

# Systematic Review of Environmental and Psychosocial Risk Factors associated with Attention Deficit Hyperactivity Disorder, Oppositional Defiant Disorder, and Conduct Disorder in Children and Adolescents

Rasha Elbagir<sup>1\*</sup>, Mohd Faisal<sup>1</sup>, Susan O'Hanharan<sup>1</sup>

<sup>1</sup>Department of Child and Adolescent Psychiatry, Mid Western Health Board, Health Service Executive West

\*Corresponding author: [rashasomy@yahoo.com](mailto:rashasomy@yahoo.com)

## Abstract

**Background:** In the majority of cases, attention deficit hyperactivity disorder (ADHD) is accompanied by one or more comorbid disorders, with the oppositional defiant disorder (ODD) being one of the most frequently diagnosed comorbid disorders. There is a lack of systematic reviews addressing the evidence for an association between the independent environmental and psychosocial risk factors associated with ADHD, ODD, and Conduct Disorder (CD).

**Objective:** This study aims to determine the link between ADHD and ODD/CD, specifically in terms of the most up-to-date environmental and psychosocial risk factors in the development of these illnesses.

**Results:** Eleven studies were included in this systematic review. Among these, ten studies involved environmental risk factors, and only one involved socioeconomic risk factors as exposure. Of the ten studies highlighting the environmental risk factors, six studies reported perinatal risk factors, three reported Atopic diseases as exposure measures, and one involved exposure to energy and coffee drinks. We have found that the most common risk factors associated with ADHD, ODD and CD in Europe and North America were Perinatal risk factors. In contrast, the risk factors of Atopic diseases were more common in Asia.

**Conclusions:** Most of the studies included in our systematic review fall within the scope of environmental risk factors were perinatal risk factors and atopic diseases are the most common risk factors. However, only one article highlighted the association of socioeconomic risk factors as an exposure. Our review results suggest the need for more research focused on psychosocial risk factors for ADHD and comorbid ODD/CD. Further research is required with the primary objective of investigating this association in greater depth and examining the possible mechanisms at varying levels is needed.

**Keywords:** Attention deficit hyperactivity disorder; Conduct disorder; Oppositional defiant disorder; Systematic Review; Environmental risk factors; Psychosocial risk factors.

## Introduction

This study aims to determine the link between Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD)/Conduct Disorder (CD), specifically in terms of the most up to date environmental and psychosocial risk factors in the development of these illnesses. Between 1% and 5% of children and adolescents worldwide suffer from ADHD (1).

ADHD is characterised by inappropriately high levels of inattentiveness, hyperactivity and impulsivity that manifest in a variety of settings, and they are inappropriate for the child's age (2). In the majority of cases, ADHD is accompanied by one or more comorbid disorders, ODD being one of the most frequently diagnosed comorbid disorders, with a prevalence rate of 60% in children and adolescents

with ADHD (3). In this situation, it is crucial to learn more about ODD. It is a persistent pattern of defiant and disobedient behaviour in the child's social connections, particularly with authority figures (such as parents and teachers) and peers (4). The estimated comorbidity rate between ADHD and CD is between 16% and 20%, with data suggesting that it is more prevalent in males than in females (5). Conduct Disorders are characterised by recurring and persistent patterns of difficulties accepting norms, violent behaviour that is frequently driven by frustration, and antisocial behaviour, including violation of the basic rights of others, theft, lying, destruction of property and harming animals and humans (4).

International classifications specify the diagnostic criteria for Disruptive Behaviour Disorders (DBD)

(4). Included in this complex group are Oppositional Defiant Disorders and Conduct Disorders.

Biopsychosocial models of ADHD postulate that genetic and environmental interactions enhance the risk of ADHD, although it is now evident that there is no straightforward causal explanation (6) consistent with this intricate etiology.

Researchers have explored a broad range of a number of potential and interdependent risk factors or causative mechanisms (7)(8). Several environmental risk factors have distinct effects on the severity of ADHD symptoms and coexisting conditions. Several pieces of research have demonstrated the effect of smoking during pregnancy on symptoms of ADHD, ADHD combined, or inattentiveness (7)(9). Some research focused specifically on the effect of prenatal smoking on CD (8)(10). When smoking during pregnancy has been adjusted for, other prenatal risk factors, such as the mother's alcohol or drug misuse, don't appear to be as specific in the development of either ADHD or CD (5). Further biological risk factors for ADHD have been identified as being a lack of iodine and hypothyroxinemia during pregnancy (11).

In addition to biological risk factors, psychological risk variables have a significant impact on the severity of ADHD and the prevalence of comorbid ODD or CD (12)(13).

We are aware that recent systematic reviews are conducted focusing mainly on the interaction between genetic and environmental risk factors. However, there is a lack of systematic reviews addressing the evidence for an association between the independent environmental and psychosocial risk factors with ADHD, ODD and CD. Therefore, this review was, thus, focused on obtaining a systematised summary of the most up to date environmental and psychosocial risk factors associated with these illnesses. Hence, we can gain knowledge of the etiological variables that exert the most effect on these disorders, which is crucial information for preventing maladaptive behaviours and their implications.

## Methods

The review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (14).

### *Eligibility criteria (inclusion/exclusion)*

The study population included children and adolescents under 18 years old with a diagnosis of Attention Deficit Hyperactivity Disorder with either comorbid Oppositional Defiant Disorder or Conduct Disorder or both. Studies set within both community and clinical populations are included. Population surveys, cross-sectional studies, cohort

studies, and case-control studies were among the research designs covered. The review did not include any case studies, editorials, reviews, or opinions. We also excluded dissertations, conference abstracts and non-English articles. Included risk factors were Environmental and psychosocial risk factors associated with ADHD and ODD or CD in children and adolescents. Excluded are studies including genetic risk factors. Studies were included if published during or from 2015 until 2021.

### *Data sources*

Five electronic databases were searched for relevant articles in February 2021. The databases searched were Cochrane, Embase(ovid), Medline EBCSO, PubMed and PsychINFO.

### *Search strategy*

The search strategy included combinations of 4 key blocks of terms (ADHD/HD, Risk factors, ODD and CD, observational studies) using medical subject headings (MESH terms) and text words.

### *Study selection*

Following the initial search and removal of duplications, the title and abstracts of the studies were screened by two independent reviewers using the eligibility criteria. Then the full texts of the remaining published articles were screened by the two reviewers. Subsequently the two reviewers met to resolve the conflicts by consensus.

### *Data collection process*

Two reviewers independently extracted data from the included published articles to ensure concordance.

### *Data items*

The following items were extracted from each publication: author name and year of publication, country of the study, the aim of the study, study design, characteristics of the population (age range, gender and the number of participants), setting, diagnostic method used for the risk factor and the outcome (ADHD, CD, ODD), results of the studies, relevant findings in discussion and conclusion, limitation and quality check of each study.

### *Definition of exposure measures*

Environmental risk factors: in our study, we defined environmental risk factor as any non-genetic biological risk factor.

Psychosocial risk factors: we defined psychosocial risk factor as any factor related to socioeconomic disadvantage (e.g., low parental income, manual occupation, poor education, and not owning the family home) (15).

**Definition of outcome variables**

In our systematic review, the outcome variable was ADHD, ODD and CD. We defined DBD as the presence of any specific categories (such as ADHD, ODD and CD) in children.

**Risk of bias**

The critical appraisal of the studies was performed using the Critical Appraisal Skills Programme (CASP) risk of bias tool. (Reference: Critical Appraisal Skills Programme (2022). We used CASP Case-Control and Cohort Study Checklist. [Online], available at: <https://casp-uk.net/> Accessed: 12.03.2022. It was chosen because it is appropriate for use for the included studies. The CASP is an appraisal tool to systematically evaluate the reliability, applicability, and outcomes of published articles. The CASP tool consists of 11 questions for the case control studies and 12 questions for the cohort studies, and we are asked to record a “yes”, “no” or “can’t tell” to 9 out of the 11/12 questions. The authors agreed to score the answer “Yes” as (score= 1), and “No” as (score= 0), and “Can’t tell” as (score=0). The remaining three questions look at the precision of the result and how strong the association is between the exposure and the outcome (treatment effect), and the implication of the study for practice. The authors agreed to rate the precision of the result as High (score=1) or Low (score=0). Similarly, the treatment effect and the implication of the study for practice were rated as either High (score=1) or Low (score=0). A total score was calculated for each study, and studies were then rated as poor (total score less than 4 points), fair (total score between 5 and 7 points), or good (total score between 8 and 11/12 points), based on the scores obtained. Two independent assessors involved in the study completed the questionnaires. In case of disagreement, a third reviewer was contacted.

**Results**

Our search yielded 1,024 results (Cochrane number= 0; Embase (Ovid) number= 93; Medline EBCSO number= 317; PubMed number= 455; PsychINFO number= 159). 755 potential articles were identified after excluding duplicate publications.

During the screening phase, the titles and abstracts of all identified studies were examined. As a result, 725 studies that did not meet the inclusion criteria were excluded. Eleven articles met the inclusion criteria for this systematic review after determining the eligibility of the remaining 30 full-text articles (Figure 1). The PRISMA flowchart (Figure 1) provides additional details about the study selection procedure.

**Study Characteristics**

The characteristics of the studies included are summarised in Table 1.

Studies were carried out in a total of nine various countries across three continents. Seven of the studies used samples from the community, most of which were population-based cohort or cross-sectional research. Four of the studies utilised samples that were recruited, at least partly through a clinical setting. This review took in two case-control studies for its consideration. All research was published between 2015 and 2021. Sample sizes ranged from 112 to 74,565, with seven of the eleven studies including over 1000 participants. The ages of participants ranged from 3 to 17 years.

Different clinical measures were used to make the diagnosis of ADHD, ODD, and CD; data on the diagnosis was provided by parents, teachers, in some studies the children themselves, and also by researcher/clinician. The majority of studies used information from parents to reach a diagnosis of ADHD, OD, or CD. Two of the included studies used more than two informants to reach the diagnosis and two studies relied on parent report of clinical diagnosis.

Of the included studies, risk factors measured included perinatal maternal distress, prenatal maternal smoking, prenatal exposure to very severe maternal obesity, maternal PCOS and hirsutism, preterm birth and low birth weight, macrosomia, allergic diseases, socioeconomic status, energy drink and coffee consumption.

The primary aim of the included publications was to examine the association between the above-mentioned risk factors with ADHD, ODD and CD.

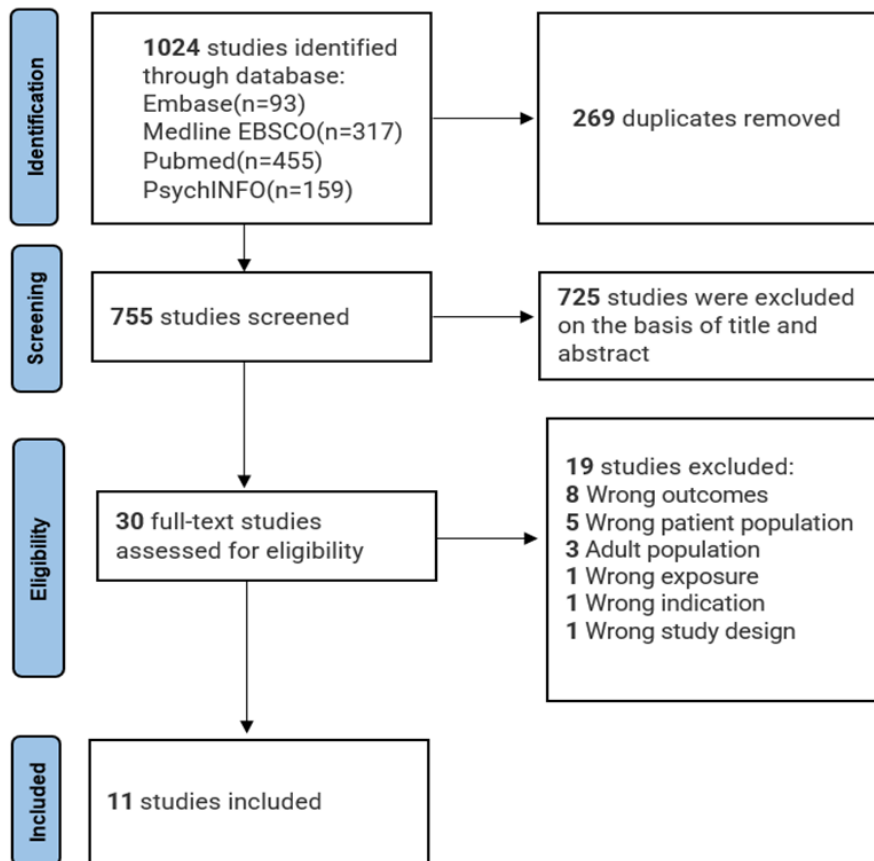
**Study quality**

The quality rating was “fair” for four studies (16–19), and “good” for the remaining seven studies (20–26). The quality of the studies is summarised in table 2.

**Risk factors associated with ADHD, ODD and CD**

The results of the individual studies are summarised in table 2.

Eleven studies were included in this systematic review. Among these, ten studies involved environmental risk factors, and only one study involved socioeconomic risk factors as exposure measures. Of the ten studies highlighting the environmental risk factors, six studies reported perinatal risk factors and three reported atopic diseases as exposure measures. And one study involved exposure to energy and coffee drinks. We have found that the most common risk factors associated with ADHD, ODD and CD in Europe and North America were perinatal risk factors. In



**FIGURE 1.** PRISMA flow chart of review search

contrast, the risk factors of atopic diseases were more common in Asia.

Among the four selected studies in North America, three were conducted in the USA and one in Canada. Three out of the four studies that were performed in North America examined the impact of the perinatal risk factor on ADHD, ODD and CD, while the remaining one selected article from this continent examined the effect of energy and coffee drinks as an environmental risk factor.

Moreover, three selected studies conducted in Europe investigated the impact of perinatal risk factors.

In Asia, four studies from this continent were included in this systematic review; three of them investigated the association between allergic diseases and ADHD, ODD and CD and one looked at the relationship between sociodemographic factors and ADHD and other DBDs.

### **Environmental risk factors**

#### *- Perinatal risk factors*

Study conducted in Norway by Bendiksen B et al. (25), examined the associations between pre- and postnatal maternal distress and ADHD, ODD and CD. Perinatal maternal distress during mid-gestation was shown to be significant but modestly associated

with symptoms of ADHD-HI (hyperactivity-impulsivity type), ODD, and CD.

While Joelsson P et al. (21) in Finland investigated prenatal smoking exposure and neuropsychiatric comorbidities with ADHD, his study showed a statistically significant association between prenatal smoking and ADHD comorbid with CD/ODD.

Another study conducted in UK by Mina TH et al. (22) explored the association between prenatal very severe maternal obesity and adverse neuropsychiatric outcomes in children. Their result showed children born to very severely obese mothers had higher scores for hyperactivity, conduct problems and other neuropsychiatric difficulties across multiple scales.

Two studies analysed the association between perinatal birth weight and ADHD, ODD and CD. Schieve LA et al. (16) in the USA, explored the impacts of preterm birth and low birth weight (LBW) on subsequent developmental disabilities including ADHD, behavioural or conduct problems or disorder (BCD), the authors found that preterm birth and/or LBW had little impact on either ADHD or BCD prevalence. Whereas the study conducted in Canada by van Lieshout RJ et al. (19) researched the association between macrosomia (birth weight > 4000 g) and adolescent psychiatric disorders, they also examined the potential moderating effects of sex

TABLE 1. Characteristics of the included studies.

Continent	First author	Year	Design	Total sample	Setting	Age Group	ADHD, ODD & CD Diagnostic tool	Risk measures
Europe	Bendixsen	2020	CO	1195	COM	3-5	PAPA	Perinatal maternal distress
Asia	Senol	2017	CR	2045	COM	7-15	T-DSM-IV-S	Socioeconomic status
Asia	Feng	2020	CR	114 with AD 201 non Atopic	CLIN	6-12	SNAP-IV Teacher and Parent 26-Item Rating Scale.	Atopic Dermatitis
Asia	Tajdini	2019	CC	80 with Asthma 92 control	CLIN	5-11	DSM-IV CSI-4	Asthma
Europe	Joelsson	2016	CC	10.132 with ADHD 38.811 Control	CLIN	All Finnish singletons born between 1991 and 2005	ADHD according to ICD-10 or ICD-9 ODD and CD according to ICD-10	Prenatal maternal smoking
Europe	Mina	2016	CO	112	CLIN	3-5	Conners' Hyperactivity Scale ESSENCE-Q SDQ CBCL	Prenatal exposure to very severe maternal obesity
North America	Van Lieshout	2020	CR	2151	COM	12-17	MINI-KID	Macrosomia
Asia	Lin	2016	CR	2.896	COM	9-10	Chinese version of the SNAP-26 questionnaire	Allergic diseases (atopic dermatitis, asthma, and allergic rhinitis)
North America	Marmorstein	2016	CR and longitudinal study	144	COM	11.9	Modified version of the CD Rating Scale ADHD CASI-4R	Energy drink and coffee consumption
North America	Robinson	2019	CO	1.915	COM	7-8	Parent/guardian report of diagnosis SDQ at 7 years Modified version of the VADPRS at 8 years	Maternal PCOS and hirsutism
North America	Schieve	2016	CR	74.565	COM	3-17	Parent/guardian report of diagnosis	Preterm birth and low birth weight

CR: cross sectional; CO: cohort; CC: case control; COM: community; CLIN: clinical; CD: Conduct Disorder, CASI-4R: The Child and Adolescent Symptom Inventory-4th edition, Revised, CBCL: Child Behavior Checklist; CSI-4: The Child Symptom Inventory-4 questionnaire; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth edition; ESSENCE-Q: Early symptomatic syndrome eliciting neurodevelopmental clinical examination Questionnaire, ICD: International Classification of Diseases; MINI-KID: The Mini International Neuropsychiatric Interview for Children and Adolescents; PAPA: Preschool Age Psychiatric Assessment, PCOS: Polycystic ovary syndrome; SDQ: Strengths and Difficulties Questionnaire, SNAP-IV: The Swanson, Nolan and Pelham IV Teacher and Parent 26-Item Rating Scale; T-DSM-IV-S: Turgay Diagnostic and Statistical Manual of Mental Disorders, fourth edition Based Child and Adolescent Behavioural Disorders Screening and Rating Scale; VADPRS: Vanderbilt ADHD Diagnostic Parent Rating Scale.

TABLE 2. Results of the individual studies.

First Author	Year	Aim of the study	Findings of the study	Quality of study
Bendixsen	2020	This research aims to evaluate the connections between prenatal and postnatal mother distress and pre-schooler symptoms of ADHD, ODD, CD, and anxiety, by time and gender.	Mid-gestational mother distress substantially raised the average number of child symptoms, which ranged 3.8% for ADHD-HI. The combination of high prenatal and postnatal mother distress ratings was linked with an elevated risk of child CD and ODD symptoms.	Good
Senol	2017	The objective of the study was to determine the prevalence of ADHD and other DBD, as well as their associations with sociodemographic variables, among schoolchildren aged 7 to 15 in Kayseri, Turkey.	The prevalence of DBDs were ADHD, 6.2%; CD, 14.4%; and ODD, 6.7%, among schoolchildren in Kayseri, Turkey. Compared to their peers, the prevalence of ADHD, CD and ODD were significantly higher among boys and children whose mothers were homemakers, as well as those from low-income and poorly educated families.	Good
Feng	2020	To evaluate the co-occurrence of symptoms of ADHD, ODD, and pertinent Atopic dermatitis (AD) risk factor, as well as their influence on the quality of life of Chinese school-aged children with AD.	AD patients were significantly more likely to exhibit ADHD symptoms and ODD symptoms than controls. In AD patients, the degree of itching and sleep loss was strongly connected with inattention, hyperactivity/impulsivity, and oppositional defiance scores. AD patients with ADHD symptoms had substantially higher CDLQI scores than those without ADHD symptoms.	Good
Tajdini	2019	The purpose of this study is to examine the prevalence of ODD, ADHD, and CD in asthmatic children.	In total, 42.5% of those in the case group and 25% of those in the control group had ADHD, with a statistically significant difference. In addition, there was a statistically significant difference between the prevalence of ODD in the case and control groups. However, the incidence of CD was 10% and 10.9% in the case and control groups, respectively, with no statistically significant difference.	Good
Joelsson	2016	This research aims to evaluate the connection between prenatal exposure to maternal smoking and offspring with ADHD, as well as to determine if the smoking-ADHD correlations are greater when ADHD is accompanied by other neuropsychiatric comorbidities.	Adjusted for confounding factors, the risk for ADHD with or without comorbidity was significantly increased among offspring exposed to maternal smoking. Subjects with comorbid CD or ODD had a significantly stronger association with smoking exposure than those with only ADHD.	Good

ADHD = Attention deficit hyperactivity disorder; ADHD-HI = ADHD hyperactive-impulsive; BCD= behavioural or conduct problems or disorder; CC = case-control; CD = Conduct Disorder, CDLQI = children's dermatology life quality index; CLIN = clinical; CO = cohort; COM = community; CR = cross-sectional; ODD = Oppositional Defiant Disorder; PAFs = population attributable fractions; PCOS = Polycystic ovarian syndrome.

Quality of the study: The critical appraisal of the studies was performed using the Critical Appraisal skills programme (CASP) risk of bias. Studies were rated as poor (total score less than 4 points out of 11/12), fair (total score between 5 and 7 points out of 11/12), or good (total score between 8 and 11/12 points).

TABLE 2 continued. Results of the individual studies.

First Author	Year	Aim of the study	Findings of the study	Quality of study
Mina	2016	To explore the association between prenatal very severe maternal obesity and adverse neuropsychiatric outcomes in children.	Prenatal mother extreme obesity remained a substantial predictor of child neuropsychiatric issues across various scales, regardless of demographic variables, prenatal characteristics, and maternal contemporaneous anxiety and depression symptoms.	Good
Van Lieshout	2020	The purpose of this study was to explore links between macrosomia (birth weight > 4000 g) and teenage mental problems and also to investigate possible moderating effects of gender and socioeconomic disadvantage on teenage mental illness.	After controlling for confounders, adolescents born macrosomic exhibited increased chances of CD, ODD and ADHD. Moderation analyses found substantial interaction effects between gender and macrosomia in predicting ODD and ADHD. Males born macrosomic were more likely than females to be diagnosed with ODD and ADHD.	Fair
Lin	2016	To investigate the connection between allergic diseases (Atopic dermatitis, asthma, and allergic rhinitis) and childhood behaviour disorders (ADHD and ODD).	Socioeconomic disadvantage multiplied the risk of ODD and ADHD posed by macrosomia. Children with a history of atopic dermatitis, asthma or allergic rhinitis had a greater likelihood of developing ADHD and ODD.	Good
Marmorstein	2016	This study explored cross-sectional and longitudinal correlations between early adolescents' energy drink intake and psychopathology. In addition, relationships between psychopathology and coffee use were investigated to determine whether the findings were exclusive to energy drinks or whether they also extended to another popular caffeinated beverage.	Cross-sectional relationships between caffeine intake and psychopathology symptoms: <ul style="list-style-type: none"> <li>• Overall, the use of energy drinks and coffee was associated with ADHD inattention and CD.</li> <li>• After adjusting for other caffeinated beverages, energy drinks were specifically related with CD.</li> </ul> Prospective correlations between caffeine intake and the development of psychopathology symptoms: Over the course of 16 months, the initial frequency of energy drink usage predicted increases in CD and ADHD inattentive symptoms. In contrast, there was no association between coffee intake and any increase or decrease in psychopathology.	Fair

ADHD = Attention deficit hyperactivity disorder; ADHD-HI = ADHD hyperactive-impulsive; BCD= behavioural or conduct problems or disorder; CC = case-control; CD = Conduct Disorder, CDLQI = children's dermatology life quality index; CLIN = clinical; CO = cohort; COM = community; CR = cross-sectional; ODD = Oppositional Defiant Disorder; PAFs = population attributable fractions; PCOS = Polycystic ovarian syndrome.

Quality of the study: The critical appraisal of the studies was performed using the Critical Appraisal skills programme (CASP) risk of bias. Studies were rated as poor (total score less than 4 points out of 11/12), fair (total score between 5 and 7 points out of 11/12), or good (total score between 8 and 11/12 points).

TABLE 2 continued. Results of the individual studies.

First Author	Year	Aim of the study	Findings of the study	Quality of study
..Continued Marmorstein			<p>After adjusting for the effects of coffee, energy drinks were shown to be linked with increases in ADHD (both inattentive and hyperactive symptoms), but the connection between energy drinks and CD symptoms decreased to a trend level.</p> <p>Prospective correlations between changes in caffeine intake and psychopathology symptoms:</p> <ul style="list-style-type: none"> <li>Initial levels of hyperactive ADHD predicted an increase in coffee consumption over time; this relationship persisted when energy drinks were controlled for.</li> </ul>	
Robinson	2019	To investigate the links between mother PCOS and hirsutism and offspring ADHD, anxiety, conduct disorder, and behavioural issues.	After controlling for confounders, the relationships between mother PCOS and offspring ADHD were positive although ambiguous. Maternal hirsutism was associated with an increased risk for children's ADHD, CD, borderline emotional symptoms, peer relationship problems, and conduct problems.	Fair
Schieve	2016	To explore the impacts of preterm birth and low birth weight on subsequent developmental disabilities including ADHD, BCD.	Summary PAFs for preterm birth and/or LBW were under 5% for ADHD and behavioural-conduct problems.	Fair

ADHD = Attention deficit hyperactivity disorder; ADHD-HI = ADHD hyperactive-impulsive; BCD= behavioural or conduct problems or disorder; CC = case-control; CD = Conduct Disorder, CDLQI = children's dermatology life quality index; CLIN = clinical ; CO = cohort; COM = community ; CR = cross-sectional; ODD = Oppositional Defiant Disorder; PAFs = population attributable fractions; PCOS = Polycystic ovarian syndrome.

Quality of the study: The critical appraisal of the studies was performed using the Critical Appraisal skills programme (CASP) risk of bias. Studies were rated as poor (total score less than 4 points out of 11/12), fair (total score between 5 and 7 points out of 11/12), or good (total score between 8 and 11/12 points).



and socioeconomic disadvantage on mental illness in adolescents. Their findings were individuals born macrosomic were more likely to develop CD, ODD, and ADHD than those born at normal birth weight. Moderation analyses revealed that boys born macrosomic were at particularly high risk for ODD and ADHD. Likewise, exposure to socioeconomic disadvantage amplified the risk of macrosomia on psychopathology, especially ODD.

Furthermore, Robinson SL et al. (17) in the USA found a positive but imprecise link between maternal Polycystic Ovary Syndrome (PCOS) and offspring ADHD. In comparison, maternal hirsutism was related to a higher risk of children's ADHD and Conduct Disorder.

#### *- Allergic diseases risk factors*

Three of the included studies in this review investigated the association between allergic diseases and ADHD, ODD and CD.

Various types of ADHD-related behavioural problems and Oppositional Defiant Disorder (ODD) may be more common in children with allergic diseases, such as atopic dermatitis (AD), asthma, and allergic rhinitis, according to research published by Lin YT et al. (26) in Taiwan. The authors also highlighted that when children had both an allergic condition and a mental health issue, including depression, stress, or poor sleep, the risk for ADHD-related behavioural disorders rose exponentially.

Similarly, research by Feng LJ et al. (20) found that children with atopic dermatitis are more likely to exhibit signs of Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD). AD-related sleep disruption may increase vulnerability to the development of attention deficit hyperactivity disorder. Their study also emphasised that patients with AD with signs of ADHD have a lower quality of life.

Moreover, a case-control study conducted by Tajdini M et al. (24) in Iran pointed out that children with asthma were significantly associated with exhibiting ADHD and ODD but not CD.

However, another environmental risk factor was examined by Marmostein et al. in the USA (18) they looked at the link between energy drink consumption and coffee consumption and psychopathology among early adolescents. Their findings suggest that energy drink consumption is a risk factor for a wide range of concurrent psychopathology symptoms, as well as an increase in ADHD and CD symptoms over time. Coffee drinking was also shown to have concomitant correlations, but it did not indicate an increase in psychopathology over time. Instead, symptoms of attention deficit hyperactivity disorder predicted an increase in coffee consumption.

#### ***Psychosocial risk factors***

Among selected studies, only one study reported the association between sociodemographic risk factors and ADHD, ODD and CD.

In Turkey, Senol V et al. (23) examined the relationships of ADHD and other DBDs with sociodemographic factors among school children in Kayseri, his results showed that compared to their peers, the prevalence of Attention Deficit Hyperactivity Disorder (ADHD) was significantly higher among boys and children whose mothers were homemakers, as well as those from low-income, and poorly educated families. CD was more prevalent among boys and children ages 13-15 whose parents had low incomes and separated. ODD was more prevalent in boys and those whose mothers were homemakers.

#### **Discussions**

##### ***Summary of main findings***

Although previous studies have investigated the risk of interaction between genetic and environmental risk factors (27-28). To the best of our knowledge, this review is the first to systematically evaluate evidence of an association between the most up to date wide range of independent environmental risk factors and psychosocial risk factors with ADHD, ODD and CD.

Studies from across three continents contributed to this review, and the conclusions drawn are relevant in many different countries.

One significant finding of the review is that six out of eleven studies explored perinatal risk factors as independent environmental risk factors associated with ADHD, ODD and CD and they were found to be more prevalent in North America and Europe. Whereas three of the included studies investigated the relationship between allergic diseases and ADHD, ODD and CD and these risk factors were more prevalent in Asia.

We found only one study which was conducted in Asia, looking at the relationship between sociodemographic factors and ADHD and other DBDs.

##### ***Comparison with other systematic reviews***

Two existing systematic reviews have examined the association between environmental perinatal risk factors and ADHD, ODD and CD (27, 29).

Both reviews highlighted that factors such as drinking, smoking, or stress during pregnancy are associated with ADHD, ODD and CD.

Our findings are in agreement with the aforementioned systematic reviews. However, Kalil et al. systematic review (27) examined the interaction between genetic and environmental risk factors, while ours didn't focus on this interaction as this was

beyond the scope of our review. Moreover, K. Latimer's study (30) included an assessment of factors present antenatally and in the first four years of life (up to 4th birthday; 0–47 month), in comparison to our review, we included the most up to date perinatal risk factors in the literature, and we examined the association of these factors with DBDs presenting up to the age of 17.

Additionally, compared to previous reviews, our study found a new result of the association between maternal PCOS, hirsutism and DBDs. However, the link is positive but imprecise. Therefore, further research is needed to determine the etiological approach towards ADHD, ODD and maternal PCOS and Hirsutism (17).

This systematic review also reports interesting findings, which is the association between allergic diseases, such as atopic dermatitis, asthma, allergic rhinitis and ADHD, ODD and CD. Among reviewed papers, three of the included studies highlighted this association (20,24,26). Existing literature seems to be consistent with our finding, Miyazaki C et al. (31) conducted a meta-analysis showing that children with ADHD are more likely to have asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis than their counterparts. Nonetheless, our review not only highlighted evidence of the association between allergic disease and ADHD (20). It also showed evidence of association with other DBDs like ODD/CD. Indeed, further studies should compare the association between these illnesses and ADHD with comorbid ODD/CD.

Another interesting finding of our study suggests that allergic risk factors are more prevalent in Asia; this could possibly be due to Asian populations being more genetically or environmentally prone to allergic diseases. This would be a fruitful area for further research in order to establish whether there is an association between the Asian population and allergic diseases, as this can play a major role in the early diagnosis and intervention of DBDs (31).

Our systematic review also highlighted energy drink consumption as an environmental risk factor for an increase in ADHD and CD symptoms over time. It would be prudent to investigate how energy drink consumption predicts an increase in ADHD and CD symptoms over time, as this could lead to the development of interventions for high-risk youth (18). However, this evidence comes from a single study and replication is required.

### **Limitations**

This study has some limitations. First, the diagnosis of ADHD and behavioural disorders were parent reported in a number of studies, so this may be influenced by recall bias. Second, due to the fact that

the evidence consists of an observational cohort, cross-sectional, and case-control studies, it is impossible to draw conclusions regarding temporality and whether the observed association constitute a causal relationship; in addition, another reason we can not clarify the exact nature of the relationship is the existence of various confounding familial and psychosocial variables. Therefore, future studies should aim to reduce this weakness by evaluating a wide range of family, social and psychological variables that may confound findings. Furthermore, certain methodological limitations inherent to this review must be acknowledged. As in most systematic reviews, there is a risk of reporting bias since only published studies in identifiable sources and articles in the English language were included. Also, some papers that have strongly influenced the field have been excluded because they focus on genetic risk factors. We also discovered that there was just one study that examined psychosocial risk variables, this may be a result of the difficulty in maintaining families facing adversity in longitudinal studies and the difficulties involved in conducting research into complicated psychosocial risk factors.

### **Conclusion**

Most of the studies included in our systematic review fall within the scope of environmental risk factors, were perinatal risk factors and atopic diseases are the most common risk factors identified. These results necessitate further evidence to strengthen and confirm the robustness of our findings.

However, only one article highlighted the association of socioeconomic risk factors as an exposure. Our review results suggest the need for more research focused on psychosocial risk factors for ADHD and comorbid ODD/CD.

Further comprehensive, high-quality prospective research is required to fully comprehend the processes behind the association between these risk factors and DBDs and, ultimately, to develop specialised preventative and treatment interventions.

### **Disclosures**

The authors have no conflict of interests to disclose.

### **Funding**

The authors received no financial support for the research, authorship, and/or publication of this article.

### **Acknowledgement**

The authors thank University hospital limerick for their support and assistance and Ms Isabelle Delaunois, Medical Librarian, for her advice and help to carry out the systematic search.

### **References**

1. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The Worldwide Prevalence of ADHD: A Systematic Review and

- Metaregression Analysis. *American Journal of Psychiatry*. 2007 Jun;164(6):942–8.
2. Guze Sb. *Diagnostic And Statistical Manual Of Mental Disorders, 4th Ed. (DSM-IV)*. American Journal Of Psychiatry. 1995 Aug;152(8):1228–1228
  3. Connor DF, Steeber J, McBurnett K. A Review of Attention-Deficit/Hyperactivity Disorder Complicated by Symptoms of Oppositional Defiant Disorder or Conduct Disorder. *Journal of Developmental & Behavioral Pediatrics*. 2010 Jun;31(5):427–40.
  4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association; 2013.
  5. Biederman J, Mick E, Faraone S V., Braaten E, Doyle A, Spencer T, et al. Influence of Gender on Attention Deficit Hyperactivity Disorder in Children Referred to a Psychiatric Clinic. *American Journal of Psychiatry*. 2002 Jan;159(1):36–42.
  6. Russell G, Ford T, Rosenberg R, Kelly S. The association of attention deficit hyperactivity disorder with socioeconomic disadvantage: alternative explanations and evidence. *Journal of Child Psychology and Psychiatry*. 2014 May 26;55(5):436–45.
  7. Linnet KM, Dalsgaard S, Obel C, Wisborg K, Henriksen TB, Rodriguez A, et al. Maternal Lifestyle Factors in Pregnancy Risk of Attention Deficit Hyperactivity Disorder and Associated Behaviors: Review of the Current Evidence. *American Journal of Psychiatry*. 2003 Jun;160(6):1028–40.
  8. Thapar A, Fowler T, Rice F, Scourfield J, van den Bree M, Thomas H, et al. Maternal Smoking During Pregnancy and Attention Deficit Hyperactivity Disorder Symptoms in Offspring. *American Journal of Psychiatry*. 2003 Nov;160(11):1985–9.
  9. Schmitz M, Denardin D, Laufer Silva T, Pianca T, Hutz MH, Faraone S, et al. Smoking During Pregnancy and Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type: A Case-Control Study. *J Am Acad Child Adolesc Psychiatry*. 2006 Nov;45(11):1338–45.
  10. Wakschlag LS, Pickett KE, Cook E, Benowitz NL, Leventhal BL. Maternal Smoking During Pregnancy and Severe Antisocial Behavior in Offspring: A Review. *Am J Public Health*. 2002 Jun;92(6):966–74.
  11. Vermiglio F, Lo Presti VP, Moleti M, Sidoti M, Tortorella G, Scaffidi G, et al. Attention Deficit and Hyperactivity Disorders in the Offspring of Mothers Exposed to Mild-Moderate Iodine Deficiency: A Possible Novel Iodine Deficiency Disorder in Developed Countries. *J Clin Endocrinol Metab*. 2004 Dec;89(12):6054–60.
  12. Blanz B, Schmidt MH, Esser G. Familial Adversities and Child Psychiatric Disorders. *Journal of Child Psychology and Psychiatry*. 1991 Sep;32(6):939–50.
  13. Copeland W, Shanahan L, Jane Costello E, Angold A. Configurations of common childhood psychosocial risk factors. *Journal of Child Psychology and Psychiatry*. 2009 Apr;50(4):451–9.
  14. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. 2009 Jul 21;6(7):e1000097.
  15. Bradley RH, Corwyn RF. Socioeconomic Status and Child Development. *Annu Rev Psychol*. 2002 Feb;53(1):371–99.
  16. Schieve LA, Tian LH, Rankin K, Kogan MD, Yeargin-Allsopp M, Visser S, et al. Population impact of preterm birth and low birth weight on developmental disabilities in US children. *Ann Epidemiol* [Internet]. 2016 Apr 1;26(4):267–74. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1047279716300680>
  17. Robinson SL, Ghassabian A, Sundaram R, Trinh MH, Bell EM, Mendola P, et al. The associations of maternal polycystic ovary syndrome and hirsutism with behavioral problems in offspring. *Fertil Steril*. 2020 Feb 1;113(2):435–43.
  18. Marmorstein NR. Energy Drink and Coffee Consumption and Psychopathology Symptoms Among Early Adolescents: Cross-Sectional and Longitudinal Associations. *J Caffeine Res*. 2016 Jun;6(2):64–72.
  19. Van Lieshout RJ, Savoy CD, Ferro MA, Krzeczowski JE, Colman I. Macrosomia and psychiatric risk in adolescence. *Eur Child Adolesc Psychiatry*. 2020 Nov 1;29(11):1537–45.
  20. Feng LJ, Chen AW, Luo XY, Wang H. Increased attention deficit/hyperactivity and oppositional defiance symptoms of 6-12 years old Chinese children with atopic dermatitis. *Medicine*. 2020 Jun 19;99(25):e20801.
  21. Joellson P, Chudal R, Talati A, Suominen A, Brown AS, Sourander A. Prenatal smoking exposure and neuropsychiatric comorbidity of ADHD: a Finnish nationwide population-based cohort study. *BMC Psychiatry* [Internet]. 2016 Dec 31;16(1):306. Available from: <http://bmcp psychiatry.biomedcentral.com/articles/10.1186/s12888-016-1007-2>
  22. Mina TH, Lahti M, Drake AJ, Rääkkönen K, Minnis H, Denison FC, et al. Prenatal exposure to very severe maternal obesity is associated with adverse neuropsychiatric outcomes in children. *Psychol Med*. 2017 Jan 1;47(2):353–62.
  23. Senol V, Unalan D, Akca RP, Basturk M. Prevalence of attention-deficit/hyperactivity and other disruptive behaviour disorder symptoms among primary school-age children in Kayseri, Turkey. *Journal of International Medical Research* [Internet]. 2018 Jan 21;46(1):122–34. Available from: <http://journals.sagepub.com/doi/10.1177/0300060517712865>
  24. Tajdini M, Effatpanah M, Zaki-Dizaji M, Movahedi M, Parvaneh N, Shariat M, et al. Associations of Behavioral Disorders with Asthma in Iranian Children [Internet]. Vol. 18, *Iran J Allergy Asthma Immunol*. Iran J Allergy Asthma Immunol. 2019. Available from: <http://ijaa.tums.ac.ir>
  25. Bendiksen B, Aase H, Diep LM, Svensson E, Friis S, Zeiner P. The Associations Between Pre- and Postnatal Maternal Symptoms of Distress and Preschooler's Symptoms of ADHD, Oppositional Defiant Disorder, Conduct Disorder, and Anxiety. *J Atten Disord*. 2020 May 1;24(7):1057–69.
  26. Lin YT, Chen YC, Gau SSF, Yeh TH, Fan HY, Hwang YY, et al. Associations between allergic diseases and attention deficit hyperactivity/oppositional defiant disorders in children. *Pediatr Res* [Internet]. 2016 Oct 2;80(4):480–5. Available from: <http://www.nature.com/articles/pr2016111>
  27. Kalil K, Gregory J, Makled M. Systematic review of risk factors associated with attention deficit hyperactivity disorder. *J Anal Res Clin Med* [Internet]. 2014;2(4):159–66. Available from: <http://journals.tbzmed.ac.ir/JARCM>
  28. Azeredo A, Moreira D, Barbosa F. ADHD, CD, and ODD: Systematic review of genetic and environmental risk factors. *Res Dev Disabil*. 2018 Nov 1;82:10–9.
  29. Latimer K, Wilson P, Kemp J, Thompson L, Sim F, Gillberg C, et al. Disruptive behaviour disorders: A systematic review of environmental antenatal and early years risk factors. Vol. 38, *Child: Care, Health and Development*. 2012. p. 611–28.
  30. Latimer K, Wilson P, Kemp J, Thompson L, Sim F, Gillberg C, et al. Disruptive behaviour disorders: a systematic review of environmental antenatal and early years risk factors. *Child Care Health Dev*. 2012 Sep;38(5):611–28.

31. Miyazaki C, Koyama M, Ota E, Swa T, Mlunde LB, Amiya RM, et al. Allergic diseases in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis. *BMC Psychiatry*. 2017 Dec 31;17(1):120.