### **Supplemental Online Content**

Constantino-Pettit A, Tillman R, Wilson J, et al. Cannabis use and trajectories of depression and stress across the prenatal period. *JAMA Netw Open.* 2024;7(12):e2451597. doi:10.1001/jamanetworkopen.2024.51597

- **eTable 1.** Percentage [95% Confidence Intervals] of Individuals with Depression Scores (EPDS) in the Putative Clinical Range (>=13) across: Individuals with No Self-Reported Cannabis Use (at T1); Individuals Using Cannabis to Cope with Mental Health Conditions; and Individuals Using Cannabis for Reasons Other than Mental Health
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This supplemental material has been provided by the authors to give readers additional information about their work.

<u>eTable 1</u>. Percentage [95% Confidence Intervals] of Individuals with Depression Scores (EPDS) in the Putative Clinical Range (>=13) across: Individuals with No Self-Reported Cannabis Use (at T1); Individuals Using Cannabis to Cope with Mental Health Conditions; and Individuals Using Cannabis for Reasons Other than Mental Health

	T1 (%, 95 C.I.)	T2 (%, 95 C.I.)	T3 (%, 95 C.I.)
No Self-Reported	19.5 [14.8-25.0]	13.5 [8.7-19.1]	13.5 [8.5-18.5]
Cannabis Use (N=251)			
<b>Using Cannabis for</b>	34.4 [26.2-43.3]	25.5 [17.5 -34.9]	19.6 [12.0-29.2]
Mental Health (N=128)			
Using Cannabis for	8.7 [3.8-16.4]	10.8 [4.8 - 20.2]	9.0 [3.4-18.5]
Other Reasons (N=92)	-		· ·

N reflects individuals with T1 EPDS scores.

### <u>eTable 2</u>. Mean EPDS and PSS scores after exclusion for discordance in Self-Reported Cannabis Use and Urine Toxicology at T1

Of those who self-reported any T1 cannabis use (i.e., either for mental health or other reasons), 48 individuals in each of the 'mental health' and 'other reason' groups did not test positive for cannabis metabolites at T1. Likewise, 44 individuals who did not self-report any T1 cannabis use tested positive for cannabis metabolites at T1.

	T1 EPDS	T2 EPDS	T3 EPDS	T1 PSS	T2 PSS	T3 PSS
Mean [SD]						
No PCU (N=253)	7.9 [6.1]*	6.3 [5.8]	6.0 [5.4]	16.7 [8.1]	15.0 [7.9]	14.6 [7.2]
Using Cannabis	5.4 [4.3]	5.5 [5.2]	5.2 [4.9]	14.4 [7.6]	13.4 [7.7]	13.1 [6.9]
for Other Reasons						
(N=131)						
Using Cannabis	10.5 [5.7]	8.4 [5.8]	7.4 [5.1]	19.5 [7.2]	18.3 [5.7]	18.0 [5.4]
for Mental Health						
Reasons (N=253)						

<sup>\*</sup>Mean T1 EPDS varied based on discordance between self-report and urine toxicology (p=0.003; 7.4 vs 7.9). No other estimates differed upon exclusion of data from discordant individuals. See footnote to Table 3 which documents that results from the multi-group model remained largely unchanged upon exclusion of data from discordant individuals.

# <u>eTable 3</u>. Association (Regression Coefficient, Standard Error, p-value) between EPDS, PSS, and Cotinine Positivity (at T1, T2, or T3) in PCU Individuals

	T1 EPDS	T2 EPDS	T3 EPDS	T1 PSS	T2 PSS	T3 PSS
Cotinine	0.52, 0.76,	0.24, 0.85,	0.34, 0.86,	0.61, 1.06,	-0.35, 1.12,	-0.85, 1.19,
positivity	0.49	0.78	0.70	0.57	0.76	0.48

eTable 4. Bivariate Pearson Correlations across EPDS, PSS, and PCU

	T1EPDS	T2EPDS	T3EPDS	T1PSS	T2PSS	T3PSS	T1PCU	T2PCU	T3PCU
T1EPDS	1								
T2EPDS	0.57*	1							
T3EPDS	0.44*	0.62*	1						
T1PSS	0.62*	0.46*	0.42*	1					
T2PSS	0.52*	0.63*	0.49*	0.59*	1				
T3PSS	0.50*	0.54*	0.64*	0.47*	0.62*	1			
T1PCU	0.11*	0.15*	0.11*	0.13*	0.12*	0.16*	1		
T2PCU	0.17*	0.17*	0.17*	0.21*	0.18*	0.21*	0.68*	1	
T3PCU	0.06	0.12*	0.18*	0.16*	0.09	0.10	0.61*	0.77*	1

<sup>\*</sup>Significant at p < 0.05

<u>eTable 5</u>. Overall and group-stratified mean change in EPDS and PSS scores between T1 and T2, and between T2 and T3. Mean absolute value (to account for increase and decrease in scores) is also shown. Results from univariate regressions (Coefficient, SE) between PCU and Difference in EPDS and PSS Scores between T1-T2 and T2-T3.

	Overall	T1 PCU	T2 PCU	T3 PCU
T1-T2 difference in	1.06 (5.3)	-	-	-
EPDS (Mean, SD)				
Absolute value (Mean,	3.88 (3.8)			
SD)	4 >			
T2-T3 difference in	0.50 (4.9)	-	-	-
EPDS (Mean, SD)				
Absolute value (Mean,	3.43 (3.5)			
SD)				
T1-T2 EPDS	-	-0.09, 0.20	-0.02, 0.21	-0.26, 0.23
T2-T3 EPDS	-	0.09, 0.20	0.04, 0.21	-0.18, 0.22
T1-T2 difference in	0.94 (6.8)	-	-	-
PSS (Mean, SD)				
Absolute value (Mean,	5.14 (4.6)			
SD)				
T2-T3 difference in	0.60 (6.2)	-	=	-
PSS (Mean, SD)				
Absolute value (Mean,	4.55			
SD)	(4.30)			
T1-T2 PSS	-	-0.17, 0.29	0.23, 0.29	0.50, 0.33
T2-T3 PSS	-	0.44, 0.29	-0.20, 0.30	-0.08, 0.33

None of the regression-based estimates are statistically significant at p < 0.05; results were unchanged when regressions were conducted using absolute value of difference in EPDS and PSS scores

<u>eTable 6</u>. Baseline Model: Standardized Estimates and 95% Confidence Intervals For Cannabis, PSS, and EPDS Trajectories; Covariate-Adjusted Model: Standardized Estimates for Covariates in the Models

Baseline Model	Prenatal Cannabis Use (n=504)			Prenatal Stress (n=417)			Prenatal Depression (n=478)		
	Intercept [95% CI]	Slope [95% CI]	Slope-Intercept Correlation [95% CI]	Intercept [95% CI]	Slope [95% CI]	Slope-Intercept Correlation [95% CI]	Intercept [95% CI]	Slope [95% CI]	Slope-Intercept Correlation [95% CI]
No covariates	0.90 <sup>&amp;</sup> [0.03-0.15]	-0.64 [95, -	-0.08 [30, 0.46]	2.59 [2.31, 2.87]	-0.29 [43, - .15]	-0.49 [62,36]	1.58 [1.40, 1.77]	-0.35 [49, -	-0.45 [58,31]
Covariate- Adjusted Model	Prenatal Cannabis Use (n=411)		Prenatal Stress (n=372)			Prenatal Depression (n=397)			
	Effect on Intercept	Effect on Slope	-	Effect on Intercept	Effect on Slope	-	Effect on Intercept	Effect on Slope	_
Age INR Mental Health History	-0.12 -0.25** 0.02	0.03 0.22 0.01	- - -	-0.15** -0.02 0.23***	0.07 -0.08 0.01	- - -	-0.12* 0.03 0.33***	0.03 -0.03 -0.17*	- - -
Psychotropic Meds	0.04	-0.02	-	0.19**	-0.11	-	0.19**	-0.11	-

Significance levels: \*.05, \*\*.01, \*\*\*.001; \*Estimated intercept and confidence intervals, not mean of raw data; Prenatal Depression (EPDS) model fit: Unadjusted (CFI = 1.00; RMSEA = 0.04); Adjusted for age, INR, mental health, and psychotropic medication (CFI = 0.99; RMSEA = 0.04); Prenatal Stress (PSS) model fit: Unadjusted (CFI = 1.00; RMSEA = 0.00); Adjusted for age, INR, mental health, and psychotropic medication (CFI = 1.00; RMSEA = 0.00); Prenatal Cannabis (PCU) model fit: Unadjusted (CFI = 1.00; RMSEA = 0.00); Adjusted for age, INR, mental health and psychotropic medications (CFI = 1.00; RMSEA = 0.00)

## <u>eTable 7</u>. Pearson Correlations between Estimated Intercept and Slopes for PCU, EPDS, and PSS, Computed Post-Estimation.

For these estimates, intercepts and slopes were saved out from the linear growth models. These extracted estimates were then correlated, post-hoc.

	PCU Intercept	PCU Slope	EPDS Intercept	EPDS Slope	PSS Intercept	PSS Slope
PCU	1		•	•		
Intercept						
PCU Slope	0.23***	1				
EPDS	0.13**	0.03	1			
Intercept						
EPDS Slope	0.01	0.13**	-0.39***	1		
PSS	0.14**	0.05	0.70***	-0.18**	1	
Intercept						
PSS Slope	-0.01	-0.01	-0.20***	0.35***	-0.48***	1

<sup>\*\*</sup>p<0.01 \*\*\*p<0.001

<u>eTable 8</u>. Individual Linear Growth Models of EPDS (Depression) and PSS (Stress) Scores across T1-T3 for: Individuals who Never Used Cannabis; Those who Used it, Either for Stress, Mental Health Symptoms, Sleep or Pain Management; and Those who Used Cannabis for Other Reasons

		EPDS (Depressio	n)	PSS (Stress)			
	Never Used Cannabis (n=253)	PCU-other motives (n=51)	PCU for stress, mental health, sleep or pain (n=174)	Never Used Cannabis (n=223)	PCU-other motives (n=44)	PCU for stress, mental health, sleep or pain (n=150)	
Initial Model							
Intercept	1.54 (0.16)***	1.38(0.30)***	1.84 (0.21)***	2.50 (0.24)***	2.62 (0.55)***	2.90 (0.31)***	
Slope	-0.36 (0.12)**	-0.14 (0.17)	-0.41 (0.15)**	-0.34 (0.14)*	0.07 (0.19)	-0.33 (0.14)*	
Slope-Intercept Correlation	-0.35 (0.14)**	-0.41 (0.02)*	-0.55 (0.13)***	-0.41 (0.14)**	-0.48 (0.19)**	-0.61 (0.10)***	
Best-fitting Model							
Intercept	1.55 (0.15)***	1.72 (0.37)***	1.83 (0.21)***	2.51 (0.24)***	3.59 (0.78)***	2.89(0.30)***	
Slope	-0.38(0.11)*** <sup>a</sup>	0.00&	-0.37 (0.12)** <sup>a</sup>	-0.36(0.13)**b	0.00	-0.30 (0.10)**b	
Slope-Intercept Correlation	-0.35 (0.13)**	0.00&	-0.55 (0.13)***	-0.41(0.14)**	0.00	-0.61 (0.10)***	

Note: All estimates are standardized. Significance levels: \*.05, \*\*.01, \*\*\*.001. \*Because there was no change in slope, it was constrained to 0; a, b Estimates with the same alphabetical superscript were equated; estimates differ slightly due to standardization

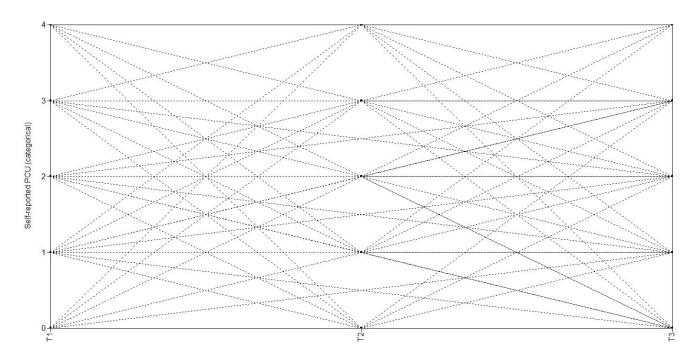
<u>eTable 9</u>. Mean EPDS by Trimester among Individuals Using for Mental Health Conditions and Individuals with No Self-Reported Cannabis Use, Stratified by Psychotropic Medication Use \*

	T1	T2	Т3
Using for Mental Health with T1 medications [n=20]	10.9 [8.3-13.6] <sup>ab</sup>	7.5 [4.7-10.4] <sup>ab</sup>	7.9 [4.9 - 10.8] <sup>abc</sup>
Using for Mental Health without	9.8 [8.6-11.1] <sup>b</sup>	8.6 [7.3-9.9] <sup>bc</sup>	7.4 [6.1-8.7] <sup>a</sup>
T1 medications [n=98] Never-Users with T1	12.5 [9.7-15.2] <sup>a</sup>	9.5 [6.2-12.9] <sup>ac</sup>	8.1[4.8-11.3] <sup>b</sup>
medication [n=26]	[	0.0 [0.2 .2.0]	
Never-Users without T1 medication [n=201]	6.6 [5.9-7.4]	5.4 [4.6-6.2]	5.4 [4.6-6.3] <sup>c</sup>

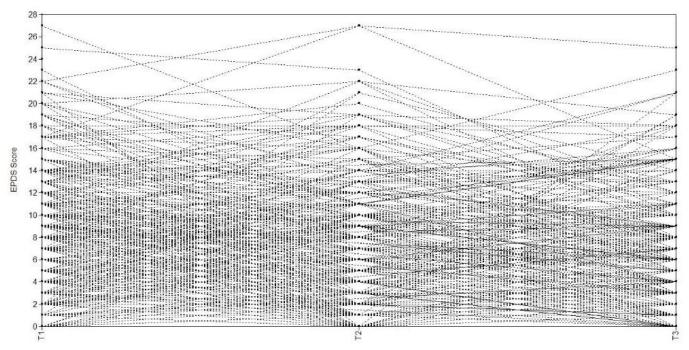
<sup>\*</sup>Individuals using for other reasons not shown as number endorsing psychotropic medications was too low (n=3); abc estimates with the same alphabetical superscript were statistically equivalent to each other. N reflects those with valid EPDS data;

<u>eFigure</u>. Sample individual observed data for PCU (Panel A), EPDS (Panel B), PSS (Panel C) across T1-T3. Plotted using the "plot" option in Mplus, within each linear growth analysis. Observed values are shown.

Panel A: PCU



#### Panel B: EPDS



#### Panel C: PSS

