Supplemental Online Content

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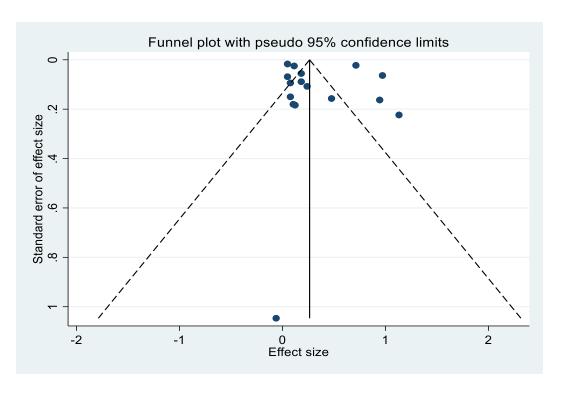
eMethods

Data extraction

Two authors (GA and BD) extracted data and independently using a standardised data extraction form. For each eligible study, we extracted the following information: first author's name, year of publication, geographic location, study design, the timing of exposure and outcomes assessment, an instrument used to assess cases in exposed and control groups, sample size, confounders adjusted for, the effects estimates (OR/RR with 95% confidence interval).

Study quality

Two investigators (GA and BD) independently evaluated the methodologic quality of the eligible articles using the Newcastle-Ottawa Scale (NOS) for observational studies ¹, with disagreements resolved by discussion. The scoring standard in the NOS scale was mainly based on three broad domains: selection of the study groups, ascertainment of outcome and exposure variables, and comparability between the groups. For cohort studies, the scoring was grouped into three categories: low quality (scored 0-3), moderate quality (scored 4-6) and high quality (scored 7-9). The maximum possible score is nine, which represents the highest methodological quality. The adapted version of NOS was used for cross-sectional studies, and scores were classified into four categories—very good quality (scored 9-10), good quality (scored 7-8), satisfactory quality (scored 5-6), and unsatisfactory (0-4 points) ².



eFigure. Funnel plot for assessing potential publication bias

eTable 1. Example search terms and strategy (PubMed)

Search: ((depression OR depressive OR psychopathology OR psychiatric disorder) AND (children OR offspring)) AND (paternal or father)

("depressed"[All Fields] OR "depression"[MeSH Terms] OR "depression"[All Fields] OR "depressions"[All Fields] OR "depression s"[All Fields] OR "depressive disorder"[MeSH Terms] OR ("depressive"[All Fields] AND "disorder"[All Fields]) OR "depressive disorder"[All Fields] OR "depressivity"[All Fields] OR "depressive"[All Fields] OR "depressively"[All Fields] OR "depressiveness"[All Fields] OR "depressives"[All Fields] OR ("depressed"[All Fields] OR "depression"[MeSH Terms] OR "depression"[All Fields] OR "depressions"[All Fields] OR "depression s"[All Fields] OR "depressive disorder"[MeSH Terms] OR ("depressive"[All Fields] AND "disorder"[All Fields]) OR "depressive" disorder"[All Fields] OR "depressivity"[All Fields] OR "depressive"[All Fields] OR "depressively"[All Fields] OR "depressiveness"[All Fields] OR "depressives"[All Fields]) OR ("psychopathologies"[All Fields] OR "psychopathology"[MeSH Terms] "psychopathology"[All Fields]) OR ("mental disorders"[MeSH Terms] OR ("mental"[All Fields] AND "disorders"[All Fields]) OR "mental disorders"[All Fields] OR ("psychiatric"[All Fields] AND "disorder"[All Fields]) OR "psychiatric disorder"[All Fields])) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields] OR "child s"[All Fields] OR "children s"[All Fields] OR "childrens"[All Fields] OR "childs"[All Fields] OR ("offspring"[All Fields] OR "offspring s"[All Fields] OR "offsprings"[All Fields])) AND ("paternal"[All Fields] OR "paternally"[All Fields] OR "paternity"[MeSH Terms] OR "paternity"[All Fields] OR "paternities"[All Fields] OR ("father s"[All Fields] OR "fathered"[All Fields] OR "fathers"[MeSH Terms] OR "fathers"[All Fields] OR "father"[All Fields] OR "fathering"[All Fields]))

eTable 2: Characteristics of included studies

| Author (year) | Country | Sample size | Effect estimate in OR (95% CI) | Study Design | Exposure measures | Outcome measures | Timing of parental depression diagnosis | Child age at outcome measure |
|---|------------------------|------------------|--|-------------------------------|-----------------------------|---------------------------|--|-------------------------------|
| Brennan et al., ³ 2002 | Australia | 522 | 1.13 (0.74 – 1.52) | Cohort | SCID (DSM–IV) | DSM–IV (K-SADS- E | Lifetime | 15 years |
| Lieb et al., ⁴ 2002 | Germany | 2,427 | 3.10 (2.00 – 4.80) | Cohort | DSM-IV | DSM-IV (M-CIDI) | 14-17 years postpartum | 17-21years |
| Klein et al., ⁵ 2005 | USA | 775 | 1.11 (0.78 – 1.58) | Cohort | DSM-IV | DSM-III R | Lifetime | 14- 24 years |
| Rohde et al., ⁶ 2005 | USA | 244 | 1.08 (0.80 – 1.44) | Cohort | DSMIV, (SCID-NP) | DSM-III-R (K-SADS) | 19 years postpartum | 24 years |
| Ramchandani et al., ⁷ 2008 | UK | 10,975 | 0.94 (0.12 – 7.26) | Cohort | EPDS | DAWBA | 18 moths antenatal and 8 weeks, 8 months and 21 months postpartum | 7 years |
| Reeb et al.,8 2010 | USA | 451 | 1.20 (1.07 – 1.33) | Cohort | SCL-90-R | SCL-90-R | 13.2 years postpartum | 13.2 years |
| Lies et al., 9 2010 | USA | 1,255 | 2.57 (1.87 – 3.54) | Cross- sectional | DSM-III R (FH-RDC) | DSM-III | Lifetime | 18 to 29 years |
| Pearson et al., ¹⁰ 2013 | UK | 4,500 | 1.08 (0.90 – 1.30) | Cohort | EPDS | CIS-R (ICD-10) | 18 and 32 weeks antenatally | 18 years |
| Reeb et al., 11 2015 | USA | 395 | 1.12 (1.07 – 1.18) | Cohort | SCL-90-R | SCL-90-R | 12.6 years postpartum | 20-22 years |
| Jacobs et al., 12 2015 | | 220 | 1.61 (1.13 – 2.09) | Cohort | KSADS-PL / SADS-LA) | DSM-IV | Lifetime | 6-23yrs |
| Musliner et al., ¹³ 2015 Middeldorp et.al., ¹⁴ 2016 | Denmark Netherlands | 2,976,264 530 | 2.04 (1.95 – 2.13) 1.05 (0.91 – 1.19) | Cohort Cross- sectional | ICD-8/10 CBCL and ASR | ICD-10 CBCL and ASR | Lifetime Lifetime | 30.5-33.6 years 7-15 years |

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| Lewis et al., ¹⁵ 2017 (a) Lewis et al., ¹⁵ 2017 (b) | Ireland UK | 6,070 7,768 | 1.27 (1.03 – 1.57) 1.20 (1.01 – 1.43) | Cohort Cohort | K6+ CES-D | SMFQ SMFQ | 9 years postpartum 7 years postpartum | 13 years 14 years |
|--|---------------|----------------|--|------------------|--------------|-------------------|--|----------------------|
| Gutierrez-Galve et al., 16 2019 | UK | 3,176 | 1.05 (1.02 – 1.09) | Cohort | EPDS | CIS-R (ICD-10) | 8 weeks and 8 months postnatally | 18 years |
| Liang et al., 17 2021 | Taiwan | 4,138,151 | 2.64 (2.33 –2.99) | Cohort | ICD-9-CM | ICD-9-CM | At childbirth | 7-20 years |

Adult self-report (ASR); Affective Disorders and Schizophrenia for School-Age Children (K-SADS); Centre for Epidemiological Studies Depression Scale (CES-D); Child Behaviour Checklist (CBCL); Clinical Interview Schedule-Revised (CIS-R); Development and Well-Being Assessment (DAWBA); Diagnostic and Statistical Manual of Mental Disorders (DSM); Diagnostic and Statistical Manual of Mental Disorders-Revised (DSM-III-R); Edinburgh Postnatal Depression Scale (EPDS); Family History - Research Diagnostic Criteria (FH-RDC); International Classification of Diseases (ICD); International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM); Kessler six-item psychological distress scale (K6+); Kiddie-Schedule for Affective Disorders and Schizophrenia Epidemiologic or Present and Lifetime version (KSADS-PL); Munich-Composite International Diagnostic Interview (M-CIDI); Schedule for Affective Disorders and Schizophrenia Lifetime version (SADS-LA); Short Mood and Feelings Questionnaire (SMFQ); Structured Clinical Interview for DSM-IV (SCID); Structured Clinical Interview for DSM-IV, non-patient version (SCID-NP); and Symptom Checklist-90-Revised (SCL-90-R).

eTable 3. Quality assessment of studies included in the final analysis according to the Newcastle-Ottawa scale (NOS)

| Study name | Selection | Comparabi lity | Exposure/ou tcome | Total | Overall quality |
|------------------------------|-----------|-------------------|----------------------|-------|-----------------|
| Cohort studies | | | | | |
| Reeb et al., 2010 | 4 | 1 | 3 | 8 | High |
| Reeb et al., 2015 | 4 | 2 | 3 | 9 | High |
| Brennan et al., 2002 | 3 | 1 | 3 | 7 | Moderate |
| Jacobs et al., 2015 | 4 | 2 | 3 | 9 | High |
| Lieb et al., 2002 | 4 | 1 | 3 | 8 | High |
| Musliner et al., 2015 | 4 | 2 | 3 | 9 | High |
| Gutierrez-Galve et al., 2019 | 4 | 1 | 3 | 8 | High |
| Pearson et al., 2013 | 3 | 1 | 3 | 7 | Moderate |
| Lewis et al., 2017 (a) | 4 | 2 | 3 | 9 | High |
| Lewis et al., 2017 (b) | 4 | 2 | 3 | 9 | High |
| Klein et al. 2005 | 4 | 2 | 3 | 9 | High |
| Ramchandani et al., 2008 | 4 | 1 | 3 | 8 | High |
| Rohde et al., 2005 | 4 | 1 | 3 | 8 | High |
| Liang et al ., 2021 | 4 | 1 | 3 | 8 | High |
| Cross-sectional studies | | | | | |
| Lies et al., 2010 | 4 | 1 | 3 | 8 | Good |
| Middeldorp et.al., 2016 | 4 | 1 | 3 | 8 | Good |

Key: For Cohort studies High quality: NOS score above or equal to 8; Moderate quality: NOS score of 6 and 7 and Low quality: NOS score below 6

For cross-sectional studies: very good quality (scored 9-10), good quality (scored 7-8), satisfactory quality (scored 5-6), and unsatisfactory studies (0-4 points)

eTable 4. Summary of the subgroup analysis

| Subgroups | OR 95% CI | | Heterogeneity across the studies | | Heterogeneity between the groups |
|-------------------------------|-----------|-----------|----------------------------------|---------|----------------------------------|
| | | | <u>I2</u> | P-value | (P-value) |
| Study design | | | | | .74 |
| Cohort $(n = 14)$ | 1.39 | 1.14-1.70 | 98.3 | <.001 | |
| Cross-sectional $(n = 2)$ | 1.62 | 0.68-3.90 | 96.1 | <.001 | |
| Study Quality | | | | | .66 |
| High (n = 12) | 1.45 | 1.16-1.81 | 98.5 | <.001 | |
| Good/moderate $(n = 4)$ | 1.32 | 0.95-1.84 | 88.7 | <.001 | |
| Tool used to assess outcome | | | | | .03 |
| Screening $(n = 5)$ | 1.14 | 1.09-1.19 | 0.00 | 0.61 | |
| Diagnostic $(n = 11)$ | 1.56 | 1.17-2.07 | 98.6 | <.001 | |
| Period outcome assessed | | | | | .21 |
| Childhood/adolescence (n = 7) | 1.33 | 0.97-1.84 | 0.00 | 0.64 | |
| Adulthood $(n = 6)$ | 1.38 | 1.02-1.86 | 99.2 | <.001 | |
| Both $(n = 3)$ | 1.74 | 1.03-2.96 | 99.3 | <.001 | |
| Tool used to assess exposure | | | | | .003 |
| Screening (n =6) | 1.12 | 1.06-1.19 | 58.7 | .03 | |
| Diagnostic (n =10) | 1.65 | 1.28-2.12 | 98.6 | <.001 | |
| Exposure time | | | | | .009 |
| Childhood $(n = 4)$ | 1.22 | 1.07-1.36 | 0.00 | 0.84 | |
| Adolescence $(n = 3)$ | 1.38 | 1.09-1.74 | 90.6 | <.001 | |
| Lifetime $(n = 5)$ | 1.58 | 1.09-2.29 | 95.9 | <.001 | |
| Postpartum $(n = 3)$ | 1.05 | 1.02-1.09 | 0.00 | 0.95 | |
| Adulthood $(n = 1)$ | 1.08 | 0.80-1.42 | - | - | |
| Adjusted for any | | | | | .004 |
| confounders | | | | | |
| Yes $(n = 13)$ | 1.51 | 1.22-1.87 | 98.4 | <.001 | |
| No $(n = 3)$ | 1.07 | 0.96-1.18 | 0.00 | 0.92 | |
| Adjusted for maternal | | | | | .26 |
| substance use | | | | | |
| Yes (n = 4) | 1.26 | 1.12-1.43 | 7.5 | 0.36 | |
| No $(n = 12)$ | 1.46 | 1.17-1.83 | 98.6 | <.001 | |
| Adjusted for maternal | | | | | .02 |
| depression | | | | | |
| Yes $(n=4)$ | 1.12 | 1.07-1.17 | 0.0 | 0.99 | |
| No $(n = 12)$ | 1.51 | 1.19-1.93 | 98.5 | <.001 | |
| Adjusted for paternal | | | | | .80 |
| mental disorders | | | | | |
| Yes (n = 2) | 1.35 | 0.94-1.94 | 58.8 | 0.12 | |
| No $(n = 14)$ | 1.43 | 1.17-1.74 | 98.1 | <.001 | |

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