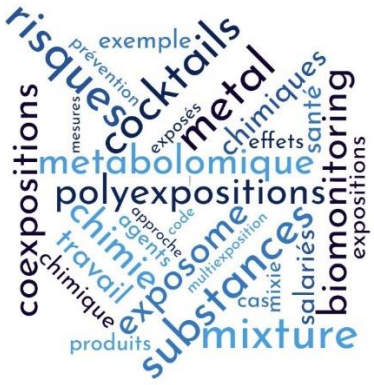

Bulletin de veille
Polyexpositions chimie-chimie
N°11 - octobre 2025

Objectif : la polyexposition homogène chimie/chimie est un sujet de plus en plus préconisé pour étudier l'évaluation du risque professionnel et sa prévention. L'objectif est de connaitre les travaux récents qui sont publiés sur le sujet et identifier des moyens d'analyse, et d'interprétation de cette co-exposition à plusieurs composés chimiques.

Ce bulletin a été réalisé à partir d'une surveillance de littérature récente sur les bases Web of Sciences et la base documentaire INRS-Biblio.

La validation des informations fournies (exactitude, fiabilité, pertinence par rapport aux principes de prévention, etc.) est du ressort des auteurs des articles signalés dans la veille. Les informations ne sont pas le reflet de la position de l'INRS. Les éléments issus de cette veille sont fournis sans garantie d'exhaustivité.

Les liens mentionnés dans le bulletin donnent accès aux documents sous réserve d'un abonnement à la ressource.

Actualités web sélectionnées

- 21 août 2025. L'EU-OSHA gère la base de données contenant des ressources sur la gestion des risques liés aux agents chimiques sur les lieux de travail. C'est un outil pratique et d'orientations sur les substances dangereuses contenant les informations utiles dans plus de 900 ressources :

https://perosh.eu/news/the-practical-tools-and-guidance-database-on-hazardous-substances/

Un certain nombre d'outils et de documents d'orientation ont été élaborés par les États membres, les institutions européennes, les associations professionnelles, les partenaires sociaux et d'autres acteurs pour aider les entreprises à réaliser des évaluations des risques complètes et efficaces. Ces outils représentent une grande variété d'approches pour gérer efficacement les substances dangereuses. Ils couvrent souvent des opérations de travail spécifiques, telles que le remplissage et le pompage de liquides ou les processus de soudage. D'autres sources donnent un aperçu complet d'un certain groupe de substances, comme les sensibilisants, ou mettent en évidence des risques typiques dans certains secteurs.

- 26 septembre 2025. L'IRSST a lancé le premier bulletin d'une veille scientifique consacrée à la métrologie des substances chimiques dans l'air. Cette veille permet à la communauté scientifique et aux praticiens et praticiennes de suivre les avancées les plus récentes en matière de méthodes d'analyse, en particulier celles sur les méthodes d'analyses émergentes concernant les substances préalablement sans méthodes analytiques. Pour plus de détails et pour s'abonner

- 15 septembre 2025. Santé publique France. PestiRiv : résultats de l'étude nationale sur l'exposition aux pesticides des riverains de zones viticoles. https://www.santepubliquefrance.fr/presse/2025/pestiriv-resultats-de-l-etude-nationale-sur-l-exposition-aux-pesticides-des-riverains-de-zones-viticoles

- 26 septembre. Blog Elle. Pourquoi le cancer touche davantage les Millenials, l'exposome en cause. Lien vers l'article de ELLE

Table des matières

1. Généralités

Cary-Clarke, R., Nguyen, L. T., Ramkissoon, C.
Occupational Co-Exposures to Noise and Chemicals - Review of Evidence and Regulatory Perspective.
Work and Health, Vol. **1** (1), (2025), 4 p.

The potential for harmful synergistic effects of workplace noise and chemical exposure is well-established. However, it is less conclusive whether such effects could still be seen if operators were complying with the relevant exposure standards for noise and/or chemicals. Bearing a regulatory perspective, this literature review explored whether any trends in the effects of combined exposure to noise and toxic chemicals could be established.
A literature search was undertaken in seven databases, using key search terms on the combined effects of occupational noise and chemical exposures. A total of 1742 articles were identified, among which 82 were assessed in greater detail.
Results in animals demonstrated a synergism of styrene, toluene and carbon disulfide when noise is delivered as a repeated 'impulse'. Other evidence suggested that noise, although at high levels, was responsible for systemic toxicity in organs other than hearing or nerves. Another significant observation was the early signs of hearing loss associated with mixed solvent exposures and noise, each below the respective occupational exposure limits (OELs). Based on these findings, we wondered whether current workplace exposure standards for noise give adequate protection against damage to hearing for workers exposed to chemicals like styrene or toluene. Additionally, they questioned whether compliance with airborne exposure standards and noise levels gave adequate protection for chemicals with a 'Skin' notation.
https://www.sciltp.com/journals/wah/articles/2505000677

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Tartaglia, M., Ge, C., Pronk, A., Costet, N., Audignon-Durand, S., Houot, M.-T.*, et al.*
Multiple maternal occupational exposures during pregnancy and intrauterine growth: analysis of the French Longitudinal Study of Children - ELFE cohort, using data-driven approaches.
International journal of hygiene and environmental health, Vol. **270**, (2025), 114666.

OBJECTIVE: To use data-driven approaches to investigate maternal multi-occupational exposures during pregnancy and their effects on intrauterine growth.
METHODS: Maternal occupational exposure to 47 factors during pregnancy was evaluated with job-exposure matrices in the French ELFE cohort. The outcomes of interest were birthweight (BW), small for gestational age (SGA) and head circumference (HC). Occupational exposures associated with these outcomes were identified by EWAS, LASSO, and random forest. The five exposures with the strongest effects selected with these approaches were included in a final multivariate model with significant interactions.
RESULTS: We included 12,851 women. The most important occupational factors predictive of SGA were endocrine disruptors, high strain, kneeling/squatting, job demands, physical effort. No significant associations were detected when these variables were combined in a final model. For BW, the most important variables were leaning forward/sideways, using a computer screen, ultrafine particles, physical effort, airborne germs, repetitive actions. The use of a computer screen significantly decreased BW and, for women not exposed to airborne germs, leaning forward/sideways significantly increased BW. For HC, repetitive actions, oxygenated solvents, kneeling/squatting, airborne germs, working outdoors were the most important predictive factors. Repetitive actions and working outdoors significantly decreased HC. HC also decreased in women exposed to both airborne germs, and oxygenated solvents. Similar results were found for women who worked during the third trimester.
CONCLUSION: Our findings highlight potential roles of chemical, biological and postural factors and their interactions in determining intrauterine growth. These results highlight the importance of considering multiple exposures in occupational health studies.
https://doi.org/10.1016/j.ijheh.2025.114666

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ROMERO-HARIOT A. ; GERARDIN K. ; DEVOY J. ; NIKOLOVA-PAVAGEAU N. ; MATER G.

Surveillance des expositions aux agents chimiques des travailleurs impliqués dans la gestion des sites et sols pollués : état des lieux et préconisations

IC RST - Grand angle. TC 184, Références en santé au travail, n° 182, avril-mai-juin 2025, pp. 37-60, 24 p.

Les catégories de travailleurs intervenant en sites et sols pollués (SSP) sont multiples et leur perception et connaissance du risque chimique sont inégales. Des sources d'information existent pour connaître les polluants présents dans les sols afin de caractériser les expositions potentielles de ces travailleurs. Un état des lieux de leur niveau d'exposition aux agents chimiques a été réalisé à partir de l'exploitation de la base Scola. Des préconisations de surveillance de l'exposition, basées sur des mesures atmosphériques, surfaciques et biométrologiques, avec l'appui notamment des services de prévention et de santé au travail, sont présentées.

Référence INRS-Biblio : 744372

Lien vers l'article : https://www.inrs.fr/media.html?refINRS=TC%20184

1.1. Exposome

Wang, B., Lan, C., Zhang, G., Ren, M., Wu, T., Gao, N.*, et al.*

ExposomeX : Development of an Integrative Exposomic Platform to Expedite Discovery of the "Exposure-Biology-Disease" Nexus.

Environ Sci Technol, Vol., (2025), p.

We proposed presenting a novel integrated platform, ExposomeX, that was created to expedite discovery of the "exposure-biology-disease" nexus. This platform has six major functions, i.e., exposome database (E-DB), biological link (E-BIO), statistical analysis (E-STAT), mass spectrometry data processing (E-MS), meta-analysis (E-META), and data visualization (E-VIZ). Twenty-three supporting databases were curated for this platform, encompassing the exposome and diseases together with their related biological pathways and molecules, to build their interaction network.
The network nodes included up to 119,247,057 unique exposures, 17,186 diseases, 153,780 proteins, 19,122 metabolites, and 572,278 annotated pathways, while the network links included 10 interaction modes, e.g., exposure and protein (3,971,005 pairs), exposure and GO (28,632 pairs), protein and disease (10,153 pairs), gene and disease (108,298,474 pairs), GO and disease (3,085,406 pairs), and associations between exposures and diseases for meta-analysis and review summary (1244 pairs). ExposomeX allows effective analysis of multidimensional exposomic data as well as investigations of the "exposure-biology-disease" nexus through explorations of the association strengths, which was well-validated by reanalyzing three typical multiomics data sets. All the aforementioned functions were implemented using R programming and integrated into a web-based server to enhance user interaction through an online interactive platform (http://www.exposomex.cn).
https://doi.org/10.1021/acs.est.5c05956

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Park, S. K., Walker, E., Arboleda-Merino, L., Fansler, S., Middleton, L. Y. M., Wang, X.*, et al.*

An Exposome-Wide Interaction Study to Identify Hidden Environmental Factors Affecting Susceptible Populations : Application to Chemical-Social Vulnerability Interactions on Cognitive Function.

medRxiv : the preprint server for health sciences, Vol., (2025), p.

Background: Exposome-wide association studies (ExWAS) systematically evaluate numerous environmental exposures, but typically focus on the mean effect, determining whether the association is statistically significant for the average individual. This approach may overlook environmental chemicals that specifically

affect susceptible subpopulations. We conducted an exposome-wide interaction study (ExWIS) to identify environmental chemicals associated with cognitive function in the context of social vulnerability.
Methods: We examined associations between 147 biomarker-based chemicals and cognitive function among 4,982 adults aged 60 and older in the National Health and Nutrition Examination Survey (NHANES) 1999-2000 and 2011-2014. Social vulnerability index (SVI) was calculated as a composite measure encompassing race/ethnicity, income, education, health insurance, housing type, food security, and employment. Initially, we ran survey-weighted linear regressions between each chemical and cognition, adjusting for SVI, age, sex, smoking status, serum cotinine, fish consumption, NHANES cycle, and urinary creatinine (marginal association models). Subsequently, we repeated these models with a linear interaction term between each chemical and SVI (interaction models).
Results: In marginal association models, 16 chemicals including smoking-related compounds, polyaromatic hydrocarbons, and metals were associated with cognitive function (unadjusted p <0.05). In interaction models, four additional chemicals-urinary mercury, diethylthiophosphate, perfluorononanoate, and perfluoroundecanoate-not identified in the marginal association models showed significant interactions with SVI.
Discussion: This study demonstrates the utility of the ExWIS framework to identify environmental factors that affect susceptible populations but may be missed by the mean effect-based ExWAS approach. Considering interaction effects is essential for accurate environmental risk assessment and identification of neurotoxicants in at-risk populations. HIGHLIGHTS: In a nationally representative sample of older adults, chemical exposures and social factors are cross-sectionally associated with cognitive function.Proof of concept exposome-wide interaction study (ExWIS) demonstrates jointly incorporating chemicals and social factors identifies exposures relevant for susceptible populations.The hypothesis generating ExWIS approach presented here may be broadly relevant for other outcomes and studies.
https://doi.org/10.1101/2025.09.17.25335908

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Crom Td, K. T., Wan W, Et Al.
Occupational exposome and the risk of COPD.
Occupational and Environmental Medicine Vol. **82** (8285318), (2025), A51.

Objectif : Les expositions professionnelles chimiques sont des facteurs de risque établis de bronchopneumopathie chronique obstructive (MPOC), mais la plupart des preuves proviennent d'études qui négligent l'impact potentiel de plusieurs expositions concomitantes. Le cadre de l'exposome professionnel aborde ce problème en saisissant un large éventail d'expositions professionnelles au cours d'une carrière. Notre objectif était d'explorer l'association entre l'exposome professionnel et le risque de BPCO.
Matériel et méthodes Nous avons inclus au départ des personnes âgées de ≥40 ans sans BPCO à partir de quatre études de cohorte basées sur des registres : la cohorte professionnelle danoise avec des données eXposure (DOC*X), la cohorte nationale suédoise sur le travail et la santé (SNOW), la cohorte sur l'état de la main-d'œuvre en Finlande (SLFF) et la cohorte norvégienne Nor-Work. (...)
https://doi.org/10.1136/oemed-2025-EPICOHabstracts.123

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1.2. Polluants environnementaux, expositions combinées

Grahn, K., Lissaker, C., Andersson, T., Gustavsson, P., Tinnerberg, H., Wiebert, P., *et al.*
Occupational exposure to chemicals and particles and incidence of myocardial infarction-a nationwide cohort study in Sweden.
Environmental research, Vol., (2025), 122783.

Cardiovascular disease (CVD) is the leading cause of death in Europe, with myocardial infarction (MI) being

one of its most severe manifestations. While many risk factors for CVD are well known, occupational exposures remain relatively understudied-especially in analyses that adjust for co-occurring workplace exposures.
This study aimed to examine the association between occupational exposure to chemicals and particles and the risk of first-time MI. The cohort included all Swedish residents born between 1930 and 1990 who were employed between 1985 and 2013 and had no prior MI. Participants were followed from 1986 to 2017, and their occupational histories were linked to the Swedish Job Exposure Matrix (SweJEM) to estimate exposure to 31 chemicals and particles. MI cases were identified through national hospital discharge and cause of death registers. Using discrete time proportional hazards regression, we estimated gender-specific hazard ratios, adjusting for age, decision authority, physical workload, noise, other chemicals/particles, and within a subset smoking and body mass index (BMI). Among 225,366 incident MI cases, the strongest increased risk was associated with both cumulative, ever, and recent exposure to diesel exhaust, polycyclic aromatic hydrocarbons, sulfur dioxide, carbon dioxide, cadmium, chromium, iron, and lead. These associations remained after adjusting for smoking, BMI, and education. Hazard ratios were generally higher among women. The attributable proportion among exposed individuals was 9%, corresponding to over 20,000 cases during the follow-up period. Our findings highlight the importance of reducing occupational exposure to harmful substances to prevent future cases of MI.
https://doi.org/10.1016/j.envres.2025.122783

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Mckeon, H., Carsique, M., Palmont, P., Machera, K., Bil, W., Bokkers, B.*, et al.*
OS02-07. The PARC Real-life Mixtures Project : Mixture Risk Assessment Results of the Case Studies on Pesticides, PFAS and Heavy Metals.
Toxicology Letters, Vol. **411**, (2025). Abstracts of the 59th Congress of the European Societies of Toxicology (EUROTOX 2025) TOXICOLOGY ADDRESSES SOCIETY'S REAL LIFE RISKS FOR SUSTAINABLE HEALTH AND WELL BEING.
https://doi.org/10.1016/j.toxlet.2025.07.166

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Tang, K. H. D.
Combined Toxicity of Microplastics and Antimicrobials on Animals : A Review.
Antibiotics-Basel, Vol. **14** (9), (2025), p.

Background/Objectives: Microplastics are ubiquitous pollutants that pose physical toxicity and serve as vectors for antimicrobial agents, altering their bioavailability and toxicity. Unlike previous reviews that focus solely on antibiotics and terrestrial or aquatic ecosystems, this review integrates recent findings on the combined impacts of microplastics and antimicrobials on both aquatic and terrestrial animals, highlighting their biological responses.
Methods: Recent experimental studies involving aquatic and terrestrial animals published in peer-reviewed journals were reviewed. These studies employed co-exposure designs using microplastics of different sizes, aging conditions, and surface chemistries in combination with antimicrobial compounds.
Results: Microplastics combined with antimicrobials cause species-specific and often synergistic toxicity in aquatic organisms, affecting reproduction, immunity, oxidative stress, gene expression, and microbiota, with co-exposure often amplifying adverse physiological and developmental effects. Similarly, co-exposure to microplastics and antimicrobials in rodents, amphibians, birds, and soil invertebrates frequently leads to synergistic toxicity, oxidative stress, disrupted gut microbiota, and enhanced accumulation and bioavailability of pollutants, promoting inflammation, neurotoxicity, metabolic dysfunction, and increased antibiotic resistance gene propagation. Particle size, aging, and antimicrobial type influence toxicity severity. Certain microplastic-antimicrobial combinations can exhibit antagonistic effects, though less frequently reported.
Conclusions: The interactions between microplastics and antimicrobials pose heightened risks to the health of organisms and ecological stability. These findings underscore the need to revise current risk assessment protocols to consider pollutant mixtures and microplastics-mediated transport. Future research should

focus on environmentally relevant exposures, mechanistic studies using omics tools, and long-term ecological impacts. Integrated regulatory strategies are essential to address the compounded effects of microplastics and chemical contaminants.
https://doi.org/10.3390/antibiotics14090896

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2. Biomonitoring, biomarqueurs

Diyabalanage, S., Manthrirathna, M. a. N. C., Lakmali, M., Jayasinghe, R. M. N. P. K., Werahera, M., Chandrajith, R.
Exposure to mercury and toxic trace elements in waste gold extraction in Sri Lanka : A study on an under-recognised occupational health hazard.
Environmental Research, Vol. **285**, (2025), p.

The "Minamata Convention on Mercury" aims to reduce and monitor environmental mercury (Hg) pollution, particularly from anthropogenic sources. The small-scale jewellery sector (SSJS) is recognised as a significant contributor to environmental Hg emissions and a critical route of exposure to humans. This study provides the first assessment of Hg and selected trace element exposure among individuals working in the SSJS. After microwave-assisted acid digestion, urinary concentrations of total Hg and selected trace elements were measured in 50 exposed subjects and 34 controls by inductively coupled plasma mass spectrometry.
In the exposed group, creatinine-adjusted urinary Hg concentrations ranged from 0.09 to 414 mu g/g creatinine, compared to 0.09-18.3 mu g/g creatinine in the control group. Notably, 8 % of exposed subjects had Hg concentrations in the alarming range (5-20 mu g/g creatinine), and 6 % exceeded the WHO occupational exposure limit by 4- to 8-fold. The highest risk of exposure was found in communities classified as waste gold processors. Increased urinary concentrations of cobalt (Co), arsenic (As), silver (Ag), cadmium (Cd), tin (Sn), vanadium (V), and chromium (Cr) in exposed individuals indicate possible co-exposure to multiple toxic elements. In addition, 30 % of the exposed individuals reported neurological symptoms, including numbness and fatigue, which may be related to Hg toxicity.
These findings suggest significant Hg exposure among SSJS workers and highlight the critical need for targeted risk communication, regulatory interventions, and enhanced biomonitoring with additional biomarkers to assess the health impacts of metal exposure in this sector.
https://doi.org/10.1016/j.envres.2025.122597

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Gand, M., Soubry, A., Mertens, B., Roosens, N. H. C., De Keersmaecker, S. C. J.
Genetic and epigenetic biomarkers in human biomonitoring : why needed and how can Oxford Nanopore sequencing contribute ?
Front Public Health, Vol. **13**, (2025), 1610248 p.

Chemical risk assessment can benefit from integrating informative biomarkers in human biomonitoring (HBM). Beyond exposure biomarkers, effect biomarkers inform on biological reactions in the body, potentially leading to adverse effects, while susceptibility biomarkers address inter-individual variability in exposure. DNA methylation of key genes shows promise as an effect biomarker but this epigenetic mark remains underexplored in the context of chemicals. Similarly, although some genetic polymorphisms are linked to increased chemical susceptibility, genetic biomarkers are rarely included in HBM.
This mini-review highlights recent literature supporting the inclusion of genetic and epigenetic biomarkers in HBM. Subsequently, we elaborate on how Oxford Nanopore Technologies as sequencing method can efficiently measure these biomarkers simultaneously, even in non-invasive samples like saliva. Widely used in other fields, this experimental set-up could facilitate the design of large-population studies paving the way for a next generation risk assessment (NGRA) of chemicals.
https://doi.org/10.3389/fpubh.2025.1610248

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Hitomi, T., Okuda, H., Takata, A., Yamauchi, H.
Interaction of coexposure to inorganic arsenic and manganese : Tight junction injury of the blood-brain barrier and the relationship between oxidative stress and inflammatory cytokines in glial cells.
Plos One, Vol. **20** (8), (2025).

Coexposure to inorganic arsenic (iAs) and manganese (Mn) may exacerbate cognitive dysfunction caused by iAs alone. In this study, we investigated the cytotoxicity of coexposure to iAs and Mn in glial cells and the expression and correlation between oxidative stress and inflammatory cytokines. Additionally, we assessed tight junction (TJ) injury using a rat in vitro blood-brain barrier (BBB) model.
In glial cells, coexposure to iAs and Mn increased cytotoxicity compared to single exposure, suggesting a likely additive effect. iAs exposure significantly increased the expression of antioxidant stress markers, including nuclear factor erythroid 2-related factor 2 (Nrf2) and heme oxygenase-1 (HO-1), relative to Mn exposure. Notably, HO-1 expression was further elevated under coexposure conditions, indicating a potential synergistic effect. Regarding inflammatory cytokines, expression of C-C motif chemokine ligand 2 (MCP-1) and interleukin-6 (IL-6) was slightly higher in the iAs exposure compared to Mn exposure.
A synergistic effect was observed in the Mn concentration-dependent increase in IL-6 under coexposure. A significant positive correlation was found between Nrf2 or HO-1 and inflammatory cytokines (MCP-1 and IL-6) ($p < 0.001$), suggesting an interaction between oxidative stress and inflammatory cytokines. The BBB TJ injury was evaluated by measuring the transendothelial electrical resistance values and the Claudin-5 and zonula occludens-1. The results showed expression in iAs exposure but not in Mn exposure. Furthermore, Mn did not affect iAs-induced TJ injury.
In conclusion, our findings demonstrate that coexposure to iAs and Mn exerts synergistic effects on oxidative stress and inflammatory cytokines in glial cells. These joint effects may increase the risk of neurotoxicity compared to single-iAs or Mn exposure.
https://doi.org/10.1371/journal.pone.0330287

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Jeddi, M. Z., Galea, K. S., Ashley-Martin, J., Nassif, J., Pollock, T., Poddalgoda, D.*, et al.*
Guidance on minimum information requirements (MIR) from designing to reporting human biomonitoring (HBM).
Environment International, Vol. **202**, (2025), p.

Human biomonitoring (HBM) provides an integrated chemical exposures assessment considering all routes and sources of exposure. The accurate interpretation and comparability of biomarkers of exposure and effect depend on harmonized, quality-assured sampling, processing, and analysis. Currently, the lack of broadly accepted guidance on minimum information required for collecting and reporting HBM data, hinders comparability between studies. Furthermore, it prevents HBM from reaching its full potential as a reliable approach for assessing and managing the risks of human exposure to chemicals. The European Chapter of the International Society of Exposure Science HBM Working Group (ISES Europe HBM working group) has established a global human biomonitoring community network (HBM Global Network) to develop a guidance to define the minimum information to be collected and reported in HBM, called the "Minimum Information Requirements for Human Biomonitoring (MIR-HBM)". This work builds on previous efforts to harmonize HBM worldwide. The MIR-HBM guidance covers all phases of HBM from the design phase to the effective communication of results. By carefully defining MIR for all phases, researchers and health professionals can make their HBM studies and programs are robust, reproducible, and meaningful. Acceptance and implementation of MIR-HBM Guidelines in both the general population and occupational fields would improve the interpretability and regulatory utility of HBM data. While implementation challenges remain-such as varying local capacities, and ethical and legal differences at the national levels, this initiative represents an important step toward harmonizing HBM practice and supports an ongoing

dialogue among policymakers, legal experts, and scientists to effectively address these challenges. Leveraging the data and insights from HBM, policymakers can develop more effective strategies to protect public health and ensure safer working environments.
https://doi.org/10.1016/j.envint.2025.109601

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Hanser, O., Remy, A. M., Melczer, M., Grova, N., Ndaw, S.
Early-effect biomarkers and hazard index approaches to assessing risks from multiple exposure to metals among battery recyclers in France.
Environ Toxicol Pharmacol, Vol 119, October 2025, 104819.

Battery-recycling can expose workers to several metals. This study aims to investigate this multiple exposure, by exploring the potential of effect biomarkers to improve risk assessment for workers, and by calculating a hazard index (HI) to assess the risk of cumulative exposure. Urine samples from 86 workers in three French recycling plants were analysed for metal biomarkers (Cd, Co, Cr, Li, Mn, Ni), kidney-injury biomarkers (alpha1-microglubulin, retinol binding protein, kidney injury molecule-1, N-acetyl-beta-D-gluocosaminidase, albumin, total proteins), and oxidative-stress biomarkers (8-hydroxydeoxyguanosine, malondialdehyde). Kidney-injury biomarker levels successfully differentiated exposed recyclers from administrative workers, while oxidative-stress biomarker levels did not allow this differentiation. The calculation of a HI proved effective in detecting the risk associated with multiple metal exposure, offering a better risk assessment than when considering metals individually. This dual approach, combining HI calculation and analyzing kidney-injury biomarkers, should be strongly considered in the risk assessment of workers exposed to multiple metals.
https://doi.org/10.1016/j.etap.2025.104819

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Lee, J., Barupal, D.
Simulating Collision-Induced Dissociation Tandem Mass Spectrometry (CID-MS/MS) for the Blood Exposome Database Using Quantum Chemistry Methods - A Pilot Study.
Journal of the American Society for Mass Spectrometry, Vol., (2025), p.

A significant number of compounds in exposome databases and chemical inventories lack mass spectral data due to the nonavailability of reference standards. To address this limitation, computational chemistry methods can be utilized to extend mass spectral libraries for a set of chemicals.
In this pilot study, we employed quantum-chemistry-based software QCxMS to generate collision-induced dissociation mass spectra for 121 compounds from the Blood Exposome Database. We developed a scalable computational framework that integrates QCxMS and additional tools, utilizing a grid-based parameter selection strategy and defined coverage criteria. Our approach systematically explored protomeric isomers and applied predefined parameter combination sets sequentially based on molecular structures. This workflow produced high-quality in silico spectra for 81 compounds that achieved entropy similarity scores >= 700 and at least two matching fragment ions against the NIST23 library, yielding 71% spectral coverage. These results highlight the importance of optimizing simulation parameters and accounting for protomeric diversity to enhance the spectral quality and computational efficiency. This workflow provides a practical strategy to add mass spectral data for most compounds in the Blood Exposome Database at reasonable computational cost, supporting the spectral library expansion for improved compound annotation in exposomics.
https://doi.org/10.1021/jasms.5c00179

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Mo, Y. Q., Zhong, J. Y., Teng, M. J., Peng, J. C., Huang, H., Aschner, M.*, et al.*
Advances in Research on Neurotoxicity and Mechanisms of Manganese, Iron, and Copper Exposure, Alone or in Combination.
Journal of Applied Toxicology, Vol. **45** n° (10), (2025), 1968-1983 p.

Manganese (Mn), iron (Fe), and copper (Cu) are all essential trace elements for the human body; however, exposure to excessive amounts of these metals, either alone or in combination, can lead to neurotoxicity. Mn, Fe, and Cu can impair the nervous system through oxidative stress, apoptosis, and mitochondrial dysfunction. Mn disrupts dopamine neurogenesis through overexpression of alpha-synuclein (alpha-syn). Fe increases oxidative damage to lipids, proteins, and DNA through the Fenton reaction, leading to ferroptosis. Cu elevates nitrite oxide levels and inhibits the antioxidant system. Compared to exposure to individual metals, combined exposure to Mn and Fe results in less toxicity, suggesting an antagonistic effect. Combined exposure to Mn and Cu may exacerbate hepatocyte injury and mitochondrial dysfunction, leading to severe brain dysfunction. In Alzheimer's disease (AD), Fe and Cu contribute to the accelerated formation and accumulation of beta-amyloid (A beta) plaques, promote Fenton chemistry, and lead to the generation of reactive oxygen species (ROS) and localized neuroinflammation.
However, the mechanistic basis of neurotoxicity arising from combined exposure to Mn, Fe, and Cu remains poorly understood, underscoring the need for further research to elucidate their synergistic effects and to inform prevention and therapeutic strategies for related neurodegenerative disorders.
https://doi.org/10.1002/jat.4833

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Motteau, S., Dervilly, G., Cariou, R., Margalef, M., Lamoree, M., Hamers, T.*, et al.*
Determination of Chemical Mixtures in Environmental, Food, and Human Samples Using High-Resolution Mass Spectrometry-Based Suspect Screening Approaches.
Environmental science & technology, Vol., (2025), p.

Chemical contaminants are widely dispersed in the environment in all its dimensions, posing significant public health problems. Comprehensive knowledge of these stressors is a prerequisite for assessing the associated risk and implementing public policy measures to reduce the level of population exposure. Nontargeted suspect screening approaches broaden the knowledge of the chemical human exposome. We developed and used a suspect screening method based on large spectral libraries. Chemical profiling was based on a combined LC- and GC-HRMS approach. The methodology was applied to 16 samples spanning the environment, food, and health continuum.
Using a combination of matching and scoring data, a total of 547 compounds were likely identified, from which the chemical structure of 63 molecules was confirmed to the highest level of certainty. Wastewater, and more generally environmental samples, had the highest number of chemicals detected, while fish samples had a lower number. Pharmaceuticals, pesticides, and personal care product-related compounds were found to be the most common compounds in and between the extracts, particularly in water and serum samples. Many natural and endogenous compounds were consistently annotated in the samples submitted for analysis, regardless of the compartment investigated.
https://doi.org/10.1021/acs.est.4c12608

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Temkin, A. M., Subramaniam, V., Friedman, A., Fleury, E., De Montagnac, D., Campbell, C.*, et al.*
A cumulative dietary pesticide exposure score based on produce consumption is associated with urinary pesticide biomarkers in a U.S. biomonitoring cohort.
International journal of hygiene and environmental health, Vol., (2025), 114654

Pesticide exposure has been linked to chronic health harms, yet the effects of cumulative dietary exposure

to pesticide mixtures are poorly understood. A pesticide load index was created to rank produce based on pesticide contamination from national pesticide residue testing data for 44 produce types, primarily collected from 2013 to 2018. Three indices were created utilizing different indicators of pesticide contamination and toxicity. Dietary pesticide exposure scores for 1837 individuals were calculated based on produce consumption from the 2015-2016 National Health and Nutrition Examination Survey (NHANES). Covariate-adjusted weighted linear regressions were used to estimate the change in average pesticide biomarker rank relative to dietary pesticide exposure scores. Pesticide load indices were calculated based on detections of 178 unique parent pesticides, or 42 parent pesticides with matched urinary biomarkers in NHANES. Increasing dietary pesticide exposure scores were not associated with average pesticide biomarker rank (beta [95% CI] = 0.02 [-0.34, 0.38]) and were consistent across scores that utilized the different indices. Matching pesticides in food and urine, results in a slightly stronger association (beta [95% CI] = 0.09 [-0.32, 0.51]). Excluding potatoes resulted in a positive significant association (beta [95% CI]=0.75 [0.35, 1.14]). When excluding potatoes, consumption of fruits and vegetables weighted by pesticide contamination was associated with higher levels of urinary pesticide biomarkers for organophosphate, pyrethroid, and neonicotinoid insecticides. Future research could use this methodology, with the recommendation to exclude potatoes, to assess the impact of dietary pesticide exposure on health outcomes.
https://doi.org/10.1016/j.ijheh.2025.114654

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3. Approches métabolomiques

Hu, H. E., Zhou, Q., Cao, K., Jiang, Y., Xiang, J. J., Wu, J., *et al.*
Metabolome-wide associations with short-term exposure to PM2.5-bound polycyclic aromatic hydrocarbons : a study in older adults.
Frontiers in Public Health, Vol. **13**, (2025).

Background: Emerging evidence links fine particulate matter (PM2.5) and its polycyclic aromatic hydrocarbon (PAH) components to adverse health outcomes. However, the biological mechanisms driving these associations remain unclear. This study innovatively integrates personal exposure monitoring and untargeted metabolomics in an older adult population to investigate the differential impacts of individual PM2.5-bound PAHs on metabolic pathways and elucidate their roles in health risks.
Methods: In this study, we enlisted the participation of 112 healthy older adults. We employed personal samplers to monitor the concentrations of pollutants throughout the study period. Furthermore, we conducted an untargeted metabolomic analysis of plasma samples using a liquid chromatograph mass spectrometer (LC-MS). A general linear regression model was utilized to investigate the significant relationships between metabolites and pollutants. Metabolic pathway enrichment analysis was performed to reveal the disturbed metabolic pathways related to PM2.5-bound PAHs.
Results: Our study demonstrated that short-term exposure to PM2.5-bound PAHs may induce acute perturbations in plasma metabolites among the older adult population. We found that exposure to LMW PAHs in PM2.5 were correlated with amino acid metabolic pathways, while HMW-PAHs are associated with fatty acid and cholesterol metabolism pathways. While PM2.5 mass was higher in summer, the toxic PAHs component of PM2.5 was substantially higher in winter, contributing to greater observed toxicity.
Conclusion: The plasma metabolome presents a promising resource for biomarkers and pathways, elucidating the biological mechanisms of PM2.5-bound PAHs. Our findings suggest that the cholesterol and citric acid metabolites, as well as the cholesterol biosynthesis and citric acid cycle pathways they affect, may play important roles in the health damage caused by PAHs, providing potential insights into the pathogenic processes underlying the impact of PM2.5-bound PAHs.
https://doi.org/10.3389/fpubh.2025.1609724

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Hu, X., Liu, Y. Y., Ma, Y. P., Zhang, J., Ma, L. A., Chen, W. Q.*, et al.*
Untargeted Metabolomics Uncovers Food Safety Risks : Polystyrene Nanoplastics Induce Metabolic Disorders in Chicken Liver.
Foods, Vol. **14** (16), (2025).

Polystyrene nanoplastics (NPs) threaten agricultural ecosystems and the food chain; however, their hepatotoxicity in chickens, a key poultry species, remains unclear. This study investigated the effects of chronic NP exposure on hepatic metabolism to evaluate food safety risks in poultry products.
Chickens were orally exposed to 100 nm polystyrene NPs via feed for 120 days. Histopathological evaluation, serum biochemical analysis revealed hepatotoxicity in NP-exposed poultry, characterized by histopathological liver injury, elevated lipid droplet accumulation, significantly increased alanine aminotransferase (ALT) activity, and elevated triglyceride (TG) levels ($p < 0.05$). Untargeted LC-MS/MS Metabolomics profiling identified 193 differentially abundant metabolites-predominantly organic acids and lipids-with L-leucine and NADH emerging as pivotal metabolic hubs. A KEGG pathway analysis demonstrated significant enrichment in purine metabolism and oxidative phosphorylation, while a gene set enrichment analysis (GSEA) confirmed the suppression of ABC transporters. Notably, the key biomarkers 9-cis-retinal and phenylalanyl phenylalanine were significantly altered, reflecting metabolic disturbances linked to NPs exposure. Overall, this study characterized exposure-associated metabolic signatures and established NP-induced hepatic injury phenotypes in poultry production systems.
https://doi.org/10.3390/foods14162781

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Oresic, M., Karu, N., Zhao, H. N., Moseley, A., Hankemeier, T., Wishart, D. S.*, et al.*
Metabolome informs about the chemical exposome and links to brain health.
Environment international, Vol. **203**, (2025), 109741-109741 p.

The metabolome is an intermediate phenotype, summarizing the profile of all small molecules (<1.5kDa) in biospecimens. The metabolome provides a readout for the net influence of the chemical exposome, diet, gut microbiome, and genome on human health. Metabolic changes observed in exposome studies may thus provide clues about adverse outcome pathways related to cancer, diabetes, heart disease, cognitive impairment and other neurological conditions such as Alzheimer's disease (AD).
Whilst the number of human cohort studies including both metabolomic and exposomic profiles is increasing, they are particularly limited in the domain of neurological conditions. Environmental exposures and chemical toxicants are known to have significant effects on the brain, gut microbiome, and gut-brain axis. Environmental chemicals of greatest interest include bisphenols, phthalates, persistent organic pollutants such as polychlorinated biphenyls (PCBs) and per- and poly-fluoroalkyl substances (PFAS), heavy metals, chemicals from household products and pesticides/herbicides ; all of which may increase the risk of AD as they impact relevant biochemical mechanisms, especially with chronic exposure.
In this review we describe how the chemical exposome can be assessed, including the approach our consortium is taking in the context of AD. Further, we review the current evidence about the impact of the chemical exposome on cognition as well as its influence on the risk and pathogenesis of AD. Finally, we highlight our approach to study the exposome in AD as part of large national and international collaborative efforts on the topic.
https://doi.org/10.1016/j.envint.2025.109741

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De Ávila, R. I., Carreira-Santos, S., Siino, V., Silic, L. L., Merényi, G., Bergendorff, O.*, et al.*
P32-07 Can we unravel cocktail effects in skin sensitization ? A proteomics-centred approach.
Toxicology Letters, Vol. **411**, (2025). Abstracts of the 59th Congress of the European Societies of Toxicology (EUROTOX 2025) TOXICOLOGY ADDRESSES SOCIETY'S REAL LIFE RISKS FOR SUSTAINABLE HEALTH AND WELL

BEING.

Des modèles cellulaires qui imitent les cellules dendritiques (CD) ont été utilisés avec succès pour développer des tests permettant de prédire la capacité des produits chimiques à provoquer une sensibilisation cutanée. Les CD jouent un rôle essentiel dans la réponse immunitaire en faisant le lien entre l'immunité innée et l'immunité adaptative. Dans le domaine de la sensibilisation cutanée, il est particulièrement important de comprendre et de prédire les effets des mélanges chimiques. Des effets combinés ou « cocktails » peuvent résulter d'une exposition simultanée à plusieurs produits chimiques et peuvent amplifier ou supprimer les effets indésirables causés par des produits chimiques individuels. Dans cette étude, nous avons examiné trois produits chimiques du caoutchouc sensibilisants, le diéthyldithiocarbamate de zinc (ZDEC) et le dibutyldithiocarbamate de zinc (ZDBC), que l'on trouve couramment dans les gants de protection, et la 1,3-diphénylguanidine (DPG), qui forment ensemble le mélange de carba. Le mélange de carba est couramment utilisé dans les tests épicutanés pour le diagnostic de la dermatite de contact allergique, bien que l'interprétation des résultats des tests puisse être difficile. (…)
https://doi.org/10.1016/j.toxlet.2025.07.981

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Chen, L., Zhao, S. S., Li, X. K., Wang, X. L., Yu, G. L.
Synergistic effects of microplastics and bioaerosols : emerging trends in urban air pollution complexification and public health implications.
Environmental Research, Vol. **286**, (2025), p.

Urban air is increasingly contaminated with complex mixtures of microplastics (MPs) and bioaerosols (BAs), whose co-exposure may pose unique health risks. This review highlights the synergistic interaction between MPs and BAs during atmospheric transport and human exposure.
We summarized the sources and physicochemical characteristics of airborne MPs (fragments and fibers from urban waste and textiles) and BAs (bacteria, fungi, and viruses from soil, water, and human activity) and their shared dispersion pathways via wind and resuspension. Both pollutants deposit in the respiratory tract upon inhalation. Notably, MPs may function as potential microbial carriers. Laboratory and field data indicate that airborne plastics harbor distinct microbial biofilms (often with antibiotic-resistant bacteria/genes) and may prolong virus survival (e.g., SARS-CoV-2 on plastic surfaces). These MP-microbe aggregates can enhance pathogen persistence and increase host exposure. In lung models, inhaled MPs disrupt epithelial barriers and surfactant layers, inhibit cell proliferation, and trigger inflammation (tumor necrosis factor-alpha, interleukin-6, IL-1 beta, and tumor growth factor-beta) and oxidative stress (depleting SOD/CAT and generating reactive oxygen species).
Assessing this co-pollution requires advanced methods. Standard spectroscopic tools (micro-Fourier-transform infrared spectroscopy and micro-Raman) and emerging methods such as laser direct infrared imaging enable polymer identification and MP sizing. Similarly, cultureindependent high-throughput sequencing techniques (e.g., 16S/18S rRNA gene profiling) elucidate airborne microbial diversity. Novel real-time aerosol counters (e.g., UV-LIF optical sensors) and machine learning analytics are being applied to monitor BA load.
Finally, we discussed implications for vulnerable subpopulations (children, the elderly, and individuals with chronic respiratory conditions) who may be more susceptible to combined MP/BA effects. The review proposes future directions, which include developing integrated toxicological models, multi-omics analyses of particle-microbe interactions, and establishing coordinated environmental health surveillance to track this emerging urban pollutant mixture.
https://doi.org/10.1016/j.envres.2025.122808

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Li, M.-Y., Chen, T.-H., Liu, Y., Xiang, M.-D., Kuang, H.-X., Yu, Y.-J.
Exploring the Impact of E-Waste Exposure on Childhood Blood Pressure : Metabolomics Analysis and Risk Prediction.
Environment & Health, Vol. **PrePrint**, (2025), p.

Le fardeau alarmant de l'hypertension dans les zones de recyclage des déchets électroniques (EA) constitue un défi de santé publique urgent. Bien que de plus en plus de preuves établissent un lien entre les changements de la pression artérielle et l'exposition aux composés organiques volatils (COV) et aux métaux (loïdes), des lacunes persistent dans la compréhension des mécanismes moléculaires et la mise au point d'outils de dépistage opérationnels. Notre objectif est d'étudier les effets de la co-exposition aux COV et aux métaux (loïdes) sur la pression artérielle des enfants atteints d'EA, de découvrir les mécanismes métaboliques via la métabolomique urinaire et de développer un modèle prédictif basé sur un algorithme d'apprentissage automatique pour identifier les enfants présentant des risques potentiels d'hypertension. Nous avons mesuré les pressions artérielles systolique (TAS) et diastolique (TAD), les métabolites urinaires des COV (COVm), les métaux (loïdes) et les profils métabolomiques chez les enfants EA (n = 426). Les résultats ont montré que la prévalence de l'hypertension dans la population étudiée (12,7 %) dépassait significativement l'estimation représentative à l'échelle nationale de 3,11 %. Des taux élevés de COVm 4 et de 5 métaïdes urinaires étaient associés à une augmentation de la TAS ou de la TAD ($p < 0,05$). L'analyse en composantes principales a permis d'identifier l'association positive entre le mélange dominé par le COVm et la TAS et la TAD, où l'acide 2-aminothiazoline-4-carboxylique (ATCA) a contribué de manière plus substantielle ($p < 0,05$). La métabolomique urinaire a révélé que la N-phénylacétyl-l-glutamine (PAGln) et l'acide pyroglutamique sont des médiateurs essentiels reliant l'exposition aux COV et aux métaux (loïdes) à l'élévation de la pression artérielle chez l'enfant, suggérant que le métabolisme du microbiote intestinal et le cycle γ-glutamyle peuvent jouer un rôle important dans l'hypertension associée aux polluants. Notamment, notre modèle prédictif a atteint une précision de 83 % pour différencier les enfants présentant un risque potentiel d'hypertension, le glucuronide d'androstane (métabolisme des stéroïdes) et le PAGln étant les caractéristiques les mieux classées.
Ces résultats ont collectivement indiqué que l'exposition aux COV et aux métaux (loïdes) peut contribuer à l'élévation de la pression artérielle chez les enfants atteints d'EA en perturbant le métabolisme du microbiote intestinal, le cycle γ-glutamyle et le métabolisme des stéroïdes. Cette étude fait progresser considérablement notre compréhension des mécanismes potentiels entre l'exposition aux COV et aux métaux (loïdes) et l'élévation de la pression artérielle chez l'enfant, tout en fournissant des outils pratiques pour la détection et l'intervention précoces des risques.
https://doi.org/10.1021/envhealth.5c00189

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Jimenez-Nieto, A., Izquierdo-Sandoval, D., Sancho, J. V., Granell, M., Gonzalez-Ruiz, A., Ballesteros, M.*, et al.*
Evaluating human serum for trace levels of lipophilic organic chemicals : A novel GC-(Q)Orbitrap methodology.
Talanta, Vol. **298** (Pt A), (2025), 128897.

The exposome encompasses all environmental exposures across the lifespan, with chemical pollutants representing a major component. A robust sample preparation and multiresidue analytical method based on GC-(Q)Orbitrap technology was developed and validated for comprehensive characterization of the human chemical exposome in serum. The method demonstrated high accuracy and satisfactory performance at validation levels of 2 and 10ngmL-1, enabling the simultaneous quantification and confirmation of 198GC-amenable compounds from diverse physicochemical properties (e.g., OPEs, PCBs, PAHs, and alkyl-PAHs). The validated methodology was applied to 24 serum samples from pregnant women participating in the INSULIN cohort (Hospital Joan XXIII, Tarragona, Spain), detecting ten chemicals (three PAHs, six alkyl-PAHs, and one synthetic antioxidant) at concentrations between 1 and 4ngmL-1. Furthermore, nontarget screening tentatively identified 64 additional compounds from various chemical

families, highlighting the potential of GC-(Q)Orbitrap for broad-spectrum non-target analysis and holistic exposome characterization. This approach overcomes LC-based analytical limitations by enabling detection of low-to-medium polarity and semi-volatile compounds, demonstrating its value for expanding chemical coverage in human biomonitoring. Overall, this validated methodology provides a powerful tool for exposome-wide association studies (ExWAS) and public health assessments by enabling more comprehensive evaluation of human chemical exposures.
https://doi.org/10.1016/j.talanta.2025.128897

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4. Modèles d'analyses, outils, méthodes

Lee, J., Barupal, D.
Simulating Collision-Induced Dissociation Tandem Mass Spectrometry (CID-MS/MS) for the Blood Exposome Database Using Quantum Chemistry Methods - A Pilot Study.
Journal of the American Society for Mass Spectrometry, Vol., (2025), p.

A significant number of compounds in exposome databases and chemical inventories lack mass spectral data due to the nonavailability of reference standards. To address this limitation, computational chemistry methods can be utilized to extend mass spectral libraries for a set of chemicals.
In this pilot study, we employed quantum-chemistry-based software QCxMS to generate collision-induced dissociation mass spectra for 121 compounds from the Blood Exposome Database. We developed a scalable computational framework that integrates QCxMS and additional tools, utilizing a grid-based parameter selection strategy and defined coverage criteria. Our approach systematically explored protomeric isomers and applied predefined parameter combination sets sequentially based on molecular structures.
This workflow produced high-quality in silico spectra for 81 compounds that achieved entropy similarity scores >= 700 and at least two matching fragment ions against the NIST23 library, yielding 71% spectral coverage. These results highlight the importance of optimizing simulation parameters and accounting for protomeric diversity to enhance the spectral quality and computational efficiency. This workflow provides a practical strategy to add mass spectral data for most compounds in the Blood Exposome Database at reasonable computational cost, supporting the spectral library expansion for improved compound annotation in exposomics.
https://doi.org/10.1021/jasms.5c00179

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Jovanovic, G., Bezdan, T., Romanic, S. H., Matek Saric, M., Biosic, M., Mendas, G., *et al.*
Application of the AI-Based Framework for Analyzing the Dynamics of Persistent Organic Pollutants (POPs) in Human Breast Milk.
Toxics, Vol. **13** (8), (2025), p.

Human milk has been used for over 70 years to monitor pollutants such as polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs). Despite the growing body of data, our understanding of the pollutant exposome, particularly co-exposure patterns and their interactions, remains limited. Artificial intelligence (AI) offers considerable potential to enhance biomonitoring efforts through advanced data modelling, yet its application to pollutant dynamics in complex biological matrices such as human milk remains underutilized. This study applied an AI-based framework, integrating machine learning, metaheuristic hyperparameter optimization, explainable AI, and postprocessing, to analyze PCB-170 levels in breast milk samples from 186 mothers in Zadar, Croatia. Among 24 analyzed POPs, the most influential predictors of PCB-170 concentrations were hexa- and hepta-chlorinated PCBs (PCB-180, -153, and -138), alongside p,p'-DDE. Maternal age and other POPs exhibited negligible global influence. SHAP-based interaction analysis revealed pronounced co-behavior among highly chlorinated congeners, especially PCB-138-PCB-153, PCB-

138-PCB-180, and PCB-180-PCB-153. These findings highlight the importance of examining pollutant interactions rather than individual contributions alone. They also advocate for the revision of current monitoring strategies to prioritize multi-pollutant assessment and focus on toxicologically relevant PCB groups, improving risk evaluation in real-world exposure scenarios.
https://doi.org/10.3390/toxics13080631

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Broughton, R., Feshuk, M., Stanfield, Z., Isaacs, K. K., Friedman, K. P.
Development of mathematical new approach methods to assess chemical mixtures.
Computational Toxicology, Vol. **35**, (2025).

The Toxicity Forecaster (ToxCast) program contains targeted bioactivity screening data for thousands of chemicals, but chemicals are often encountered as co-exposures. This work evaluated the feasibility of using single chemical ToxCast data to predict mixture bioactivity assuming chemical additivity. Twenty-one binary mixtures and their single components, inspired by consumer product chemical exposures, were screened in concentration-response using a multidimensional in vitro assay platform for transcription factor activity.
Three models were applied to simulate mixtures' concentration-responses : concentration addition (CA), independent action (IA), and a model that treats the mixture as the most potent single chemical component (MP). Uncertainty in the modeled and observed mixture points of departure and full concentration-responses was considered using bootstrap resampling and a Bayesian statistical framework. Approximately 80 % of the predicted mixture point of departure values were within +/- 0.5 on a log10-micromolar scale of the observed concentrations ; a majority of these predicted points of departure were protective (90-96 %), whether using CA, IA, or MP derived with the screened single components, when compared to the observed mixture. For most mixtures, >= 80 % of the observed mixture concentration-response data points fell within the modeled 95 % prediction interval, suggesting it would be difficult to observe deviations from additivity when accounting for experimental and mixtures modeling uncertainties. As it is resource-prohibitive to screen all mixtures, a case study to estimate bioactivity : exposure ratios for mixtures of per-and polyfluoroalkyl chemicals demonstrated the utility of operationalizing existing ToxCast data with mixtures modeling that includes uncertainty to predict potential risk from co-exposures.
https://doi.org/10.1016/j.comtox.2025.100376

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Dai, R., Zhang, H., Yang, W., Wang, X., Li, X., Yu, Y.*, et al.*
A simple and high-throughput ICP-MS method for the determination of 46 elements in urine : Biomonitoring of occupational exposure in automotive workers.
Talanta Open, Vol. **12**, December 2025, 100559

Monitoring urinary metal concentrations is crucial for assessing occupational exposure and associated health risks. Inductively coupled plasma mass spectrometry (ICP-MS) is widely considered the method of choice for multi-element analysis due to its high sensitivity, low detection limits, and broad dynamic range. This study presents a simple and rapid ICP-MS method for the simultaneous determination of 46 elements in urine, utilizing 2 % nitric acid and 1.5 % ethanol (v/v) for sample pretreatment.
This approach effectively mitigates matrix effects and carbon-based interferences. The method demonstrated excellent linearity (coefficient of determination, $R^2 \geq 0.9985$), precision (relative standard deviation, RSD < 8 %), and accuracy (recoveries 80–120 %). The method was applied to analyze 268 urine samples from automotive manufacturing workers. Several elements of occupational relevance, including Nickel (Ni), tungsten (W), molybdenum (Mo), titanium (Ti) and Cadmium (Cd), as well as essential elements such as iron (Fe), copper (Cu), and zinc (Zn), were elevated compared with general population references, indicating complex multi-metal exposure profiles.
This work provides a validated and efficient tool for occupational biomonitoring and delivers valuable

elementomic data to support exposure assessment, workplace interventions, and future research on the health effects of multi-metal exposure.
https://doi.org/10.1016/j.talo.2025.100559

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Lamon, L., Paini, A., Siccardi, M., Doyle, J., Mcnamara, C., Galea, K.*, et al.*
Physiologically based toxicokinetic models in aggregate exposure : a review.
Toxicology letters, Vol., (2025), 111725.

This literature review explores the application of Physiologically Based Kinetic (PBK) models in aggregate exposure (AE) assessment across different chemical classes. It builds on the screening of 1119 publications and the identification of 40 relevant articles. The most frequently studied chemicals include volatile organic compounds and plant protection products, with metals, personal care products, persistent organic pollutants and plasticisers also represented. Most studies reported in this review are applied to human populations and build on human biomonitoring (HBM) data to enhance model reliability. However, some studies use animal models (primarily rat models) and apply cross-species extrapolation to the human AE scenario. Occupational exposure is taken into consideration as part of the AE scenario in a few studies. Many of the reviewed studies are designed in support of chemical risk assessment (CRA), illustrating the wide applicability of PBK models.
The review discusses the joint role of HBM data and PBK model in AE scenarios, highlighting its importance for a reliable risk assessments. The studies identified and discussed in this review suggest a broad interpretation of AE. The diversity across case reported studies is attributed to varying interpretations and existing definitions of AE. Finally, the roles of forward and reverse dosimetry in refining AE assessments are discussed, highlighting their importance for future research.
This scoping review provides a comprehensive overview of PBK model applications in addressing AE, serving as a valuable foundation for future research and development aimed at advancing human health protection towards the Next-Generation Risk Assessment (NGRA). Copyright © 2025 Elsevier B.V. All rights reserved.
https://doi.org/10.1016/j.toxlet.2025.111725

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Young, A. S., Gennings, C., Eick, S. M., Liang, D., Walker, D. I.
A Statistical Workflow for Analyzing the Untargeted Chemical Exposome and Metabolome in Epidemiologic Studies Using High-Dimensional Mixture Methods.
Exposome, Version manuscrite pre-print, (2025). osaf010.

Les humains sont exposés simultanément à plus de milliers de produits chimiques, mais la recherche s'est traditionnellement concentrée sur les effets sur la santé d'un seul produit chimique à la fois. Non seulement les analyses monochimiques sous-estiment le risque total pour la santé, mais elles ignorent également le biais lié à la multicolinéarité et à la confusion entre les produits chimiques. Des méthodes statistiques avancées de mélange permettent de relever ces défis et de nous permettre à la fois d'estimer l'effet cumulatif sur la santé des mélanges chimiques et d'identifier les principaux contributeurs chimiques. Dans le même temps, le profilage non ciblé des exposomes chimiques par spectrométrie de masse à haute résolution (HRMS) permet désormais de mesurer plus de 100 000 signaux chimiques dans des échantillons biologiques. Cependant, la plupart des méthodes de mélange ne peuvent pas évaluer les données d'exposome non ciblées contenant plus de variables chimiques que d'échantillons. La régression à somme quantile pondérée avec sa récente implémentation de sous-ensembles aléatoires (WQSRS) est une méthode de mélange unique et statistiquement puissante pour les données d'exposome de grande dimension. Il estime les poids des produits chimiques par rapport à l'indice de mélange sur de nombreuses répétitions différentes dans lesquelles seul un petit sous-ensemble aléatoire de produits chimiques est utilisé à la fois, ce qui permet de décorréler les données et d'éviter le surapprentissage.
Dans cet article, nous discutons de notre flux de travail statistique et des considérations importantes pour l'application de WQSRS à l'épidémiologie des exposomes, y compris la quantification manuelle des non-

détections, les exclusions répétées personnalisées pour les données appariées, la présélection de produits chimiques exogènes, les décisions de paramètres, les options d'interprétation et les visualisations. Nous décrivons ensuite son application à l'analyse de l'enrichissement des voies fonctionnelles avec des données intégrées d'exposome-métabolome pour explorer les mécanismes biologiques sous-jacents. Ces approches de science des données permettront à l'épidémiologie des exposomes de découvrir des facteurs de risque jusque-là inconnus, d'estimer les risques cumulatifs pour la santé à partir de mélanges chimiques totaux et d'obtenir des informations mécanistes.
https://doi.org/10.1093/exposome/osaf010

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5. Coexpositions aux métaux lourds

Effets neurologiques
Effets rénaux et cardio-vasculaires
Effets respiratoires
Grossesse, reproduction

Dan, Y., Long, P., Jiang, Q., Wang, Y., Zhang, X., Yuan, R., *et al.*
Multiple plasma metal exposures and incident anemia in middle-aged and elderly individuals: The Dongfeng-Tongji cohort.
Ecotoxicol Environ Saf, Vol. **303**, (2025), 118820.

Anemia is a global health concern. However, prospective studies on the relationships between multiple metal exposures and incident anemia remain limited. This study included 3928 participants from the Dongfeng-Tongji cohort. Using the generalized linear (GLM) model to estimate the associations between individual metals and anemia. The least absolute shrinkage and selection operator (LASSO) regression model identified metals associated with anemia. Additionally, Bayesian kernel machine regression (BKMR) and Quantile g-computation (Q-g) regression models were employed to identify the significant contributing metals. Compared to the lowest quartiles, the odds ratios (ORs) and 95 % confidence intervals (CIs) for the fourth quartiles were: aluminum 1.64 (1.17, 2.32), arsenic 1.57 (1.12, 2.20), barium 1.56 (1.12, 2.19), molybdenum 1.92 (1.38, 2.69), rubidium 0.71 (0.51, 0.98), strontium 1.55 (1.13, 2.14), vanadium 1.67 (1.18, 2.37). The ORs and 95 % CIs for the risk of incident anemia per one interquartile range (IQR) increase were: selenium 0.88 (0.78, 1.00), and zinc 1.20 (1.04, 1.38). LASSO regression models identified eight plasma metals potentially associated with incident anemia. Six metals, significant in both the GLM and LASSO models, were selected for further analysis. The BKMR model demonstrated a positive association between mixed metals and anemia. Q-gcomp regression indicated rubidium mainly contributed to negative weights, while molybdenum and vanadium contributed to positive weights. This study found that elevated plasma levels of arsenic, molybdenum, strontium, and vanadium were associated with higher risks of incident anemia, while rubidium and selenium had a protective role. These findings indicated that controlling metal exposures would be important in preventing anemia.
https://doi.org/10.1016/j.ecoenv.2025.118820

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5.1. Effets neurologiques

Sarmah, D., Nirala, A., Hazarika, H.
Heavy metal-induced neurotoxicity and endocrine disruption from e-waste : emerging health challenges and intervention strategies.
Toxicology and Environmental Health Sciences, (2025), Preprint.

The global rush of electronic waste has raised serious health problems and environmental issues, particularly in areas that do not have proper disposal facilities. E-waste contains a wide range of diverse toxic heavy metals, such as lead, cadmium, mercury, and arsenic. Chronic or repeated exposure can cause damage to both the nervous and endocrine systems, which may lead to risk factors for neurotoxicity, such as Alzheimer's disease, Parkinson's disease, and endocrine disruption, by interfering with hormone production.
The purpose of this review is to investigate how exposure to heavy metals from e-waste leads to neurological impairment and endocrine disruption and to highlight recent advances in public health control to combat these risks.
Information on this review article was collected from the literature available in online scientific databases such as PubMed, Google Scholar, Springer, the Wiley Online Library, and Science Direct. The work was chosen on the basis of the inclusion criteria agreed upon by all the authors.
This study suggested that some heavy metals can penetrate the CNS, which induces oxidative stress, inflammation, and cell damage that can lead to cognitive dysfunction and neurological disorders. Moreover, these metals are capable of mimicking and blocking hormones, causing endocrine disruption.
Exposure to heavy metals from e-waste is a growing problem for both endocrine and brain health. Preventive measures should be taken through synergistic efforts involving policy changes, recycling practices, public health interventions, and specific treatments. Identification of these health risks is essential to avoid long-term health effects.
https://doi.org/10.1007/s13530-025-00268-6

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Gonzales, G. F., Ordonez-Aquino, C.
Neurodegeneration and Environmental Health: Emerging Role of Polluting Metals in Alzheimer's Disease (AD): A Narrative Review.
Vol., (2025), p.

Alzheimer's disease (AD) is a complex neurodegenerative condition characterized by progressive cognitive decline and neuronal dysfunction. In addition to the known, genetic factors, such as the APOE ε4 allele, growing evidence points to the influence of environmental elements, particularly polluting metals and air pollution, in the development and progression of AD.
This review explores how metals like iron (Fe), copper (Cu), and manganese (Mn), when present in excess or dysregulated, contribute to oxidative stress, neuroinflammation, mitochondrial damage, and pathological protein aggregation in the brain. Moreover, air pollution, especially exposure to particulate matter, has been associated with higher AD risk. The role of gut dysbiosis and systemic inflammation is also discussed as a potential link between environmental exposure and neurodegeneration. This synthesis of current literature highlights the importance of recognizing environmental metals as modifiable risk factors for AD and the urgent need to incorporate environmental health considerations into dementia prevention strategies.
https://doi.org/10.20944/preprints202508.0197.v1

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Yuanxin Guo, Y. C., Houfeng Zhou Et Al. .
Association between heavy metals'exposure and depression: Findings of the NHANES from 2003 to 2020.
Vol. PREPRINT (Version 1) available at Research Square.

Heavy metal exposure is established as depression-related, yet limited research examines combined metal impacts. This study assessed multi-metal exposure's collective risk and identified key contributors.
Analyzing National Health and Nutrition Examination Survey data, adults with complete data on nine urinary metals (antimony, barium, cadmium, cobalt, cesium, molybdenum, lead, thallium and tungsten),

three blood metals (cadmium, mercury and lead), depression status, and key covariates were assessed via four methods (multivariate logistic regression, restricted cubic spline (RCS) regression, weighted quantile sum (WQS) regression and Bayesian kernel machine regression (BKMR) to evaluate metal-depression associations.
Among 8,814 participants (731 with depression), those with depression showed higher urine and blood cadmium levels, but lower blood mercury and urine thallium levels compared to controls. Adjusted analyses linked elevated urine antimony (OR = 1.34, p = 0.029) and tungsten (OR = 1.42, p = 0.008) to increased depression risk, while higher urine thallium (OR = 0.52, p < 0.001) and blood mercury (OR = 0.7, p = 0.005) reduced risk. RCS analysis revealed nonlinear relationships between depression and urine cadmium (p = 0.004), cobalt (p = 0.005), lead (p = 0.024), antimony (p < 0.001), tungsten(p < 0.001), as well as blood cadmium (p < 0.001) and mercury (p < 0.001). However, the WQS index was postive associated with depression (OR:1.17, 95% CI: 1.02–1.35, p = 0.026) but a negative correlation (OR:0.81, 95% CI: 0.7–0.94, p = 0.006). BKMR analysis confirmed multi-metal co-exposure elevates depression risk, and urinary barium showed the highest BKMR-derived posterior inclusion probability (PIP = 0.448).
Heavy metal mixture exposure elevates depressive disorder risk, with tungsten and antimony as key risk drivers, mercury and thallium showing protective effects, and barium emerging as a potential contributor. Further studies needed to validate these metal-specific impacts and uncover additional depression-linked metals.
https://doi.org/10.21203/rs.3.rs-7038470/v1

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Yang, W., Yang, Y., Cao, W., Xie, Q., Wei, M., Wang, S.*, et al.*
Association between mixed exposure to multiple metal elements and cognitive decline in older adults: The moderating role of sleep quality.
Ecotoxicology and environmental safety, Vol. **303**, (2025), 118941.

BACKGROUND: Cognitive decline among older adults has become an increasingly serious public health issue. Metal exposure may contribute to neurodegenerative processes; however, the combined effects of multiple metals and the potential moderating role of sleep quality on cognitive function remain unclear.
OBJECTIVE: To examine the associations between combined exposure to six metal elements-molybdenum (Mo), vanadium (V), nickel (Ni), strontium (Sr), arsenic (As), and cadmium (Cd)-in whole blood and cognitive function among community-dwelling older adults, and to assess whether these associations are modified by sleep quality.
METHODS: A total of 1273 older adults participated in the study. The concentrations of metal elements in whole blood were determined using Inductively coupled plasma mass spectrometer (ICP-MS). Cognitive performance was evaluated with the Mini-Mental State Examination (MMSE), while sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). Associations between individual metals and cognitive function were examined through multivariable linear regression. The combined impact of metal mixtures was analyzed using Bayesian kernel machine regression (BKMR) and weighted quantile sum (WQS) models. Additionally, interaction effects involving sleep quality were explored. RESULTS: Elevated levels of Mo, V, Ni, Sr, and Cd were significantly associated with lower MMSE scores. Significant interactions were observed between V and sleep quality and between Sr and sleep quality, suggesting that poor sleep may exacerbate the neurotoxic effects of metal exposure.
CONCLUSION: Exposure to various metal elements has been linked to reduced cognitive function in older adults, with the magnitude of this association varying by sleep quality. These results highlight the need to consider both environmental metal exposure and sleep health in efforts to prevent cognitive deterioration. To establish causal relationships and clarify underlying pathways, longitudinal research incorporating objective assessments of sleep is warranted.
https://doi.org/10.1016/j.ecoenv.2025.118941

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Li, Q., Liu, X., Zhou, Y., Wang, K., Liu, H., Fu, X.*, et al.*
The association between heavy metals co-exposures and depression: a convergence of network toxicology and epidemiology.
J Affect Disord, Vol., (2025), 120290 p.

As neurotoxic agents, heavy metals have been implicated in depression pathogenesis, yet epidemiological evidence on metal mixture associations remain limited. This study examined associations between cadmium (Cd), lead (Pb), selenium (Se), manganese (Mn), and their mixtures with depression in US adults. Using 2011-2018 NHANES data from 8565 participants (>/=20 years), we applied logistic regression, weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR) to evaluate individual and mixture associations. Subgroup analyses by age/sex, mediation analysis, and network toxicology for molecular mechanisms were conducted. The logistic regression revealed significant Cd-depression associations [OR (95 %CI): 1.43 (1.24,1.65)]. Mixture analyses demonstrated positive exposure-response relationships, with Cd contributing 75.4 % to the WQS mixture index and exhibiting the strongest association in BKMR. Network toxicology identified CASP3, TNF, ALB, AKT1, and JUN as core genes, with oxidative stress, transcription factor Ap-1 complex and protein serine/threonine kinase inhibitor activity emerging as key mechanistic components. Our findings highlight heavy metal mixtures, particularly Cd-dominated combinations, exhibit significant depression associations, and reveal the neurotoxic synergy in metal mixtures and identify molecular targets for intervention.
https://doi.org/10.1016/j.jad.2025.120290

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5.2. Effets rénaux, et cardio-vasculaires

Wagoner, R. S., Lopez-Galvez, N. I., Casarez, I. J., Canales, R. A., Beamer, P. I., Farland, L. V.*, et al.*
Longitudinal associations and interactions of heat and metal(loid) exposure with kidney outcomes in Mexican agricultural workers.
Environmental research, Vol. **285** (Pt 3), (2025), 122533.

BACKGROUND: Agricultural workers perform physically demanding labor in extreme heat, increasing their risk for kidney injury. Agricultural workers are also exposed to nephrotoxic metal(loid)s, yet little research examines the combined effects of heat and metal(loid) exposure on kidney health.
OBJECTIVE: This study assessed how simultaneous exposure to metal(loid)s and heat impacts acute kidney injury (AKI) and kidney function over time.
METHODS: As part of a longitudinal study, we followed a cohort of male grape farmworkers near the Arizona-Sonora border (n=77), collecting biological samples and questionnaires at two timepoints: at the beginning (i.e., baseline) and again at the end of the work season (i.e., follow-up). Physiological strain index (PSI) was estimated using inner ear temperature and heart rate. Urine samples were analyzed for metal(loid)s, specific gravity, and neutrophil gelatinase-associated lipocalin (uNGAL), while blood serum was used to calculate estimated glomerular filtration rate (eGFR). Linear mixed effect and linear regression models evaluated the impact of metal(loid)s and PSI on kidney health, incorporating interaction terms for chronic (seasonal) and acute (PSI) heat exposure.
RESULTS: Participants averaged 29 years old, with 35% primarily speaking an Indigenous language. Urinary arsenic (beta=0.35, 95%CI: 0.15, 0.55), cadmium (beta=0.27, 95%CI: 0.14, 0.40), and chromium (beta=0.54, 95%CI: 0.20, 0.88) were associated with increased uNGAL, while increased uranium was associated with reduced eGFR (beta=-2.45, 95%CI: 4.81, -0.08). Effects were attenuated in stratified models. Interactions showed chronic heat exposure exacerbated arsenic and cadmium's effects (arsenic-uNGAL, $p<0.01$; cadmium-uNGAL, $p=0.02$). No significant interactions were observed for acute heat stress.
DISCUSSION: Heat may modify the impact of toxic metal(loid)s on kidney health, emphasizing the need for workplace policies that mitigate heat stress among agricultural workers.

https://doi.org/10.1016/j.envres.2025.122533

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Wang, J., Wu, Q., Chen, B., Li, J., Jiang, J., Liao, X.*, et al.*
Urinary heavy metal burden and overactive bladder risk: a cross-sectional study based on NHANES 2005-2018.
Int J Surg, p. 10.1097/JS9.0000000000003214, August 19, 2025.

OBJECTIVE: We aimed to explore the relationship between urinary heavy metals and overactive bladder (OAB) among U.S. adults.
METHOD: Data were obtained from the National Health and Nutrition Examination Survey (NHANES) 2005-2018. Concentrations of heavy metals in urine were determined by laboratory tests and corrected for urinary creatinine using natural logarithm (ln) transformation. OAB was assessed using questionnaires. The association between each urinary heavy metal and OAB was first explored using multivariate logistic regression, followed by nonlinear correlation analyses and smoothed curve fitting, with stratified analyses and interaction tests for age and sex. In addition, weighted quantile sum (WQS) regression and quantile-based g-computation (qgcomp) analyses were implemented to explore the relationship between mixed heavy metal and OAB.
RESULTS: A total of 9086 participants were included in the final study. Multifactorial logistic regression analysis showed that cobalt (Co), lead (Pb), cadmium (Cd), and uranium (Ur) were positively associated with the risk of developing OAB, whereas barium (Ba) and thallium (Tl) were negatively associated with OAB. Nonlinear correlation analysis showed that the associations between the concentrations of Ba and Tl and OAB risk were nonlinear, and Pb, antimony (Sb), tungsten (Tu), Ur, and Cd showed significant positive correlations with OAB. WQS regression showed that OAB risk increased with increasing quartiles of the WQS index (odds ratio (OR) 1.202, 95% confidence interval (CI) 1.064, 1.357), with Cd showing the strongest positive correlation with OAB. When the mixture effect was constrained to be negative, an increase in the WQS index quartile corresponded to a 14.3% reduction in OAB risk (OR 0.857, 95% CI 0.778, 0.943), with Ba standing out as the most dominant. The results of qgcomp analysis showed that Cd had the largest positive weight of 0.5098, and Ba had the largest negative weight of 0.5976. CONCLUSION: Urinary heavy metals are significantly associated with OAB risk among U.S. adults. The metal contributing most to the positive correlation with OAB risk is Cd, while the metal contributing most to the negative correlation with OAB risk is Ba.
https://doi.org/10.1097/JS9.0000000000003214

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Zhong, J., Xu, Z., Yang, T., Liu, L., Zhang, R., Wang, Y.*, et al.*
Exploring the Impact of Urinary Metal Exposure on Blood Lipid Profiles in Chinese Adults: Mediating Roles of Health-Related Indicators.
Journal of the American Heart Association, Vol. **14** (16), (2025).

Background The relationship between urinary metal exposure and lipid profiles remains unclear, particularly regarding potential mediators. This study aimed to investigate associations between urinary metals and lipid levels and to explore mediating health indicators.
Methods We included 14 817 participants in the CMEC (Chinese Multi-Ethnic Cohort) study baseline data. Twenty-one urinary metals, 16 health indicators, and lipid profiles were measured to explore their relationships.Results In single-metal models, each unit increase in urinary zinc was associated with higher total cholesterol by 12%, triglycerides by 29%, and low-density lipoprotein cholesterol by 14%, along with lower high-density lipoprotein cholesterol by 3%, and increased odds of dyslipidemia (odds ratio, 1.76 [95% CI, 1.55-2.01]). In contrast, higher urinary sodium was associated with lower total cholesterol (-12%), triglycerides (-6%), low-density lipoprotein cholesterol (-7%), and decreased dyslipidemia risk (odds ratio, 0.87 [95% CI, 0.83-0.92]). In mixed exposure models, zinc, manganese, and cobalt were major contributors to dyslipidemia. Quantile regression revealed stronger effects of zinc in individuals with higher lipid levels.

Mediation analysis showed that waist-to-hip ratio and uric acid mediated 27.2% and 12.0% of the metal-dyslipidemia relationship, respectively.
Conclusions Urinary metal exposure is significantly associated with lipid abnormalities, particularly among individuals with higher lipid levels. Specific metals may influence lipid metabolism via adiposity and uric acid pathways. Therefore, reducing exposure to certain urinary metals may contribute to dyslipidemia prevention and cardiovascular risk reduction.
https://doi.org/10.1161/jaha.125.042597

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Ponnusamy, B., Veeraraghavan, V. P., Al-Huseini, I., Woon, C. K., Jayaraman, S., Sirasanagandla, S. R.
Heavy Metal Exposure-Induced Cardiovascular Diseases: Molecular Mechanisms and Therapeutic Role of Antioxidants.
Current Medicinal Chemistry, Vol. **32** (17), (2025), 3438-3465.

Globally, cardiovascular diseases (CVDs) are the main cause of mortality every year worldwide. CVD health is influenced by various health factors, such as blood pressure, cholesterol levels, and glucose control. The main risk factors include smoking, physical activity, food intake, and body mass index. Around 90% of CVDs could be prevented by controlling these risk factors. Heavy metals are indigenous to the environment of the earth. However, modern lifestyles have led to the exploitation of our environment by unconstrained use of heavy metals. Though heavy metals are essential components, they are hazardous to humans and living systems due to their persistent and non-degradable nature. The main purpose of this study is to provide a literature review on the mechanisms of heavy metals, particularly arsenic, lead, and cadmium, that cause cardiovascular diseases. The major mechanism by which heavy metals result in various modalities of cardiovascular disease is the generation of reactive species and the depletion of the antioxidant reserves inside the biological system. The generation of reactive species gradually leads to the activation of various signaling pathways, resulting in either apoptosis or unrestricted cell growth. These unfavorable conditions result in a state when there is an imbalance between reactive species generation and antioxidant activity. Both endogenously present antioxidants and dietary antioxidants are very much essential in regulating the redox potential of the body. They help in the detoxification and excretion of heavy metals and their metabolites in the biological system. Therefore, recognizing the role of heavy metals in cardiovascular health is crucial for developing preventive strategies and interventions aimed at mitigating their adverse effects on human health.
https://doi.org/10.2174/0109298673307446240514064253

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Ma, J., Li, P., Tao, L., Yang, X., Luo, Y., Guo, X.*, et al.*
Environment-wide association study of cardiovascular-kidney-metabolic syndrome based on NHANES 2013-2016.
Ecotoxicology and Environmental Safety, Vol. **303**, (2025), p.

Background: Environmental chemical exposure has emerged as an important risk factor for cardiometabolic and other chronic diseases. Cardiovascular-kidney-metabolic (CKM) syndrome conceptualizes the overlap of cardiovascular, kidney, and metabolic diseases as a systemic condition, providing a comprehensive framework for systematically identifying their risk factors. This study aimed to assess the associations between multiple environmental chemicals and CKM syndrome and to examine the potential mediating role of inflammation.
Methods: The analysis was based on NHANES data from the 2013-2016 period. An exposome-wide approach was applied to identify environmental chemicals associated with CKM syndrome. Restricted cubic splines (RCS) were used to examine potential nonlinear associations. To evaluate the joint associations of multiple exposures, both weighted quantile sum (WQS) regression and quantile-based g-computation (Qgcomp) were employed. Mediation analyses were performed to explore inflammation as a possible pathway.

Results: Six environmental chemicals were found to be associated with CKM syndrome, including metals (tin), volatile organic compound metabolites (VOCMs: n-A-S-(3-hydrxprpl-1-metl)-L-cys, n-ace-S-(3,4-dihidxybutl)-L-cys), polycyclic aromatic hydrocarbons (PAHs: 1-hydroxyphenanthrene, 2&3-hydroxyphenanthrene), and iodine. A U-shaped relationship was observed between barium, cobalt, strontium, thallium, nitrate, and 2&3-hydroxyphenanthrene and the risk of advanced CKM syndrome. Mixed exposure analyses suggested that combined exposure to multiple metals was associated with a higher risk of advanced CKM syndrome. Moreover, inflammation may mediate the association between environmental chemicals and CKM syndrome.
Conclusion: This study underscored the importance of controlling exposure to harmful environmental chemicals in the prevention and control of chronic multisystem diseases, and provided new research perspectives for elucidating the potential biological mechanisms underlying CKM syndrome.
https://doi.org/10.1016/j.ecoenv.2025.118993

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Zhao, X., Liu, B., He, H., Zhou, L., Gong, X., Fan, Y.*, et al.*
Associations Between Blood Metal Exposure and Hypertriglyceridemia Among Adults in NHANES, 2011-2018.
Food Sci Nutr, Vol. **13** (9), (2025), e71001.

Growing evidence indicates associations between blood metal exposure and dyslipidemia. However, the relationships between hypertriglyceridemia (HTG), the most prevalent form of dyslipidemia, and blood metal exposure remain unclear. Our study aimed to evaluate both single and combined effects of blood metals on HTG risk. This study included 4182 adults from the 2011-2018 National Health and Nutrition Examination Survey. We assessed single and combined associations between blood metals (cadmium, mercury, lead, selenium, and manganese) and HTG. In single metal analysis, elevated blood selenium concentrations were significantly associated with increased HTG risk and triglyceride (TG) levels, with OR (95% CI) and β (95% CI) of 1.78 (1.36, 2.32) and 0.21 (0.13, 0.29), respectively, in the highest tertile group. Restricted cubic splines revealed a positive linear correlation between selenium and HTG. No significant associations were observed between HTG and blood cadmium, mercury, lead, or manganese in the overall population. In metal mixture analysis, blood metal co-exposure was positively related to HTG risk across WQS, qgcomp, and BKMR models, particularly in females and individuals under 60 years old. Furthermore, selenium was identified as the primary contributor to the overall mixture effect. The positive directional influence of selenium was further confirmed on the overall effect. Collectively, these findings indicate that elevated blood selenium concentrations are associated with increased HTG risk and higher TG levels. The results provide novel epidemiological evidence for the associations between multi-metal co-exposure and HTG risk, particularly in females and individuals under 60 years old.
https://doi.org/10.1002/fsn3.71001

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Bulat, Z., Bulat, P.
Toxicité cardiovasculaire des métaux.
In: Toxicité cardiovasculaire. Progrès de la biochimie dans la santé et la maladie.
Springer, Cham.; 2025. 427-441 p.

Les métaux toxiques affectent tous les organes et systèmes organiques, y compris le système cardiovasculaire. L'objectif de ce chapitre est de compiler et de présenter les recherches récentes sur l'impact des métaux uniques et des mélanges de métaux sur les maladies cardiovasculaires (MCV) chez l'homme. Le plus souvent, les études se sont concentrées sur les effets sur la pression artérielle et le développement de l'hypertension. En dehors d'une augmentation de la pression artérielle et de l'hypertension suite à une exposition à des niveaux croissants de plomb, le rôle précis que jouent les métaux dangereux dans le développement des MCV n'a pas encore été déterminé. Les données sur les effets cardiovasculaires de l'exposition au cadmium, à l'arsenic et au mercure sont contradictoires, et même dans

les études qui montrent une corrélation entre l'exposition à ces métaux et les MCV, elle est généralement modeste. L'exposition à des mélanges de métaux, avec des concentrations et des compositions variables, rend plus difficile la recherche de ces effets. Des études prospectives de haute qualité examinant les effets de la cardiotoxicité des mélanges de métaux dans des populations exposées à un plus large éventail d'expositions aux métaux sont nécessaires. À la lumière de tout ce qui précède, un plan complet pour éviter la morbidité ainsi que les décès dus aux MCV devrait inclure des efforts pour réduire l'exposition aux métaux toxiques.

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5.3. Grossesse, reproduction

Yu, T., Zhang, D., Li, Z., Zhai, M., Lin, W., Ren, S.*, et al.*
Evaluating the association between exposure to multiple metals and adverse pregnancy outcomes based on a multi-step statistical analysis strategy.
Ecotoxicol Environ Saf, Vol. **303**, (2025), 118768 p.

BACKGROUND: Adverse pregnancy outcomes (APOs) pose a serious threat to the safety of both the mother and the fetus. The association between metal exposure during pregnancy and the risk of APOs remains inconsistent. Therefore, this study aimed to evaluate the association between exposure to multiple metals and the risk of APOs based on a multi-step statistical analysis strategy.
METHODS: A birth cohort study including 707 pregnant women was performed in the present study, and 182 women were ultimately diagnosed with APOs. Blood levels of arsenic (As), cadmium (Cd), mercury (Hg), lead (Pb), barium (Ba), cobalt (Co), chromium (Cr), manganese (Mn), molybdenum (Mo), nickel (Ni), thallium (Tl), and vanadium (V) were measured in pregnant women. Multi-step statistical analyses were conducted to evaluate the associations between metals exposure and APO risk. First, cluster and scatter clustering analyses were used to assess the overlap for high exposure levels of metals among participants. Second, binary logistic regression was performed to assess the association between each single metal level and APO risk, respectively. Third, weighted quantile sum (WQS) regression and quantile-based g-computation (QGC) were conducted to identify the key metals contributing most to APO risk. Finally, Bayesian kernel machine regression (BKMR) evaluated the joint effects of these key metals on APO risk.
RESULTS: The results from cluster analyses revealed that there were substantial overlaps for high exposure levels of metals among pregnant women. Higher blood levels of Ba and Tl were associated with an increased APO risk (Ba: adjusted odds ratio [aOR] = 2.03, 95 % confidence interval [CI]: 1.33-3.10; Tl: aOR = 1.73, 95 % CI: 1.13-2.63). Consistently, results from the WQS regression model suggested that Ba (0.27), Tl (0.16), Pb (0.01) and V (0.01) were major contributors to APO risk ($p < 0.05$), which was further supported by the results from QGC regression model. The BKMR model indicated that the mixtures of Ba, Tl, Pb and V, identified through the WQS and QGC models, were positively associated with the risk of APOs. CONCLUSIONS: In this study, we observed substantial overlaps in high exposure levels of metals among pregnant women. Ba, Tl, Pb, and V were identified as the major contributors to the risk of APOs. Co-exposure to these metals was linked to an increased risk of APOs. This highlights the importance of avoiding metal exposure during pregnancy to protect maternal and fetal health.
https://doi.org/10.1016/j.ecoenv.2025.118768

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Zhang, L., Feng, M., Zhang, J., Wang, Z., Kang, W., Liu, Y.*, et al.*
Mixed exposure to lithium-battery related metals and menstrual health among young Chinese women: A cross-sectional study.
J Hazard Mater, Vol. **498**, (2025), 139783.

Environmental contamination from lithium battery waste poses health risks, but the impacts of constituent

metals (Li, Ni, Co, Mn) on menstrual health are unclear. This study investigated associations between blood concentrations of these metals and menstrual characteristics in 504 healthy young women. Metals concentrations in whole blood were measured using inductively coupled plasma mass spectrometry. The qgcomp, BKMR, and SHAP models were used to analyse the association and contribution of mixed metal exposure to menstrual outcomes. The average concentrations of whole blood Ni, Li, Co, and Mn of participants reached 1.16, 0.94, 0.27, and 2.87 ng.mL(-1). Single-metal analyses showed that Co and Mn were significantly negatively correlated with menstrual cycle, while Li was positively correlated with menstrual bleed duration. The overall metal mixture demonstrated negative associations with menstrual cycle and positive associations with menstrual bleed duration. Specifically, increasing Co (25th to 50th percentile) significantly decreased cycle length (-0.684 days [95 %CI: -1.025, -0.341]), while increasing Li significantly increased duration (0.557 days [95 %CI: 0.133, 0.981]), with other metals fixed at the 25th percentile. These findings highlight environmentally relevant Co and Li exposure as potential modifiable risk factors for female reproductive health disturbances.
https://doi.org/10.1016/j.jhazmat.2025.139783

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5.4. Effets respiratoires

Liu, J., Yang, L., Chen, J., Man, Y. B., Wong, M. H., Cheng, Z.
Cadmium and Benzo[a]pyrene Co-exposure Synergistically Induces Apoptosis in Bronchial Epithelium : Mechanistic Insights and Predictive Risk Modeling for Indoor Dust.
Biol Trace Elem Res, Vol., (2025), p.

Cadmium (Cd) and benzo[a]pyrene (BaP) are widely present in indoor dust. However, research on their combined health impacts on humans remains insufficient. To this end, this study employs human bronchial epithelial cells (16HBE) as an exposure model to elucidate the combined toxic effects of Cd and BaP in indoor dust. Cellular studies have demonstrated that Cd and BaP in dust exhibit synergistic toxicity in inducing apoptosis. Compared to the control group, as the combined concentration of Cd and BaP increased (from 5 + 5 to 40 + 100 muM, Cd + BaP), the synergistic toxicity significantly exacerbated cellular damage: Cell viability decreased to as low as 34.1%, lactate dehydrogenase (LDH) release rates rose to 140.2%, and oxidative stress (with catalase (CAT) activity dropping to 73.4%) drove a sharp increase in apoptosis (early apoptosis increased from 6.76% to 15.4%, while late apoptosis rose from 1.90% to 10.9%). Additionally, the expression levels of the pro-apoptotic gene Bcl-2-associated X protein (Bax) and executioner caspase gene Caspase-3 were upregulated by 1.8-fold and 3.7-fold, respectively. Cadmium and BaP promote late apoptosis and early apoptosis, respectively. However, their co-exposure synergistically exacerbates the apoptotic process by complementarily enhancing these pathways in cellular mechanisms. The fitting of the linear equation for Cd-BaP composite pollution lays the foundation for predicting the potential impacts of composite concentrations on the respiratory system. The research findings provide a scientific basis for determining the safety threshold values of Cd and BaP in indoor dust pollutants and for implementing environmental remediation strategies in residential settings.
https://doi.org/10.1007/s12011-025-04797-6

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6. Multiples expositions aux pesticides, BTEX, VOCs

Eid, A., Jodeh, S., Hanbali, G., Hawawreh, M., Chakir, A., Roth, E.
Multi-Output Machine-Learning Prediction of Volatile Organic Compounds (VOCs): Learning from Co-Emitted VOCs.
Environments, Vol. **12** (7), (2025).

Volatile Organic Compounds (VOCs) are important contributors to indoor and occupational air pollution, such as environments involving the extensive use of paints and solvents. The routine measurement of VOCs is often limited by resource constraints, creating a need for indirect estimation techniques.
This work presents the need for a predictive framework that offers a practical, interpretable alternative to a full-spectrum chemical analysis and supports early exposure detection in resource-limited settings, contributing to environmental health monitoring and occupational risk assessment.
This study explores the capability of machine learning to simultaneously predict the concentrations of five paint-related VOCs using other co-emitted VOCs along with demographic variables. Three models-Multi-Output Gaussian Process Regression (MOGP), CatBoost Multi-Output Regressor, and Multi-Output Neural Networks-were calibrated and each achieved a high predictive performance. Further, a feature importance analysis is conducted and showed that certain VOCs and some demographic variables consistently influenced the predictions across all models, pointing to common exposure determinants for individuals, regardless of their specific exposure setting. Additionally, a subgroup analysis identified the exposure disparities across demographic groups, supporting targeted risk mitigation efforts.
https://doi.org/10.3390/environments12070216

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Muñoz-Quezada, M. T., Hojas, R., Toro, J., Norambuena, J., Lucero, B., Bekinschtein, T.*, et al.*
Exposition simultanée à des pesticides organophosphorés et pyréthrinoïdes et effets sur la santé du cerveau chez l'homme. Une revue systématique.
medRxiv 2025.08.19.25334018. Preprint, not reviewed.

Les pesticides organophosphorés et pyréthrinoïdes sont largement utilisés, mais leurs effets combinés sur la santé du cerveau restent incertains. Cette étude a analysé la recherche observationnelle de 2014 à 2024 sur leur exposition simultanée et son association avec des troubles neurocomportementaux, neurodégénératifs et neurologiques par le biais d'une revue systématique suivant les directives PRISMA dans PubMed et Web of Science.
Les études évaluant la co-exposition avec des méthodes validées et rapportant des résultats sur la santé cérébrale ont été incluses, tandis que les revues, les études animales et celles sans données d'exposition simultanée ont été exclues. Le risque de biais dans les études de cohorte a été évalué à l'aide de l'étude ROBINS-E. Sur les 34 études incluses, neuf étaient des études de cohorte, quatre avec un faible risque de biais et quatre avec des préoccupations liées à la taille de l'échantillon ou à l'évaluation de l'exposition. Trois ont établi un lien entre la co-exposition aux déficits de l'attention et le déclin cognitif chez les enfants. Les preuves sur les maladies neurodégénératives et les troubles du spectre autistique étaient incohérentes en raison de résultats contradictoires. Des études transversales et cas-témoins ont associé la co-exposition à la dépression et à l'anxiété, mais manquaient de données de suivi. La variabilité de l'évaluation de l'exposition a réduit la comparabilité. Les recherches restent limitées, ce qui indique de possibles effets sur le développement neurologique et la nécessité de méthodologies normalisées pour affiner l'évaluation des risques.
https://doi.org/10.1101/2025.08.19.25334018

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Julien, C.
Étude de l'influence des polluants environnementaux sur l'incidence du diabète de type 2.
Thèse. Université de Liège, (2025). Thèse présentée en vue de l'obtention du grade de Doctorat en Sciences Biomédicales et Pharmaceutiques.

Nous avons investigué le lien entre le diabète de type 2 et la contamination en mettant en place une étude transversale au cours de laquelle nous avons comparé les niveaux de contamination pour 51 perturbateurs endocriniens (plusieurs substances per- et polyfluoroalkylées, plusieurs polychlorobiphényles, des bisphénols, des métabolites des phtalates, des pesticides organophosphorés et des pesticides organochlorés, la benzophénone 3 et le triclosan) chez 105 patients diabétiques et 98 volontaires sains. Au cours de cette étude, nous avons mis en évidence plusieurs associations positives entre différents polluants et le diabète de type 2.
En plus de l'approche monopolluants, nous avons investigué l'effet de la coexposition simultanée à plusieurs polluants de l'étude en utilisant deux méthodes statistiques : la weighted quantile sum regression et la Bayesian Kernel machine regression. Ces analyses ont permis de mettre en évidence que les mélanges de polluants étaient positivement associés au risque de diabète de type 2. Nous avons également montré que certains polluants étaient identifiés comme principalement associés à la pathologie.
Le nombre de substances anthropogènes présentes dans l'environnement ne cesse d'augmenter, et les effets de certaines d'entre elles sur le système endocrinien se précisent. Plusieurs composés sont mis en évidence pour leurs impacts sur la santé et leurs effets sur l'homéostasie du glucose. Par nos travaux, nous avons souhaité contribuer à l'investigation de l'incidence des perturbateurs endocriniens sur le diabète de type 2 en intégrant la recherche de solutions pour le dosage des composés non persistants ainsi qu'une approche statistique mixte permettant de mettre en évidence les effets cocktails.
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De Morais Valentim, J. M. B., Pizzatti, L., Coradi, C., Cristina Cazagranda, I., Fadel, B., Vacario, B. G. L., *et al.*
Pesticide exposome reveals oxidative stress and immune response disruptions in occupationally exposed women with breast cancer.
Scientific reports, Vol. **15** (1), (2025), 30910.

Rural women are at a higher risk of developing breast cancer, but the molecular mechanisms involved remain poorly understood. This study investigates the impact of chronic pesticide exposure on systemic and tissue-level protein expressions in women diagnosed with breast cancer.
Plasma and tumor samples were collected from 215 women diagnosed with breast cancer; among them, 128 patients were occupationally exposed (n=128) and 87 patients were not occupationally exposed (87) were analyzed for further studies. High-throughput proteomic analyses of plasma revealed distinct protein expression profiles between the groups, primarily associated with inflammation, oxidative stress, and immune deregulation. Validation analysis showed that cytokines such as IL-1beta, IL-12, IL-17A, and TNF-alpha were significantly reduced in both plasma and tumor samples from exposed patients compared to unexposed women. This reduction in cytokines, coupled with decreased tumor-infiltrating leukocytes (TILs) and CTLA-4 overexpression, suggests pesticide-induced immune compromise. Circulating IL-12 levels were significantly reduced in younger, eutrophic, and at menacme exposed patients. Pesticide exposure also influenced nitrosative stress production, leading to reduced NOx levels in plasma and impaired iNOS expression in TILs.
These results suggest a potential link between pesticide exposure and the pathophysiology of breast cancer, offering new insights into the underlying molecular mechanisms.
https://doi.org/10.1038/s41598-025-12870-2

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Hojas, R., Norambuena, J., Ponce, A., Toro, J., Adonis, J., Al., E.
Environmental co-exposure to organophosphate and pyrethroid pesticides and mental health status in rural communities near an industrial pig farming facility.
3 September 2025, PrePrint (Version 1) available at Research Square

Chronic exposure to pesticide residues from large-scale agro-livestock operations remains poorly characterized, particularly among rural populations living near industrial pig farming facilities. This study examined the association between co-exposure to organophosphate and pyrethroid pesticide residues in soil and well water and mental health outcomes among adults residing near an industrial pig farming facility in rural Chile.
A cross-sectional analysis was conducted with a sample of 82 adults. Peridomestic soil and well water samples were analyzed using gas chromatography–tandem mass spectrometry to detect five pesticides: chlorpyrifos, diazinon, pirimiphos-methyl, cypermethrin, and lambda-cyhalothrin. Mental health was assessed using validated instruments measuring depressive symptoms, anxiety, emotional affect, and health-related quality of life. Robust linear regression models were employed, adjusting for age, sex, education level, and body mass index. Chlorpyrifos in water was associated with more depressive symptoms (β = 0.180; 95% CI: 0.016, 0.345) and lower mental quality of life (β = − 0.713; 95% CI: − 1.288, − 0.137). Cypermethrin in water was linked to greater psychological distress (β = 0.913; 95% CI: 0.193, 1.632). Pirimiphos-methyl in soil was associated with higher emotional affect scores (β = 21.29; 95% CI: 1.78, 40.79), while cypermethrin in soil showed an inverse association (β = − 3.66; 95% CI: − 6.99, − 0.33). Lambda-cyhalothrin in soil was linked to lower quality of life (β = − 15.13; 95% CI: − 27.42, − 2.83). Male sex was positively associated with quality of life (β = 14.96; 95% CI: 3.14, 26.79).
These findings suggest the presence of measurable associations between environmental pesticide residues and various dimensions of mental health in rural populations living near industrial pig farming operations. Longitudinal studies are needed to follow up on these communities and better understand the potential long-term health implications.
https://doi.org/10.21203/rs.3.rs-7459878/v1

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Li, H., Xiao, L., Wang, Y., Yin, X., Li, L., Duan, Y.*, et al.*
Volatile organic compounds exposure with risk of thyroid function in U.S. general population : 2007-2012 NHANES.
Ecotoxicol Environ Saf, Vol. **303**, (2025), 118987.

BACKGROUND: The link between exposure to environmental hazards and thyroid function has been relatively well established. However, evidence on environmental exposure to volatile organic compounds (VOCs) and thyroid function in the general population remains unclear.
OBJECTIVES: To assess the impact of individual and joint effects of VOCs exposure on thyroid function in a representative sample of U.S. general population.
RESULTS: The findings from the WQS suggested a positive correlation between VOCs co-exposure and FT3 (beta = 0.033, 95 % CI: 0.014, 0.025), as well as a negative correlation with FT4/FT3 (beta = -0.084, 95 % CI: -0.127, -0.040). Specifically, 1,4-dichlorobenzene (29.2 %) was identified as the primary contributor to elevated serum FT3 concentrations, while tetrachloroethylene, 2,5-dimethylfuran, and furan (18.3 %) were the major contributors to the decreased FT4/FT3 ratio. Thyroid hormones, including FT3 and FT4, are key indicators of thyroid function, with the FT4/FT3 ratio serving as an important marker of thyroid homeostasis. Subgroup analysis showed a positive association between VOC exposure and FT3 in females (beta = 0.045, 95 % CI: 0.019, 0.071), with 1,4-dichlorobenzene as the strongest contributor. In participants aged >/= 60 years, VOC exposure was positively associated with FT3 (beta = 0.107, 95 % CI: 0.006, 0.208) and negatively with FT4/FT3 (beta = -0.103, 95 % CI: -0.202, -0.003). In this subgroup, ethylbenzene and 1,4-dichlorobenzene were the major contributors to FT3, while o-xylene was the primary contributor to the FT4/FT3 ratio. No significant associations were found in males or participants < 60 years.
CONCLUSION: These results suggest that VOCs exposure has a detrimental impact on thyroid function,

especially in females and individuals aged 60 years and older. VOCs exposure may accelerate the onset of thyroid function impairment and lead to changes in thyroid hormone levels. This study may inform the development of early monitoring and regulatory measures for VOCs exposure, thereby reducing the incidence of thyroid dysfunction.
https://doi.org/10.1016/j.ecoenv.2025.118987

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