HHS Public Access

Author manuscript

Curr Environ Health Rep. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:

Curr Environ Health Rep. 2020 September ; 7(3): 256–271. doi:10.1007/s40572-020-00280-7.

A Scoping Review of Non-Occupational Exposures to Environmental Pollutants and Adult Depression, Anxiety, and Suicide

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Abstract

Purpose of Review: Despite a call for better understanding of the role of environmental pollutant influences on mental health and the tremendous public health burden of mental health, this issue receives far less attention than many other effects of pollutants. Here we summarize the body of literature on non-occupational environmental pollutant exposures and adult depression, anxiety, and suicide—in PubMed, Embase, Web of Science, and PsychINFO through the end of year 2018.

Recent Findings: One hundred twelve articles met our criteria for further review. Of these, we found 88 articles on depression, 33 on anxiety, and 22 on suicide (31 articles covered multiple outcomes). The earliest article was published in 1976, and the most frequent exposure of interest

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Compliance with Ethical Standards

Conflict of Interest

Aisha S. Dickerson, Alexander C. Wu, Zeyan Liew, and Marc G. Weisskopf declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any data directly collected from human or animal subjects by any of the authors.

was air pollution (n=33), followed by secondhand smoke (n=20), metals (n=18), noise (n=17), and pesticides (n=10). Other exposures studied less frequently included radiation, magnetic fields, persistent organic pollutants (POPs), volatile organic compounds, solvents, and reactive sulfur compounds.

Summary: The current literature, although limited, clearly suggests many kinds of environmental exposures may be risk factors for depression, anxiety, and suicide. For several pollutants, important limitations exist with many of the studies. Gaps in the body of research include a need for more longitudinal, life-course studies, studies that can measure cumulative exposures as well as shorter-term exposures, studies that reduce the possibility of reverse causation, and mechanistic studies focused on neurotoxic exposures.

Keywords

Mental Health; Environmental Pollutants; Depression; Anxiety; Suicide

Introduction

Depression and anxiety are the two most prominent mental health conditions worldwide [1]. Suicide is perhaps the most dramatic outcome of mental health disorders. Depression is the third most prevalent cause of disease burden worldwide [2], and affects about 300 million people globally [3]. In 2010, depression attributed to the most disability-adjusted life years (DALYs) lost among mental and substance use disorders—accounting for approximately 74.5 million DALYs worldwide [4]. The lifetime prevalence of Major Depressive Disorder (MDD) in the US is 17% [5] and 7% have experienced an MDD in the past year [6, 7]. The personal costs from MDD include significant clinical morbidity, increased mortality from suicide, and loss of quality of life [8]. Financial costs from MDD to employers in the US in 2000 measured $83 billion, with the majority (62% or $52 billion) due to lost workplace productivity [9]. Furthermore, the cost of MDD to employers in lost work days is as great or greater than the cost of many other common medical conditions, including heart disease, diabetes, or back problems [10]. Anxiety disorders are the most common types of psychiatric disorder in the general population [6], and affect around 270 million people worldwide [1]. Approximately 29% of people have an anxiety disorder in their lifetime [5], and 18% have experienced an anxiety disorder in the past year [6]. Anxiety disorders are associated with reduced productivity and increased psychiatric and non-psychiatric medical care, absenteeism, and risk of suicide [11]. The monetary cost of anxiety disorders is also substantial; in the US, the annual direct cost of anxiety disorders in the 1990s has been estimated to be $42.3 billion [12]. In 2012, there was an estimated 804,000 suicide deaths worldwide with an annual age-standardized suicide rate of 11.4 per 100,000 people (15.0 for males, 8.0 for females) [13]. Although suicides accounted for about 1.4% of deaths globally in 2012, it is the second leading cause of death after traffic accidents among young-adults age 15 to 29 years and the fifth leading cause of death among adults age 30 to 49 years [14]. In 2016, suicides accounted for nearly 45,000 deaths (rates increased >30% in half of states since 1999) in the US and was the 2nd leading cause of death among people age 10 to 43 years [14, 15].

Exposure to environmental contaminants may be important modifiable risk factors for depression, anxiety, and suicide—individually and through public policy. Many environmental toxicants can cause oxidative stress that can contribute to such negative effects, but many also have known effects on more specific neural systems that underlie depression and anxiety. For example, effects on synaptic transmission [16, 17], dopaminergic systems [18], and glucocorticoid signaling and the hypothalamic-pituitary axis [19, 20] could be potential mechanisms. Furthermore, in many occupational and other high contaminant exposure settings strong associations between toxicants and mood or psychological distress have been seen [21–23]. Despite a decades-old call by a panel convened by the National Institute for Mental Health to study the link between environmental pollution and mental health, this area of research has received limited attention [24]. Over the last decade, several reviews of epidemiologic literature have addressed various aspects of individual toxicant exposures in relation to mental health outcomes as systematic [25–33], scoping [34–36], and narrative reviews [37–44]. However, some of these reviews only focused on individual metals [30, 31, 44, 45], certain components of air pollution like ozone [28] or particulate matter [46], and particular pesticides like organophosphate (OP) pesticides [33, 37]. Some of these previous reviews also limited included literature to outcomes reported in very specific populations, such as pregnant women [27], subjects in Bangladesh [30], and agricultural workers [33, 42], while others utilized a much broader definition of mental health outcomes that included personality and developmental disorders [28, 34, 43]. This scoping review advances upon these in using multiple data sources to obtain the most comprehensive collection of literature on non-occupational exposures to toxicants and risk of highly prevalent frequently co-occurring mental health outcomes: depression, anxiety, and suicide. As a scoping review, we will not systematically evaluate study quality, but we will describe the research that has been conducted and identified thus far and identify future directions for research in this field.

Methods

We conducted a scoping review [47, 48] by selecting, collecting, and summarizing the existing literature on environmental pollutants and depression, anxiety, and suicide. We defined “environmental” as a person’s surroundings, and “pollutants” as metals, pesticides, particles (air pollution, secondhand smoke), noise, and radiation that pollute a person’s surroundings. Our definition of “pollutants” did not include personal lifestyle factors such as diet, tobacco use, medications, or psychosocial factors, nor did we consider biological agents (e.g., viruses, bacteria, and mold). We searched for English articles on human subjects published through December 31, 2018 utilizing four databases: PubMed (US National Library of Medicine, Bethesda, Maryland), Web of Science (Thomson Reuters Corporation, New York, New York), PsychINFO (American Psychological Association, Washington, D.C.), and Embase (Elsevier, Amsterdam, Netherlands). Table 1 details search terms used in each database.

After removing duplicates, titles and abstracts through 2016 were screened for potential relevance by at least two of three reviewers (M.G.W., A.C.W., and Z.L.) and articles for 2017 and 2018 were screened by two others (A.S.D and J.G.). Questions or discrepancies were resolved by consensus with the lead author (M.G.W.). After the initial title and abstract

screening, full texts of articles were further reviewed and information on authors, year, study design, study populations, outcome measurements (i.e. depression, anxiety, and/or suicide), and markers and type of exposure (i.e. metals, air pollution, pesticides, noise, secondhand smoke, or other) were extracted and entered into Excel files. If any papers were thought to potentially be ineligible at this stage, the decision was made by consensus. Additionally, we hand searched reference lists in review papers and journal articles captured by our search terms for additional relevant papers. We excluded articles based on the following criteria: 1) study designs (not human studies, assessments in childhood (≤18 years) without results reported separately for adults); 2) reported exposures (occupational cohorts, did not study environmental pollutants, acute poisonings, exposure due to an environmental health incident or disaster); 3) reported outcomes (did not study depression, anxiety, or suicide independent of other psychological outcomes); and 4) article types (review papers, commentaries, conference abstracts, dissertations, and case studies). After full-text review, any discrepancies about which articles would be included in the scoping review were discussed and, when necessary, adjudicated by the lead author (M.G.W.). We present these articles organized by outcome and subdivided by exposure, and presented in visualized, interactive format using Tableau Public (version 2019.2; Tableau, https://public.tableau.com/authoring/EnvironmentalPollutantsandMentalHealthReview/Dashboard). For each exposure of interest, we summarize the number of studies included, range of sample sizes, countries of origin, and study design.

Results

We identified 14,323 articles by searching PubMed (1,642), Embase (1,532), Web of Science (10,145), and PsychINFO (1,004). Of these, there were 13,302 unique articles. Following exclusions and hand searches among references, we ended with 112 relevant articles for further review (Figure 1). Of these, we found 88 articles on depression, 33 on anxiety, and 22 on suicide, with 31 articles covering multiple outcomes. The majority (75 articles) of included articles were published after 2011 with the earliest article published in 1976 (Figure 2). Details on individual study designs, exposures, outcomes, study populations, sample sizes, confounders, and overall results can be found in Excel Table S1 and https://public.tableau.com/profile/aisha.dickerson#!/vizhome/EnvironmentalPollutantsandMentalHealthReview/Dashboard.

Depression

Of the 88 studies of depression, a large majority (n=60) were cross-sectional studies, followed by 20 cohort, 4 case-crossover, 3 case-control (1 nested) studies, and 1 ecological study. A variety of methods for assessing depression were used across studies, including self-reported depression symptoms or diagnosis via health questionnaires and several validated depression scales, and 8 studies used ICD codes. Of the depression diagnostic tools used, the Centre for Epidemiologic Studies Depression Scale (CES-D) (n=14) and Patient Health Questionnaire (PHQ) (n=10) were most frequently used, while others were also common, including the Composite International Diagnostic Interview (CIDI) (n=5), Generic Depression Scale (GDS) (n=4), Edinburgh Postnatal Depression Scale (EPDS) (n=4), Beck's Depression Inventory (BDI) (n=3), General Health Questionnaire (GHQ)

(n=2), and Hospital Anxiety Depression Scale (HADS) (n=2). Additional study information can be found in the Excel Supplemental Table and https://public.tableau.com/authoring/EnvironmentalPollutantsandMentalHealthReview/Dashboard.

Metals—Sixteen studies examined exposure to metals and depression (Figure 3, Excel Table S1) with sample sizes ranging from 210 to 15,140 subjects. Only 4 of the studies were not conducted in the US, with 2 in Québec [49, 50], 1 in Korea [51], and 1 in India [52]. The most studied metal was lead (Pb) (n=7), followed by cadmium (Cd) (n=5), manganese (Mn) (n=3), mercury (Hg) (n=2) and arsenic (As) (n=2), and strontium (Sr) (n=1), with Shiue *et al.* (2015) also incorporating antimony, beryllium, cesium, cobalt, molybdenum, selenium, thallium, tin, tungsten, and uranium.

The majority of the studies (n=14) were cross-sectional in design with blood concentrations of metals used for exposure assessment, which may not capture the relevant exposure window and can be susceptible to reverse causation. Most of these used National Health and Nutrition Examination Survey (NHANES) data. Six other cross-sectional studies also examined concurrent short-term metal biomarkers in settings other than NHANES. These studies were smaller than the NHANES studies and not representative samples of the populations from which samples were drawn. Blood concentrations of Cd (n=4), Mn (n=2), Pb (n=5), and Hg (n=2) have been examined in such studies. Other markers of exposure to metals included urine (n=3), bone Pb (n=2), and drinking water for As (n=2). Of the 2 cohort studies, 1 was a study of childhood (before age 7) blood Pb and depression at 25–29 years of age [53], while the other assessed bone Pb, a marker of cumulative exposure in adulthood, via K-shell X-Ray Fluorescence (KXRF) [54].

Air Pollution—There were 22 studies on exposure to air pollution and depression (Figure 3, Excel Table S1), with sample ranging from 102 to 124,205 subjects. Although one of these studies was global, [55] most were set in the US (n=5) and China (n=5), followed by Korea (n=4), Canada (n=3), Europe (n=3), and India (n=1). All but one of these involved outdoor exposure estimates independent of the participant—e.g. based on air monitor data or distance to road, which avoids much reverse causation [56]. Most of the studies were cross-sectional (n=10) and the rest were cohort (n=8) and case-crossover (n=4) studies. While 5 of the cohort studies only looked at long-term exposures, 2 only examined short-term exposures [57, 58], and 1 investigated both short-and long-term air pollution exposures [59]. All other studies, except 2 cross-sectional studies [60, 61] focused on short-term exposures. There was a variety of air pollutants covered by the included studies, with the most frequently studied being particulate matter (PM) (i.e. $PM_{2.5}$, n=12; PM_{10}, n=9), ozone (O_3) (n=9), nitrogen oxides (n=12), sulfur dioxide (SO_2) (n=10), carbon monoxide (CO) (n=8), black carbon (n=1), smog (n=1), and sulfates (n=1). There was one study of indoor biomass burning, which would be expected to measure much higher levels of exposure, and was the only study that used personal-based exposure monitoring [62].

Pesticides—There were 7 studies of exposure to pesticides and depression (Figure 3, Excel Table S1), with samples ranging from 149 to 29,074 study participants. Many had important limitations, such as self-reported exposures (n=4). Of the 5 studies conducted in the US, 3 were conducted in spouses of agricultural workers [63–65], while 1 was in Turkey

[66] and the other was in Brazil [67]. Regarding study design, 3 were cohort studies, 3 were cases-control (1 nested), 1 was cross-sectional, and 1 was an ecological study. Additionally, 1 of the case-control studies was the only to use a biological measure as a proxy for a specific pesticide exposure – red blood cell acetylcholine esterase (AChE) for OP pesticide exposure [66].

Noise—We found 13 studies of exposure to noise and depression (Figure 3, Excel Table S1) with sample sizes ranging from 144 to 77,295 people. Most studies assessed exposure based on where people lived, with 1 case-control study, 1 cohort study, and the rest (11 studies) being cross-sectional. Most studies were set in European countries, including Germany (n=2), the UK (n=2), Serbia (n=1), Italy (n=1), Finland (n=1), and Norway (n=1), while the rest were in Asia, including Japan (n=2), Korea (n=1), India (n=1), and Iran (n=1). Eight articles addressed road traffic noise and depression symptoms as measured by scales [68–75]. Five additional studies considered noise around airfields [76–80]. One study in India investigated indoor noise pollution and neighborhood noise with depression, but not street noise, although no details on how the noise was assessed were provided [74]. Another conducted small randomized trials of ear plugs or sound cancelling headphones in a noisy hospital setting and found no differences in depression scores between any of the trial conditions [73].

Secondhand Smoke—We found 19 studies describing depression and exposure to secondhand smoke (SHS) (Figure 3, Excel Table S1), with sample sizes ranging from 162 to 123,665 people. Eight of these studies took place in the US, with others located in various countries, including Taiwan (n=2), Canada (n=2), China (n=2), Korea (n=3), Germany (n=1), and the Netherlands (n=1). Three of these studies used blood or salivary cotinine as biomarkers of exposure [81–83]. Of 14 studies that determined SHS exposure by questionnaire [84–97], 5 of these were among pregnant women [87–90, 97] and 1 specifically examining post-partum depression [88]. Two of the pregnancy studies were in Taiwan where maternal smoking during pregnancy is illegal, presumably increasing the likelihood that mothers truly did not smoke during pregnancy and so were only exposed to SHS [89, 90]. Three of the studies considered earlier life (*in utero* and childhood) exposures to SHS and later life depression [94, 96, 97].

Other—There were 13 studies evaluating depression and other environmental pollutants including polyfluorinated compounds (n=1), phthalates (n=4), polychlorinated biphenyls (PCBs) (n=2), volatile organic compounds (VOCs) (n=1), trichloroethylene (TCE), and electromagnetic and gamma radiation (n=3) (Figure 3, Excel Table S1). With sample sizes ranging from 143 to 15,140 people, most (n=10) were cross-sectional in design, and 3 were cohort studies. Of the 7 studies conducted in the US, 3 used NHANES data [98–100]. There were also 2 studies set in Taiwan, while others were distributed to Australia, Egypt, New Zealand, and Korea. Phthalate exposure was primarily determined through urine measurements [99–102]. Three studies used NHANES data and examined contaminants in biosamples collected from participants [98–100]. Three studies considered electromagnetic fields (EMF) [103–105]. One related to living or working near a mobile phone base station

antenna and was quite small with a high risk of confounding [103]. The other two examined living near high-voltage power transmission lines [104, 105].

Anxiety—There were 33 papers on anxiety; most of which were cross-sectional studies (n=20). Eight of the studies were cohort studies, 2 randomized experiments, 1 case-crossover, 1 case-control, and 1 time-series study. Two studies used anxiety diagnosis as indicated by ICD codes in hospital records [57, 106], and 3 were based on self-reported diagnosis or symptoms [92, 107, 108]. Other studies used various anxiety measurement scales, including the State-Trait Anxiety Inventory (STAI) (n=6), CIDI (n=5), Brief Symptom Inventory (BSI) (n=2), Crown-Crisp Index (CCI) (n=2), HADS (n=2), Profile of Mood States (POMS) (n=2), Symptom Checklist-90 (SCL-90) scale (n=1), CES-D (n=1), and the World Health Organization Neurobehavioral Core Test Battery (WHO-NCTB) (n=1).

Metals—There were 8 studies that examined exposure to metals and anxiety (Figure 3, Excel Table S1) with sample sizes ranging from 190 to 654 adults. Half of the studies were set in the US (n=4), 2 in Canada, and the others in Australia and India. Most of these were cross-sectional studies (n=5) of Pb, Mn, and As, 2 were cohort investigations of Pb, and 1 case-control study examined Mn. Four studies considered anxiety in association with blood (n=3) and bone (n=2) Pb measures, and one specifically investigated childhood blood levels and anxiety in adulthood [53, 54, 109, 110]. A study in India also examined the association between As concentrations in drinking water and anxiety symptoms [52]. Three studies considered Mn exposure: two assessing exposure via blood Mn levels [49, 50], and the other based on ambient air concentrations [111]. Because blood Mn is under tight homeostatic control, it is possible that it is not as effective at identifying higher Mn exposures as is simply living in the area with higher air Mn concentrations [56].

Air Pollution—There were 7 studies on air pollution and anxiety (Figure 3, Excel Table S1), with sample sizes ranging from 102 to 71,271 study participants. There were 4 cohorts set in the US (n=3) and Canada (n=1), 1 cross-sectional study in Spain, 1 case-crossover study in China, and 1 time-series study in Korea. Two of the cohort studies only assessed long-term exposures [112, 113], 1 only used short-term exposures [57], and 1 examined both short- and long-term air pollution exposures [59]. All other study designs investigated anxiety in relation to short-term air pollution exposures. Different aspects of air pollution were studied: particulate matter (i.e. PM_{10}, n=4; $PM_{2.5}$, n=5), nitrogen oxides (n=4), CO (n=2), SO_2 (n=2), O_3 (n=2), and smog (n=1). Two of these considered daily concentrations of several different ambient air pollutants and hospital emergency department (ED) visits for anxiety [57, 106], 4 studies explored individual level anxiety symptoms [59, 112–114], and 1 considered self-reported history of anxiety [108].

Pesticides—The review found no studies on pesticides and anxiety.

Noise—There were 9 studies on noise and anxiety (Figure 3, Excel Table S1) with sample sizes ranging from 48 to 2898 people. Although most (n=6) of the studies were cross-sectional, 2 were randomized experiments and one was a cohort study. Both randomized experiments were conducted in North American (Canada and the US) psychology classes

[115, 116], while the only cohort study was conducted in the UK [69]. The remaining cross-sectional studies were distributed among Germany, Italy, Finland, and Norway (each with n=1), while the rest were in Asia, including Japan (n=2), Korea (n=1), India (n=1), and Iran (n=1). Two studies were of noise around airfields [77, 78], 4 others considered road traffic noise [68, 69, 72, 107], and 1 of these also examined exposure to railway noise and overall outdoor noise (i.e. commercial properties, renovations, etc.) [107]. Three studies took an experimental approach to assessing noise and anxiety [73, 115, 116].

Secondhand Smoke—Six studies examined secondhand smoke (SHS) and anxiety (Figure 3, Excel Table S1), with sample sizes ranging from 162 to 49,701 subjects. All studies were cross-sectional studies, except 1 cohort study of pregnant women [89]. Study locations included Taiwan (n=2), Canada, the US, the Netherlands, and Germany. Two studies considered SHS exposure during pregnancy specifically and came to opposite conclusions [89, 90]. Another study considered adult anxiety incidence and SHS exposure during childhood and adulthood separately [96].

Other—Three studies examined other exposures and anxiety (Figure 3, Excel Table S1), with sample sizes ranging from 143 to 540. All were cross-sectional studies examining magnetic field exposure in New Zealand [104], TCE exposure in the US [117], and serum PCB concentration in the US [118].

Suicide

We included 22 papers on environmental exposures and suicide. Of these, 7 were cohort studies, 7 were cross-sectional studies, 6 were case-crossover, 1 was a case-control, and 1 was an ecological study. Over half of these studies were set in Asian populations, including Korea (n=7), Taiwan (n=2), China (n=1), Japan (n=1), and Iran (n=1), while 3 were conducted in US populations, along with 3 in European countries (Belgium, Denmark, and the UK), 2 in South America (Brazil and Columbia), 1 in Australia, and 1 in Turkey. We included studies that evaluated completed suicides (n=15), attempts (n=4), and ideation of suicides (n=3). Completed suicide was determined via ICD codes in mortality records (n=11) and police or medical examiner records (n=3). All ideation was determined through self-report (n=3) while suicide attempts were determined via hospital records (n=2) and self-report (n=2).

Metals—There was 1 study of completed suicides and metals in adults, which was a prospective population-based study in Denmark (Figure 3, Excel Table S1). Specifically, this study examined the association with area lithium concentration in drinking water [119].

Air Pollution—We identified 9 studies on completed suicide and 1 on suicide attempts and air pollution (Figure 3, Excel Table S1), with samples sizes ranging from 1546 to 265,749 people. One study was in the US [120], 1 was in South America [121], 1 was in Europe [122], and the rest were in Asia. Of these, 6 were case-crossover, 2 were cohort studies, 1 was cross-sectional, and 1 was an ecological study. All studies used air pollution exposure estimates based on ambient monitoring data. All studies examined particulate matter (PM_{10}, n=8; $PM_{2.5}$, n=5) and nitrogen oxides (n=7), followed by SO_2 (n=8), O_3 (n=4), and CO

(n=4). There were also slight differences in timing of exposure examined (preceding days, weeks, or years).

Pesticides—In relation to studies examining exposure to pesticides, there were 3 on completed suicides, 1 focused on suicide ideation, and 1 on suicide attempts with sample sizes ranging from 149 to 81,988 people (Figure 3, Excel Table S1). Regarding study design, 2 were cohort, 1 was case-control, and 2 were cross-sectional. The largest studies were among spouses of participants in the Agricultural Health Study (AHS) [123, 124]. Only 1 study considered a biomarker of exposure, red blood cell AChE activity (a specific molecular target of organophosphate and carbamate pesticides) in relation to attempted suicide [66].

Noise—There was 1 cohort study of outdoor noise and completed suicides, as indicated by ICD-10 codes in the Korean Statistical Office database [125].

Secondhand Smoke—Two cross-sectional studies explored suicide ideation and 1 cohort study examined suicide attempts and secondhand smoke (SHS) (Figure 3, Excel Table S1). These studies took place in Australia, Korea, and Taiwan and ranged from 2736 to 6043 subjects, with the smallest sample belonging to the cohort study [126].

Other—Two cross-sectional studies examined other exposures in relation to suicide, including hydrogen sulfide (H_2S) from ambient natural gas [127] and magnetic fields [128].

Discussion

The number of studies on general population environmental exposures and depression, anxiety, or suicide has increased over the last two decades (Figure 2). However, we found this literature to be rather limited for specific exposures of interest. Additionally, the vast majority of studies of depression and anxiety have important limitations, including small sample sizes, comparisons between crude proxies of exposure such as distinct communities, limited control for confounding, and designs that raise concern of reverse causation. Many of the studies were cross-sectional in nature, such as studies based on NHANES data. Because mental health conditions affect behavior, this study design aspect makes it difficult to conclude that the exposures are causally related to the depression, anxiety, or suicide as opposed to the mental health issues affecting measured exposure levels.

Mental health diagnosis

Our review demonstrated that several (n=15) of the studies of depression, anxiety, and suicide were based on ICD diagnosis codes provided in medical records. However, numerous studies have shown differences in likelihood of seeking mental health care as well as disparities in referrals and treatment provided based on gender [129] and socioeconomic status [130, 131]. Thus, studies using ICD codes from medical records may underrepresent depression and/or anxiety in populations considered underserved. However, there were several assessment scales utilized in other studies. Some studies used outcome-specific assessments, while others assessed depression and/or anxiety as a subpart of overall general health. Mental health screens should be provided as part of general healthcare visits, but for

the purposes of research, continuous scales suited for assessing severity of depression and anxiety may be more appropriate. Additionally, it is important to note that depression and anxiety are often co-occurring conditions [132], and that suicide is commonly the result of these underlying conditions [133]. For these reasons, the authors suggest future studies of environmental exposures and depression and anxiety should investigate these disorders using both symptoms and scale measures in order to capture preclinical influence of exposures on mental health. Furthermore, although 20 of the discussed studies considered depression and anxiety in conjunction, and 8 considered other co-occurring mental health outcomes, including panic disorder [53, 109], psychotic episodes [49, 50], paranoia and obsessive-compulsive disorder [49], aggression [49, 50, 117], memory and learning [52, 118], executive function and impulse control [50, 118], drug and alcohol abuse [53, 95], and post-traumatic stress disorder [53], we believe that future studies should consider a broader spectrum of outcomes and evaluate comorbidity whenever possible.

Metal exposures

Studies of metal exposures were mostly cross-sectional, many using US NHANES data [98, 100, 109, 134–137]. For most of these, reverse causation is hard to rule out. However, several other studies used exposure assessments that more readily avoid reverse causation, including some related to metals in drinking water [52, 138] and bone measurements [54, 110], while a protective association was seen between water selenium concentrations and depression [139]. Only 3 studies used biomarkers of exposure that more readily captured past exposure—all were biomarkers of Pb. One used child blood Pb levels and found no association with young adult depression, but a nearly significant association with anxiety [53]. Two others used bone Pb in adults as a marker of cumulative exposure and did find associations with worse depression and anxiety [54, 110].

The only studies to not find higher metal concentrations associated with depression were 2 studies of Hg [98, 135], 1 of As [100], and 2 of Pb [98, 100]. Analyses of Hg are complicated because the primary source of Hg exposure is fish consumption, which could have beneficial neurological effects [140, 141]. One of these studies suggested the lack of association with Hg could be related to protection from fish consumption [98], although the other study attempted to control for fish consumption and fish oil intake [135]. Only one study of blood Pb used an assessment tool (the CIDI) to identify a clinical disorder (major depressive disorder [MDD]) as the outcome [109]. The study reported differences among smokers and non-smokers, which could relate to increased exposure from more hand-to-mouth activity among smokers. Smoking could be a form of self-medication to reduce symptoms (and therefore their CIDI score) [142, 143], highlighting the concern of the possibility of reverse causation with such cross-sectional studies. Three studies of depression and metals used exposure metrics that involved measures independent of the participants to estimate individual exposures. Although this approach can result in a less accurate assessment of true exposure—which is likely non-differential and so biases effect estimates to the null—it avoids problems of reverse causation and confounding by personal behaviors [56].

Air Pollution

Studies of air pollution exposures more readily avoid reverse causation than many studies of other exposures because the exposure estimates typically are not affected by personal behaviour [56]. Although each paper reported the primary source of air pollution data, very few mentioned the specific air dispersion models used for these sources, including Gaussian line-source dispersion, inverse distance weighting, and land-use regression modeling. Furthermore, time series and case-crossover designs are commonly used in air pollution studies, and these study designs eliminate concern for confounding by time-invariant factors. The largest group of any type of study examined associations between same day or recent days' ambient pollutant concentrations and the number of hospital visits for depression or anxiety using a time series or case-crossover design [57, 58, 144–146]. While these study designs help avoid confounding by time-invariant factors, ED visits are a crude method for capturing depression. Different components of air pollution, including PM and metal, have been established as neurotoxic [147]. The mechanisms are not fully understood, but animal and human studies have suggested that this may be through cerebrovascular dysfunction, oxidative stress or inflammation [148, 149]. While 17 of the included studies only looked at short-term exposures, this may only be a reflection of triggered inflammation. Conversely, long-term exposures, examined in 10 of the included studies, are indicators of chronic exposure and are more likely to result in overall poorer health and subsequent mental health decline.

Pesticides

Of work on pesticides and depression, the most compelling studies on non-occupational exposures were in the AHS cohort in part because of its size, ability to control for covariates, and, in one case, a prospective follow-up design. The AHS was established to examine health effects of pesticide exposures primarily among pesticide applicators who presumably would be much better than the general public at recalling past pesticide use and exposures [150], but as an occupational group fall outside the scope of this review. However, the AHS also enrolled spouses of the applicators and we considered AHS studies among these non-workers. Although participants self-reported past exposures, the analyses of prevalent depression could still suffer from reverse causation if reporting of past exposures was influenced by depression. It should be noted that while studies among spouses were not among workers, spouses of workers likely have different exposure routes and profiles than the general public. No studies were identified of pesticide exposures and anxiety.

Other studies of pesticide exposures were more limited. A large study using NHANES data assessed associations between urinary pesticides (including organophosphates) and depression [98], but as a cross-sectional study with a short half-life biomarker of exposure. The only other study to use a biomarker of exposure used red blood cell acetylcholinesterase (AChE) activity as an indicator of exposure to organophosphate (OP) pesticides in a study of only 149 patients with MDD and 64 patients without [66].

Noise

We found several studies of noise with most estimating outdoor noise levels. Assessments of noise was done by various methods including simply living near an airfield or not,

residential address combined with different noise maps, or direct noise measurements outside the home. One study assessed indoor and neighbor noise although did not provide details of the approach [74], one considered self-report of noise levels [107], one considered noise reduction through use of earplugs [73], and two delivered white noise experimentally [115, 116]. Several studies also asked about noise sensitivity and considered outcomes relative to that. For these studies, many alternate explanations other than a causal association are hard to rule out, including chance (many studies were small) and confounding by SES. Some study designs make it difficult to ascribe depression or anxiety differences specifically to noise exposure, as higher noise exposure would likely be almost completely co-linear with other aspects of living nearer noisy places such as airports. In addition, noise represents a complex exposure for these types of studies, as individuals are generally aware of these exposures, which is not the case with many other environmental contaminants. As a result, a participants' responses regarding depression and anxiety could be influenced by recognition of their exposure. At the same time, recognition of exposure could lead to annoyance and stress, which could then lead to biological effects resulting in more depression and/or anxiety. This would nonetheless be a somewhat different causal path to worse mental health than would be postulated for most of the other environmental exposures considered here.

Secondhand smoke

Secondhand smoke (SHS) is an exposure that could conceivably suffer from some of the same issues outlined above for noise since people are generally aware of their exposure to SHS. Nonetheless, there are also more direct biological actions of SHS that could conceivably lead to depression, anxiety, and suicide. Overall, the studies tended to reasonably account for confounding, in particular by SES factors, and many were quite large. The few studies on associations between childhood SHS exposure, or the combination of childhood and adult exposure, and adult depression and anxiety suffer less from the issue of reverse causation or the exposure causing the outcome because of annoyance or stress, since the exposures were very removed in time. In addition, one study avoided these problems in considering SHS indirectly by examining the association between depression and smoking policies both at home and work [151].

Other exposures

Several other contaminants have also been explored, including more recently explored chemicals like polyfluorinated compounds, phthalates, and triclosans, as well as older ones such as PCBs, TCE and different types of EMF. There were analyses of many compounds with shorter half-lives—such as phenols, phthalates, and polyaromatic hydrocarbons in urine. Given the short half-lives of the biomarkers, one measure may not reflect longer-term exposure well, which could add error to the estimation of exposures over relevant time periods and contribute to differences in findings particularly in cross-sectional studies such as NHANES. However, 1 of these studies examined blood polyfluorinated compounds, which can have much longer half-lives [98]. Polychlorinated biphenyls (PCBs) have even longer half-lives in blood than polyfluorinated compounds, so one blood measure is a good cumulative exposure estimate. However, many of these studies also suffered from the kinds of limitations discussed above.

Future directions

Previous reviews of environmental exposures and mental health outcomes restricted inclusion criteria to specific metals, air pollution components, and particularly volatile toxicants. However, our scoping method used multiple data sources to obtain the most comprehensive collection of literature on non-occupational exposures to toxicants. We also provided a thorough synopsis of the studies included, with searchable data on modes of assessment of both exposures and assessment. Though we did summarize and interpret included studies, as this is not a systematic review, we did not appraise overall weight of evidence based on sample size, study design, risk of bias, or other factors commonly evaluated for study quality. The wealth of available data ascertained in our scoping review suggests that a systematic review and/or meta-analysis would be an appropriate next step, though it would need to have more restrictions on publication range. However, we recognize that harmonizing certain outcomes may be difficult due to the variety of methods used in each study. Current literature on pesticides is overall crude and particularly difficult to provide comparative reviews. Thus, the authors believe that future studies of these exposures should assess particular types of pesticides grouped by their potential toxicity and mechanism of action. Additionally, we recommend that future individual studies of environmental exposures and depression, anxiety, and suicide should investigate a broader range of validly measured mental health outcomes using repeated symptom and scale measures in order to mitigate reverse-causation with both cumulative and short-term exposures.

Conclusion

Given the tremendous public health impact of adverse mental health conditions, understanding the contribution of environmental exposures—often modifiable—should be of paramount importance. The current literature, although limited, clearly suggests many kinds of environmental exposures may be risk factors for depression, anxiety, and suicide. Gaps in the body of research include a need for more longitudinal studies, studies that can measure cumulative exposures as well as shorter-term ones, and studies that control well for potential confounders and reduce the possibility of reverse causation. Furthermore, there should be more examination into the potentially mediating impact of pharmacological treatment in these exposure-outcome relationships.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank Scott Lapinski, Digital Resource and Services Librarian at the Francis A. Countway Library of Medicine, for his counsel and constant assistance in honing our literature review. We also thank Julie Goodman for extending the literature search and Maggie Mittleman and Christian Hoover for checking our review for missed articles. No authors received compensation for their participation in this project. All authors declare no financial interest. Drs. Weisskopf, Wu, and Dickerson had full access to all of the references in the review and take responsibility for the integrity and accuracy of the review. This work was supported by NIH grant P30 ES000002. Dr. Wu was supported by the NIOSH ERC training-grant, T42 OH008416. Dr. Dickerson was supported in part by a National Institutes of Health training grant T32 ES007069. Dr. Liew was partly supported by the NIH/NIEHS Pathway to Independence Award (K99ES026729/R00ES026729).

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* Of importance

** Of major importance

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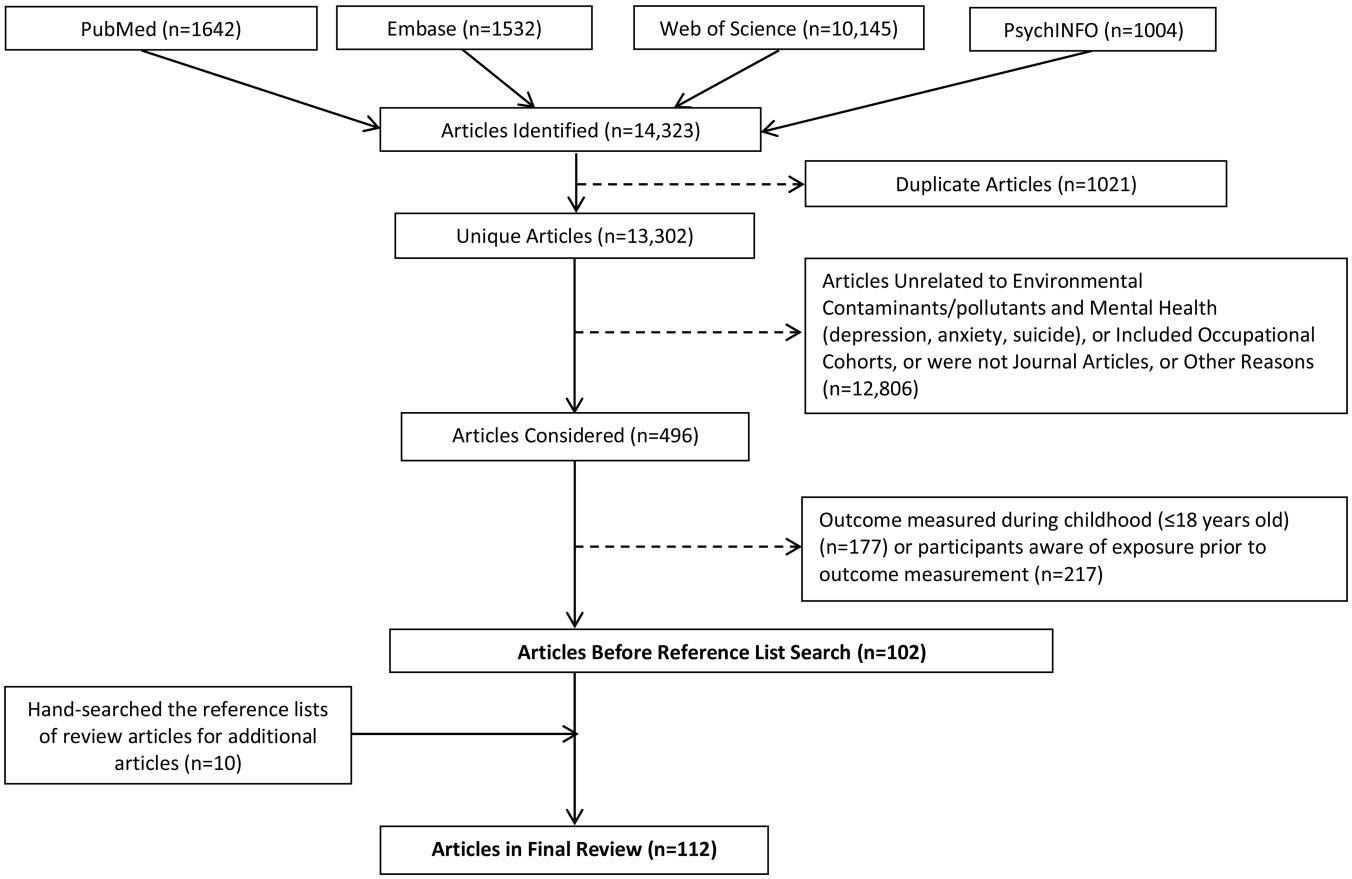


Figure 1.

Article search and selection method utilized in reviewing studies on the associations between environmental contaminants/pollutants and depression and anxiety among non-occupational cohorts. Solid lines represent articles included and dashed lines denote excluded articles. The final search included articles published before Dec. 31, 2018.

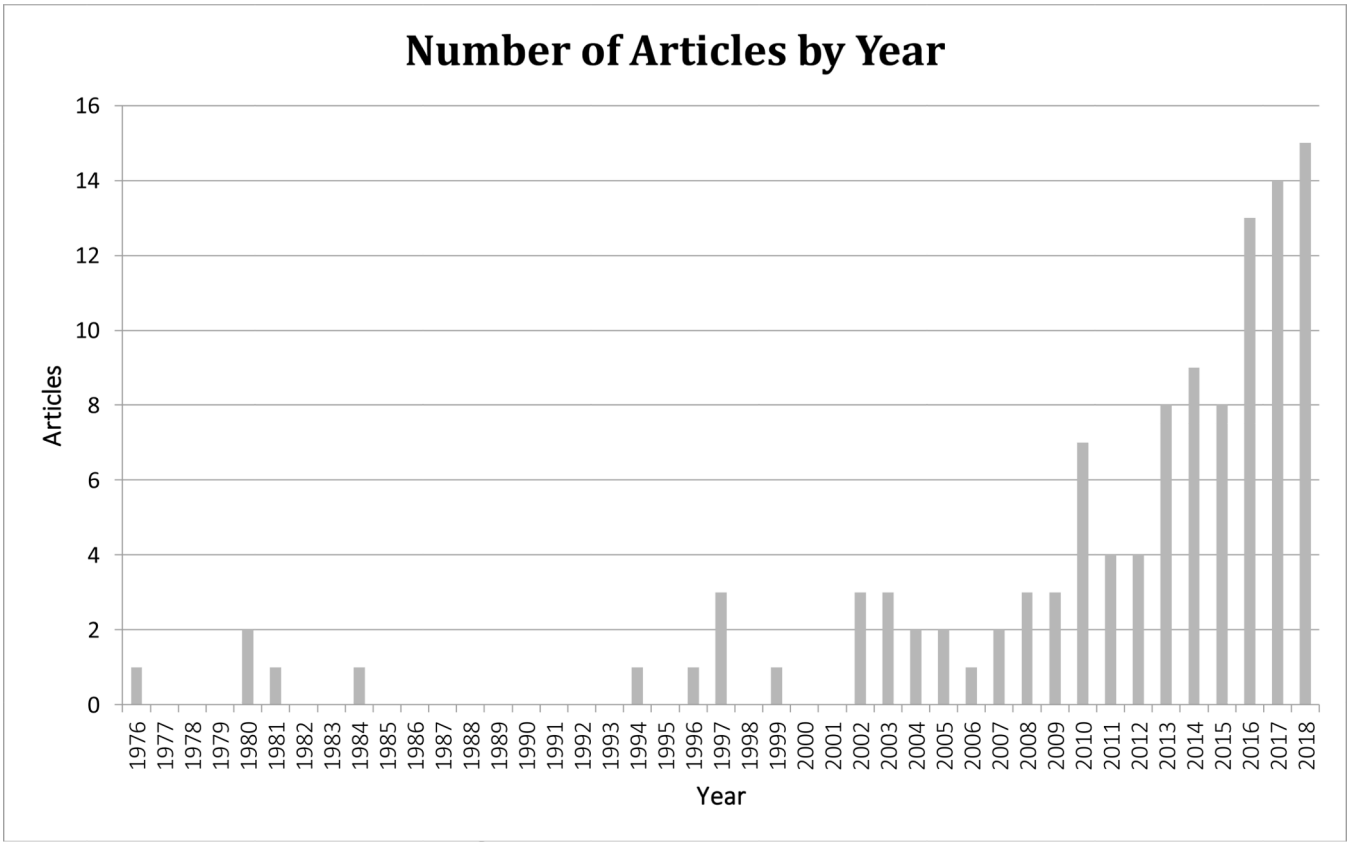
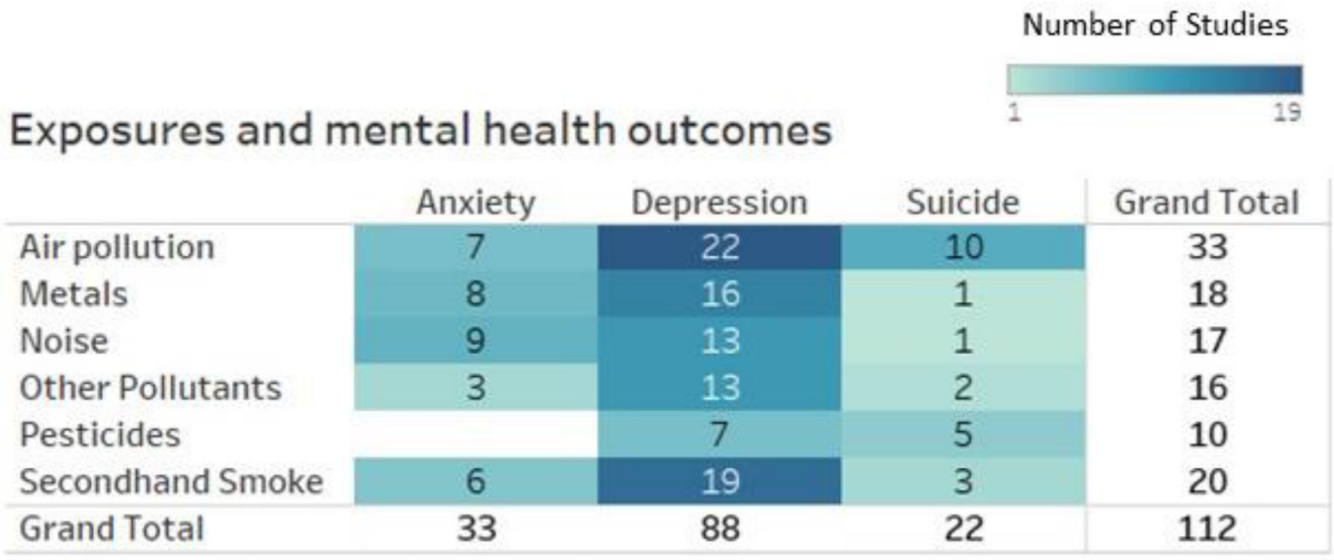


Figure 2.
Number of articles included in the review by year (112 total articles).



	Anxiety	Depression	Suicide	Grand Total
Air pollution	7	22	10	33
Metals	8	16	1	18
Noise	9	13	1	17
Other Pollutants	3	13	2	16
Pesticides		7	5	10
Secondhand Smoke	6	19	3	20
Grand Total	33	88	22	112

Figure 3.
Heat map of included studies by exposure category and mental health outcome.

Table 1.

Journal database search terms utilized in identifying studies.

Database	Search terms
PubMed (n=1642)	"Environmental Pollution"[Mesh] OR Pollut*[tw] OR ((Environment*[tw] OR water[tw] OR Hazardous[tw]) AND (waste[tw] OR radioactive*[tw] OR radiation[tw]))
	AND
	"Depression"[Mesh] OR "Depression"[tiab] OR "Depressions"[tiab] OR "Depressive"[tiab] OR "Anxiety"[Mesh] OR
	"Anxiety"[tiab] OR "Catastrophization"[tiab] OR "Hypervigilance"[tiab] OR "Suicide"[Mesh] OR "Suicide"[tiab] OR
	"Internalizing"[tiab] OR "externalizing"[tiab]
	AND
	"cohort studies"[mesh] OR "case-control studies"[mesh] OR "comparative study"[pt] OR "risk factors"[mesh] OR
	"cohort"[tw] OR "compared"[tw] OR "groups"[tw] OR "case control"[tw] OR "multivariate"[tw] OR "Epidemiologic
	Research Design"[Mesh] OR "Epidemiologic Study Characteristics as Topic"[Mesh] OR
	"Depression/epidemiology"[Mesh] OR "Anxiety/epidemiology"[Mesh]
	NOT
	("invertebrates"[Mesh] OR "Rodentia"[Mesh])
	Filters: date to Dec. 31, 2018
Embase (n=1532)	'pollution and pollution related phenomena'/exp OR 'pollut*':ab,ti OR (('environment*' OR 'water' OR 'hazardous') AND ('waste' OR 'radioactive*' OR 'radiation'))
	AND
	'depression'/exp OR 'depression':ab,ti OR 'depressions':ab,ti OR 'depressive':ab,ti
	OR 'anxiety'/exp OR 'anxiety disorder'/exp OR 'anxiety':ab,ti OR 'catastrophization':ab,ti OR 'hypervigilance':ab,ti
	OR 'suicide'/exp OR 'suicidal behavior'/exp OR 'suicide':ab,ti OR 'internalizing':ab,ti OR 'externalizing':ab,ti
	AND
	'clinical article'/exp OR 'controlled study'/exp OR 'major clinical study'/exp OR 'prospective study'/exp OR 'cohort analysis'/exp OR 'cohort':ab,ti OR 'compared':ab,ti OR 'groups':ab,ti OR 'case control':ab,ti OR 'multivariate':ab,ti
	AND
	(1952:py OR 1958:py OR 1959:py OR 1960:py OR 1961:py OR 1962:py OR 1963:py OR 1964:py OR 1965:py OR 1966:py OR 1967:py OR 1969:py OR 1970:py OR 1971:py OR 1972:py OR 1973:py OR 1974:py OR 1975:py OR 1976:py OR 1977:py OR 1978:py OR 1979:py OR 1980:py OR 1981:py OR 1982:py OR 1983:py OR 1984:py OR 1985:py OR 1986:py OR 1987:py OR 1988:py OR 1989:py OR 1990:py OR 1991:py OR 1992:py OR 1993:py OR 1994:py OR 1995:py OR 1996:py OR 1997:py OR 1998:py OR 1999:py OR 2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py)
Web of Science (n=10,145)	TS=(Environmental pollution OR Pollut* OR air pollution OR water pollution OR pesticide* OR environmental exposure* OR environmental monitoring OR radiation OR noise OR waste water OR wastewater OR toxi* OR metal* OR pesticide* OR particle* OR particulate*)
	OR
	TS=((Environment* OR water OR Hazardous OR industrial OR solid OR radioactive) SAME (waste OR radioa ctive* OR radiation))
	AND
	TS=(depression OR depressions OR depressive OR anxiety OR catastrophization OR hypervigilance OR hypervigilant OR suicid* OR internalizing OR externalizing)
	AND

Database	Search terms
	TS=((cohort NEAR/1 studies) OR (case NEAR/1 control) OR (comparative NEAR/1 study) OR (risk NEAR/1 factors) OR cohort OR compared OR groups OR multivariate OR (cross NEAR/1 sectional)) Filters: date 1900 – 2018
PsychINFO (n=1004)	DE “Hazardous Materials” OR DE “Insecticides” OR DE “Teratogens” OR DE “Toxins” OR DE “Toxic Disorders” OR DE “Acute Alcoholic Intoxication” OR DE “Carbon Monoxide Poisoning” OR DE “Drug Induced Congenital Disorders” OR DE “Lead Poisoning” OR DE “Mercury Poisoning” OR DE “Narcosis” OR DE “Neuroleptic Malignant Syndrome” OR DE “Thyrotoxicosis” OR DE “Toxic Encephalopathies” OR DE “Toxic Hepatitis” OR DE “Toxic Psychoses” OR DE “Pollution” OR DE “Passive Smoking” OR DE “Prenatal Exposure” OR DE “Noise Effects” OR TX (pollut* OR ((Environment* OR water OR Hazardous) AND (waste OR radioactive* OR radiation))) AND DE “Major Depression” OR DE “Anaclitic Depression” OR DE “Dysthymic Disorder” OR DE “Endogenous Depression” OR DE “Late Life Depression” OR DE “Postpartum Depression” OR DE “Reactive Depression” OR DE “Recurrent Depression” OR DE “Treatment Resistant Depression” OR DE “Atypical Depression” OR DE “Bipolar Disorder” OR DE “Cyclothymic Personality” OR DE “Depression (Emotion)” OR DE “Euthymia” OR DE “Neurosis” OR DE “Childhood Neurosis” OR DE “Experimental Neurosis” OR DE “Occupational Neurosis” OR DE “Traumatic Neurosis” OR DE “Pseudodementia” OR DE “Seasonal Affective Disorder” OR DE “Anxiety” OR DE “Computer Anxiety” OR DE “Mathematics Anxiety” OR DE “Performance Anxiety” OR DE “Social Anxiety” OR DE “Speech Anxiety” OR DE “Test Anxiety” OR DE “Anxiety Disorders” OR DE “Acute Stress Disorder” OR DE “Castration Anxiety” OR DE “Death Anxiety” OR DE “Generalized Anxiety Disorder” OR DE “Obsessive Compulsive Disorder” OR DE “Panic Disorder” OR DE “Phobias” OR DE “Post-Traumatic Stress” OR DE “Posttraumatic Stress Disorder” OR DE “Separation Anxiety Disorder” OR DE “Anxiety Management” OR DE “Generalized Anxiety Disorder” OR DE “Panic” OR DE “Panic Attack” OR DE “Panic Disorder” OR DE “Externalization” OR DE “Internalization” OR DE “Introjection” OR DE “Suicide” OR DE “Assisted Suicide” OR DE “Attempted Suicide” OR DE “Suicidal Ideation” OR TX (depression OR depressions OR Depressive OR anxiety OR catastrophization OR hypervigilance OR suicide OR internalizing OR externalizing) AND TX (“case control” OR “comparative study” OR “comparative studies” OR “risk factor” OR “risk factors” OR cohort OR compared OR groups OR multivariate) Filters: publication year 1936–2018