

Health consequences of exposure to e-waste: a systematic review



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Summary

Background The population exposed to potentially hazardous substances through inappropriate and unsafe management practices related to disposal and recycling of end-of-life electrical and electronic equipment, collectively known as e-waste, is increasing. We aimed to summarise the evidence for the association between such exposures and adverse health outcomes.

Methods We systematically searched five electronic databases (PubMed, Embase, Web of Science, PsycNET, and CINAHL) for studies assessing the association between exposure to e-waste and outcomes related to mental health and neurodevelopment, physical health, education, and violence and criminal behaviour, from Jan 1, 1965, to Dec 17, 2012, and yielded 2274 records. Of the 165 full-text articles assessed for eligibility, we excluded a further 142, resulting in the inclusion of 23 published epidemiological studies that met the predetermined criteria. All studies were from southeast China. We assessed evidence of a causal association between exposure to e-waste and health outcomes within the Bradford Hill framework.

Findings We recorded plausible outcomes associated with exposure to e-waste including change in thyroid function, changes in cellular expression and function, adverse neonatal outcomes, changes in temperament and behaviour, and decreased lung function. Boys aged 8–9 years living in an e-waste recycling town had a lower forced vital capacity than did those living in a control town. Significant negative correlations between blood chromium concentrations and forced vital capacity in children aged 11 and 13 years were also reported. Findings from most studies showed increases in spontaneous abortions, stillbirths, and premature births, and reduced birthweights and birth lengths associated with exposure to e-waste. People living in e-waste recycling towns or working in e-waste recycling had evidence of greater DNA damage than did those living in control towns. Studies of the effects of exposure to e-waste on thyroid function were not consistent. One study related exposure to e-waste and waste electrical and electronic equipment to educational outcomes.

Interpretation Although data suggest that exposure to e-waste is harmful to health, more well designed epidemiological investigations in vulnerable populations, especially pregnant women and children, are needed to confirm these associations.

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Introduction

Electronic and electrical waste (e-waste), also referred to as waste electrical and electronic equipment, is defined as any end-of-life "equipment which is dependent on electrical currents or electromagnetic fields in order to work properly".¹ Included in this definition are small and large household appliances; information technology and telecommunications equipment; lighting equipment; electrical and electronic tools, toys, and leisure and sports equipment; medical devices; monitoring and control instruments; and automatic dispensers.² Components of electrical and electronic equipment such as batteries, circuit boards, plastic casings, cathode-ray tubes, activated glass, and lead capacitors are also classified as e-waste.³ Although e-waste is informally processed in many regions, high-volume informal recycling has been reported in China, Ghana, Nigeria, India, Thailand, the Philippines, and Vietnam.

Pollutants are released as a mixture, and the effects of exposure to a specific compound or element cannot be considered in isolation. However, a more complex understanding of the interactions between the chemical components of e-waste is needed. Exposure to e-waste is a complex process in which many routes and sources of exposure, different lengths of exposure time, and possible inhibitory, synergistic, or additive effects of many chemical exposures are all important variables. Exposure to e-waste is a unique variable in itself and the exposures implicated should be considered as a whole. Sources of exposure to e-waste can be classified into three sectors: informal recycling, formal recycling, and exposure to hazardous e-waste compounds remaining in the environment (ie, environmental exposure). Informal electronic waste recycling includes the dismantling of end-of-life electronics to retrieve valuable elements with primitive techniques, without or with very little technology to minimise exposure or protective



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equipment, allowing the emission of dangerous chemicals.^{4,5} Formal electronic waste recycling facilities use specifically designed equipment to safely remove salvageable materials from obsolete electronics while protecting workers from adverse health effects. However, these centres are very expensive to build and run and are rare in less developed countries. Varying national safety standards can mean that workers at formal or semiformal recycling centres still risk exposure at low doses.⁶ Because of the high levels of environmental, food, and water contamination, residents living within a specific distance of e-waste recycling areas are also at risk of environmental exposure, although at lower levels than through occupational exposure.^{5,7,8}

Exposure routes can vary dependent on the substance and recycling process (table 1). Generally, exposure to the hazardous components of e-waste is most likely to arise through inhalation, ingestion, and dermal contact. In addition to direct occupational (formal or informal) exposure, people can come into contact with e-waste materials, and associated pollutants, through contact with contaminated soil, dust, air, water, and through food sources, including meat.^{9–21} Children, fetuses, pregnant women, elderly people, people with disabilities, workers in the informal e-waste recycling sector, and other vulnerable populations face additional exposure risks. Children are a particularly sensitive group because of additional routes of exposure (eg, breastfeeding and placental exposures), high-risk behaviours (eg, hand-to-mouth activities in early years and high risk-taking behaviours in adolescence), and their changing physiology (eg, high intakes of air, water, and food, and low rates of toxin elimination).²² The children of e-waste recycling workers also face take-home contamination from their parents' clothes and skin and direct high-level exposure if recycling is taking place in their homes.

Specific chemical elements and compounds are associated with e-waste, either as components of the equipment or released during the recycling process (table 1).²³ Persistent organic pollutants are a group of lipophilic, bioaccumulative substances that are very resistant to breakdown because of long half-lives. Common persistent organic pollutants found in electrical and electronic equipment components include: brominated flame retardants (polybrominated diphenyl ethers), polybrominated diphenyls, dibrominated diphenyl ethers, polychlorinated biphenyls, polychlorinated or polybrominated dioxins and dibenzofurans dioxins, hexabromocyclododecanes, and perfluoroalkyls. Persistent organic pollutants released during dismantling, typically from incineration and smelting, include polychlorinated dibenzodioxins, polychlorinated dibenzofurans, and dioxin-like polychlorinated biphenyls. Polycyclic aromatic hydrocarbons are naturally occurring, hydrophobic substances that are formed during

incomplete combustion of coal, gas, oil, meat, tobacco, incense, and wood.^{10,24} These hydrocarbons are formed and released into the environment during the burning of e-waste materials.²⁵ Potentially hazardous chemical elements are also components of electrical and electronic equipment; the most common are lead, cadmium, chromium, mercury, copper, manganese, nickel, arsenic, zinc, iron, and aluminium.²⁶

Regional intergovernmental organisations, international organisations, national governments, and non-governmental organisations have actively worked to address the practical application of e-waste regulations and initiatives to prevent negative effects on health from the informal recycling of e-waste. However, the focus of e-waste policies and initiatives is only now beginning to shift from a mainly environmental emphasis to one that includes health. New challenges are emerging, and international conventions such as those in Basel,³ Rotterdam,²⁷ and Stockholm²⁸ will struggle to effectively address growing domestic e-waste streams in developing countries. Evidence of the human health effects of e-waste exposure will be key to the development of effective protective policies. We aimed to summarise the evidence relating to the possible association between exposure to e-waste and health, and outcomes related to education and violence.

Methods

Search strategy and selection criteria

We undertook a systematic review that followed the 2009 PRISMA guidelines.²⁹ We developed a review protocol with methods and inclusion criteria we specified in advance (appendix). We incorporated epidemiological studies meeting the following inclusion criteria: the aim of the study was to explore an association between exposure to e-waste and waste electrical and electronic equipment and outcomes related to mental health and neurodevelopment, physical health (including mechanistic events such as DNA damage and effects on gene expression), education, violence, and criminal behaviour; the study was published in a peer-reviewed journal, and reported original research; and the study examined outcomes in human beings. We excluded studies reporting results in plants, animals, and in-vivo or in-vitro populations; reviews, letters to the editor, and abstracts; and those that did not report an outcome related to exposure to e-waste.

We searched five electronic databases (PubMed, Embase, Web of Science, PsycNET, and CINAHL) from , Jan 1, 1965, to Dec 17, 2012, with the search terms: (e-waste OR electronic waste OR WEEE) AND (health OR development OR mental OR education OR behaviour OR learning OR psychological OR psychiatric* OR environment* OR exposure* OR food OR fish OR human breast milk; appendix). We used broad search terms to ensure that publications were not overlooked, and many were then excluded. Our search was not

See Online for appendix

restricted to the English language, nor by any other means. Relevant articles published in languages other than English were translated. We also assessed reference lists of included studies for other relevant studies.

Data collection

After preliminary screening, studies deemed relevant were retrieved for assessment. Eligibility was assessed independently by two reviewers (KG and FCG), and disagreements were resolved by consensus for all included reports. A data extraction sheet was pilot tested and revised to include: publication details, study characteristics (period, design, location, and sample size), exposure and outcome measures, exposure variables (exposure sector, and chemicals included and analysed), and study outcome (appendix). All possible

reported measures of effect size were included. We assessed risk of bias by focusing on a set of methodological issues including whether or not the sample was representative of the population; study design (prospective, retrospective, or ecological); ascertainment of exposure to e-waste (whether objective markers of exposure were used and individual biological samples were taken or whether samples were pooled or residence in an e-waste recycling area was used as a proxy for exposure); assessment of health outcome (clinical diagnosis or physical measurements and tests vs self-reported) and whether masking of outcome assessment was done; selection of the non-exposed controls and appropriate methods to control confounding that might affect the results of this systematic review.

	Component of electrical and electronic equipment	Ecological source of exposure	Route of exposure
Persistent organic pollutants			
Brominated flame retardants Polybrominated diphenyl ethers Polychlorinated biphenyls	Fire retardants for electronic equipment Dielectric fluids, lubricants and coolants in generators, capacitors and transformers, fluorescent lighting, ceiling fans, dishwashers, and electric motors	Air, dust, food, water, and soil Air, dust, soil, and food (bio-accumulative in fish and seafood)	Ingestion, inhalation, and transplacental Ingestion, inhalation or dermal contact, and transplacental
Dioxins			
Polychlorinated dibenzodioxins and dibenzofurans Dioxin-like polychlorinated biphenyls Perfluoroalkyls	Released as combustion byproduct Released as a combustion byproduct but also found in dielectric fluids, lubricants and coolants in generators, capacitors and transformers, fluorescent lighting, ceiling fans, dishwashers, and electric motors Fluoropolymers in electronics	Air, dust, soil, food, water, and vapour Released as combustion byproduct, air, dust, soil, and food (bioaccumulative in fish and seafood) Water, food, soil, dust, and air	Ingestion, inhalation, dermal contact, and transplacental Ingestion, inhalation, and dermal absorption Ingestion, dermal contact, inhalation, and transplacental
Polyaromatic hydrocarbons			
Acenaphthene, acenaphthylene, anthracene, benzo[a]anthracene, benzo[a]pyrene, benzo[e]pyrene, benzo[b]fluoranthene, benzo[g,h,i]perylene, benzo[j]fluoranthene, benzo[k]fluoranthene, chrysene, dibenz[a,h]anthracene, fluoranthene, fluorene, indeno[1,2,3-c,d]pyrene, phenanthrene, and pyrene	Released as combustion byproduct	Released as combustion byproduct, air, dust, soil, and food	Ingestion, inhalation, and dermal contact
Elements			
Lead Chromium or hexavalent chromium Cadmium Mercury Zinc Nickel Lithium Barium Beryllium	Printed circuit boards, cathode ray tubes, light bulbs, televisions (1.5–2.0 kg per monitor), and batteries Anticorrosion coatings, data tapes, and floppy disks Switches, springs, connectors, printed circuit boards, batteries, infrared detectors, semi-conductor chips, ink or toner photocopying machines, cathode ray tubes, and mobile phones Thermostats, sensors, monitors, cells, printed circuit boards, and cold cathode fluorescent lamps (1–2 g per device) Cathode ray tubes, and metal coatings Batteries Batteries Cathode ray tubes, and fluorescent lamps Power supply boxes, computers, x-ray machines, ceramic components of electronics	Air, dust, water, and soil Air, dust, water, and soil Air, dust, soil, water, and food (especially rice and vegetables) Air, vapour, water, soil, and food (bioaccumulative in fish) Air, water, and soil Air, soil, water, and food (plants) Air, soil, water, and food (plants) Air, water, soil, and food Air, food, and water	Inhalation, ingestion, and dermal contact Inhalation and ingestion Ingestion and inhalation Inhalation, ingestion, and dermal contact Ingestion and inhalation Inhalation, ingestion, dermal contact, and transplacental Inhalation, ingestion, and dermal contact Ingestion, inhalation and dermal contact Inhalation, ingestion, and transplacental

Table 1: Chemical classification of e-waste components and sources and routes of exposure

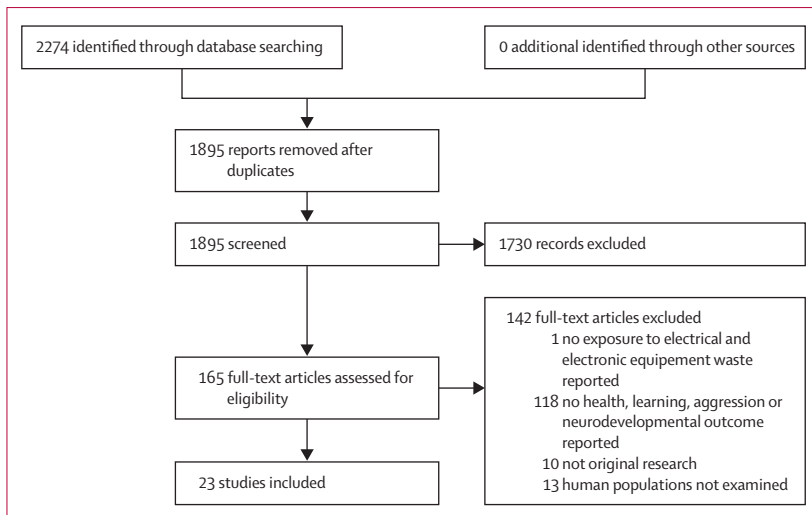


Figure: Study selection for inclusion in systematic review

Results

Of the 165 studies that we screened and assessed for eligibility, 23^{30–51} reported associations between exposure to e-waste or waste electrical and electronic equipment and physical health, mental health, neurodevelopment, and learning outcomes (figure). All included studies were from southeast China, and almost all included the major e-waste recycling towns of Guiyu (n=14), Taizhou (n=1), and Luqiao (n=1). We excluded most studies because they did not assess the health, educational, and behavioural consequences of exposure to e-waste (n=118; figure).

Findings of 16 of the 23 studies^{30–45} showed associations between exposure to e-waste and physical health outcomes, including thyroid function, reproductive health, lung function, growth, and changes to cell functioning. Although all studies investigated the association between exposure to e-waste and outcomes, the chemical components of e-waste analysed differed between studies, and included polybrominated diphenyl ethers, polychlorinated dibenzodioxins and polychlorinated dibenzofurans, polycyclic aromatic hydrocarbons, polychlorinated biphenyls (including dioxin-like polychlorinated biphenyls), perfluoroalkyls, and chemical elements (chromium, lead, manganese, and nickel). Outcomes were reported from Guiyu and Taizhou in southeast China, and included environmental, informal, and formal exposure routes.

Five studies^{30–34} have examined the effects of exposure to e-waste on thyroid function (table 2). These studies included mainly ecological assessments that compared health outcomes of populations in towns involved in e-waste recycling with those in non-exposed (control) towns. The reported effects on thyroid-stimulating hormone (TSH) are not consistent, with two studies reporting increased TSH concentrations in the exposed populations^{30,31} and three reporting decreased concen-

trations associated with e-waste exposure (table 2).^{32–34} Similarly, concentrations of tetraiodothyronine (T4) in the exposed population have either been lower^{30,32} or no different³³ from those in the control population. Although Yuan and colleagues³¹ showed that working with e-waste was an independent predictor of serum TSH concentrations,³¹ the investigators acknowledged limitations in the interpretation of results because of a failure to account for other effects on TSH concentrations, including T4 concentrations not measured.

Zheng and colleagues³⁵ investigated associations between exposure to metals (eg, chromium, manganese, and nickel) and lung function in 144 schoolchildren (aged 8–13 years) from Guiyu, an e-waste dismantling site, and from Liangying, a control town with no evidence of e-waste recycling.³⁵ Boys aged 8–9 years living in Guiyu had a lower forced vital capacity than those living in Liangying (1859 mL vs 2121 mL, p=0.03).³⁵ Findings from height-adjusted multivariate regression analysis showed significant negative correlations between blood chromium concentrations and forced vital capacity in children aged 11 and 13 years ($\beta=-14.02$, p=0.018, and $\beta=-43.23$, p=0.027, respectively), and serum nickel concentrations in children aged 10 years ($\beta=-18.47$, p=0.035).³⁵

Pregnancy outcomes in populations exposed to e-waste have been investigated in seven studies (table 2).^{41–47} Despite different exposure settings and toxicants assessed, there have been consistent effects of exposure with increases in spontaneous abortions,⁴⁰ stillbirths,^{37,42} and premature births,^{37,40,42} and reduced birthweights^{37,40,42} and birth lengths^{39,40} in most studies. Adverse birth outcomes have been associated with increased exposures to polycyclic aromatic hydrocarbons³⁷ and persistent organic pollutants, including polybrominated diphenyl ethers,³⁶ polychlorinated biphenyls,³⁷ and perfluoroalkyls.⁴⁰ The main exception to these effects is the lack of association between exposures to metals and adverse birth outcomes.³⁶

Findings from the two ecological studies^{35,43} showed that physical growth indicators, such as weight, height, and body-mass index, were significantly lower in children living in the e-waste recycling town of Guiyu than in those living in the control area Liangying (table 2).³⁵ Height and weight were also negatively correlated with concentrations of blood manganese and serum nickel in one of these ecological studies. However, findings from the other did not show adverse effects of lead on growth in young children.⁴³

In two studies,^{44,45} lead was investigated as the main chemical agent associated with mental health outcomes related to e-waste exposure (table 2). In one study,⁴⁴ investigators assessed temperament in children, and measured neonatal behavioural neurological assessment scores in another.⁴⁵ Children in Guiyu had higher concentrations of lead in their blood than did those living in towns with no e-waste recycling, which was

	Exposure setting	Exposed population	Primary toxicant	Health effect
Thyroid function				
Ju et al ³⁰	Ecological: exposed town vs control town	Mothers and newborn babies (n=93)	Not assessed	Maternal: TSH higher (2.63 vs 2.10 mIU/L) and free T4 lower (16.47 vs 160.76 pmol/L) in exposed group. Cord blood: TSH (6.35 vs 5.47 mIU/L), free T4 (8.45 vs 9.52 pmol/L)
Yuan et al ³¹	Formal recycling	Formal and informal workers vs not exposed (n=49)	PDBE	Serum PDBE: 382 vs 158 ng/g lipid weight, p=0.045. Serum TSH: 1.7×10^{-6} vs 1.1×10^{-6} mIU/L, p<0.01
Zhang et al ³²	Ecological: exposed town vs control town	Pregnant women (n=50)	PCCDs and PCCFs, PCBs and PDBEs	Higher body burdens of PCCD and PCCFs, PCBs, and PDBEs. Serum TSH: 1.15 vs 2.65 nmol/L, p=0.015. Free T4: 112.5 vs 139.0 nmol/L, p=0.015
Wang et al ³³	Ecological: workers in exposed town vs those in control town	Population (n=442)	PBDEs	Lower TSH (1.26 vs 1.57 μ U/mL), T3 (1632.4 vs 1817.2 pmol/L), and free T3 (4188.8 vs 4404.4 pmol/L), all p<0.001. No difference in T4.
Han et al ³⁴	Ecological: exposed town vs control town	Population (n=369)	Not assessed	Serum TSH: 1.8×10^{-6} vs 3.3×10^{-6} mIU/L. No p value reported
Lung function				
Zheng et al ³⁵	Ecological: exposed town vs control town	School children (aged 8–13 years; n=144)	Chromium, manganese, and nickel	Blood manganese: 374.92 nmol/L vs 271.18 nmol/L, p<0.01. Nickel: 5.3 vs 3.0 mg/L, p<0.01. FVC in boys aged 8–9 years: 1859 vs 2121 mL, p=0.03. Decrease in FVC with increased chromium (11-year-old β = -14.02, p=0.018, 13-year-old β = -43.23, p=0.027), decreased FVC with increased nickel (10-year-olds β = -18.47, p=0.035)
Reproductive health				
Guo et al ³⁶	Ecological: exposed town vs control town	Mother–infant pairs (n=220)	Lead, chromium, cadmium, and nickel	No differences in birthweight, birth length, or gestational age. Negative correlation between placental nickel and gestational age (r_s = -0.16, p=0.017)
Guo et al ³⁷	Ecological: exposed town vs control town	Mother–infant pairs (n=183)	PAHs	Cord blood total PAH: 108.5 vs 79.63 ppb, p=0.003, chromium: 1.57 vs 1.05 ppb, p=0.049, BaP: 2.14 vs 1.64 ppb, p=0.001. DahA 12.26 vs 11.59 ppb, p=0.031. Increased BaA, chrysene, and BaP in neonates with adverse birth outcomes (prematurity, low birthweight, still birth, and malformations) (p<0.05). BaA negatively associated with neonatal height (r = -0.23, p=0.006); chrysene and BaP negatively associated with gestational age (r = -0.20, p=0.013; r = -0.17, p=0.042, respectively).
Wu et al ³⁸	Ecological: exposed town vs control town	Mother–infant pairs (n=153)	PBDEs	Higher total PBDEs in those with adverse birth outcomes (41.97 vs 9.88 ng/g, p=0.004). No effect on neonatal length, GA, or infant sex
Wu et al ³⁹	Informal recycling	Mother–infant pairs (n=167)	PCBs	Cord blood PCBs: 338.6 vs 140.2 ng/g, correlated with mothers' recycling activity. Higher total PCBs with adverse birth outcomes (t = -2.26, p=0.03). Negative associations between individual PCB congeners and neonatal height, neonatal weight, Apgar score, gestational age, and BMI (all p<0.05)
Wu et al ⁴⁰	Informal recycling	Pregnant women (n=167)	PFOA	Serum PFOA: 17.0 vs 8.7 ng/mL (p<0.001) correlated with recycling activity. Negative association between PFOA and spontaneous abortion (t = -3.035, p=0.003), preterm birth (t = -2.209, p=0.029), 1 log increase in PFOA associated with 15.99 (95% CI 2.72–4.25) reduction in GA, 267.3 g (37.2–573.3) reduction in birthweight, 1.91 cm (0.52–3.31) reduction in birth length and 1.37 (0.32–2.42) reduction in Apgar score
Li et al ⁴¹	Ecological: exposed town vs control town	Newborn infants (302)	Chromium	Cord blood chromium, 2006: 306.2 vs 1.95 mg/L; 2007: 99.9 vs 32.48. No association with birthweight or birthlength
Xu et al ⁴²	Informal recycling	Newborn infants (n=531)	Lead	Cord blood lead: 10.87 vs 2.25 mg/dL (p<0.01), correlated with recycling activity. Higher rates of adverse birth outcomes: stillbirth (4.72% vs 1.03%, p<0.05), preterm birth (5.68% vs 5.24%, p<0.05), lower birthweight (3168 vs 3258 g, p<0.05), and lower Apgar scores (9.6 vs 9.9, p<0.05)
Growth				
Zheng et al ³⁵	Ecological: exposed town vs control town	School children (aged 8–13 years; n=144)	Manganese and nickel	Height: 126.8 vs 135.0 cm, p<0.001. Weight: 24.7 vs 30.2 kg, p<0.01. BMI: 15.2 vs 16.5, p<0.01. Negative correlations between serum manganese and height (r_s = -0.303, p<0.001) and weight (r_s = -0.228, p=0.006) and serum nickel and height (r_s = -0.417, p<0.001), weight (r_s = -0.399, p<0.001), and BMI (r_s = -0.213, p=0.011)
Huo et al ⁴³	Ecological: exposed town vs control town	Children (younger than 6 years; n=226)	Lead	Blood lead: 15.3 vs 9.94 mg/dL (p<0.01). No differences in height, weight, chest circumference, or head circumference
Mental health outcomes				
Liu et al ⁴⁴	Ecological: exposed town vs control town	Children (aged 3–7 years; n=303)	Lead	Blood lead: 0.64 vs 0.40 μ mol/L (13.2 vs 8.3 mg/dL), p<0.01. Temperament scores: activity level (mean \pm SD 4.53 \pm 0.83 vs 4.18 \pm 0.81, t = 3.377), adaptability (4.96 \pm 0.73 vs 4.67 \pm 0.83, t = 2.96) and approach withdrawal (4.62 \pm 0.85 vs 4.3 \pm 0.89, t = 2.877)
Li et al ⁴⁵	Ecological: exposed town vs control town	Newborn babies (n=152)	Lead	Cord blood lead: 11.3 vs 6.0 mg/dL, p<0.001; meconium lead: 2.5 vs 1.2 mg/g, p<0.001. NBNA scores: total (38.45 vs 38.92, Z = -2.023, p=0.043), behaviour cluster (10.91 vs 11.29, p=0.012). Negative associations between meconium lead and total NBNA (r = -0.903, p<0.01), activity tone (r = -0.637, p<0.01), and behavioural (r = -0.826, p<0.01) scores

TSH=thyroid-stimulating hormone. T4=tetraiodothyronine. PDBE=polybrominated diphenyl ethers. PCCD=polychlorinated dibenzodioxins. PCCF= polychlorinated dibenzofurans. PCB=polychlorinated biphenyls. FVC= forced vital capacity. PAH= polycyclic aromatic hydrocarbons. BaP=benzo[a]pyrene. DahA=dibenz[a,h]anthracene. BaP=benzo[a]pyrene. BMI=body-mass index. ppb=parts per billion. NBNA=neonatal behavioural neurological assessment.

Table 2: Health effects of exposure to e-waste

	Exposure setting	Exposed population	Main toxicant	Effect
DNA damage				
Chen et al ⁴⁷	Ecological: exposed town vs control town	Population (n=138)	Not assessed	Micronuclei in binucleated cells: median 4.0% (range 2.0–7.0) vs 1.0% (0.0–2.0), p<0.01
Yuan et al ³¹	Recycling activity	Recycle workers vs farmers (n=49)	Not assessed	Micronuclei in binucleated cells: median 5.0% (range 0.0–96.0) vs 0.0% (0.0–5.0), p<0.01
Wang et al ⁴⁸	Recycling activity	Recycle workers vs not exposed (n=104)	Lead, copper, and cadmium	Micronuclei in binucleated cells: median 4.0% (range 2.0–7.0) vs 1.0% (0.0–2.0), p<0.01. Positive correlation between blood lead and micronuclei in binucleated cells ($r=0.245$, p<0.01). No associations with copper or chromium
Liu et al ⁴⁶	Recycling activity	Recycle workers vs not exposed (n=201)	Not assessed	Micronuclei in binucleated cells: median 16.92% vs 3.47%, p<0.01, chromosomal aberration (5.5% vs 1.7%), and DNA damage (comet assay). Women more affected than men (p<0.05)
Li et al ⁴⁴	Ecological: exposed town vs control town	Newborn infants (n=302)	Chromium	Comet assay: DNA damage (33.2% vs 10.7%, p<0.01), length of tail (4.49±1.92 μ M vs 2.09±0.65, p<0.01). Blood chromium correlated with DNA damage ($r_s=0.95$, p<0.01) and tail length ($r_s=0.95$, p<0.01)
Gene expression				
Li et al ⁴⁹	Ecological: exposed town vs control town	Men	Not assessed	miRNA expression profiles in spermatozoa: differential regulation (109 downregulated, 72 upregulated)
Li et al ⁵⁰	Ecological: exposed town vs control town	Newborn infants (n=423)	Cadmium	Metallothionein expression in placenta: 67.0% vs 3.7%, p<0.01; and correlated with cord blood ($r^2=0.21$, p=0.01) and placenta ($r^2=0.76$, p=0.01) cadmium concentrations
Zhang et al ⁵¹	Ecological: exposed town vs control town	Pregnant women (n=105)	Not assessed	Placental S100P protein (0.026 vs 0.032, p=0.045) and mRNA (0.175 vs 1.462, p<0.001); metallothionein expression (0.051 vs 0.035, p=0.003)

Table 3: Changes at the cellular level resulting from exposure to e-waste

correlated with location of residence in Guiyu (particularly having an e-waste workshop within 50 m), parents' involvement in e-waste recycling, (including time involvement), the use of the home as a recycling workshop, and the gnawing of toys by children.⁴² Neonates had increased lead concentrations in cord blood and meconium, which were correlated with maternal involvement in e-waste recycling, time spent living in Guiyu before and during pregnancy, time spent in recycling facilities while pregnant, and the father's involvement in e-waste activities.⁴⁵ Neonatal behavioural neurological assessment scores differed significantly between the Guiyu group and the control group.⁴⁵ Increased concentrations of lead were associated with abnormalities in temperament scores⁴⁴ and low neonatal behavioural neurological assessment scores⁴⁵ (table 2).

We identified eight studies that included health outcomes at the cellular level caused by exposure to e-waste and waste electrical and electronic equipment.^{31,41,46–51} All study populations were from southern China and studies were cross-sectional (table 3).

People living in e-waste recycling towns or working in e-waste recycling had evidence of greater DNA damage than did those living in the control down, with increased frequencies of micronucleated binucleated cells in peripheral blood.^{31,46–48} Although exposure to e-waste is implicated in this DNA damage, the studies generally do not have the power to exclude other contributory factors. In one study,³¹ no significant differences were recorded in other measures of oxidative DNA damage (ie, serum levels of superoxide dismutase, malondialdehyde, glutathione peroxidase, and 8-hydroxy-2'-deoxyguanosine) between the exposed and control groups. Additionally, the exposed group had higher chromosomal aberration rates than did the control group (5.5% vs 1.7%), and

significant differences in DNA damage in the comet assay (one cell gel electrophoresis) between the two populations were recorded (significant increases in percentage of DNA in the tail, and differences in tail moments).⁴⁶ In this study, the potential confounding effect of cigarette smoking was excluded.⁴¹ Higher rates of DNA damage were reported in women than in men, which the investigators attributed to greater exposure to pollutants because of time spent indoors.⁴⁶

Significant differences were reported in lymphocytic DNA damage in neonates between the e-waste recycling town of Guiyu and the neighbouring fishing town Chaonan.⁴¹ Neonates from Guiyu had greater DNA damage with significantly higher injury rates and lengths of tails in the comet assay than did neonates from Chaonan (table 3).⁴¹ The investigators detected significant correlations between blood chromium concentrations and DNA damage in neonates.⁴¹ A possible correlation was found between exposure to e-waste and changes in miRNA expression profiles in spermatozoa.⁴⁹ Li and colleagues⁴⁹ identified differential expression for 182 miRNAs by comparing the exposed and unexposed population, and noted a potential association between environmental exposure to e-waste and sperm quality and count.

Neonates from Guiyu had higher placental metallothionein expression (a biomarker of exposure to toxic metals) than did those from Chaonan.⁵⁰ Zhang and colleagues⁵¹ noted significant downregulation of S100P proteins, higher expression of metallothionein, and higher placental cadmium concentrations in mothers exposed to e-waste from Guiyu than in non-exposed mothers from the control town Shantou (table 3). Mean relative mRNA and protein S100P concentrations were significantly lower in pregnant women from Guiyu than

in those from Shantou (table 3), and metallothionein expression was higher in Guiyu than in Shantou (table 3).⁵¹ However, potential confounders were recorded that might account for these results: S100P concentrations were negatively correlated with gestational age; metallothionein expression was positively correlated with gestational age and Apgar score, but negatively correlated with maternal age.⁵¹

We identified one study⁵² that related exposure to e-waste and waste electrical and electronic equipment to educational outcomes. Lead was analysed as the main chemical agent due to environmental exposure routes. Wang and colleagues⁵² assessed the effects of blood lead concentrations on intelligence quotient (IQ) in children aged 11–12 years in the e-waste recycling town of Luqiao, the tinfoil manufacturing area Lanxi, and the control town Chun'an. Researchers identified no significant differences in IQ at the three sites. Because of small individual site sample sizes, the results were combined, and intellectual deficits were recorded in children with blood lead concentrations lower than 0.48 µmol/L every 0.04 µmol/L increase in blood lead level resulted in a 0.71 (95% CI -1.30 to -0.12) point decrease in IQ.⁵² No studies investigated an association between e-waste exposure and aggression, violence, or criminal behaviour.

We assessed evidence for causality between exposure to e-waste and outcomes within the Bradford Hill framework.⁵³ We used the criteria for grading evidence developed by the World Cancer Research Fund (WCRF) as a guideline.⁵⁴

Discussion

To the best of our knowledge, this report is the first systematic review of published studies assessing the evidence of the effects of exposure to e-waste in children and adults. We identified 23 studies that examined associations between exposure to e-waste and health and learning outcomes, but no studies in which an association between exposure to e-waste and violence or criminal behaviour was investigated. We included violence and criminal behaviour as potential outcomes because of proposed associations between exposure to heavy metals, aggression, and violent crime.^{55,56} We assessed evidence of causality between exposure to e-waste and many outcomes within the Bradford Hill framework, focusing on temporality, strength, and consistency of the associations, dose–response relation, plausibility, and the consideration of alternative explanations.

Our ability to assess temporality of associations was limited by the absence of prospective or longitudinal studies. Temporal associations, by definition, were not possible to establish in cross-sectional studies. We recorded weak associations between e-waste exposure and changes in thyroid function, adverse neonatal outcomes, changes in temperament and behaviour, decreases in lung function, and changes in cellular expression and function. Most associations remained significant when confounding

variables were considered. However, the absence of prospective and longitudinal studies, and the small sample sizes (only one study had a sample size >450 people),⁴² are concerns. Of note is the issue of the transport of environmental contamination. Substantial quantities of pollution are found not only very close to e-waste recycling locations, but, because of contamination of the surrounding environment (specifically soil and water) and the resulting food chain, high levels of pollution due to e-waste are also found throughout southern China, including control population locations.^{47,57} Nonetheless, we still recorded differences between exposed and control populations in many studies, even without controlling for exposure in control groups.

Consistency of associations was hard to assess because of diverse outcomes and variation in chemical exposure variables. However, we noted consistent associations in studies assessing the effects of e-waste exposure on measures of DNA damage and cellular expression. In all studies, investigators reported higher frequencies of micronucleated binucleated cells in all e-waste-exposed populations than in unexposed controls. DNA damage (ie, DNA injury rates and tail length) was more prevalent in all e-waste-exposed populations than in controls—a finding consistent across studies. In the four studies assessing the effects of the components of e-waste on neonatal birth outcomes, the infants with adverse birth outcomes had increased concentrations of polybrominated diphenyl ethers,^{38,39} polycyclic aromatic hydrocarbons,³⁷ and perfluoroalkyls.⁴⁰ However, these conclusions need to be further substantiated because both cases (neonates with adverse birth outcomes) and controls (neonates with healthy birth outcomes) were taken from the study and not the general population.

We did not establish a dose–response relation for exposure to e-waste. Because the chemical elements and compounds to which people are exposed are released as a very complex mixture, the physiological response is to the mixture, instead of to individual chemicals. Dose–response relations of the chemical mixtures that arise in e-waste have not been extensively studied. Additionally, a typical linear dose–response pattern is not predicted for many of the chemicals involved in e-waste, especially compounds that have endocrine-disrupting effects.⁵⁸ Non-monotonic (ie, non-linear), or low-dose associations have typically been associated with some of these chemical compounds.⁵⁸ An association between exposure to e-waste and various outcomes in human beings is very likely. Mechanisms of action, from animal and in-vitro models, have been developed for individual and mixtures of chemical compounds implicated in e-waste. Additionally, important associations have been recorded between the chemical compounds found in e-waste and mental, physical, and learning outcomes due to non-e-waste sources of exposure (appendix). Many of the individual chemical pollutants found in e-waste have substantial effects on human health (appendix). The International Agency for Research on

Cancer has identified TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin), cadmium, hexavalent chromium, and beryllium as carcinogenic;⁵⁹⁻⁶¹ some polychlorinated biphenyls and some polycyclic aromatic hydrocarbons as probably carcinogenic;^{62,63} and polybrominated diphenyl ethers, metallic nickel, and some polycyclic aromatic hydrocarbons as possibly carcinogenic.^{60,62,64} Because of insufficient evidence, mercury, some dioxins, and some polycyclic aromatic hydrocarbons cannot be classified as carcinogenic.^{59,61,62,65} Polybrominated diphenyl ethers, polycyclic aromatic hydrocarbons, chromium, nickel, and aluminium are confirmed genotoxins,⁶⁶⁻⁷¹ because these compounds have damaged DNA in vitro, and in tests on animals and human beings. Copper, iron, and aluminium are known cytotoxins.^{69,71,72} Exposure to dioxins, dioxin-like polychlorinated biphenyls, perfluoroalkyls, lead, and possibly cadmium has been associated with increased incidence of

chronic diseases later in life, including obesity, type 2 diabetes, hypertension, and cardiovascular diseases.⁷³⁻⁷⁹ Lung cancer, lung damage, and decreased lung function are also associated with compounds common in e-waste, including polycyclic aromatic hydrocarbons, hexavalent chromium, cadmium, nickel, arsenic, and lithium.^{59,60,62,68,80-87}

We recorded adverse perinatal and neonatal outcomes, such as impaired fetal growth, low birthweight and birth length, low head circumference, stillbirth, preterm delivery, and below average childhood growth in mothers exposed to polybrominated diphenyl ethers, polychlorinated biphenyls, dioxins, perfluoroalkyls, polycyclic aromatic hydrocarbons, and cadmium.^{73,88-94} Exposure to hazardous e-waste compounds affected reproductive development and fertility. Lead has been linked to delayed puberty in girls;⁹⁵ polychlorinated biphenyls, TCDD, and perfluoroalkyls decrease sperm quality;⁹⁶⁻⁹⁸ and exposure to polybrominated diphenyl ethers seems to decrease female fertility.⁹⁹ Many persistent organic pollutants are also endocrine disruptors, with an especially strong effect from early life exposure.^{100,101}

The hazardous compounds found in e-waste have strong neurodevelopmental and neurobehavioural effects, especially in children. Polybrominated diphenyl ethers, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, lead, cadmium, and mercury are associated with decreased intelligence (as measured by IQ) and impaired cognitive functioning,^{49,102-113} whereas polybrominated diphenyl ethers, polychlorinated biphenyls, mercury, and cadmium have been linked to neurodevelopmental abnormalities. Changes in mental health, including behavioural disturbances, attention deficits, hyperactivity, and conduct issues have been reported after childhood exposures to polychlorinated biphenyls, lead, mercury, and aluminium.¹¹⁴⁻¹¹⁸ Some investigators have proposed associations between lead and polychlorinated biphenyl exposure and an increased risk of aggression and international rates of violent crime.^{55,56} Data also suggest that lead exposure, combined with genetic predisposition, can trigger schizophrenia.¹¹⁹⁻¹²¹ Although debated, heavy metals might have a role in the development of the neurodegenerative diseases Alzheimer's disease (aluminium)¹²² and Parkinson's disease (lead).¹²³

The effects of simultaneous exposure to many chemicals—eg, involvement in e-waste recycling—are not well explored or understood. This knowledge gap becomes an even larger problem in areas where other hazardous wastes are present in the environment. Although e-waste contains a unique combination of persistent hazardous compounds, other sources of exposure are difficult to rule out, especially in China, where all included studies were undertaken. However, in studies that accounted for confounding variables, investigators still recorded significant associations between e-waste and adverse outcomes in exposed populations. Working with e-waste was an independent risk factor

Panel: Research gaps and recommendations for future study

Gaps in research

- Retrospective studies are not effective measures of the long-term health effects of e-waste exposure
- Issues in study design, particularly the pooling of samples, restrict the analysis and comparison of results
- All the studies qualifying for inclusion in our report focus on study sites in China, despite evidence of dangerous informal e-waste processing in many countries; although research has been published from other regions, a direct association between e-waste exposure and health outcomes in human beings has not been assessed
- Large gaps exist in the physical health, mental health, educational, and behavioural outcomes of exposure to individual chemical compounds released during e-waste recycling
- More understanding of potential synergistic and inhibitor effects of exposure to chemical mixtures, the effects of long-term exposure, and the outcomes of low-dose exposure to e-waste is needed
- The unique risks to children and vulnerable populations have not been given enough consideration

Recommendations

- Prospective, long-term cohort studies are needed to study exposed children and adults from the time of exposure, measuring body burden and investigating health and educational, employment, and other outcomes of interest
- A standardised and validated questionnaire should be introduced to remove the issues of different definitions of electronic waste, confounding factors, and health effects, and to standardise exposure recall data collection
- Additional research into the potential combination and inhibitor effects of the unique chemical mixtures present in e-waste is needed
- Additional research should be done in the growing e-waste regions of Africa, India, and Brazil
- A collaborative research agenda should be determined by international experts
- Although additional evidence is needed, rapidly growing streams of e-waste, the involvement of vulnerable populations, direct evidence of health effects, and biological plausibility of additional health effects need timely investigation and implementation of exposure-minimising interventions
- Public health professionals are not sufficiently aware of the health consequences of e-waste exposure; increased awareness and capacity building is needed within the health sector

associated with genotoxic damage when other variables, such as smoking and age, were accounted for.^{31,48} The mechanisms of action of the mixture of chemicals that make up e-waste are not completely known, nor are the full range of effects that arise from the combined exposure to many chemical elements and compounds. We used the grading system developed by the WCRF⁵⁴ as a guideline to assess the level of evidence. We concluded that the evidence is suggestive of an association between e-waste exposure and change in thyroid function, changes in cellular function and expression, adverse neonatal outcomes, changes in temperament and behaviour, and decreases in lung function.

Extensive use of an ecological study design in the included reports introduced a risk of ecological fallacy (in which associations at the individual level are deduced from those found at the population level) in the interpretation of results. Although populations exposed to e-waste generally had a higher frequency of adverse health effects—especially for thyroid functioning, adverse birth outcomes, and changes in cellular functioning—the use of ecological data limits conclusions made at the individual level. Some studies relied on pooling of serum samples from exposed and control populations to make associations between adverse effects and chemical exposure. Studies based on retrospective assessment can be prone to information bias⁴² and possible overreporting of disease in exposed groups, especially when child outcomes were measured by parent reports.⁴⁴ Although the investigators who associated adverse birth outcomes in neonates with concentrations of serum and umbilical cord chemical compounds did find significant associations,^{37–40,42} the cases and controls were chosen from the study and not the general population, creating a sample bias (in which non-random population selection arises) or diagnostic bias (in which the exposure is already known for the cases and controls). Widespread environmental pollution from e-waste recycling sites hinders the identification of specific sources and routes of exposure. Additionally, alternative sources of local pollution, remote industrial pollution, and the biomagnification of pollutants in the food chain create complexity in exposure and body burden measurements.

At the outcome level, several studies that used a retrospective case–control design did not adjust results for confounding variables. In some studies, investigators did not adjust for the effect of confounders, especially smoking and age, on neonatal outcomes.^{37–40} Possible alternative sources of exposure including outdoor air pollution, pesticides, and industrial pollution, have not been accounted for in the interpretation of results, which has diminished the plausibility of certain health outcomes being due to e-waste exposure alone. Our report might also have been biased by the inclusion of only published scientific literature because studies with findings showing significant (*vs* null) associations are more likely to be published.

In conclusion, few epidemiological data, weak associations, inconsistent findings across studies, and poor understanding of biological mechanisms preclude the establishment of a causal relation between exposure to e-waste and adverse health outcomes in the assessment of evidence by conventional epidemiological approaches. However, the widespread production and use of electronic and electrical equipment, the increasing contamination of the environment, and the persistence and bioaccumulation of these chemical components warrant special consideration of e-waste as an emerging health risk for many populations. A precautionary approach towards exposure, especially in children, seems warranted. Additionally, we recorded extensive evidence of a causal link between exposure to individual chemical compounds common in e-waste and negative health outcomes (appendix). The strong biological plausibility of an association between e-waste exposure and health outcomes justifies investment in further research into the unique exposure scenarios and potential health consequences of e-waste exposure. Several research gaps have been identified by our report, and we provide recommendations to fill these gaps (panel).

The health effects of exposure to e-waste must become a priority of the international community. Informal e-waste recycling has long been accepted as a source of dangerous environmental pollution, but the health risks it poses to exposed populations are only beginning to be recognised. An international research agenda should be set by experts to increase the body of evidence of the health effects of e-waste exposure, especially in children and vulnerable populations. Simultaneously, the international health community, academia, policy experts, and non-governmental organisations, in conjunction with national governments, should create policy solutions, educational programmes, and interventions to reduce e-waste exposure and its health effects.

Contributors

PDS, M-NB, and MN initiated the report. KG, REN, and MvdB wrote the review protocol. KG did the initial search and collection of articles. KG and FG independently reviewed articles and determined included articles. KG, FCG, REN, PDS, and M-NB wrote the first and final versions. All authors independently reviewed and approved the final manuscript.

Conflicts of interest

We declare that we have no conflicts of interest.

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