International Journal of Environmental Health Research

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/cije20

Neurodevelopmental outcomes in children living near hazardous waste sites: a systematic review

Edoardo Miotto, Anna Maria Tartaglione, Ivano Iavarone, Laura Ricceri, Amerigo Zona, Alessandra Ceccarini, Sabrina Rossi & Lucia Fazzo

To cite this article: Edoardo Miotto, Anna Maria Tartaglione, Ivano Iavarone, Laura Ricceri, Amerigo Zona, Alessandra Ceccarini, Sabrina Rossi & Lucia Fazzo (07 Aug 2024): Neurodevelopmental outcomes in children living near hazardous waste sites: a systematic review, International Journal of Environmental Health Research, DOI: 10.1080/09603123.2024.2384963

To link to this article: https://doi.org/10.1080/09603123.2024.2384963

Published online: 07 Aug 2024.

INTERNATIONAL JOURNAL OF ENVIRONMENTAL HEALTH RESEARCH
https://doi.org/10.1080/09603123.2024.2384963

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

OPEN ACCESS Check for updates

Neurodevelopmental outcomes in children living near hazardous waste sites: a systematic review

Edoardo Miotto[a‡], Anna Maria Tartaglione[b‡], Ivano Iavarone[c,d], Laura Ricceri[b], Amerigo Zona[c,d], Alessandra Ceccarini[e], Sabrina Rossi[c] and Lucia Fazzo[c,d]

[a]Department of Medicine, University of Udine, Udine, Italy; [b]Centre for Behavioural Sciences and Mental Health, Istituto Superiore di Sanità, Roma, Italy; [c]Department Environment and Health, Istituto Superiore di Sanità, Roma, Italy; [d]World Health Organization Collaborating Centre for Environmental Health in Contaminated Sites; [e]Scientific Knowledge Unit, Istituto Superiore di Sanità, Roma, Italy

ABSTRACT

Mismanagement of hazardous waste (HW) causes severe threats to ecosystems and human health. We conducted a systematic literature review and evaluated the evidence regarding the association between residential exposure to HW and childhood neurobehavioral effects. We consulted international agencies websites and conducted a search on MEDLINE and EMBASE databases by applying a "Population-Exposure-Comparator-Outcome" question. The evidence evaluation, based on the quality of the studies and their concordance, was graded in sufficient/limited/inadequate. Documents from international agencies were not found. Of the seventy-five studies screened, nine met the eligibility criteria. Studies agree on the association between residential exposure to HW sites and negative neurodevelopmental effects. The evidence of the association was attributed limited to cognitive and behavioral outcomes, and inadequate to Autism Spectrum Disorder. The evidence was evaluated sufficient for HW sites releasing lead and cognitive disorders. Residential exposure to unsafe HW sites may contribute to childhood neurobehavioral alterations. It is urgent to implement environmental remediation of contaminated sites and counteracting illegal and unsafe HW management practices.

ARTICLE HISTORY
Received 23 January 2024
Accepted 22 July 2024

KEYWORDS
Hazardous waste; neurodevelopment; behavior; e-waste; children

Introduction

Hazardous waste (HW) encompasses material that, due to its characteristics, poses significant risks to human health and the environment (https://www.eea.europa.eu/help/glossary/eea-glossary/hazardous-waste.; https://www.epa.gov/hw/learn-basics-hazardous-waste#hwid). Over recent years, electronic waste (e-waste) has emerged as a pressing global issue (Forti et al. 2020).

Unsafe management of HW, including illegal waste dumping, can lead to contamination of soil, water, and air, with profound implications for ecosystems and human well-being.

The Basel Convention, adopted in 1989 by 188 countries and enacted in 1992, aims to regulate the transboundary movements of HW to prevent environmental and health hazards (UNEP 2011).

CONTACT Lucia Fazzo lucia.fazzo@iss.it Department Environment and Health, Istituto Superiore di Sanità, Viale Regina Elena 299, Roma, Italy

‡First authors

This article has been republished with minor changes. These changes do not impact the academic content of the article.
Supplemental data for this article can be accessed online at https://doi.org/10.1080/09603123.2024.2384963.

The World Health Organization (WHO) has prioritized effective HW management as part of its efforts to achieve Sustainable Development Goals by 2030, emphasizing sound practices and contrasting illegal trafficking and mishandling of waste (World Health Organization Declaration of the Sixth Ministerial Conference on Environment and Health 2017).

In Europe, the management of contaminated sites is a significant concern, with waste disposal and treatment accounting for approximately 38% of the estimated 342,000 contaminated sites across 27 European Environment Agency (EEA) member states. As of 2021, only 15% of these sites had been remediated; the large volume of waste production and the widespread use of chemicals over the past decades have caused local soil contamination due to inadequate or unauthorized waste disposal, unsafe handling of dangerous substances within industrial or commercial processes, as accidents (https://www.eea.europa.eu/data-and-maps/indicators/progress-in-management-of-contaminated-sites-3/assessment/view, last accessed: 14 December 2023).

In the United States, the Environmental Protection Agency (EPA) oversees its National Priority List of the contaminated sites (Superfund sites), which currently numbers 1,336 HW sites (https://www.epa.gov/superfund/current-npl-updates-new-proposed-npl-sites-and-new-npl-sites; last accessed: 7 September 2023).

Low- and middle-income countries face particular challenges, exacerbated by illegal transboundary of waste from industrialized nations. This issue has been identified as a major environmental and health risk factor in African regions, where HW has been implicated in widespread contamination (McCormack and Schüz 2012). In seven Asian countries, 679 areas have been identified as contaminated by HW (Caravanos et al. 2013), and in three Latin American countries (Mexico, Uruguay, and Argentina), hundreds of thousands of people have been exposed to hazardous lead contamination from 129 HW sites (Caravanos et al. 2016).

Increased risks of cancer, respiratory and cardiovascular diseases, as well as negative reproductive effects, have been reported in populations living near HW sites. There is limited evidence of the association between the residence close to HW sites and liver, bladder, breast and testis cancers, non-Hodgkin lymphomas, asthma, congenital anomalies overall and anomalies of the neural tube, urogenital connective and musculoskeletal systems, low birth weight and pre-term birth. Moreover, there is sufficient evidence of the association between the exposure to oil industry waste releasing high concentrations of hydrogen sulfide and acute symptoms of respiratory and digestive systems (Fazzo et al. 2017).

The risk of adverse neurodevelopmental outcomes has yet to be thoroughly investigated and WHO explicitly recommended focusing on neurological and behavioral effects of HW sites in children (World Health Organization 2016).

Furthermore, there is growing evidence linking prenatal and childhood exposure to chemical substances, potentially emitted by HW, with neurodevelopmental disorders in children (Environmental Protection Agency 2000; World Health Organization 2017b; Rebelo and Dutra Caldas 2016). Exposure, even at very low levels, to environmental pollutants, such as lead (Pb), methylmercury, and selected pesticides, flame retardants (polybrominated diphenyl ethers: PBDEs) and polychlorinated biphenyls (PCBs), affects the brain and nervous system development, increasing the risk of neurobehavioral alterations in children and higher susceptibility to neurodegenerative diseases later in life (Carroquino et al. 2012; Gomes et al. 2024; Grandjean and Landrigan 2014; World Health Organization 2017a). Pre- and postnatal exposure to air pollutants has also been implicated in neurodevelopmental and behavioral disorders, those related to autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD) (World Health Organization 2018).

Specifically, neurodevelopmental disorders (NDDs) refer to a group of heterogeneous conditions that manifest early in childhood, including ASD, ADHD and intellectual disability (ID). Notably, it has been hypothesized that the significant rise in the prevalence of NDDs over the past few decades could be explained, at least in part, by increased exposure to environmental contaminants (Grandjean and Landrigan 2014). Synergistic actions of environmental exposure with genetic factors and developmental timing have been hypothesized to influence neurodevelopment from the embryonic stage through adulthood (Scattolin et al. 2022).

Our systematic review aims to comprehensively summarize existing studies exploring possible association between residential exposure, including maternal and prenatal exposure, to HW sites (including illegal dumps, and e-waste sites) and neurobehavioral outcomes in children.

Materials and methods

The reporting of this systematic review was guided by the standards of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al. 2021). A five-step process, as described by Woodruff, was followed: 1. Specify the research question, 2. Carry out the literature search, 3. Select studies for inclusion, 4. Assess the quality of individual selected studies, 5. Rate the confidence in the body of evidence for each outcome (Woodruff and Sutton 2014).

Eligibility criteria

The **eligibility** criteria for the inclusion of the studies in the review were formulated in terms of Population-Exposure-Comparator-Outcomes (PECO) question. The population of interest consisted of children, infants, or toddlers residentially exposed to waste sites, including prenatal exposure. Exposure considered HW sites, including industrial and electronic waste landfills and illegal dumps. There were no limitations on the comparators considered. The outcomes of interest were neurodevelopmental and behavioral disorders: ASD, ADHDs, cognitive alterations, and language disorders, and alterations in emotional and conduct domains. The **exclusion** criteria involved discrepancies with the PECO question, i.e. excluding human adult population, and laboratory and animal studies.

Information sources

International agencies' documents and reports and original articles complying with the eligibility criteria were searched.

International agencies' documents

The following websites were browsed (January 2023) to locate documents and/or reports addressing the topic of interest, searching with specific website *ad hoc* filters and keywords matching the PECO search question: United States Environmental Protection Agency – EPA (https://www.epa.gov); International Programme on Chemical Safety – IPCS INCHEM (http://www.inchem.org); Toxicology Excellence for Risk Assessment – TERA (http://tera.org); Agency for Toxic Substances and Disease Registry – ATSDR (http://atsdr.cdc.gov); Office of Environmental Health Hazard Assessment – OEHHA (https://oehha.ca.gov); World Health Organization – WHO (https://www.who.int); National Institute of Environmental Health Sciences – NIEHS (https://seek.niehs.nih.gov/texis/); Centers for Disease Control and Prevention – CDC (https://www.cdc.gov/index.htm); International Agency for Research on Cancer – IARC (https://www.iarc.who.int).

Original papers

To highlight the published articles, MEDLINE and EMBASE databases were searched through the STN International platform (on 14 December 2022). The International Prospective Register of

Systematic Reviews (PROSPERO) was last consulted in April 2023. Reference lists or bibliographies of included studies were not examined.

Finally, the authors checked the list to add relevant articles that did not emerge from the database systematic research.

Search strategy

The search strategy, based on the aforementioned PECO, is reported in Table 1. Boolean operators were used to combine exposure and outcome terms (Table 1).

All original publications and reviews written in English, Italian and French were considered, with no restriction on the publication year.

Selection process

Each study/record was screened independently by two reviewers, and a third investigator was consulted in case of discrepancies. Screening was done in a first step by reading the title and abstract, and in a second step based on the full-text analysis.

Data collection process and data items

Data extraction of the selected articles was performed by the entire reviewer team, and each article was analyzed independently by two reviewers. Study design, characteristics of the population, exposure assessment and its measurement, statistical analyses and funding source were sought.

Quality and risk of bias assessment

The quality assessment of each selected article was performed independently by two reviewers, and in case of disagreement the whole team of reviewers was consulted.

An adapted version of the Newcastle-Ottawa Quality Assessment Scale (NOQAS, https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.) was used as an assessment tool for original studies (Wells et al. 2023). The scale contains a list of items, grouped by domains (selection, comparability, outcome) and a scoring system that allows rating each study from 0 to 9 stars. The reliability of the studies is divided into three classes: "good" (7–9 stars), "satisfactory" (5–6 stars), or "unsatisfactory" (0–4 stars). The modifications of the scale concern some aspects of the ascertainment of the exposure (in the selection domain) and the control of confounding factors (in the comparability domain). For systematic reviews, a Measurement Tool to Assess Systematic Reviews (AMSTAR 2,

Table 1. Search strategy: descriptors and text words searching in MEDLINE and EMBASE.

Phase 1: Descriptors	
# 1 Exposure	(ELECTRONIC WASTE/CT OR HAZARDOUS WASTE+NT/CT OR INDUSTRIAL WASTE/CT OR E-WASTE/CT OR HAZARDOUS WASTE+NT/CT OR INDUSTRIAL WASTE+N/CT) AND (ENVIRONMENTAL EXPOSURE+NT/CT OR ENVIRONMENTAL HEALTH+NT/CT OR ENVIRONMENTAL EXPOSURE+NT/CT OR ENVIRONMENTAL HEALTH/CT)
# 2: Outcomes	(NEURODEVELOPMENTAL DISORDERS+NT/CT) OR (MENTAL DISEASE+NT/CT)
#3	#1 AND #2
PHASE 2: TEXT WORDS	
# 4: Exposure	(INDUSTR? OR ILLEGAL OR HAZARDOUS OR TOXIC OR ELECTRONIC)(W)(WAST? OR LANDFILL OR DUMP?) OR E(W)WASTE(3A)(LANDFILL OR DUMP?)
# 5: Outcomes	(NEURODEVELOP? OR NEURO?(W) DEVELOP? OR NEURO? OR NEURAL OR (NEURODEVELOP? OR NEURO?(W) DEVELOP? OR NEURO? OR NEURAL OR COGNITIVE OR BRAIN OR BEHAVIOUR? OR PSYCHO? OR LANGUAGE OR SOCIAL OR DEVELOPMENT? OR INTELLECTUAL OR AUTISM OR AUTISTIC)(3A)(DISORDER OR SKILL OR DEFICIT OR DELAY OR DISABILITY)
#6	#4 AND #5
PHASE 3: DESCRIPTORS OR TEXT WORDS, AND POPULATION	
#7	#3 OR #6
#8: Population	#7 AND (CHILD OR BABY OR INFANT OR NEWBORN OR TODDLER OR HUMAN)

https://amstar.ca/Amstar-2.php.) was used (Shea et al. 2017). The tool counts 16 items, with a focus on seven critical items. The overall confidence in the results of the review could be rated in four classes: "high" (no or one "non-critical" item not satisfied), "moderate" (more than one non-critical item not satisfied), "low" (one critical item not satisfied), "critically low" (more than one critical item not satisfied).

Quality assessment was not performed for institutional reports and documents, as they were published by experts and multidisciplinary evaluation teams.

Synthesis methods/evaluation of strength of the body of evidence

No meta-analysis was conducted, since the aim of the study is to offer a synthesis of the evidence, and because of the low number of the selected articles, often using different and heterogeneous methods for the outcomes' assessment and different measurements of the risk, to allow a quantitative overall estimate.

The strength of the evidence of association between each neurodevelopmental outcome and HW exposure was evaluated taking into account the reliability of each study, and the concordance between study findings. Among the concurring different risk estimates, those from higher quality studies were given higher weight. The body of the evidence was evaluated separately for the following outcomes: "cognitive outcomes", including alterations in cognitive (e.g. intelligence quotient, IQ) and language disabilities; "behavioral outcomes", including alterations in emotional social, and conduct domains; "ASD".

The evidence was rated in three grades: Sufficient/Limited/Inadequate, partly derived from the approach used by the International Agency for Research on Cancer (IARC) Monograph (https://monographs.iarc.who.int/wp-content/uploads/2019/07/Preamble-2019.pdf.), but specifically defined, as reported in Table 2.

Results

International agencies' documents

The results of the search on websites of the main international agencies are described in Supplementary materials S1.

Eight documents fitting the PECO question were selected. HW was mentioned among the potential sources of exposure to contaminants with effects on childhood neurodevelopment, but reports that estimated the risk in children and adolescents living near illegal and HW sites specifically were not found. There are several indications that make HW a potential risk factor for childhood neurodevelopmental disorders, based on the neurotoxicity and behavioral effects (including ADHD, ASD, learning disabilities) of specific contaminants potentially emitted by unsafe handling of waste (heavy metals and PCBs, in particular); further defined and harmonized *ad hoc* epidemiological studies were recommended (Environmental Protection Agency 2000; Environmental Protection Agency 2003; ATSDR, 1995; Environmental Protection Agency 2013; Environmental Protection Agency 2019; UNICEF and Pure Earth 2020; World Health Organization 2021; World Health Organization WHO Initiative on E-waste and Child Health 2021).

Characteristics of included articles

From MEDLINE and EMBASE searches, 75 records were retrieved, excluding 11 duplicates. Out of them, 46 were considered not relevant for the present review because they did not fit the PECO question, based on title and abstract. The evaluation of the 29 remaining articles, based on the reading of the full text, highlighted seven papers concerning the object of the present investigation.

Table S2 (Supplementary Material) describes the excluded articles and the motivations for their exclusion.

Table 2. Criteria used to rate the evidence of the association between each outcome and the exposure to hazardous waste.

Grading of the evidence	Criteria
SUFFICIENT: the evidence is sufficient to infer the presence of a causal association. The strength of association, considerations on dose-response relationship, time coherence and biological plausibility further support causality. Alternative explanations, in particular the role of random variability, bias, confounding factors, can be reasonably excluded.	• one or more than one international and national Agency documents state as "sufficient" the evidence of the association or provide information at this regard; • quantitative meta-analyses or more than one original study of "satisfactory" quality report positive findings with strong, precise and consistent association.
LIMITED: the evidence is limited, but not sufficient to infer the presence of a causal association.* A role of random variability, bias and confounding factors may not be completely excluded.	• one or more than one international and national Agency documents/reviews of "high" or "moderate" quality report "suggestive" or "limited" evidence; • quantitative meta-analyses/more than one original study of "satisfactory" or "good" quality report positive findings; • one original study of "satisfactory" or "good" and one or more reviews of "low" quality" provide positive results.
INADEQUATE: the evidence is not adequate to infer the presence or the absence of a causal association.*	• more than one international and national Agency document/review investigate the association, but the results are not consistent (conflicting evidence); • one or more than one reviews report positive findings, but the quality of the reviews has been evaluated "low/ critically low"; • only one original study reports positive findings; • more than one original study report positive results, but the quality of the studies has been evaluated "unsatisfactory"; • two original studies of "satisfactory" or "good" quality investigate the association, but the results are not consistent (conflicting evidence).

*Among the concurring different risk estimates, those from higher quality studies were given higher weight.

Two articles (Grant et al. 2013; Liu et al. 2015) known by the authors but not retrieved by the search were added.

Finally, the evaluation of the evidence was based on nine articles.

Figure 1 shows the flow chart of the literature search and screening process, based on PRISMA 2020 flow diagram for new systematic reviews.

The nine selected articles include two reviews, the first on the association of several health outcomes with e-waste sites (Grant et al. 2013), the second on ASD in children living in US Superfund contaminated sites with HW (Rossignol et al. 2014), and seven cross-sectional studies, four carried out in China, one in the USA, one in Chile, and one in several countries with Pb contaminated HW sites. The seven original studies concern children living in areas contaminated by HW (Wright et al. 2006; Chatham-Stephens et al. 2014; Burgos et al. 2017), in some cases with a specific focus on HW, including e-waste (Liu et al. 2015, 2018; Zeng et al. 2021, 2022). Supplementary Table 3 reports the characteristics of the nine articles considered.

Based on NewCastle Ottawa and AMSTAR 2 scales, the quality of the seven original studies was evaluated as satisfactory/good quality, while the quality of the two reviews was rated as low or critically low (see Supplementry Table 3).

Effects on cognitive outcomes

Wright et al. (2006) investigated the association between hair metal levels and neuropsychological outcomes in children aged 11–13 years living in an area with a 100-year history of Pb and zinc mining, where waste was dumped on the ground. They found that hair arsenic (As) and manganese (Mn) levels were negatively associated with scores on the Full-Scale IQ and Verbal IQ as measured by the Wechsler Abbreviated Intelligence Scale (WASI), as well as with verbal learning and memory as measured by the

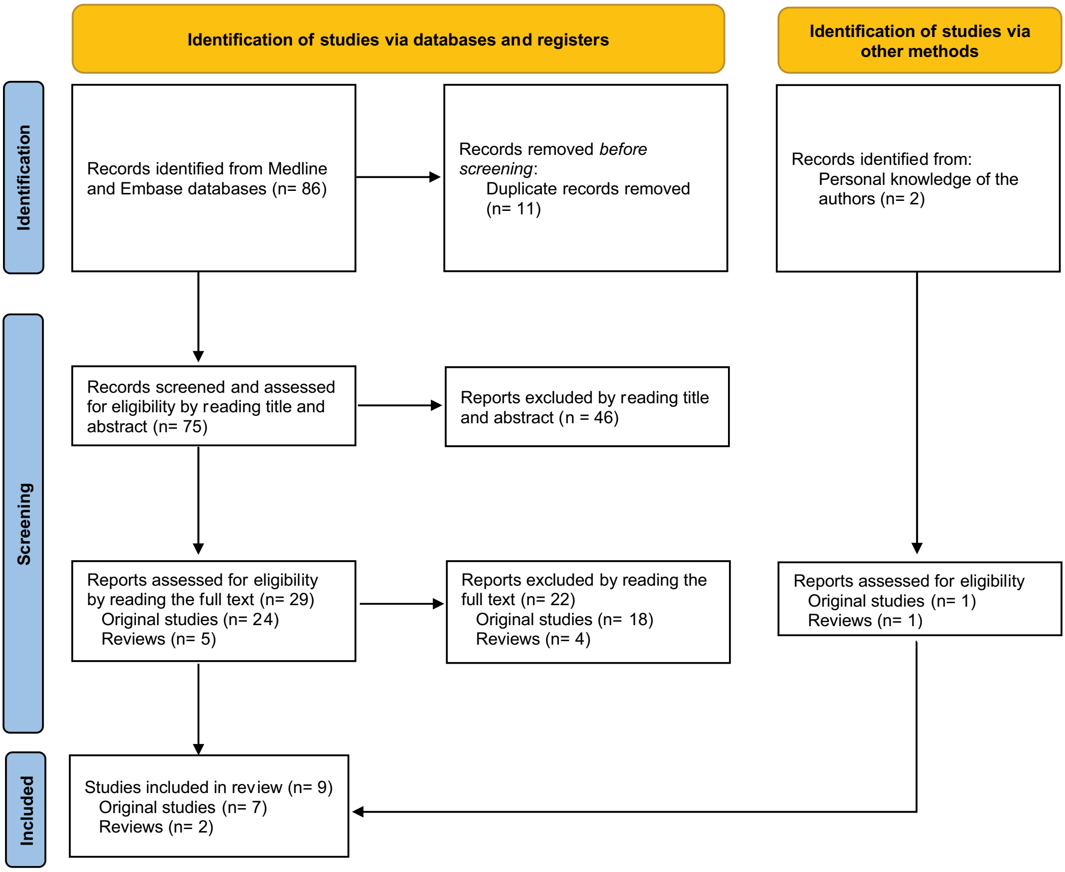

Figure 1. Flow diagram for identification of included studies.

California Verbal Learning Test-Children (CVLT-C) and the story memory subtest of the Wide Range Assessment of Memory and Learning (WRAML), respectively. Moreover, these scores were lower in children with higher exposure to both As and Mn. Hair cadmium (Cd) levels were not associated with scores on any neuropsychological tests. Liu et al. (2015) found that 3-year-old children living in Guiyu, a town with a more than 30-year history of informal e-waste recycling, have significantly lower cognitive and language scores, as assessed by the Bayley Scales of Infant Development, third edition (BSID-III), and higher Pb blood levels compared with the reference group. In a subsequent study (Liu et al. 2018), they also measured Cd blood levels: mediation analysis showed that only Pb negatively correlated with both cognitive and language scores, as already reported in the previous study. Another study investigated cognitive performance as assessed by the Wechsler Intelligence Scale for Children, Third Edition (WISC-III) in children aged 12–16 years living in the neighborhood of Arica (Chile) close to waste sites polluted by heavy metals (Burgos et al. 2017). They found that children born in the study area during the period of the highest exposure (before the remediation of waste sites) had an average total IQ 10 points lower compared to those born afterward (81.9 points vs. 91.1 points). Chatham-Stephens et al. (2014) calculated that nearly 800,000 children under 4 years of age were potentially exposed to Pb from 200 toxic waste sites in 31 low–middle income countries, the majority of whom were predicted to have mean blood Pb levels (BLLs) greater than 5 µg/dL. The authors estimated that these BLLs result in a loss of 5.41 to 8.23 IQ points, an incidence of 6.03 cases of mild mental retardation per 1,000 population, and 76.1 disability adjusted life years (DALYs) per 1,000 inhabitants.

Effects on behavioral outcomes

In the same area considered by Liu et al. (2015, 2018), Zeng et al. (2021) investigated the effects of Pb exposure in children aged 3–7 years on behavioral outcomes, as assessed by the emotional symptoms subscale of the Strengths and Difficulties Questionnaire (SDQ), and on serum levels of dopamine, substance P, and neuropeptide Y (NPY), all neuromodulators involved in the regulation of emotional behavior. They found that children of both sexes from the exposed area, Guiyu, exhibited higher "behavioral symptom scores" (as defined by the authors, the score relative to the emotional symptoms SDQ subscale) than the reference group, with exposed girls being more impaired. Children living in the exposed area also had significantly higher levels of dopamine and substance P, and lower levels of NPY compared to those living in the reference area. They found that the behavioral symptom score was positively correlated with blood Pb and substance P levels, and negatively correlated with NPY. Additionally, the authors investigated the prevalence rate of behavioral symptoms, classifying children as "normal" or "at-risk" based on the scores obtained in the SDQ subscale. They found that the prevalence rate of behavioral difficulties was higher in the exposed group compared to the reference group (48.2% vs. 13.9%).

In a subsequent study, the same authors (Zeng et al. 2022) extended the behavioral assessment to all subscales of the SDQ, finding that SDQ scores for emotional symptoms, conduct problems, hyperactivity-inattention, peer relationship problems, and total difficulties were higher in Guiyu than in the reference area, while prosocial behavior scores were lower in Guiyu than in children from the reference area. Additionally, they also found a significant increase in serum levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α), in children living in Guiyu.

The review published on 2013 considered two studies investigating mental health outcomes and Pb exposure from e-waste: the evidence of an association between e-waste exposure and changes in childhood temperament and behavior was evaluated as suggestive (Grant et al. 2013).

In contrast with what was reported for cognitive outcomes, Wright et al. (2006) did not find significant associations between hair metal levels and behavioral outcomes in children, as assessed by self-report, parent, and teacher questionnaires (see Supplementry Table 3, for major details).

Effects on autism spectrum disorder

Only one systematic review has been found on ASD and HW sites (Rossignol et al. 2014), based on two cross-sectional studies performed in US Superfund sites with HW, evaluated that the studies provided evidence for an association between ASD prevalence and HW sites, although the limits due to the study design did not allow firm conclusions on causation.

Grade of evidence

The grade of the evidence of the association between neurodevelopmental outcomes and residential exposure to HW sites, following the criteria described in Table 2, was attributed as follows: limited for "cognitive outcomes" and for "behavioral outcomes", and inadequate for "ASD". In addition, considering the strength of association, dose–response relationship, time coherence and biologic plausibility, the evidence was defined as sufficient for the association between HW sites releasing Pb and cognitive outcomes.

Supplementry Table 3 reports the characteristics of the considered papers and the attributed grade of the evidence for each outcome. Wright et al. (2006) was reported twice, since it considered both cognitive and behavioral outcomes.

Discussion

The present review highlights the possible association between residential exposure to HW sites (including prenatal and maternal exposure) and cognitive and behavioral disorders in children. The evidence supporting this association is limited: while multiple studies show positive results, the role of random variability, bias and confounding factors cannot be completely excluded.

Specifically concerning HW releasing Pb, the evidence for its association with cognitive outcomes was evaluated as sufficient, based on considerations of dose–response relationship, temporal coherence, and biological plausibility supporting causality. Considering the etiology of the outcomes, the exposure to contaminants through HW could contribute, along with other risk factors, to influencing brain development. As for ASD, current literature did not allow for the inference of the presence or absence of a causal association and the evidence was defined as inadequate.

Our review focused on studies involving populations living near inadequately managed HW sites. These practices occur in various regions, including both high- and middle- to low-income countries, with a notable increase in the latter. This situation poses a global emergency for public health (World Health Organization Declaration of the Seventh Ministerial Conference on Environment and Health 2023). The absence of environmental regulations, such as a proper waste management control, leads to illegal dumping and burning by crime organizations, and fosters illegal and uncontrolled international movements of HW, often from the industrialized to middle- and low-income countries.

The present review employed rigorous and established methodology and *a priori* criteria for reviewing literature and assessing evidence strength. The topic is complex in terms of exposure and outcome characterization and is associated with significant sources of heterogeneity that require specific considerations.

Firstly, HW sites as contamination sources involve a wide range of materials and chemicals of various origins, resulting in exposures to mixtures of contaminants through different routes (inhalation, dermal absorption, dietary ingestion). These factors studies' limit the ability to identify all potentially harmful contaminants, determine correct exposure time windows and the related health effects, and provide a comprehensive understanding of HW related environmental health scenarios. Suitable exposure assessment approaches capable of addressing these sources of heterogeneity might benefit from multimedia exposure assessment procedures developed for risk assessment purpose, which could be ideally integrated into environmental epidemiological studies (Hoech et al. 2018; European Commission 2020; Luijten et al. 2023; Cattaneo et al. 2023).

Another source of heterogeneity among studies lies in health outcome assessment. The outcomes and assessment tools vary across studies, hindering direct comparison and quantitative assessment of the association between HW exposure and neurodevelopmental outcomes.

Furthermore, the etiology of the investigated health outcomes, such as cognitive and behavioral disorders and ASD, is multifactorial and not fully understood in a significant proportion of cases, despite their prevalence (from 5% to 20%) in the general population (Patel and Merrick 2020), with an increased trend in 5–17 years-olds from 1997 to 2019 (Environmental Protection Agency 2019). Exposure to both psychosocial and environmental risk factors often varies by social class and ethnicity, with populations in HW contaminated sites frequently experiencing socio-economic deprivation. Thus, it is essential to consider the broader developmental environment encompassing psychosocial adversity, environmental toxicants and malnutrition (Volk and Sheridan 2020).

Additionally, this review primarily relied on cross-sectional studies. Although many used biological monitoring for exposure assessment and controlled for major risk factors, the role of random variability, bias and confounding factors cannot be entirely excluded. These studies, in fact, are designed to analyze both exposure and health outcomes data from a population at a single point in time. Longitudinal analytical studies, such as residential cohorts following individuals over extended periods, are crucial to providing more robust evidence, particularly for investigating medium- to long-term effects like the neurodevelopmental disorders (NDDs). The complexity and limitations of existing research on the neurodevelopmental effects of HW in children are compounded by low environmental exposure levels and small relative risks. These factors, combined with the relatively small proportion of children exposed in residential settings, limit the power to analyze the associations of interest. Residential cohort studies that include all children residing in a HW contaminated area are recommended to better evaluate potential associations, particularly for medium- to long-term effects. Specifically, ASD requires further investigation using specialized methods for exposure and outcome assessment, given the limited available literature at the time of this review.

Despite the overall scarcity and heterogeneity of available data, the results from selected studies align with the robust epidemiological and preclinical evidence demonstrating detrimental effects of early life exposure to heavy metals commonly found in HW sites, as reported in Agencies' reports (ATSDR, 1995; Environmental Protection Agency 2003, 2013, 2019; UNICEF and Pure Earth 2020; World Health Organization 2021; World Health Organization WHO Initiative on E-waste and Child Health 2021).

The susceptibility of organogenesis and early childhood to chemical exposure, as well as physiological and behavioral factors, is well documented (Environmental Protection Agency 2000; World Health Organization 2017b). The developing brain is particularly vulnerable due to immature condition of both detoxification mechanisms and the blood–brain barrier. Increased risks of behavioral disorders in children have been linked to the transfer of chemical substances (As, Pb, Hg) via placental and breast milk pathways (Rebelo and Dutra Caldas 2016).

Specifically, we evaluated sufficiently the evidence supporting an association between residence near HW sites emitting or releasing lead and cognitive impairments, considering the strength of association, dose–response relationship, temporal coherence and biological plausibility. This conclusion is supported by extensive literature on the neurotoxic effects of lead exposure (Bellinger et al. 2017; Santa Maria et al. 2019; Dinçkol et al. 2022). Mechanisms of lead neurotoxicity include interference with neuronal calcium ion neuronal functions, including membrane excitability, synaptic transmission, signal transduction, neurotransmitter release, neuronal signaling, and NMDA receptor distribution (Tartaglione et al. 2020; Bjørklund et al. 2024). Other mechanisms include increased oxidative stress leading to reactive oxygen species (ROS) production due to glutathione depletion and elevated neuroinflammatory profile, due to an increase of pro-inflammatory cytokines, such as IL-6, IL-1β, and TNF-α reported in the forebrain and hippocampus following Pb exposure (Zeng et al. 2022). Epigenetic alterations, such as global decreases in DNA methyltransferase (DNMT), have also been observed, potentially affecting brain function and aging (Eid and Zawia 2016).

Similar mechanisms of action may apply to e-waste which contains various chemicals and metals (Pb, Cd, Hg, etc.) as recently reported for different e-waste in Africa (Okeke et al. 2024), as well as organic compounds like polycyclic aromatic hydrocarbons (PAHs), flame retardants such as PBDEs, and polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs). Additionally, emerging evidence suggests that environmental pollutants may influence the microbiota-gut-brain axis by altering commensal microbe compositions and their metabolites with known effects on brain function (Teffera et al. 2024). Notably, gut microbiota modulation appears crucial for neurodevelopmental trajectories (Cowan et al. 2020).

E-waste, often disposed alongside chemical HW, poses a growing global health issue (Parvez et al. 2021). Global e-waste generation reached 53.6 million tons in 2019 and could rise to 74.7 million tons by 2030. Most e-waste is illegally disposed or informally recycled, considering that only 17.4% of e-waste generated in 2019 reached formal waste management or recycling systems. Informal e-waste processing is present in Africa, Asia, Latin America, and in certain industrialized economies where impoverished individuals live near informal dumps and landfills (World Health Organization 2021). Annually, 1.3 million tons of discarded electronic products are illicitly exported from the EU to other countries, highlighting the global challenge of illegal e-waste trafficking (World Economic Forum 2019).

Given the significant impact of contaminated sites on both human well-being and environmental sustainability, it is crucial to prioritize their identification and remediation within policy discussion. Soil protection has been integrated into the Sustainable Development Goals (SDGs) endorsed by the 193 members of the United Nations General

Assembly (United Nations General Assembly 2015). Measures to reduce mortality and illnesses from hazardous substances include restoring degraded land and soil, promoting the best practices for chemical and waste management to minimize environmental release and mitigating adverse impacts (Payá Pérez and Rodríguez Eugenio 2018; World Health Organization Declaration of the Seventh Ministerial Conference on Environment and Health 2023).

The findings of this review underscore the necessity for further investigations into neurodevelopmental outcomes among children living in HW contaminated sites. Addressing the limited evidence of the association between cognitive and behavioral outcomes and residential HW exposure requires implementing target public policies to reduce environmental exposures and supporting families, pregnant women and children in these areas. Neurodevelopmental disorders occurring in early childhood appear to be more severe, especially if not identified on time. The adoption of screening tools and intervention actions before health effects get worse (or to prevent their appearance) would therefore allow more effective healthcare, education and social pathways, thereby reducing developmental inequities and social inequalities (Scattolin et al. 2022).

Promoting waste reduction, recycling and reuse in a circular economy framework, represents a priority step toward minimizing environmental exposures to harmful substances. Moreover, efforts to contrast illegal and informal waste management practices, and to curtail illegal HW trafficking must be implemented at both local and international levels. Simultaneously, environmental remediation and redevelopment of contaminated sites, involving local communities and stakeholders in a participatory process, are essential for promoting health and well-being, in socioeconomically disadvantaged areas frequently affected by HW contamination, thereby addressing environmental inequalities.

Conclusions

To the best of our knowledge, our systematic review is the first to examine the association between residential HW exposure and neurobehavioral outcomes, evaluating the overall evidence based on the quality of the studies and its findings' concordance. The evidence regarding the association between the residence in HW contaminated sites and cognitive and behavioral disorders was evaluated limited. Specifically, evidence was evaluated sufficient for HW sites releasing lead and cognitive disorders. The association between residential exposure to HW and ASD was evaluated as inadequate. Despite the paucity of studies included, this systematic review poses urgent issues in terms of both research and public health policies. Besides the need for further investigations, the results highlight that unsafe and uncontrolled HW management practices may contribute to cognitive and behavioral disorders in children residing near HW sites. This conclusion, added with existing knowledge on the health impacts of these sites, emphasizes the necessity for implementing appropriate public health actions. These actions include environmental remediation of contaminated sites, and efforts to counteract illegal and unsafe HW management practices.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by Italian National Institute for Health intramural fundings and by Italian Space Agency (Agenzia Spaziale Italiana ASI) Project "STOPP Strumenti e Tecniche di Osservazione della Terra in Prossimità e Persistenza", F45F21001650005.

ORCID

Edoardo Miotto http://orcid.org/0000-0001-9167-1798
Lucia Fazzo http://orcid.org/0000-0002-6465-1780

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Authors'contributions

LF, II, LR: conceptualization; LF, II, LR, AC: discussed investigation methodology; AC, EM: collected the data; EM, LF, AMT: wrote the original draft; EM, AMT, II, LR, AZ, SR, LF: performed data analysis and contributed to result interpretation. All authors read and approved the final manuscript.

References

ATSDR 1995. Agency for toxic substances and disease registry [Pamela Tucker editor]. Report of the Expert Panel Workshop on the Psychological Responses to Hazardous Substances; [accessed 14 Dec 2023]. https://www.atsdr.cdc.gov/risk/prhs/index.html.

Bellinger DC, Chen A, Lanphear BP. 2017. Establishing and achieving national goals for preventing lead toxicity and exposure in children. JAMA Pediatr. 171(7):616–618. doi: 10.1001/jamapediatrics.2017.0775.

Bjørklund G, Tippairote T, Hangan T, Chirumbolo S, Peana M. 2024. Early-life lead exposure: risks and neurotoxic consequences. Curr Med Chem. 31(13):1620–1633. doi: 10.2174/0929867330666230409135310.

Burgos S, Tenorio M, Zapata P, Cáceres DD, Klarian J, Alvarez N, Oviedo R, Toro-Campos R, Claudio L, Iglesias V. 2017. Cognitive performance among cohorts of children exposed to a waste disposal site containing heavy metals in Chile. Int J Environ Health Res.27(2):117–125.doi: 10.1080/09603123.2017.1292494.

Caravanos J, Carrelli J, Dowling R, Pavilonis B, Ericson B, Fuller R. 2016. Burden of disease resulting from lead exposure at toxic waste sites in Argentina, Mexico and Uruguay. Environ Health. 15(1). doi: 10.1186/s12940-016-0151-y.

Caravanos J, Chatham-Stephens K, Ericson B, Landrigan PJ, Fuller R. 2013. The burden of disease from pediatric lead exposure at hazardous waste sites in 7 Asian countries. Environ Res. 120:119–125. doi: 10.1016/j.envres.2012.06.006.

Carroquino MJ, Posada M, Landrigan PJ. 2012. Environmental toxicology: children at risk. Environ Toxicol. 4:239–291. doi: 10.1007/978-1-4614-5764-0_11.

Cattaneo I, Kalian AD, Di Nicola MR, Dujardin B, Levorato S, Mohimont L, Nathanail AV, Carnessechi E, Astuto MC, Tarazona JV, et al. 2023. Risk assessment of combined exposure to multiple chemicals at the European food safety authority: principles, guidance documents, applications and future challenges. Toxins. 15(1):40. doi: 10.3390/toxins15010040.

Chatham-Stephens K, Caravanos J, Ericson B, Landrigan P, Fuller R. 2014. The pediatric burden of disease from lead exposure at toxic waste sites in low and middle income countries. Environ Res. 132:379–383. doi: 10.1016/j.envres.2014.04.018.

Cowan CS, Dinan TG, Cryan JF. 2020. Annual research review: critical windows–the microbiota–gut–brain axis in neurocognitive development. Child Phychol Psychiatry. 61(3):353–371. doi: 10.1111/jcpp.13156.

Dinçkol Ö, Fuentes B, Tartaglione AM, Pino A, Calamandrei G, Ricceri L. 2022. Low-level lead exposure during development differentially affects neurobehavioral responses in male and female mouse offspring: a longitudinal study. Neurotoxicology. 91:188–199. doi: 10.1016/j.neuro.2022.05.007.

Eid A, Zawia N. 2016. Consequences of lead exposure, and it's emerging role as an epigenetic modifier in the aging brain. Neurotoxicology. 56:254–261. doi: 10.1016/j.neuro.2016.04.006.

Environmental Protection Agency. 2000. America's children and the environment a first view of available measures. accessed 14 Dec 2023. https://www.epa.gov/system/files/documents/2022-10/ace-report.pdf. First Edition, EPA 24O-R-00-0006.

Environmental Protection Agency. 2003. America's children and the environment: measures of contaminants, body burdens, and illnesses. 240–R-03–001 edition, EPA. [accessed 14 Dec 2023]. https://www.epa.gov/system/files/documents/2022-10/ace_2003.pdf. Second.

Environmental Protection Agency. 2013. America's children and the environment. 240–R-13–001 edition, EPA. [accessed 14 Dec 2023]. https://www.epa.gov/system/files/documents/2022-10/ace3_2013.pdf. Third.

Environmental Protection Agency. 2019. America's children and the environment. Publ Number. 100K(19004): [accessed 14 Dec 2023]. https://www.epa.gov/sites/default/files/2019-10/documents/ace2019-v17s.pdf.

European Commission. 2020) 250 final. Progress report on the assessment and management of combined exposure to multiple chemicals (chemical mixture) and associated risks. SWD. [accessed 2 July 2024]. https://op.europa.eu/en/publication-detail/-/publication/2e7f5564-0f02-11eb-bc07-01aa75ed71a1/language-en.

Fazzo L, Minichilli F, Santoro M, Ceccarini A, Della Seta M, Bianchi F, Comba P, Martuzzi M. 2017. Hazardous waste and health impact: a systematic review of the scientific literature. Environ Health. 16(1). doi: 10.1186/s12940-017-0311-8.

Forti V, Baldé CP, Kuehr R, Bel G. 2020. The global E-waste monitor 2020: quantities, flows and the circular economy potential. United nations university (unu)/united nations institute for training and research (UNITAR) – co-hosted SCYCLE programme, international telecommunication union (ITU) & international solid waste association (ISWA. Bonn/Geneva/Rotterdam ISBN Digit. 978–92–808–9114–0. [accessed 14 December 2023]. https://www.itu.int/en/itu-d/environment/documents/toolbox/gem_2020_def.pdf.

Gomes J, Begum M, Kumarathasan P. 2024. Polybrominated diphenyl ether (PBDE) exposure and adverse maternal and infant health outcomes: systematic review. Chemosphere. 347:140367. doi: 10.1016/j.chemosphere.2023.140367.

Grandjean P, Landrigan PJ. 2014. Neurobehavioural effects of developmental toxicity. Lancet Neurol. 13(3):330–338. doi: 10.1016/S1474-4422(13)70278-3.

Grant K, Goldizen FC, Sly PD, Brune MN, Neira M, van den Berg M, Norman RE. 2013. Health consequences of exposure to e-waste: a systematic review. Lancet Glob Health. 1(6):e350–61. doi: 10.1016/S2214-109X(13)70101-3.

Hoech G, Ranzi A, Alimehmeti I, Ardeleanu ER, Arrebola JP, Avila P, Candeias C, Colles A, Crisan GC, Dack S, et al. 2018. A review of exposure assessment methods for epidemiological studies of health effects related to industrially contaminated sites. Epidemiol Prev. 42(5–6) :21–36. doi: 10.19191/EP18.5-6.S1.P021.085.

Liu L, Xijin X, Yekeen TA, Lin K, Li W, Huo X. 2015. Assessment of association between the dopamine D2 receptor (DRD2) polymorphism and neurodevelopment of children exposed to lead. Environ Sci Pollut Res. 22 (3):1786–1793. doi: 10.1007/s11356-014-2565-9.

Liu L, Zhang B, Lin K, Zhang Y, Xu X, Huo X. 2018. Thyroid disruption and reduced mental development in children from an informal e-waste recycling area: a mediation analysis. Chemosphere. 193:498–505. doi: 10.1016/j.chemosphere.2017.11.059.

Luijten M, Vlaanderen J, Kortenkamp A, Antignac JP, Barouki R, Bil W, van den Brand A, den Braver Sewradi S, van Klaveren J, Mengelers M, et al. 2023. Mixture risk assessment and human biomonitoring: lessons learnt from HBM4EU. Int J Hyg Environ Health. 249:114135. doi: 10.1016/j.ijheh.2023.114135.

McCormack VA, Schüz J. 2012. Africa's growing cancer burden: environmental and occupational contributions. Cancer Epidemiol. 36(1):1–7. doi: 10.1016/j.canep.2011.09.005.

Okeke ES, Enochoghene A, Ezeudoka BC, Kaka SD, Chen Y, Mao G, ThankGod Eze C, Feng W, Xiangyang W. 2024. A review of heavy metal risks around e-waste sites and comparable municipal dumpsites in major African cities: recommendations and future perspectives. Toxicology. 501:153711.doi: 10.1016/j.tox.2023.153711

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 372:n71. doi: 10.1136/bmj.n71.

Parvez SM, Jahan F, Brune MN, Gorman JF, Rahman MJ, Carpenter D, Islam Z, Rahman M, Airch N, Knibbs L, et al. 2021. Health consequences of exposure to e-waste: an updated systematic review. Lancet Planet Health. 5(12): e905–e920. doi: 10.1016/S2542-5196(21)00263-1.

Patel DR, Merrick J. 2020. Neurodevelopmental and neurobehavioral disorders. Transl Pediatrics. 9(S1):S1–S2. doi: 10.21037/tp.2020.02.03.

Payá Pérez A, Rodríguez Eugenio N. 2018. & European commission joint research centre. Status of local soil contamination in Europe: revision of the indicator "progress in the management contaminated sites in Europe". [accessed 14 Dec 2023]. https://data.europa.eu/doi/10.2760/093804.

Rebelo FM, Dutra Caldas E. 2016. Arsenic, lead, mercury and cadmium: toxicity, levels in breast milk and the risk for breastfed infants. Environ Res. 151:671–688. doi: 10.1016/j.envres.2016.08.027.

Rossignol DA, Genuis SJ, Frye RE. 2014. Environmental toxicants and autism spectrum disorders: a systematic review. Transl Psychiatry. 4(2):e360. doi: 10.1038/tp.2014.4.

Santa Maria MP, Hill BD, Kline J. 2019. Lead (pb) neurotoxicology and cognition. Appl Neuropsychol Child. 8 (3):272–293. doi: 10.1080/21622965.2018.1428803.

Scattolin MAA, Resegue RM, Rosário MCD. 2022. The impact of the environment on neurodevelopmental disorders in early childhood. J Pediatr (Rio J). 98(1):S66–S72. doi: 10.1016/j.jped.2021.11.002.

Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 358:j4008. doi: 10.1136/bmj.j4008.

Tartaglione AM, Serafini MM, Raggi A, Iacoponi F, Zianni E, Scalfari A, Minghetti L, Ricceri L, Cubadda F, Calamandrei G, et al. 2020. Sex-dependent effects of developmental lead exposure in Wistar rats: evidence from behavioral and molecular correlates. Int J Mol Sci. 21(8):2664. doi: 10.3390/ijms21082664.

Teffera M, Veith AC, Ronnekleiv-Kelly S, Bradfield CA, Nikodemova M, Tussing-Humphreys L, Malecki K. 2024. Diverse mechanisms by which chemical pollutant exposure alters gut microbiota metabolism and inflammation. Environ Int. 190:108805. doi: 10.1016/j.envint.2024.108805.

UNEP. 2011. The Basel convention on the control of transboundary movements of hazardous wastes and their disposal. [accessed 14 Dec 2023]. https://www.unep.org/resources/report/basel-convention-control-transboundary-movements-hazardous-wastes.

UNICEF and Pure Earth. 2020. The toxic truth: children's exposure to lead pollution undermines a generation of future potential. [accessed 14 Dec 2023]. https://www.unicef.org/reports/toxic-truth-childrens-exposure-tolead-pollution-2020.

United Nations General Assembly. 2015. Resolution adopted by the general assembly- A/70/1: transforming our world: the 2030 agenda for sustainable development. [accessed 14 Dec 2023]. https://daccess-ods.un.org/access.nsf/Get?OpenAgent&DS=A/RES/70/1&Lang=E.

Volk H, Sheridan MA. 2020. Investigating the impact of the environment on neurodevelopmental disorder. J Neurodevelop Disord. 12(1):43. doi: 10.1186/s11689-020-09345-y.

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa scale [NOS] for assessing the quality of observational studies in meta- analyses. 2021 Ottawa hospital research institute. [accessed 14 Dec 2023]. https://www.ohri.ca/programs/clinical_epidemiology/oxford.Asp.

Woodruff TJ, Sutton P. 2014. The navigation systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Persp. 122(10):1007–1014. doi: 10.1289/ehp.1307175.

World Economic Forum & Platform for Accelerating the Circular Economy. 2019. A new circular vision for electronics: time time for a global reboot. [accessed 14 Dec 2023]. https://wedocs.unep.org/20.500.11822/32762.

World Health Organization. 2017a. Don't pollute my future! The impact of the environment on children's health. Geneva. [accessed 14 Dec 2023]. https://www.who.int/publications/i/item/WHO-FWC-IHE-17.01.

World Health Organization. 2017b. Inheriting a sustainable world? Atlas on children's health and the environment. Geneva. [accessed 14 Dec 2023]. https://www.who.int/europe/publications/i/item/WHO-EURO-2017-3898-43657-61366.

World Health Organization. 2018. Air pollution and child health: prescribing clean air. Summary. Geneva. [accessed 14 Dec 2023]. https://www.who.int/publications/i/item/WHO-CED-PHE-18-01.

World Health Organization. 2021. Children and digital dumpsites: e-waste exposure and child health. [accessed 14 Dec 2023]. https://www.who.int/publications/i/item/9789240023901.

World Health Organization. Declaration of the Seventh Ministerial Conference on Environment and Health. 2023. [accessed 14 Dec 2023]. https://www.who.int/europe/publications/i/item/EURO-Budapest2023-6.

World Health Organization. Declaration of the Sixth Ministerial Conference on Environment and Health. 2017. [accessed 14 Dec 2023]. https://www.who.int/europe/publications/i/item/WHO-EURO-2017-3895-43654-61359.

World Health Organization. Regional Office for Europe. Waste and human health: evidence and needs. WHO meeting report 5-6 November 2015: bonn, Germany. WHO regional office for Europe. 2016. [accessed 14 Dec 2023]. https://iris.who.int/handle/10665/354227.

World Health Organization. WHO Initiative on E-waste and Child Health. 2021. [accessed 14 Dec 2023]. https://www.who.int/publications/i/item/WHO-HEP-ECH-CHE-21-01.

Wright RO, Amarasiriwardena C, Woolf AD, Jim R, Bellinger DC. 2006. Neuropsychological correlates of hair arsenic, manganese, and cadmium levels in school-age children residing near a hazardous waste site. Neurotoxicology. 27(2):210–216. doi: 10.1016/j.neuro.2005.10.001.

Zeng X, Xu C, Xu X, Huang Y, Wang Q, Huo X. 2022. Combined toxicity of air pollutants related to e-waste on inflammatory cytokines linked with neurotransmitters and pediatric behavioral problems. Ecotoxicol Environ Saf. 239:113657. doi: 10.1016/j.ecoenv.2022.113657.

Zeng X, Xu C, Xu X, Zhang Y, Huang Y, Huo X. 2021. Elevated lead levels in relation to low serum neuropeptide Y and adverse behavioral effects in preschool children with e-waste exposure. Chemosphere. 269:129380. doi: 10.1016/j.chemosphere.2020.129380.