**Appendix A:** full search strategy

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Database* | *1. infant/child/ adolescent* | *2. parent* | *3. Mental disorder* | *4. mental disorder categories* | *5. Physical illness* | *6. Disease categories* | *7. study type* | *8.combin-ation* | *9. restrictions* | *Number of hits* |
| Medline | exp infant/ or adolescent/ or child/ or child, preschool/ or "child of impaired parents"/ or (infant or new?born or girl$ or boy$ or child or adolescent$ or teen\* or offspring).ti,ab,kw | father-child relations/ or fathers/ or maternal behavior/ or mother-child relations/ or mothers/ or parent-child relations/ or paternal behavior/ or parenting/ or parents/ or single parent/ or single-parent family/ or (father\* or mother\* or parent\* or maternal or paternal).ti,ab,kw. | ((mental adj3 disorder$) or (mental adj3 illness) or (psychiatric adj3 disorder$) or (psychiatric adj3 illness) or (mental adj3 health)).ti,ab,kw | exp mood disorders/ or substance-related disorders/ or alcohol-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or opioid-related disorders/ or exp psychotic disorders/ or exp "schizophrenia spectrum and other psychotic disorders"/ or exp Anxiety Disorders/ or exp Stress Disorders, Traumatic/ or exp "Feeding and Eating Disorders"/ or (((affective or psychosocial or emotional or neurot\*) adj2 disorder$) or neuros\* or affective personality or depress\* or ((substance or alcohol or drug) adj3 (misuse or abuse or dependence)) or addiction or psychotic or psychosis or schizo\* or anxiety or phobi\* or (obsessive adj3 disorder) or ocd or post?traumatic stress disorder or PTSD or ((eating adj3 disorder) or bulimia or anorexia)).ti,ab,kw | exp morbidity/ or (morbidity or (somatic adj3 disease) or (somatic adj3 illness) or (physicaladj3 illness)).ti,ab,kw | "wounds and injuries"/ or allergy/ or arthritis/ or asthma/ or atopy/ or cancer/ or cardiovasular disease/ or congenital heart disease/ or diabetes/ or eczema/ or endocrine disease/ or epilepsy/ or gastroenteritis/ or gastrointestinal diseases/ or haematological disease/ or exp infection/ or meningitis/ or migraine/ or musculoskeletal diseases/ or obesity/ or rheumatic disease/ or (accidents or allerg\* or arthritis or asthma or atopy or cancer or cardiovascular disease or congenital heart disease or diabetes or eczema or endocrine disorders or epilepsy or gastroenteritis or gastrointestinal diseases or haematological disorders or infect\* or meningitis or migraine or musculoskeletal or obesity or rheumatological disorders or injury or "malignant neoplasms" or atopic dermatitus or "diarrhoea and vomiting" or rheumato\*).ti,ab,kw | (Case-Control Studies/ or Control Groups/ or Matched-Pair Analysis/ or ((case\* adj5 control\*) or (case adj3 comparison\*) or control group\*).ti,ab.) or (cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/ or cohort.ti,ab. or longitudinal.ti,ab. or prospective.ti,ab. or retrospective.ti,ab.) or epidemiological studies/ or Incidence/ or prevalence/ or (incidence or prevalence or (rate adj ratio) or (hazard adj ratio) or (relative adj risk) or (odds adj ratio)).ti,ab,kw. | 1 and 2 and (3 or 4) and (5 or 6) and 7 | limit 8 to (yr="1970 -Current") | 6403 |
| Ovid PsycINFO | exp infant development/ or child.mp. or exp parent child relations/ or (infant or new?born or girl$ or boy$ or child or adolescent$ or teen\* or offspring).ti,ab,id | exp parents/ or exp father child relations/ or exp mother child relations/ or (father\* or mother\* or parent\* or maternal or paternal).ti,ab,id. | ((mental adj3 disorder$) or (mental adj3 illness) or (psychiatric adj3 disorder$) or (psychiatric adj3 illness) or (mental adj3 health)).ti,ab,id. | exp affective disorders/ or drug abuse/ or alcohol abuse/ or drug dependency/ or polydrug abuse/ or psychosis/ or Schizophrenia/ or exp anxiety disorders/ or Obsessive Compulsive Disorder/ or Posttraumatic Stress Disorder/ or exp Eating Disorders/ or (((affective or psychosocial or emotional or neurot\*) adj2 disorder$) or neuros\* or affective personality or depress\* or ((substance or alcohol or drug) adj3 (misuse or abuse or dependence)) or addiction or psychotic or psychosis or schizo\* or anxiety or phobi\* or (obsessive adj3 disorder) or ocd or post?traumatic stress disorder or PTSD or ((eating adj3 disorder) or bulimia or anorexia)).ti,ab,id. | morbidity/ or epidemiology/ or exp physical disorders/ or (morbidity or (somatic adj3 disease) or (somatic adj3 illness) or (physicaladj3 illness)).ti,ab,id. | exp accidents/ or exp allergic disorders/ or exp arthritis/ or exp rheumatoid arthritis/ or asthma/ or exp neoplasms/ or cardiovascular disorders/ or diabetes/ or exp eczema / or endocrine disorders/ or exp epilepsy/ or exp gastrointestinal disorders/ or "blood and lymphatic disorders"/ or infectious disorders/ or meningitis/ or migraine headache/ or exp musculoskeletal disorders/ or obesity/ or (accidents or allerg\* or arthritis or asthma or atopy or cancer or cardiovascular disease or congenital heart disease or diabetes or eczema or endocrine disorders or epilepsy or gastroenteritis or gastrointestinal diseases or haematological disorders or infect\* or meningitis or migraine or musculoskeletal or obesity or rheumatological disorders or injury or neoplasms or atopic dermatitus or "diarrhoea and vomiting" or rheumato\*).ti,ab,id. | ((case\* adj5 control\*) or (case adj3 comparison\*) or case-comparison or control group\*).ti,ab,id. or (cohort or longitudinal or prospective or retrospective or incidence or prevalence or (rate adj ratio) or (hazard adj ratio) or (relative adj risk) or (odds adj ratio)).ti,ab,id. or longitudinal study.md. or prospective study.md. or retrospective study.md. not "Literature Review".md. | 1 and 2 and (3 or 4) and (5 or 6) and 7 | limit 8 to (yr="1970 -Current") | 2543 |
| Ovid PsychARTICLES | (infant or new?born or girl$ or boy$ or child or adolescent$ or teen\* or offspring) | (father\* or mother\* or parent\* or maternal or paternal) | ((mental adj3 disorder$) or (mental adj3 illness) or (psychiatric adj3 disorder$) or (psychiatric adj3 illness) or (mental adj3 health)) | (((affective or psychosocial or emotional neurot\*) adj2 disorder$) or neuros\* or affective personality or depress\* or ((substance or alcohol or drug) adj3 (misuse or abuse or dependence)) or addiction or psychotic or psychosis or schizo\* or anxiety or phobi\* or (obsessive adj3 disorder) or ocd or post?traumatic stress disorder or PTSD or (eating adj3 disorder) or bulimia or anorexia) | (morbidity or (somatic adj3 disease) or (somatic adj3 illness) or (psychical adj3 illness)) | accidents or allerg\* or arthritis or asthma or atopy or cancer or cardiovascular disease or congenital heart disease or diabetes or eczema or endocrine disorders or epilepsy or gastroenteritis or gastrointestinal diseases or haematological disorders or infect\* or meningitis or migraine or musculoskeletal or obesity or rheumatological disorders or injury or neoplasms or atopic dermatitus or "diarrhoea and vomiting" or rheumato\* | (case\* adj5 control\*) or (case adj3 comparison\*) or case-comparison or control group\* or cohort or longitudinal or prospective or retrospective or incidence or prevalence or (rate adj ratio) or (hazard adj ratio) or (relative adj risk) or (odds adj ratio) or (longitudinal adj study) or (prospective adj study) or (retrospective adj study) | 1 and 2 and (3 or 4) and (5 or 6) and 7 | limit 8 to (yr="1970 -Current") | 5932 |
| Ovid EMBASE | exp infant/ or adolescent/ or child/ or child, preschool/ or "child of impaired parents"/ or (infant or new?born or girl$ or boy$ or child or adolescent$ or teen\* or offspring).ti,ab,kw | parent/ or father/ or mother or (father\* or mother\* or parent\* or maternal or paternal).ti,ab,kw. | ((mental adj3 disorder$) or (mental adj3 illness) or (psychiatric adj3 disorder$) or (psychiatric adj3 illness) or (mental adj3 health)).ti,ab,kw | exp mood disorder/ or drug dependence/ or alcoholism/ or substance abuse/ or drug abuse/ or addiction/ or exp psychosis/ or exp anxierty disorder/ or exp eating disorder/ or (((affective or psychosocial or emotional or neurot\*) adj2 disorder$) or neuros\* or affective personality or depress\* or ((substance or alcohol or drug) adj3 (misuse or abuse or dependence)) or addiction or psychotic or psychosis or schizo\* or anxiety or phobi\* or (obsessive adj3 disorder) or ocd or post?traumatic stress disorder or PTSD or (eating adj3 disorder) or bulimia or anorexia).ti,ab,kw. | morbidity/ or epidemiology/ or (morbidity or (somatic adj3 disease) or (somatic adj3 illness) or (physicaladj3 illness)).ti,ab,kw. | accident/ or injury/ or allergy/ or rheumatoid arthritis/ or arthritis/ or Asthma/ or atopy/ or malignant neoplasm/ or cardiovasular disease/ or congenital heart disease/ or diabetes mellitus/ or eczema/ or endocrine disease/ or epilepsy/ or gastroenteritis/ or gastrointestinal diseases/ or haematological disease/ or exp infection/ or meningitis/ or migraine/ or musculoskeletal disease/ or obesity/ or childhood obesity/ or rheumatic disease/ or (accidents or allerg\* or arthritis or asthma or atopy or Cancer or cardiovascular disease or congenital heart disease or diabetes or eczema or endocrine disorders or epilepsy or gastroenteritis or gastrointestinal diseases or haematological disorders or infect\* or meningitis or migraine or musculoskeletal or obesity or rheumatological disorders or injury or neoplasms or atopic dermatitus or "diarrhoea and vomiting" or rheumato\*).ti,ab,kw. | exp case control Study/ or ((case\* adj5 control\*) or (case adj3 comparison\*) or control group\*).ti,ab. or (cohort analysis/ or cohort study/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/ or cohort.ti,ab. or longitudinal.ti,ab. or prospective.ti,ab. or retrospective.ti,ab.) or epidemiological studies/ or Incidence/ or prevalence/ or (incidence or prevalence or (rate adj ratio) or (hazard adj ratio) or (relative adj risk) or (odds adj ratio)).ti,ab,kw. | 1 and 2 and (3 or 4) and (5 or 6) and 7 | limit 8 to (yr="1970 -Current") | 6251 |
| Web of Science | (infant OR new?born OR girl$ OR boy$ OR child OR adolescent$ OR teen\* OR offspring) | (father\* OR mother\* OR parent\* or maternal or paternal) | ((mental NEAR/3 disorder$) OR (mental NEAR/3 illness) OR (psychiatric NEAR/3 disorder$) OR (psychiatric NEAR/3 illness) OR (mental NEAR/3 health)) | ((affective or psychosocial or emotional or personality or neurot\*) NEAR/2 disorder$) or neuros\* or affective personality or depress\* or ((substance or alcohol or drug) NEAR/3 (misuse or abuse or dependence)) or addiction or psychotic or psychosis or schizo\* or anxiety or phobi\* or (obsessive NEAR/3 disorder) or ocd or posttraumatic stress disorder or PTSD  or (eating NEAR/3 disorder) or bulimia or anorexia | (morbidity OR (somatic NEAR/3 disease) OR (somatic NEAR/3 illness) OR (physical NEAR/3 illness)) | (accidents OR allerg\* OR arthritis OR asthma OR atopy OR Cancer OR cardiovascular disease OR congenital heart disease OR diabetes OR eczema OR endocrine disorders OR epilepsy OR gastroenteritis OR gastrointestinal diseases OR haematological disorders OR infect\* OR meningitis OR migraine OR musculoskeletal OR obesity OR rheumatological disorders OR injury OR neoplasms OR atopic dermatitus OR "diarrhoea and vomiting" OR rheumato\*) | (case\* NEAR/2 control\*) or (case NEAR/2 comparison\*) or control group\* or cohort or longitudinal or prospective or retrospective or incidence or prevalence or "rate ratio" or "hazard ratio" or "relative risk" or "odds ratio" | 1 and 2 and (3 or 4) and (5 or 6) | - | 3690 |
| proquest ASSIA | infant OR newborn OR new-born OR girl\* OR boy\* OR child OR adolescent\* OR teen\* OR offspring | father\* OR mother\* OR parent\* or maternal or paternal | ((mental NEAR/3 disorder\*) OR (mental NEAR/3 illness) OR (psychiatric NEAR/3 disorder\*) OR (psychiatric NEAR/3 illness) OR (mental NEAR/3 health)) | ((affective or psychosocial or emotional or personality or neurot\*) NEAR/2 disorder$) or neuros\* or affective personality or depress\* or ((substance or alcohol or drug) NEAR/3 (misuse or abuse or dependence)) or addiction or psychotic or psychosis or schizo\* or anxiety or phobi\* or (obsessive NEAR/3 disorder) or ocd or posttraumatic stress disorder or PTSD or | (morbidity OR (somatic NEAR/3 disease) OR (somatic NEAR/3 illness) OR (physical NEAR/3 illness)) | (accidents OR allerg\* OR arthritis OR asthma OR atopy OR Cancer OR cardiovascular disease OR congenital heart disease OR diabetes OR eczema OR endocrine disorders OR epilepsy OR gastroenteritis OR gastrointestinal diseases OR haematological disorders OR infect\* OR meningitis OR migraine OR musculoskeletal OR obesity OR rheumatological disorders OR injury OR neoplasms OR atopic dermatitus OR "diarrhoea and vomiting" OR rheumato\*) | (case\* NEAR/2 control\*) or (case NEAR/2 comparison\*) or "control group" or cohort or longitudinal or prospective or retrospective or incidence or prevalence or "rate ratio" or "hazard ratio" or "relative risk" or "odds ratio" | 1 and 2 and (3 or 4) and (5 or 6) | - | [349](http://apps.webofknowledge.com/summary.do?product=WOS&doc=1&qid=26&SID=S187XnTTIHPmhm3aogs&search_mode=AdvancedSearch&update_back2search_link_param=yes) |

**Appendix B:** Fully summary of included studies

| **Study** | **Design, setting, country and sample size** | **Exposure: Measures** | **Outcome: Measures** | **Effect measure/Analysis** | **Unadjusted effect size (95% CI)** | **Adjusted effect size (95%CI)** | **Methods/Variables used for confounder control** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Accidents/injuries** | | |  |  |  |  |  |
| *Wilson 1981*34 | Prospective maternity cohort, US N =125 | Maternal substance misuse:  Review of treatment and medical records, and urine sampling.  Categorised into:1) heroin-dependent mothers; 2) methadone-treated mothers; and 3) drug-free mothers. | Accidents: Clinical assessment, including a physical and neurological examination. | OR drug-dependent vs. drug-free | 1.90 (0.80 to 4.54) | - | Matched on maternal age, race, socio-economic level, marital status, gestational age |
| *Howard 2003*36 | Retrospective primary care matched cohort, UK, N=986 | Maternal psychosis: Diagnosis of psychotic disorder or a prescription for a neuroleptic depot, an atypical antipsychotic drug or lithium. | Accidents: Self-referrals to accident and emergency departments, referrals to hospital out-patient departments, hospital admissions and primary care consultations. | RR | 0.98 (0.55 to 1.74) | - | Matched on age and general practice |
| *Phelan 2007*27 | Prospective cohort of young mothers, US N=1,106 | Maternal depression: Centre of Epidemiologic Studies Depression Scale (CES-D). <16 non-depressed; >16 for depressed. | Injuries: An injury requiring medical attention. | OR per unit increase in depression score | Not reported | 1.04 (1.01 to 1.08) | Adjusted for: family income, family size, maternal education, child race, child’s age and gender |
| *Winqvist 2007*33 | Retrospective cohort of population and hospital discharge registries, Finland  N= 12,058 | Maternal or paternal alcohol misuse: Hospital Discharge Register diagnosis of: alcoholic psychoses, alcohol dependence syndrome, alcohol abuse, alcoholic liver disease and alcoholic pancreatic disease. | Traumatic brain injuries: Clinical diagnosis of TBI from the Hospital Discharge Register. | RR | 1.90 (1.13 to 3.17) | 1.99 (1.19 to 3.33) | Adjusted for: father's occupation, family background, place of residence, family history of alcohol misuse, child’s gender |
| *McKinlay 2010*28 | Prospective birth cohort, New Zealand, N= 1,265 | Maternal depression: Levine-Pilowsky Depression Inventory. Continuous scale used. | Traumatic brain injuries: diagnosis at general practice or emergency department or hospital admission of a TBI or concussion. Excluding those who had an intentional injury. | HR  Low depression score  Medium depression score  High depression score | REF  1.22 (1.0 to 1.5)  1.49 (1.0 to 2.3) | - | None |
| *Schwebel 2010*32 | Prospective hospital birth cohort, US, N=584 | Maternal and paternal depression: Centre for Epidemiological Studies Depression Scale. Continuous scale used. | Injury: Determined by mothers reporting their children’s history of injuries requiring professional medical attention at least once a year from grade 6 to 12. | OR per unit increase in depression score  Maternal  Paternal | 1.00 (0.98 to 1.03)  1.00 (0.97 to 1.03) | - | None |
| *Myhre 2012*29 | Prospective pregnancy cohort, Norway, N=26,087 | Maternal depression: Symptom Checklist SCL-8. Continuous scale used. | Injury: Self-reporting of a clinical event. | OR high mental distress vs. low | 1.12 (1.06 to 1.18) | 1.09 (1.03 to 1.16) | Adjusted for: older siblings, maternal age, maternal education, employment, child not living with father, financial problems, child’s gender, gestational age, motor/ social/ communication development, temperament, externalising behaviours. |
| *Orton 2012*30 | Nested case-control study, primary care records, UK, N=104,512 | Maternal depression: Clinical diagnosis | Injuries: thermal, fractures, poisonings: Clinical diagnosis of thermal injury, fracture or poisoning | OR  Thermal injuries  Fractures  Poisoning | 1.22 (1.08 to 1.39)  1.06 (0,93 to 1.20)  1.50 (1.29 to 1.75) | 1.15 (1.02 to 1.32)  Not reported *p* > 0.05  1.45 (1.24 to 1.70) | Matched on general practice. Adjusted for: child’s gender, age at injury, birth order, maternal age at birth, household composition, harmful alcohol consumption, area-level deprivation |
| *Baker 2016*31 | Retrospective cohort primary care records, UK, N= 54,702 | Maternal depression or anxiety: Child was considered exposed for six months from the point when there was diagnostic, symptom, hospital, or treatment record for depression/anxiety. The episode was considered to have ended if there were no further recordings within the subsequent 6 months, after which the child was considered unexposed. | Injuries by: poisoning, fractures, burns or serious injuries: Clinical diagnosis of incident poisonings, fractures, and burns from primary care or hospital record | RR (time-varying exposure)  Poisonings:  Depression  Anxiety  Anxiety and depression  Fractures  Depression  Anxiety  Anxiety and depression  Burns  Depression  Anxiety  Anxiety and depression  Serious injuries  Depression  Anxiety  Anxiety and depression | 1.62 (1.39 to 1.88)  1.65 (1.11 to 2.47)  2.43 (2.03 to 2.90)  1.18 (1.05 to 1.32)  0.90 (0.64 to 1.28)  1.28 (1.10 to 1.49)  1.33 (1.17 to 1.51)  1.45 (1.04 to 2.03)  1.59 (1.34 to 1.88)  1.28 (0.97 to 1.68)  0.94 (0.39 to 2.26)  0.98 (0.62 to 1.54) | 1.52 (1.31 to 1.76)  1.63 (1.09 to 2.43)  2.30 (1.93 to 2.75)  1.15 (1.03 to 1.28)  0.87 (0.61 to 1.23)  1.24 (1.06 to 1.44)  1.31 (1.15 to 1.48)  1.47 (1.05 to 2.05)  1.53 (1.29 to 1.81)  1.25 (0.95 to 1.65),  0.95 (0.39 to 2.29),  0.95 (0.60 to 1.50) | Adjusted for: area level deprivation, calendar year and region |
| *Raitasalo 2017*35 | Retrospective population and hospital cohort, Finland, N=113,813 | Maternal and paternal substance abuse: Clinical diagnosis of substance-use related disorder and/or treatment thereof. | Injuries: Register entries for inpatient treatment or hospitalisation for ICD-10 diagnosis until 6th birthday. | OR  Maternal substance abuse  Paternal substance abuse | 1.26 (0.94 to 1.68)  1.16 (0.97 to 1.38) | 1.12 (0.84 to 1.50)  1.03 (0.86 to 1.23) | Adjusted for: parental education, social assistance, child’s gender |
| ***Asthma*** |  |  |  |  |  |  |  |
| *Klinnert 2001*42 | Prospective cohort of children with asthmatic mothers, US, N=133 | Maternal depression: First exposure measured using the Perinatal Depression Scale. Continuous measure used. The second time exposure was measured using a 5-point scale focusing on depressive effect | Asthma: Clinically diagnosed. | OR | 1.41 (0.98 to 2.03) | - | None |
| *Kozyrskyj 2008*44 | Retrospective cohort insurance registry, Canada, N=13,907 | Maternal mood or anxiety: Physician visits, hospitalizations, or prescription medications for depression or anxiety. | Asthma: Defined as at least two physician visits for asthma, one asthma hospitalization, or two prescriptions for any asthma in the year after the child’s 7th birthday. | OR  First year only  Short-term  Long-term | 1.14 (0.86 to 1.52)  1.22 (0.89 to 1.66)  1.63 (1.33 to 2.00) | 1.05 (0.79 to 1.41)  1.00 (0.72 to 1.37)  1.25 (1.01 to 1.37) | Adjusted for: maternal asthma, child’s gender, urban/rural location, family income, number of health care visits, number of siblings, number of respiratory/non-respiratory tract infections, course of antibiotic prescriptions |
| *Cookson 2009*37  *Cookson 2009*37 | Prospective birth cohort, UK, N=5,810 | Maternal anxiety: Anxiety measured using the Crown-Crisp Experimental Index. Depression measured using the Edinburgh Postnatal Depression Scale. | Asthma: Clinical diagnosis of symptoms of wheezing or treatment for asthma, retrieved through a review of medical records. | OR vs. 1st quartile of anxiety score, 32 weeks gestation  2nd quartile  3rd quartile  4th quartile  8 months postnatal  2nd quartile  3rd quartile  4th quartile | 1.37 (1.09 to 1.73)  1.51 (1.21 to 1.89)  1.79 (1.41 to 2.26)  1.12 (0.91 to 1.39)  1.48 (1.17 to 1.87)  1.37 (1.10 to 1.72) | 1.33 (1.05 to 1.68)  1.46 (1.16 to 1.83)  1.68 (1.32 to 2.13)  1.09 (0.88 to 1.35)  1.40 (1.10 to 1.77)  1.26 (1.00 to 1.59) | Adjusted for: child’s gender, preterm delivery, multiple birth, number of siblings, maternal age, maternal education, maternal history of asthma and allergy, prenatal tobacco smoke exposure, problems during pregnancy (diabetes, hypertension, steroid intake) |
| *Lange 2011*39 | Prospective twin birth cohort, Puerto Rico, N=339 pairs | Maternal or paternal depression and paternal PTSD: Maternal depressive symptoms measured using the mood and feelings questionnaire. Paternal major depressive episode and PTSD were measured using the Composite International Diagnostic Interview. | Asthma: Parental report of physician diagnosed asthma. | OR, maternal:  Depressive symptoms  Paternal:  Major depressive episode  PTSD | 1.13 (1.02 to 1.24)  2.24 (0.71 to 7.10)  1.04 (0.99 to 1.09) | 1.13 (1.01 to 1.27)  1.30 (0.32 to 5.16)  Not reported | Adjusted for: household income and parental asthma, maternal depressive symptoms, paternal depression |
| *Giallo 2015*38 | Prospective national cohort, Australia, N=4,165 | Maternal depression: Measured using the Kessler-6 instrument, using cut-off: <13 for no depression; >13 for depression | Asthma: Determined through report of ever having a diagnosis of asthma, symptoms of wheezing in the last 12 months, and a receipt of asthma medication in last 12 months. | OR after latent class analysis to identify depression trajectories:  Minimal symptoms  Subclinical symptoms  Persistent and increasing high symptoms | REF  1.31 (0.94 to 1.85) 2.81 (1.68 to 4.69) | REF  1.33 (0.94 to 1.87)  2.70 (1.59 to 4.59) | Adjusted for: maternal smoking, use of asthma/ antidepressant medication during pregnancy, child gender, instrumental delivery, prematurity, birth weight, breastfeeding, child-care attendance, socioeconomic status, single parent, maternal age, other siblings, urban/rural residency. |
| *Kozyrskyj 2017*43 | Prospective youth cohort, Canada N=1,696 | Maternal depression: Measured using a rescaled Centre for Epidemiological Studies scale. A cut-off was used: <12 for no postpartum depression; >12 for depression. | Asthma: Clinical diagnosis of either: 1) an asthma attack in the last 12 mths; 2) wheezing or whistling in the chest area in the last 12 mths; or 3) taking asthma medications on a regular basis. | OR, postpartum depression | 1.11 (0.83 to 1.50) | 1.15 (0.85 to 1.56) | Adjusted for: child’s gender, maternal asthma, urban/rural, immigrant status |
| *Magnus 2017*41 | Prospective pregnant cohort, Norway, N=63,626 | Maternal or paternal major depression: Life time history of major depressive symptoms: at least three affirmative answers on questionnaire. | Asthma: Medication in past year. | OR  Maternal major depression  Paternal major depression | 1.31 (1.20 to 1.42)  0.97 (0.83 to 1.12) | 1.19 (1.09 to 1.30)  0.95 (0.81 to 1.11) | Adjusted for: age, parity asthma, education, pre-pregnancy BMI, smoking and history of asthma |
| *Brew 2018*40 | Retrospective population cohort, Sweden,  N = 360,526 | Maternal or paternal depression or anxiety: Diagnosis of anxiety or depression or treatment with antidepressant or anxiolytic medication. | Asthma: 1) Clinical diagnosis during 5th year or 2) asthma diagnosis age 1-6 and asthma medication age 5-6. | OR, maternal anxiety or depression (cumulative exposure)  Pre-conception only  Plus pregnancy  Plus postnatal  Plus current  Paternal  Pre-conception only  Plus pregnancy  Plus postnatal  Plus current | 1.36 (1.32 to 1.41)  1.54 (1.47, 1.62)  1.49 (1.40, 1.60)  1.59 (1.48, 1.71)  1.11 (1.06 to 1.16)  1.16 (1.09 to 1.25)  1.13 (1.03 to 1.24)  1.14 (1.05 to 1.25) | 1.30 (1.26 to 1.35)  1.44 (1.38 to 1.52)  1.39 (1.30 to 1.49)  1.44 (1.34 to 1.56)  1.09 (1.04 to 1.13)  1.13 (1.06 to 1.21)  1.08 (0.98 to 1.19)  1.11 (1.01 to 1.21) | Adjusted for: maternal/paternal education, maternal/paternal asthma, parity, child’s gender |
| **Other atopic diseases** | | |  |  |  |  |  |
| *Wang 2016*45 | Prospective national cohort study, Taiwan, N=18,024 | Maternal depression: Determined by self-reporting of a clinical diagnosis of postpartum depression. | Atopic dermatitis: Maternal self-reporting of a child clinical diagnosis. | OR | 1.65 (1.44 to 1.88) | 1.42 (1.21 to 1.66) | Adjusted for: prenatal maternal stress, breastfeeding, family income, number of siblings, help for child care, residential location, maternal health index |
| *Letourneau 2017*46 | Prospective birth cohort, Canada, N=242 | Maternal depression/ Anxiety: Depression measured by the Edinburgh Depression Scale. A continuous scale was used. Anxiety measured by the Symptom Checklist-90 item-Revised. A cut-off was used: <63 for no anxiety; >63 for anxiety. Antenatal anxiety measured by the Pregnancy-Specific Anxiety Scale. A continuous scale was used | Atopic dermatitis: Clinical assessment, wherein mothers were asked if child had received a clinical diagnosis of atopic dermatitis in the last 6 months. | OR  Depression  Anxiety | 0.97 (0.87 to 1.08) 1.08 (0.98 to 1.18) | 0.93 (0.82 to 1.05)  1.13 (1.01 to 1.28) | Adjusted for: maternal sensitivity, social support and anxiety, pregnancy specific anxiety, maternal asthma |
| *Elbert 2017*47 | Prospective population birth cohort, Netherlands, N=5,205 | Maternal/paternal anxiety or depression: Brief symptom inventory mothers or fathers: ≥ 0.80 or ≥ 0.71 on the depressive symptom scale and ≥ 0.71 or ≥ 0.65 on the anxiety scale, respectively. | Inhalant or food allergy: Parental report of a clinical diagnosis. | OR, Maternal depression  Inhalant  Food  Maternal anxiety  Inhalant  Food  Paternal depression  Inhalant  Food  Paternal anxiety  Inhalant  Food | Not reported | 2.07 (1.43 to 2.97)  0.75 (0.29 to 1.97)  1.51 (1.06 to 2.16)  0.43 (0.14 to 1.32)  1.58 (0.89 to 2.80)  0.87 (0.18 to 4.14)  1.38 (0.89 to 2.15)  0.56 (0.14 to 2.32) | Adjusted for: Maternal age at enrolment, education, ethnic origin, history of allergy, eczema or asthma, parity, pet keeping, body mass index at enrolment, smoking, and child’s gender, gestational age and birth weight, inhalant/food allergy |
| **Obesity/overweight** | | |  |  |  |  |  |
| *Bronte-Tinkew 2007*49 | Prospective infant cohort, US, N=8,693 | Maternal depression: The Centre for Epidemiological Studies of Depression. Cut off: <5 for not depressed; >5 for depressed | Overweight: Clinical assessment using Centre for Disease Control weight charts, with children who had weight for length >95th percentile classed as overweight. | Structural equation model, Standardised path coefficient | -0.025, *p* = 0.29 | - | Adjusted for: food insecurity, infant feeding practices, positive parenting practices, child’s gender, age, family structure, household poverty, parent education level, maternal employment, age at birth, welfare receipt, smoking in child’s home, receipt of well-baby visit |
| *De Sousa 2009*48 | Case-control study primary schools, India, N=160 | Maternal depression/anxiety: Exposure measured using the Depression Anxiety Stress Scales. A continuous scale used. | Obesity: Clinical assessment using BMI charts | Mean depression score (SD)  Obese group  Control group  Mean anxiety score (SD)  Obese group  Control group | 7.75 (4.31)  3.69 (2.95), *p*<0.005;  4.59 (5.52)  2.41 (4.13), *p*<0.005 | - | None |
| *Ajslev 2010*50  *Ajslev 2010 cont,*50 | Prospective birth cohort, Denmark, N=21,121 | Maternal depression/ anxiety: Items taken from the Symptom Distress Checklist (SCL-90) and the General Health Questionnaire (GHQ 60) relating to depression/anxiety. | Overweight: BMI-growth charts to assess BMI>25on a corresponding adult chart. | OR  Depression  Anxiety | 1.02 (0.98 to 1.07) 1.02 (0.98 to 1.07) | 1.01 (0.96 to 1.07)  1.00 (0.96 to 1.06) | Adjusted for: maternal age, socioeconomic status, parity, smoking, pre-pregnancy BMI, gestational weight gain, paternal BMI, gestational age, child’s age and gender |
| *Santos 2010*51 | Prospective cohort maternity hospital, Brazil, N=3,792 | Maternal depression: Edinburgh Postnatal Depression Scale. A cut-off was used: <13 for not depressed; >13 for depressed. | Overweight: Clinical assessment according to World Health Organization criteria. | OR maternal depression vs not  At 1-2 follow-ups  At 3 follow-ups | Not reported | 1.0 (0.8 to 1.3)  1.6 (1.0 to 2.6) | Adjusted for: family income, maternal skin colour, marital status, maternal age, maternal schooling, parity, pre-pregnancy BMI, smoking during pregnancy, preterm birth |
| *Wojcicki 2011*56 | Prospective cohort of Latina women recruited from prenatal clinic, US , N=166 | Maternal depression: Edinburgh Postpartum Depression Scale, with a cut-off >16 for depressed, < for not depression. The Centre for Epidemiologic Studies Depression Scale was used for current depression, with a cut-off of >13 for depressed, <13 for not depressed | Overweight: BMI >85th percentile | OR  Episodic depression  Chronic depression | 0.68 (0.29 to 1.60)  0.29 (0.09 to 0.98) | 0.61 (0.26 to 1.44)  0.28 (0.03 to 0.92) | Adjusted for: maternal postnatal BMI, Mexican ethnicity, breastfeeding at 6 months, maternal age, gestational age, birthweight |
| *Guxens 2013*52 | Prospective pregnancy cohort, Netherlands, N=5,283 | Maternal/ paternal depression and anxiety: Global Severity Index. For depression, a cut-off of 0.80 was used for mothers and 0.71 for fathers. For anxiety, a cut-off of 0.71 was used for mothers and 0.65 for fathers. | Overweight: BMI z-score between 1.10 and 2.30. | OR  Maternal depression  Maternal anxiety  Paternal depression  Paternal anxiety | 1.43 (1.23 to 1.66)  1.37 (1.16 to 1.67).  0.97 (0.65 to 1.41)  0.96 (0.67 to 1.78) | 1.09 (0.92 to 1.30)  1.00 (0.83 to 1.19) 0.71 (0.46 to 1.09) 0.81 (0.55 to 1.18) | Adjusted for: maternal education, ethnicity, age, smoking and alcohol use during pregnancy, parity, gestational age at enrolment, marital status, and maternal and paternal body mass index |
| *Wang 2013*53 | Prospective birth cohort, US, N=1,090 | Maternal depression: Centre for Epidemiologic Studies Depression Scale. Cut-off: <16 for not depressed; >16 for depressed. | Overweight: BMI >85th percentile | OR, maternal depression at  Month 1  Month 24  Month 36 | 1.20 (0.92 to 1.56)  1.38 (1.03 to 1.86)  1.40 (1.03 to 1.89) | 1.05 (0.71 to 1.57)  1.16 (0.77 to 1.75)  1.50 (0.96 to 2.33) | Adjusted for: child’s gender, birth weight, ethnicity, maternal age, education marital status, income, breastfeeding, smoking status prior to birth, employment status, social support |
| *Audelo 2016*54 | Prospective birth cohort of Mexican-American children from rural community, US, N=332 | Maternal depression: Centre for Epidemiologic Studies-Depression Scale. A cut-off was used: <16 for not depressed; >16 for depressed. | Obesity: BMI >85th percentile | OR depression at child’s age  Never  Year 1 only  Years 1 and 3.5  Year 3.5 only  Years 3.5 and 7  Year 7 only  Year 1 and 7  Years 1, 3.5 and 7 | REF  1.0 (0.5 to 2.0)  1.2 (0.6 to 2.3)  1.3 (0.6 to 2.8)  2.0 (0.6 to 7.1)  1.1 (0.4 to 3.2)  0.6 (0.2 to 2.1)  2.0 (1.0 to 4.2) | REF  1.2 (0.6 to 2.6)  1.4 (0.7 to 3.1)  1.3 (0.5 to 3.1)  2.2 (0.6 to 8.4)  1.1 (0.4 to 3.4)  0.6 (0.2 to 2.0)  2.4 (1.1 to 5.6) | Adjusted for: maternal years in US, pre-pregnancy maternal weight status, pregnancy smoking, family poverty status, housing density, social support, birthweight, food security |
| *Blanco 2017*55  *Blanco 2017*55  *cont,* | Case-control study cases primary care, controls schools, Spain,  N=100 | Maternal depression: The Beck Depression Inventory‐II (BDI) was used to assess depression. A cut-off was used: <20 for not depressed; >20 for depressed.  Maternal Anxiety: The State Trait Anxiety Inventory for state and trait anxiety (STAI): <31 was neither state nor trait anxiety; 31-33 for state anxiety; >34 for trait anxiety. | Obesity: BMI >85th percentile | Mean (SD) maternal depression score  Obese  Not obese  BDI>20  Obese  Not obese  Mean (SD) maternal state anxiety score  Obese  Not obese  Mean (SD) maternal trait anxiety score  Obese  Not obese  N (%) STAI>34  Obese  Not obese | 9.56 (8.11)  7.28 (5.52)  *p* = 0.086  8 (16)  2 (1)  *p*=0.036  20.84 (10.78)  17.26 (9.72)  *p*= 0.064  20.72 (10.46) 1  5.9 (8.16)  *p*<0.05  5 (10)  2 (4)  *p*=0.11 | - | None |
| *Figueiredo 2017*57 | Prospective cohort of teenagers, Finland,  N=4,525 | Maternal alcohol misuse: Alcohol Use Disorders Identification Test (AUDIT). A cut-off was used: <5 for low-moderate drinkers; >5 for harmful drinkers. | Overweight: Cole and Lobstein Classification. | OR | Not reported | 1.00 (0.81 to 1.23) | Adjusted for: age, child’s gender, maternal age, educational attainment, maternal BMI, language spoken at home. |
| **Other studies from low and middle-income countries** | | |  |  |  |  |  |
| *De Miranda 1996*58 | Case-control study, primary health care patients, Brazil, N=105 | Maternal psychiatric morbidity: The Adult Psychiatric Morbidity Questionnaire. A cut-off was used: <6 for no psychiatric morbidity difficulties; >6 for psychiatric morbidity difficulties. | Malnutrition: Comparing weight measurements with a growth curve (Gomez criteria). | OR | 2.8 (1.2 to 6.9) | 2.9 (1.3 to 6.8) | Adjusted for: maternal age, number of children, birthweight |
| *Anoop 2004*59 | Case-control study, community health rural setting, India, N=144 | Maternal depression: Clinical assessment using the Structured Clinical Interview for DSM III Revised, assessing for current major depression or postpartum depression. | Malnutrition: Weight between 50% and 80% of their expected weight for age. | OR  Postnatal depression  Current depression | 5.0 (1.0 to 24.0)  3.2 (1.1 to 9.5) | 7.4 (1.6 to 38.5)  3.1 (0.9 to 9.7) | Matched on: age, child’s gender and locality. Multivariable models adjusted for low maternal intelligence, low birth weight, socioeconomic status, duration of breast feeding (exclusive and supplementary), immunisation status, mother's literacy |
| *Rahman 2004*63 | Prospective cohort, rural community, Pakistan, N=320 | Maternal depression: Clinical assessment using the Schedules for Clinical Assessment in Neuropsychiatry. | Diarrhoea, acute respiratory infection; Fortnightly visits from a health-visitor | OR  Diarrhoea  Acute respiratory infection | 2.4 (1.7 to 3.3)  1.1 (0.9 to 1.4) | - | None |
| *Adewuya 2008*60 | Prospective cohort Women attending infant immunisation clinics, Nigeria, N=142 | Maternal depression: Structured Clinical Interview for DSM-III-R (SCID-NP). | Malnutrition: Clinical assessment | OR | 2.84 (0.98 to 8.24) | - | Matched on: maternal age, marital status, socio-economic class, parity, infant gender, birthweight and gestational age |
| *Santos 2011*61 | Case-control study, health centres, Brazil, N=294 | Maternal common mental disorder: The Self-Report Questionnaire. A cut-off was used: <8 for no mental disorder; >8 for common mental disorder. | Malnutrition: Weight-for-height z-score below –2 standard deviations. | OR | 2.1 (1.23 to 3.58) | 2.04 (1.10 to 3.78) | Matched on: age and child’s gender. Adjusting for number of children in house, maternal employment status, family income, maternal schooling, maternal age |
| *Okronipa 2012*64 | Prospective cohort study from antenatal clinics in area of high HIV prevalence, Ghana, N=492 | Maternal depression: The Edinburgh Postnatal Depression Scale. A continuous scale used. | Diarrhoea: Clinical assessment by collecting information on infant health, including total number of stools and stool characteristics, every two weeks. | OR | 2.36 (1.53 to 3.67) | 2.89 (1.71 to 4.89) | Adjusted for: HIV status, prenatal stress, marital status, LBW, cooking fuel |
| *Ashaba 2015*62 | Case-control study from hospital in urban setting, Uganda, N=166 | Maternal depression: The Mini International Neuropsychiatric Interview. A cut off was: <5 for not depressed; >5 for depressed. | Malnutrition: Clinical assessment based on WHO child growth standards. | OR | 2.4 (1.18 to 4.79) | 2.4 (1.11 to 5.18) | Matched on: child’s age and gender. Adjusted for maternal age, marital status, education attained, occupation, source of income, number of children |
| *Weobong 2015*65 | Prospective cohort study, rural/peri-urban setting, Ghana, N=12,618 | Maternal depression: Patient Health Questionnaire. A cut-off was used: <8 for no depression; >8 for depression. | Diarrhoea: Clinical assessment every 4 weeks until 1 year after birth. | OR | 2.17 (1.73 to 2.60) | 1.80 (1.45 to 2.14) | Adjusted for: maternal age, education, occupation, ethnicity, religion, urban/rural, parity, preterm delivery, mode of delivery, size of child, socio-economic status |
| **Other studies from high-income countries** | | |  |  |  |  |  |
| *Ban 2010*66 | Retrospective cohort, primary care data and hospital registries, UK, N=107,587 | Maternal depression: Clinical diagnosis of perinatal depression during pregnancy or during the first 6 months postpartum. | Gastrointestinal infections, lower respiratory tract infections (RTI): Clinical diagnosis of gastrointestinal infection, recorded in their general practice records. | Gastrointestinal infections  RD  RR  Lower RTI  RD  RR | 0.97 (0.90 to 1.03)  1.40 (1.37 to 1.42)  0.19 (0.16 to 0.23)  1.27 (1.22 to 1.32) | - | None |
| *Sarkola 2011*67 | Retrospective cohort, population and healthcare registries, Finland, N=2,552 | Maternal alcohol or substance misuse: Determined by a referral history of signiﬁcant alcohol and/or substance misuse during pregnancy. | Diseases of the eye, ear and mastoid process: Clinical diagnosis of disease of the eye, ear and/or respiratory system. | OR  With Out-of-Home Care (OHC)  Without OHC | Not reported | 1.34 (1.03 to 1.73)  1.10 (0.85 to 1.44) | Matched on: maternal age, parity, number of foetuses, birth month, and hospital. Adjusted for: birthweight (adjusted for gestational age), maternal SES |

**Appendix C:** quality assessment of included studies

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Criteria\* | | | | | | | | | | | | | |  |
| Study | Study design | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13\*\* | 14\*\* | Grade |
| Wilson 1981 | cohort | no | yes | yes | NR | no | yes | yes | yes | no | yes | no | yes | yes | No | poor |
| Howard 2003 | case control | yes | yes | yes | yes | yes | yes | NR | yes | yes | yes | yes | yes |  |  | good |
| Phelan 2007 | cohort | yes | yes | yes | no | no | yes | yes | yes | yes | no | yes | yes | no | yes | fair |
| Winqvist 2007 | cohort | yes | yes | yes | yes | no | no | no | no | NA | no | no | yes | NR | yes | poor |
| McKinlay 2010 | cohort | yes | yes | yes | yes | no | CD | no | yes | yes | yes | yes | yes | yes | yes | poor |
| Schwebel 2010 | cohort | yes | yes | no | yes | no | yes | yes | yes | yes | no | no | yes | no | yes | poor |
| Myhre 2012 | cohort | yes | yes | no | yes | no | yes | yes | yes | yes | no | no | yes | no | yes | poor |
| Orton 2012 | cohort | yes | yes | yes | yes | yes | CD | yes | yes | yes | no | no | yes | yes | yes | fair |
| Baker 2016 | cohort | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | good |
| Raitasalo 2017 | case control | yes | yes | no | yes | yes | yes | yes | no | yes | yes | yes | yes |  |  | good |
| Klinnert 2001 | cohort | yes | no | NR | no | no | yes | yes | yes | yes | no | no | no | no | yes | poor |
| Kozyrskyj 2008 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | yes | no | yes | fair |
| Cookson 2009 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | yes | no | yes | fair |
| Lange 2010 | cohort | yes | yes | yes | yes | no | CD | CD | no | no | no | yes | NR | no | yes | poor |
| Giallo 2015 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | yes | no | yes | fair |
| Kozyrskyj 2017 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | yes | no | yes | fair |
| Magnus 2017 | cohort | yes | yes | no | yes | no | yes | yes | yes | yes | yes | yes | yes | no | yes | fair |
| Brew 2018 | cohort | yes | yes | yes | yes | no | no | no | yes | yes | yes | yes | yes | yes | yes | fair |
| Wang 2016 | cohort | yes | yes | no | yes | no | yes | yes | yes | yes | no | yes | NA | yes | yes | good |
| Letourneau 2017 | cohort | yes | yes | no | yes | no | yes | yes | yes | yes | yes | no | NA | no | no | fair |
| Elbert 2017 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | yes | no | yes | fair |
| Bronte-Tinkew 2007 | cohort | yes | yes | NR | NR | no | yes | yes | no | yes | no | yes | NR | yes | yes | fair |
| De Sousa 2009 | case control | no | yes | no | NR | yes | yes | NR | NR | no | yes | NR | no |  |  | poor |
| Ajslev 2010 | cohort | yes | yes | no | yes | no | yes | yes | yes | yes | no | no | yes | no | yes | fair |
| Santos 2010 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | NR | yes | yes | good |
| Wojcicki 2011 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | yes | yes | NR | yes | yes | good |
| Guxens 2013 | cohort | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | NR | yes | yes | good |
| Wang 2013 | cohort | yes | yes | NR | yes | yes | yes | yes | yes | yes | yes | yes | NR | yes | yes | good |
| Audelo 2016 | cohort | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | NR | no | yes | fair |
| Blanco 2017 | case control | yes | yes | no | no | yes | yes | no | no | no | yes | NR | no |  |  | poor |
| Figueiredo 2017 | cohort | yes | yes | no | yes | no | no | no | yes | yes | no | yes | NR | yes | yes | poor |
| De Miranda 1996 | case control | yes | yes | yes | yes | yes | yes | NA | no | no | yes | yes | no |  |  | fair |
| Anoop 2004 | case control | yes | yes | yes | yes | yes | yes | no | no | yes | yes | yes | yes |  |  | good |
| Rahman 2004 | cohort | yes | yes | yes | yes | yes | yes | yes | yes | yes | no | yes | NA | yes | yes | fair |
| Adewuya 2008 | cohort | yes | yes | yes | yes | no | yes | yes | yes | yes | no | yes | NR | yes | no | fair |
| Santos 2011 | case control | yes | yes | yes | yes | yes | yes | NA | no | no | yes | NR | yes |  |  | fair |
| Okronipa 2012 | cohort | yes | yes | CD | CD | no | yes | yes | yes | yes | no | no | NR | no | CD | poor |
| Ashaba 2015 | case control | yes | no | yes | no | no | no | no | no | no | no | NR | yes |  |  | poor |
| Weobong 2015 | cohort | yes | yes | yes | yes | no | yes | yes | no | yes | no | no | NR | yes | yes | fair |
| Ban 2010 | cohort | yes | yes | yes | yes | yes | yes | yes | no | yes | NA | yes | yes | no | yes | fair |
| Sarkola 2011 | cohort | yes | yes | yes | yes | yes | yes | yes | no | yes | NA | yes | NA | yes | yes | good |

\* Studies graded according to criteria for cohort or case-control studies <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>

\*\*criterion for cohort study only

NR: Not reported; CD: Cannot determine; NA: Not Applicable;

Appendix D: sensitivity analysis showing forest plot after removal of studies ranked poor quality**

Appendix E: subgroup analysis showing forest plot of case-control and cohort studies

