

## Supplemental Online Content

Nelson HD, Darney BG, Ahrens K, et al. Associations of unintended pregnancy with maternal and infant health outcomes: a systematic review and meta-analysis. JAMA. doi:10.1001/jama.2022.19097

### **eMethods**

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### **eReferences**

This supplemental material has been provided by the authors to give readers additional information about their work.

## eMethods

### Search Terms

Database: Ovid MEDLINE(R) ALL <1946 to June 17, 2020> Updated June 15, 2022

Search Strategy (KQ4):

- 
- 1 pregnancy, unplanned/ or pregnancy, unwanted/ (4341)
  - 2 (unintended or unintentional or unplanned or unwanted or accidental or (contraceptive adj3 fail\*) or ("not" adj3 planned) or ("not" adj3 wanted)).ti,kf. (18265)
  - 3 2 and (pregnant or pregnancy or birth\*).ti,kf. (2326)
  - 4 1 or 3 (5512)
  - 5 Mothers/ (43332)
  - 6 women/ or pregnant women/ (22608)
  - 7 (mother or maternal or woman or women).ti,ab,kf. (1379043)
  - 8 exp Infant/ (1134191)
  - 9 (infant\* or infancy or child\* or baby or neonate\*).ti,ab,kf. (1798714)
  - 10 or/5-9 (3380913)
  - 11 4 and 10 (3815)
  - 12 limit 11 to english language (3509)
  - 13 limit 12 to humans (3116)
  - 14 limit 13 to yr="2000 -Current" (2358)
  - 15 "in-process".st. (340437)
  - 16 "aheadofprint".pp. (245247)
  - 17 12 and (15 or 16) (67)
  - 18 14 or 17 (2425)

## U.S. Preventive Services Task Force Criteria for Rating Study Quality of Cohort Studies<sup>1</sup>

- Initial assembly of comparable groups: Consideration of potential confounders, with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- All important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies.

Definition of ratings based on above criteria:

**Good:** Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up  $\geq 80\%$ ); reliable and valid measurement instruments are used and applied equally to all groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, intention-to-treat analysis is used for RCTs.

**Fair:** Studies are graded “fair” if any or all of the following problems occur, without the fatal flaws noted in the “poor” category below: Generally comparable groups are assembled initially, but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is used for RCTs.

**Poor:** Studies are graded “poor” if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Intention-to-treat analysis is lacking for RCTs.

<sup>1</sup> U.S. Preventive Services Task Force. Methods and Processes. Accessed September 15, 2022.  
<https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes>

## Grading Strength of Evidence<sup>1</sup>

Grades are based on:

- Study limitations (low, medium, or high level)
- Consistency (consistent, inconsistent, or unknown/not applicable)
- Directness (direct or indirect)
- Precision (precise or imprecise)
- Reporting bias (suspected or undetected)

The strength of evidence is assigned an overall grade of high, moderate, low, or insufficient by evaluating and weighing the combined results of the above domains.

**High:** high confidence that the estimate of effect lies close to the true effect for the outcome; the body of evidence has few or no deficiencies; and the findings are stable, (i.e., another study would not change the conclusions).

**Moderate:** moderate confidence that the estimate of effect lies close to the true effect for the outcome; the body of evidence has some deficiencies; and the findings are likely to be stable, but some doubt remains.

**Low:** limited confidence that the estimate of effect lies close to the true effect for the outcome; the body of evidence has major or numerous deficiencies (or both); and additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.

**Insufficient:** no evidence, unable to estimate an effect, or there is no confidence in the estimate of effect for the outcome; and no evidence is available or the body of evidence has unacceptable deficiencies, precluding conclusions.

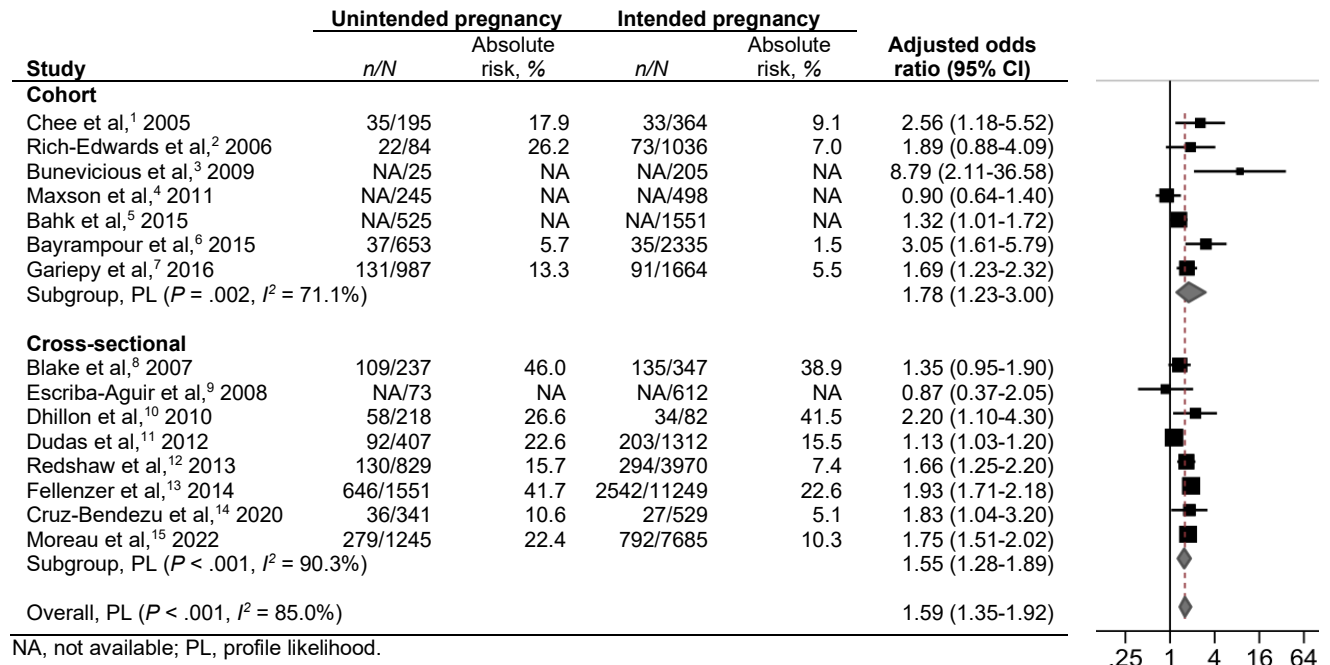
<sup>1</sup> Berkman ND, Lohr KN, Ansari MT, et al. Grading the strength of a body of evidence when assessing health care interventions: an EPC update. *J Clin Epidemiol.* 2015;68(11):1312-24. doi:10.1016/j.jclinepi.2014.11.023

<b>eTable. Strength of Evidence</b>							
<b>Outcome</b>	<b>Outcome measure</b>	<b>Studies; design; participants (N)</b>	<b>Summary of findings</b>	<b>Consistency; directness; precision</b>	<b>Reporting bias</b>	<b>Study Limitations</b>	<b>Strength of evidence</b>
Maternal depression	Prenatal depression	7 cohort and 8 cross-sectional studies (302,633)	Higher rates of prenatal depression with unintended vs intended pregnancies (aOR, 1.59 [95% CI, 1.35-1.92]; 15 studies [ <i>n</i> = 41,054]).	Consistent; indirect; precise	Undetected	Medium: multiple measures of depression used; adjustment for confounders varied across studies	High
	Postpartum depression	4 cohort and 6 cross-sectional studies (157,198)	Higher rates of postpartum depression with unintended vs intended pregnancies (aOR, 1.51 [95% CI, 1.40-1.70]; 10 studies [ <i>n</i> = 82,673])	Consistent; indirect; precise	Undetected	Medium: multiple measures of depression used; adjustment for confounders varied across studies	High
Maternal interpersonal violence	Interpersonal violence during pregnancy	5 cross-sectional studies (186,503)	Higher rates of interpersonal violence with unintended vs intended pregnancies (aOR, 2.22 [95% CI, 1.41-2.91]; 5 studies [ <i>n</i> = 42,306])	Consistent; indirect; precise	Undetected	Medium: few studies although high enrollment; difficulty measuring experience of violence	Moderate
Preterm birth	<37 weeks gestation	4 cohort and 6 cross-sectional studies (294,553)	Higher rates of preterm birth with unintended vs intended pregnancies (aOR, 1.21 [95% CI, 1.12-1.31]; 10 studies [ <i>n</i> = 94,351])	Consistent; indirect; precise	Undetected	Medium: adjustment for confounders varied across studies	Moderate
Low birth weight	<2500 grams birth weight	3 cohort and 5 cross-sectional studies (281,720)	Higher rates of low birth weight with unintended vs intended pregnancies (aOR, 1.09 [95% CI, 1.02-1.21]; 8 studies [ <i>n</i> = 87,547])	Consistent; indirect; precise	Undetected	Medium: adjustment for confounders varied across studies	Moderate

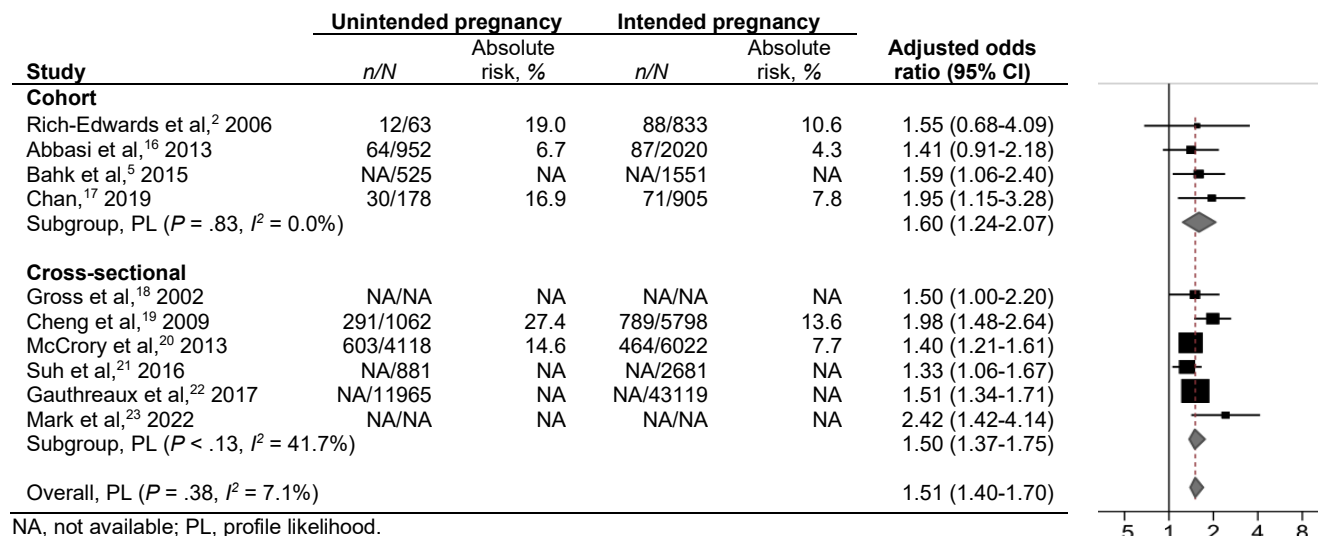
Abbreviations: CI, confidence interval; aOR, adjusted odds ratio.

## eFigure 1. Sensitivity Analysis for Depression by Study Design

### Prenatal Depression



### Postpartum Depression

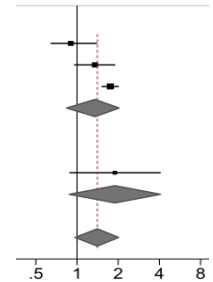


## eFigure 2. Sensitivity Analysis for Depression by Unwanted Pregnancy

### Prenatal Depression

	Unwanted pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
Study	n/N	Absolute risk, %	n/N	Absolute risk, %	
Not controlled for history of depression					
Maxson et al, <sup>4</sup> 2011	NA/245	NA	NA/498	NA	0.90 (0.64-1.40)
Blake et al, <sup>8</sup> 2007	109/237	46.0	135/347	38.9	1.35 (0.95-1.90)
Moreau et al, <sup>15</sup> 2022	279/1245	22.4	792/7685	10.3	1.75 (1.51-2.02)
Subgroup, PL ( <i>P</i> = .005, <i>I</i> <sup>2</sup> = 81.2%)					1.35 (0.84-2.03)
Controlled for history of depression					
Rich-Edwards et al, <sup>2</sup> 2006	22/84	26.2	73/1036	7.0	1.89 (0.88-4.09)
Overall, PL ( <i>P</i> = .01, <i>I</i> <sup>2</sup> = 72.3%)					1.41 (0.97-2.01)

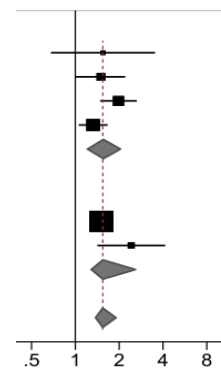
NA, not available; PL, profile likelihood.



### Postpartum Depression

	Unwanted pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
Study	n/N	Absolute risk, %	n/N	Absolute risk, %	
Not controlled for history of depression					
Rich-Edwards et al, <sup>2</sup> 2006	12/63	19.0	88/833	10.6	1.55 (0.68-4.09)
Gross et al, <sup>18</sup> 2002	NA/NA	NA	NA/NA	NA	1.50 (1.00-2.20)
Cheng et al, <sup>19</sup> 2009	291/1062	27.4	789/5798	13.6	1.98 (1.48-2.64)
Suh et al, <sup>21</sup> 2016	NA/881	NA	NA/2681	NA	1.33 (1.06-1.67)
Subgroup, PL ( <i>P</i> = .21, <i>I</i> <sup>2</sup> = 34.3%)					1.56 (1.21-2.04)
Controlled for history of depression					
Gauthreaux et al, <sup>22</sup> 2017	NA/11965	NA	NA/43119	NA	1.51 (1.34-1.71)
Mark et al, <sup>23</sup> 2022	NA/NA	NA	NA/NA	NA	2.42 (1.42-4.14)
Subgroup, PL ( <i>P</i> = .09, <i>I</i> <sup>2</sup> = 64.7%)					1.55 (1.29-2.59)
Overall, PL ( <i>P</i> = .19, <i>I</i> <sup>2</sup> = 32.4%)					1.54 (1.38-1.90)

NA, not available; PL, profile likelihood.

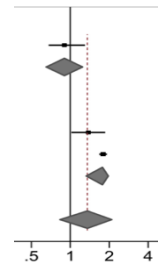


### eFigure 3. Sensitivity Analysis for Depression by Mistimed Pregnancy

#### Prenatal Depression

	Mistimed pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
Study	n/N	Absolute risk, %	n/N	Absolute risk, %	
<b>Cohort</b>					
Maxson et al, <sup>4</sup> 2011	NA/578	NA	NA/498	NA	0.90 (0.68-1.30)
<b>Cross-sectional</b>					
Blake et al, <sup>8</sup> 2007	199/423	47.0	135/347	38.9	1.38 (1.02-1.86)
Fellenzer et al, <sup>13</sup> 2014	2173/5288	41.1	2542/11249	22.6	1.79 (1.67-1.93)
Subgroup, PL ( <i>P</i> = .10, <i>I</i> <sup>2</sup> = 64.2%)					1.77 (1.33-1.97)
Overall, PL ( <i>P</i> < .001, <i>I</i> <sup>2</sup> = 89.4%)					1.36 (0.83-2.09)

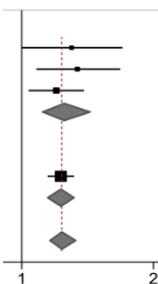
NA, not available; PL, profile likelihood.



#### Postpartum Depression

Study	Mistimed pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
	n/N	Absolute risk, %	n/N	Absolute risk, %	
Not controlled for history of depression					
Gross et al, <sup>18</sup> 2002	NA/NA	NA	NA/NA	NA	1.30 (1.00-1.70)
Cheng et al, <sup>19</sup> 2009	438/2188	20.0	789/5798	13.6	1.34 (1.08-1.68)
Suh et al, <sup>21</sup> 2016	NA/1987	NA	NA/2681	NA	1.20 (1.04-1.39)
Subgroup, PL ( <i>P</i> = .68, <i>I</i> <sup>2</sup> = 0.0%)					1.25 (1.12-1.43)
Controlled for history of depression					
Gauthreaux et al, <sup>22</sup> 2017	NA/11965	NA	NA/43119	NA	1.23 (1.15-1.32)
Overall, PL ( <i>P</i> = .84, <i>I</i> <sup>2</sup> = 0.0%)					1.23 (1.16-1.33)

NA, not available; PL, profile likelihood.





## eFigure 4. Sensitivity Analysis for Preterm Birth by Unwanted and Mistimed Pregnancy

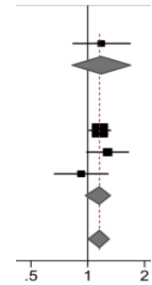
### Unwanted Pregnancy

	Unwanted pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
Study	n/N	Absolute risk, %	n/N	Absolute risk, %	
<b>Cohort</b>					
Lindberg et al, <sup>24</sup> 2015	125/891	14.0	496/4133	12.0	1.18 (0.83-1.69)
<b>Cross-sectional</b>					
Mohllajee et al, <sup>25</sup> 2007	1133/9684	11.7	3578/44178	8.1	1.16 (1.01-1.33)
Afable-Munsuz et al, <sup>26</sup> 2008	NA/827	NA	NA/6114	NA	1.28 (0.98-1.66)
Mark et al, <sup>23</sup> 2022	NA/NA	NA	NA/NA	NA	0.92 (0.66-1.29)
Subgroup, PL ( <i>P</i> = .32, <i>I</i> <sup>2</sup> = 12.3%)					1.15 (0.97-1.32)
Overall, PL ( <i>P</i> = .51, <i>I</i> <sup>2</sup> = 0.0%)					1.15 (1.01-1.30)

NA, not available; PL, profile likelihood.

Study	Adjusted Odds Ratio (95% CI)
Lindberg et al, 2015 (Cohort)	1.18 (0.83-1.69)
Mohllajee et al, 2007 (Cross-sectional)	1.16 (1.01-1.33)
Afable-Munsuz et al, 2008 (Cross-sectional)	1.28 (0.98-1.66)
Mark et al, 2022 (Cross-sectional)	0.92 (0.66-1.29)
Subgroup, PL	1.15 (0.97-1.32)
Overall, PL	1.15 (1.01-1.30)

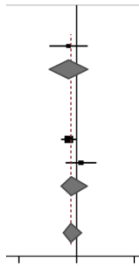
NA, not available; PL, profile likelihood.



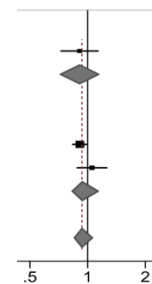
### Mistimed Pregnancy

Study	Mistimed pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
	n/N	Absolute risk, %	n/N	Absolute risk, %	
<b>Cohort</b>					
Lindberg et al, <sup>24</sup> 2015	165/1492	11.0	496/4133	12.0	1.91 (0.72-1.14)
<b>Cross-sectional</b>					
Mohllajee et al, <sup>25</sup> 2007	2345/27271	8.6	3578/44178	8.1	0.91 (0.83-1.00)
Afable-Munsuz et al, <sup>26</sup> 2008	NA/2381	NA	NA/6114	NA	1.05 (0.88-1.27)
Subgroup, PL ( <i>P</i> = .16, <i>I</i> <sup>2</sup> = 48.8%)					0.94 (0.83-1.14)
Overall, PL ( <i>P</i> = .36, <i>I</i> <sup>2</sup> = 1.0%)					0.93 (0.85-1.06)

NA, not available; PL, profile likelihood.



NA, not available; PL, profile likelihood.



## eFigure 5. Sensitivity Analysis for Infant Low Birth Weight by Unwanted and Mistimed Pregnancy

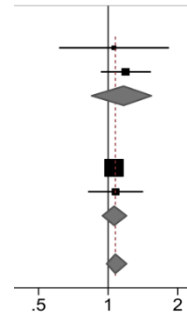
### Unwanted Pregnancy

	Unwanted pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
Study	n/N	Absolute risk, %	n/N	Absolute risk, %	
<b>Cohort</b>					
Joyce et al. <sup>27</sup> 2000	NA/NA	NA	NA/NA	NA	1.06 (0.61-1.83)
Lindberg et al, <sup>24</sup> 2015	73/916	8.0	297/4247	7.0	1.19 (0.93-1.53)
Subgroup, PL ( <i>P</i> = .71, <i>I</i> <sup>2</sup> = 0.0%)					1.17 (0.85-1.54)
<b>Cross-sectional</b>					
Mohllajee et al, <sup>25</sup> 2007	755/9684	7.8	2209/44178	5.0	1.06 (0.97-1.16)
Mark et al, <sup>23</sup> 2022	NA/NA	NA	NA/NA	NA	1.08 (0.82-1.42)
Subgroup, PL ( <i>P</i> = .91, <i>I</i> <sup>2</sup> = 0.0%)					1.06 (0.94-1.20)
Overall, PL ( <i>P</i> = .86, <i>I</i> <sup>2</sup> = 0.0%)					1.07 (0.99-1.20)

NA, not available; PL, profile likelihood.

Study	Adjusted Odds Ratio (95% CI)
Joyce et al. <sup>27</sup> 2000	1.06 (0.61-1.83)
Lindberg et al, <sup>24</sup> 2015	1.19 (0.93-1.53)
Subgroup, PL ( <i>P</i> = .71, <i>I</i> <sup>2</sup> = 0.0%)	1.17 (0.85-1.54)
Mohllajee et al, <sup>25</sup> 2007	1.06 (0.97-1.16)
Mark et al, <sup>23</sup> 2022	1.08 (0.82-1.42)
Subgroup, PL ( <i>P</i> = .91, <i>I</i> <sup>2</sup> = 0.0%)	1.06 (0.94-1.20)
Overall, PL ( <i>P</i> = .86, <i>I</i> <sup>2</sup> = 0.0%)	1.07 (0.99-1.20)

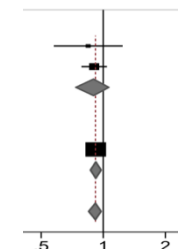
NA, not available; PL, profile likelihood.



### Mistimed Pregnancy

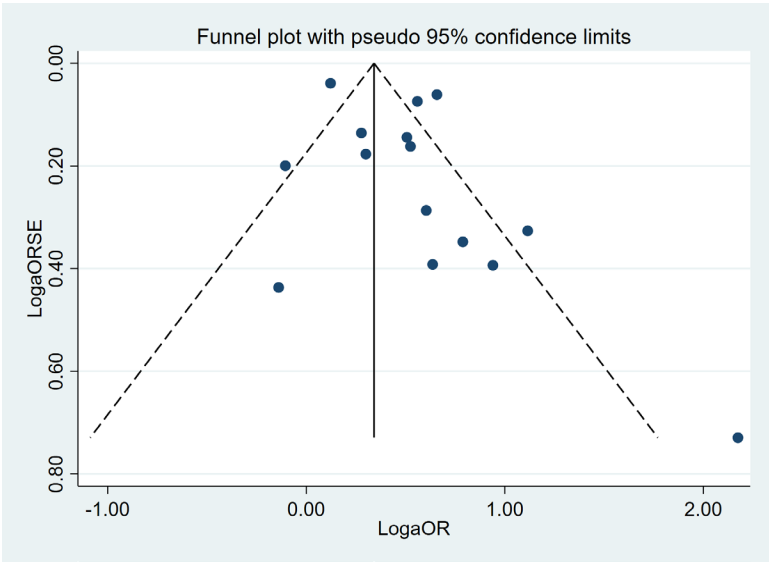
	Mistimed pregnancy		Intended pregnancy		Adjusted odds ratio (95% CI)
Study	n/N	Absolute risk, %	n/N	Absolute risk, %	
<b>Cohort</b>					
Joyce et al, <sup>27</sup> 2000	NA/NA	NA	NA/NA	NA	0.85 (0.58-1.24)
Lindberg et al, <sup>24</sup> 2015	240/3164	7.6	297/4247	7.0	0.90 (0.78-1.04)
Subgroup, PL ( <i>P</i> = .75, <i>I</i> <sup>2</sup> = 0.0%)					0.90 (0.74-1.06)
<b>Cross-sectional</b>					
Mohllajee et al, <sup>25</sup> 2007	1718/27271	6.3	2209/44178	5.0	0.92 (0.86-0.97)
Overall, PL ( <i>P</i> = .90, <i>I</i> <sup>2</sup> = 0.0%)					0.92 (0.85-0.98)

NA, not available; PL, profile likelihood.



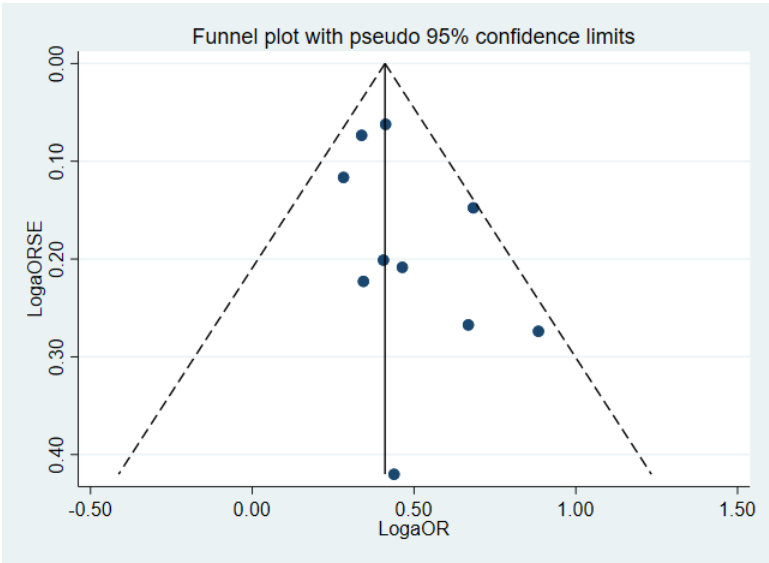
**eFigure 6. Funnel Plots**

**Prenatal Depression**



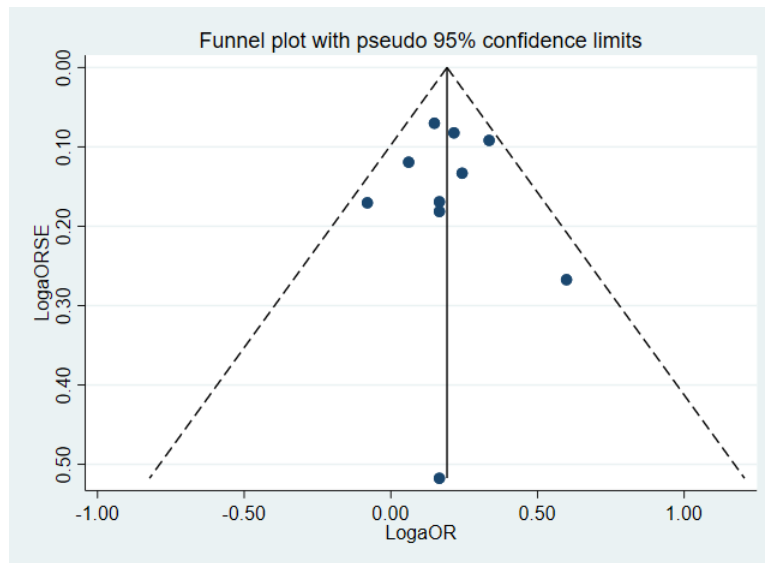
Egger's test:  $P = .14$  indicates no small-study effects.

**Postpartum Depression**



Egger's test:  $P = .16$  indicates no small-study effects.

## Preterm Birth



Egger's test:  $P = .94$  indicates no small-study effects.

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