPDS Item Response Probabilities
Percent
100
80
60
40
20
0
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Q9
Q10
EPDS Score
0
1
2
3


Site 9
EPDS Item Response Probabilities
Percent
100
80
60
40
20
0
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Q9
Q10
EPDS Score
0
1
2
3


Site 10
EPDS Item Response Probabilities
Percent
100
80
60
40
20
0
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Q9
Q10
EPDS Score
0
1
2
3





Note: Sample sizes are not consistent across sites.