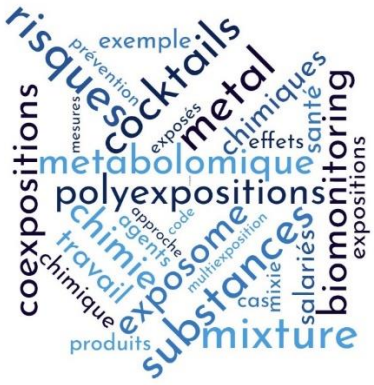

Bulletin de veille
Polyexpositions chimie-chimie
N°13 – février 2026

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

- 29 décembre 2025. Article sur l'avantage de la spectrométrie de masse de haute résolution pour l'évaluation de microéchantillonnage sanguin pour l'évaluation à grande échelle des exposomes chimiques. Pour en savoir plus

- 31 décembre 2025. L'EPA (l'Agence de Protection de l'Environnement américaine) annonce son intention de réglementer des dizaines d'utilisations de cinq produits phtalates pour protéger les travailleurs et l'environnement. https://www.epa.gov/newsreleases/epa-announces-intent-regulate-dozens-uses-five-phthalate-chemicals-protect-workers-and

- 13 janvier 2026. Article des Echos en « Santé et environnement : sur les traces de notre exposition aux polluants ». https://www.lesechos.fr/idees-debats/sciences-prospective/sante-et-environnement-sur-les-traces-de-notre-exposition-aux-polluants-2209245

- 15 janvier 2026. Inrae. FOCAL : un laboratoire international associé pour approfondir l'étude des contaminants chimiques dans l'alimentation. Etude de l'exposome alimentaire et substances chimiques, incluant les polluants environnementaux.
  https://www.inrae.fr/actualites/focal-laboratoire-international-associe-approfondir-letude-contaminants-chimiques-lalimentation

- 29 janvier 2026. Le réseau PAN Europe (Pesticides Action Network), dénonce le cocktail dangereux de pesticides présents dans les pommes de 13 pays européens, selon l'étude que l'organisation a réalisée.
  https://www.pan-europe.info/press-releases/2026/01/european-apples-contaminated-cocktails-pesticides-pfas-neurotoxins-and-other

- Janvier 2026. Article de santé publique : évaluation des risques sanitaires liés à l'exposition à des composés organiques volatils intérieurs dans les bâtiments éducatifs européens. L'exposition au formaldéhyde et au benzène présentent un risque accru d'effets respiratoires et neurologiques chez les jeunes et les adolescents fréquentant les écoles, les lycées et universités. https://www.nature.com/articles/s41598-026-37072-2

Sommaire

1. Généralités

Sarazin, P., Pomerleau, M., Almadin, C., Ho, V., Bosson-Rieutort, D., Labreche, F., *et al.*
Cumulative chemical risk and associated toxic effect classes across US industries from regulatory inspections.
Annals of work exposures and health, Vol. 70 (2), March 2026, wxag002.

OBJECTIVES: Workers are often exposed to multiple chemical agents, which should be accounted for in risk assessment. However, few data are yet available to prioritize specific agents, toxic effects, or industries for cumulative risk assessment (CRA). This study aimed to characterize the cumulative chemical risk in US workplaces using over 600,000 exposure measurements carried out in numerous industries by the Occupational Safety and Health Administration (OSHA), to quantify the frequency of cumulative risk exceedances, and to identify recurring combinations of agents associated with these elevated risks.
METHODS: Data on airborne exposure to 195 chemical agents from the OSHA database for the period 1971 to 2021 were grouped by workplace situation (WS, a job title within a company within a calendar year) to observe the co-presence of chemicals. WSs were then linked via their chemicals to one or several toxicological classes from MiXie, a tool which systematically associates several hundreds of chemicals to a standard list of 24 toxicological classes. CRA was then conducted for all WSs across toxicological classes by calculating the agent-specific hazard quotients (HQ, ratio of a chemical measurement to its occupational exposure limit) and summing them into the WS- and class-specific hazard index (HI, sum of HQ of chemicals relevant to a toxicological class). WSs with HI > 1 were flagged as "hazardous," and hazardous WSs with all HQ < 1 were flagged as "missed risk" as assessment of a single agent would not have detected overexposure. Frequent itemset mining (FIM) was used to identify frequent combinations of chemicals in hazardous multiexposed WSs, by toxicological class and across 51 industry groups.
RESULTS: From 607,676 measurements, 38,512 unexposed WSs and 123,118 exposed WSs were identified. Among the latter, 33% were considered multiexposed (median 3 agents/WS). The following toxicological classes were associated with more than half of all exposed WSs: Carcinogenicity and/or mutagenicity (60%), central nervous system damage (58%), lower airway damage (54%), and upper airway damage (53%). Toxicological classes co-occurred frequently across WSs, with 94% of WSs linked to ≥2 classes. Clustering analyses revealed strong co-association patterns, especially between irritation effects (eyes/airways) and between metal-related effects (blood/kidney/nervous system). Across the 24 toxicological classes, the proportion of hazardous WSs among multiexposed WSs was highest for carcinogenicity and/or mutagenicity (65%), while the proportion of missed risk among hazardous multiexposed WSs was highest for ototoxicity (19%). Among all industries, the highest proportion of hazardous multiexposed WSs was in boat building and repairing (81%), while the highest proportion of missed risk was in general industrial machinery and equipment (30%). FIM revealed recurring hazardous combinations of agents-primarily involving solvents and metals-which varied across toxicological classes and industries (eg toluene/xylene and copper compounds/iron oxides frequent for upper airway damage; toluene/styrene/acetone frequent for boat building and repairing).
CONCLUSIONS: Overall, our study suggests that workers in US workplaces are often exposed to hazardous combinations of chemical agents targeting a wide variety of organ systems. Our results should help prioritize industries and agents likely necessitating CRA.
https://doi.org/10.1093/annweh/wxag002

****

Leung, L., Koushik, A., Cordina-Duverger, E., Siemiatycki, J., Guenel, P.
Exploratory research on occupational exposures and breast cancer risk in the CECILE study.
Occup Environ Med, Vol. 82 (3), (2025), 139-147.

Les auteurs ont examiné de manière exploratoire les associations entre l'exposition professionnelle à 49 agents chimiques prévalents et le risque de cancer du sein. Dans une étude cas-témoins en population générale menée en France sur le cancer du sein (2005-2007), les antécédents professionnels de 1 230 cas

incidents et de 1 315 témoins ont été recueillis. Un hygiéniste industriel a codé chaque profession occupée par les participantes. Les codes professionnels ont ensuite été liés à une matrice emploi-exposition canadienne, et des estimations du niveau d'exposition pour de nombreux agents chimiques ont été générées. Les associations entre l'exposition professionnelle à 49 agents chimiques prévalents et le risque de cancer du sein ont été estimées en tenant compte des facteurs de risque établis et de certaines covariables sociodémographiques. Des OR (odds ratios) accrus ont été observés chez les femmes du tertile le plus élevé d'exposition cumulée par rapport aux femmes non exposées aux 12 agents suivants : carbonate de sodium, fibres synthétiques, fibres de laine, fibres de soie, colorants et pigments organiques, poussières de plastique, fumées de pyrolyse du plastique, ozone, oxydes d'azote, gaz anesthésiants, cétones aliphatiques et hydrocarbures aromatiques monocycliques.
Stratifiés selon le statut relatif à la ménopause, les OR pour plusieurs de ces agents étaient plus élevés chez les femmes préménopausées que chez les femmes ménopausées.
En conclusion, ces résultats suggèrent le rôle possible dans le cadre du travail de certains produits chimiques dans l'étiologie du cancer du sein. D'autres études, basées sur des échantillons de grande taille et une évaluation de l'exposition de haute qualité, sont nécessaires pour confirmer les résultats.
Référence INRS-Biblio : 751135
https://doi.org/10.1136/oemed-2024-110021

****

Anderson, K. R., Callaway, P., Virjii, M. A.
Evaluation of chemical exposures generated from n-free nail polishes.
J Occup Environ Hyg 2025, Vol. 22 (6), 482-494.

Nail polishes contain over a dozen chemical compounds, including chemicals that can cause adverse reproductive outcomes and pose a risk to the high proportion of nail salon workers who are women of childbearing age. Consumer demand has resulted in a shift toward more natural products, with manufacturers attempting to remove harmful ingredients (n-free products). Many products that claim to have eliminated toluene, formaldehyde, and dibutyl phthalate (DBP) are labeled as "3-free"; however, studies have found these products often contain higher concentrations of toluene and DBP compared to products with no such claims. Products used only at salons are not required to list ingredients, leading to uncertainties as to the exact chemical composition and potential exposures. A better understanding of chemical exposures associated with nail polish products is necessary to understand potential worker exposures and develop effective control options.
This study evaluated chemical exposures generated while painting nails with 20 n-free polishes using real-time and time-integrated air sampling. Total volatile organic compounds (TVOCs, PID, ION Science Inc.) and 22 individual compounds (FTIR, Gasmet Technologies) were measured in the breathing zone of the manicurist while two coats of polish were applied to artificial nails on a manikin in an exposure chamber and for 2 hr afterwards. Formaldehyde and toluene were measured in all polishes using the real-time FTIR, despite all claiming to be 3-free. Normalized geometric mean (GM) formaldehyde exposures from the FTIR ranged from 0.021 to 0.273 ppm/g, GM toluene exposures ranged from 0.068 to 0.534 ppm/g, and GM benzene exposures ranged from 0.076 to 0.752 ppm/g. Notably, formaldehyde, toluene, and benzene exposures did not significantly differ between different products. Neither DBP nor triphenyl phosphate (TPhP) was detected in any of the polishes.
This study highlights that despite industry claims, n-free polishes may still contain chemicals associated with negative health effects and that more studies are necessary to understand the true chemical exposures of nail salon workers.
https://doi.org/10.1080/15459624.2025.2468931

****

Jensen, M. B., Alfonso, J. H., Seibel, A. T., Mollerup, S., Wilks, M. F., Selvestrel, G.*, et al.*
Chemical Mixture Exposures and Their Effects on Sensitisation and Elicitation Responses : A Systematic Review.
Contact dermatitis, 2026, Vol 94 p 105-119.

Consumers and workers are generally exposed to multiple allergens and irritants simultaneously in products. This systematic review of 13 studies : 4 clinical, 6 animal, and 3 invitro studies, suggests that co-exposure often enhances both sensitisation and elicitation reactions. When an irritant is combined with an allergen, the threshold for sensitisation and elicitation is lowered, and the severity of reactions is increased. Animal models suggest that weak allergens, when combined, can elicit responses at individual subthreshold doses, supporting their role as immune-enhancing adjuvants. Current regulations generally assess allergens or irritants in isolation, potentially overlooking the combined effects of low-level exposures from everyday products.
There is a need to refine safety standards and ensure that risk assessment tools reflect real-world interactions between multiple allergens and irritants. Contact allergy is frequent and increasing in the population. A clearer understanding of mixture effects in sensitisation and elicitation responses is essential to protect the general population from developing contact allergy.
https://doi.org/10.1111/cod.70069

****

Ogunsina, K., Richardson, K. A., White, A., Chang, C. J., Sandler, D. P., O'brien, K. M.
Occupational exposures among hairdressers and the occurrence of hormone-related conditions.
Occup Environ Med, January 2026

OBJECTIVE: To investigate the association between hairdresser exposures and hormone-related conditions.
METHODS: Using data from 50 800 eligible Sister Study participants (enrolled 2003-2009, aged 35-74 years), we estimated ORs and 95% CIs for associations between ever working as a hairdresser (n=1803) and prevalent fibroids, endometriosis, hysterectomy and oophorectomy. We estimated HRs and 95% CI for incident fibroids, endometriosis, breast, uterine and ovarian cancers among ever hairdressers versus never hairdressers. We also examined associations of hormone-related diseases and professional use of products such as bleach, perms, chemical straighteners, permanent hair colour, hairspray, barbicide, formaldehyde and alcohol, comparing data from 985 long-term hairdressers who worked >/=2 years to non-long-term hairdressers (never workers and those working <2 years).
RESULTS: Ever-hairdressers were more likely than never-hairdressers to have had a prebaseline hysterectomy (OR=1.23: 95% CI 1.11 to 1.36). Hysterectomies were more common among long-term hairdressers with more frequent applications of perms, chemical straighteners and permanent hair colour compared with less frequent applicators or never hairdressers. Ever-hairdressers had higher rates of incident endometriosis (477 cases, HR=1.61: 95% CI 1.08 to 2.38) compared with never-hairdressers, but there were no notable associations between working as a hairdresser and fibroids (1805 cases, HR=1.04: 95% CI 0.80 to 1.34), breast cancer (4628 cases, HR=0.98: 95% CI 0.83 to 1.16), ovarian cancer (300 cases, HR=1.33: 95% CI 0.77 to 2.29) or uterine cancer (447 cases, HR=1.04: 95% CI 0.60 to 1.77). In race-stratified analyses, Black hairdressers were more likely to be diagnosed with fibroids than Black never-hairdressers (201 cases, HR=1.56: 95% CI 0.93 to 2.62).
CONCLUSIONS: Hairdresser occupation was associated with increased odds of hysterectomy and increased rates of incident endometriosis and possibly fibroids among Black women.
https://doi.org/10.1136/oemed-2025-110207

****

Wu, D., Bing, S., Qiu, H., Wang, S., Zhang, Y.
Association Between Mixed Exposure to Endocrine-Disrupting Chemicals and Cardiovascular Health : Results from the 2003-2016 NHANES.
Cardiovascular Toxicology, 2026. Vol. 26 (7)

Accumulating evidence supports the association between endocrine disrupting chemicals (EDCs) exposure and cardiovascular disease (CVD). However, the link between EDCs and cardiovascular health (CVH) prior to CVD onset remains unclear. This study investigates the relationship between individual and combined EDC exposure and Life's Essential 8 (LE8).
We included 9,940 participants from the National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2016, excluding adults with known CVD. Twenty-two types of EDCs were detected in urine samples, including three phenols, two phenolic pesticides, eleven phthalates, and six polycyclic aromatic hydrocarbons (PAHs). Weighted generalized linear models (GLM) and weighted quantile sum (WQS) regression to explore the relationship between single/mixed exposure to EDCs and CVH. Overall, 9,940 individuals (weighted mean [SE] age, 42.53 [0.26] years; 5,313 women [weighted 53.7%]) without CVD were included, with a mean score of LE8 at 68.70. The GLM model reveals that specific exposures to EDCs are inversely associated with LE8, serving as independent risk factors contributing to poorer CVH. The WQS index of EDCs was independently associated with overall CVH, with an adjusted odds ratio (OR) of 3.00 (95% confidence interval [CI]: 2.30-3.90; P < 0.001). 2-Fluorenone (2-FLU) emerged as the most heavily weighted component in the overall CVH model.
This study emphasizes the association between exposure to EDCs is correlated with a higher odds ratio for decline in CVH among American adults. 2-FLU emerges as a prominent contributor. It provides epidemiologic evidence for the detrimental effects of these chemicals on CVH.
https://doi.org/10.1007/s12012-025-10084-6

****

Généralités, Exposome

Hahad, O., Wass, S., Rajagopalan, S., Abohashem, S., Hao, H., Navas-Acien, A.*, et al.*
The environmental exposome in heart failure risk and progression.
Nat Rev Cardiol, 2026. https://doi.org/10.1038/s41569-026-01247-1

Environmental exposures have a crucial role in the incidence and progression of heart failure (HF) by exacerbating genetic predisposition and other pathophysiological mechanisms. The exposome - encompassing pollution, climate and the urban environment - and the biological responses to these factors shape cardiovascular health in complex ways. Air, noise and light pollution, exposure to toxic metals, and extremes of temperature adversely affect HF outcomes. Social determinants of health, including socioeconomic status, amplify these environmental risks, disproportionately affecting vulnerable populations. Conversely, green spaces and walkable neighbourhoods are linked to a reduced risk of HF, improved vascular health and medication adherence. Emerging evidence suggests that environmental stressors influence HF outcomes from early life by altering gene expression through epigenetic mechanisms. Despite these insights, research gaps remain. Future studies must integrate environmental, genetic and multiomics data to refine risk prediction and guide targeted public health interventions. A comprehensive understanding of the exposome in the aetiology of HF is essential for developing prevention strategies that address both biological and social determinants of cardiovascular health.
https://doi.org/10.1038/s41569-026-01247-1

****

Vogli, M., Jeong, A., Yu, Z., Vonk, J. M., Ibi, D., Kronberg, J.*, et al.*
The impact of environmental exposures on DNA methylation in the EXPANSE project.
EBioMedicine, Vol. 123, (2025), 106084.

BACKGROUND: Living in an urban environment exposes the population to a mix of environmental and social factors, known as the Urban Exposome, that can influence health via changes in DNA methylation. We hypothesised that linking urban exposures with epigenome-wide DNA methylation in blood can reveal impacts across the lifespan.
METHODS: In the EXPANSE project, we conducted an inverse variance-weighted meta-analysis of epigenome-wide association studies of seven European cohorts. Urban exposures were estimated at participants' home addresses and included air pollution (PM2.5, NO2, O3), light at night, modified soil-adjusted vegetation index, and urbanicity.
FINDINGS: DNA methylation was measured in blood samples from 1778 children (4-10 years), 878 adolescents (16 years), and 5975 adults (18-87 years). PM2.5, NO2, and greenness were associated with methylation differences in children, while greenness and urbanicity showed associations in adults. Regional analyses showed differentially methylated regions (DMRs) across all life stages. Pathway analysis showed that monthly NO2 in children was linked to immune and infectious disease pathways, whereas adult urbanicity was associated with immune pathways as well as PD-L1 expression and the PD-1 checkpoint pathway in cancer.
INTERPRETATION: Urban environmental factors induce DNA methylation changes across life stages, with stronger associations in young children and adults. We observed a distinct contrast in the methylation changes associated with greenness compared to other urban environmental factors. However, disentangling exposure-specific methylome signatures remains a challenge.
FUNDING: This work was supported by the EXPANSE project, funded by the European Union's Horizon 2020 research and innovation programme under grant agreement No. 874627.
https://doi.org/10.1016/j.ebiom.2025.106084

****

Perez-Vazquez, F. J., Reyes-Zavala, A., Marin-Jauregui, L. S., Mendez-Rodriguez, K. B., Van-Brussel, E., Fernandez-Macias, J. C.
Assessment of environmental pollutant exposure and cardiovascular risk in Mexican brick-making communities.
Environ Geochem Health 2025, Vol. 48 (1), 25

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide and are strongly influenced by both environmental and socioeconomic determinants. Populations engaged in informal and hazardous occupations, such as brickmaking, may experience elevated cardiovascular risk due to chronic exposure to environmental pollutants, including heavy metals (arsenic and lead) and polycyclic aromatic hydrocarbons (PAHs).
This study aimed to assess occupational exposure to heavy metals and PAHs and to evaluate atherogenic indices as indicators of cardiovascular risk among brickmakers in the Bajio region of Mexico. A cross-sectional study was conducted among 113 male adults from brickmaking communities in San Luis Potosi (SLP), Guanajuato (GTO), and Queretaro (QRO). Urine and blood samples were analyzed to quantify heavy metals and PAHs, while lipid profiles were used to calculate Castelli's Risk Indices (CRI-I and CRI-II) and the Atherogenic Index of Plasma (AIP). GTO exhibited the highest urinary arsenic concentrations (42.5 microg/l), whereas SLP showed the highest blood lead levels (1.52 microg/dl). PAH exposure was also highest in GTO (2.25 micromol/mol creatinine). Correspondingly, the highest atherogenic index values were observed in GTO: CRI-I (4.28 +/- 0.97), CRI-II (2.54 +/- 0.64), and AIP (0.145 +/- 0.28). A considerable proportion of participants presented moderate to high CVD risk profiles. Significant associations were found between arsenic and lead exposure and elevated CRI-II values, suggesting potential disruption of lipid metabolism.
These findings confirm occupational exposure to environmental pollutants in brickmaking populations and

indicate that chronic exposure to arsenic and lead may contribute to increased cardiovascular risk, as reflected by higher atherogenic indices.
https://doi.org/10.1007/s10653-025-02910-1

****

Zhang, X. Q., Hai, P., Xue, J. J., Cai, Q. Z., Zhang, J., Zhang, J. X.*, et al.*
Combined effect of biological age and fine particulate matter pollution with risk of nonalcoholic fatty liver disease in the UK Biobank : a prospective cohort study.
American Journal of Epidemiology 2025, kwaf046.

Aging and long-term exposure to fine particulate matter (PM2.5) are associated with a higher risk of nonalcoholic fatty liver disease (NAFLD), but evidence on their combined effect is limited. We thus evaluated the joint effects of accelerated biological aging and PM2.5 exposure on incident NAFLD in a UK cohort. We included 296 917 UK Biobank participants without NAFLD at baseline.
Annual mean PM2.5 concentration was evaluated using a land use regression model. Biological age was assessed using the Klemera-Doubal method (KDM-BA) and PhenoAge algorithm. Cox proportional hazards models were used to assess the effects on incident NAFLD. Both chronic PM2.5 exposure and older biological age were linked to higher risk of NAFLD, with HRs of 1.07 (95% CI, 1.04-1.10) per SD increase in PM2.5, 1.47 (95% CI 1.43-1.52) in per SD increase KDM-BA, and 1.38 (95% CI 1.35-1.41) in per SD increase PhenoAge-BA, respectively.
Participants with low PhenoAge and low PM2.5 had a lower NAFLD risk than those with high PhenoAge and high PM2.5. Positive additive interactions were observed. This study suggests that both PM2.5 exposure and biological aging increase NAFLD risk, with simultaneous exposure to high levels potentially intensifying their effects.
https://doi.org/10.1093/aje/kwaf046

****

2. Biomonitoring

Dai, Y., Van De Water, B., Telleria, J., Furlong, L. I., Vermeulen, R. C. H., Vlaanderen, J.
Integrating human exposome data into next-generation risk assessment : a systematic framework to infer real-life exposure levels and prioritize chemical compounds for testing.
Environment international, Vol. 208, (2026), 110110.

Exposome research and next-generation risk assessment (NGRA) share the goal of improving the human relevance of chemical safety evaluations, yet practical integration remains limited.
We developed a flexible framework that combines human biomonitoring (HBM) data, exposome datasets, and exposure modeling results with chemical property, toxicity, and bioactivity information to support NGRA and chemical prioritization. The framework comprises three modules: a curated human exposome database, model-based exposure estimates, and toxicity/bioactivity data integration. Its application was demonstrated in two case studies. Case study 1 focused on organ-specific carcinogens, prioritizing candidate hepatocarcinogens. Case study 2 adopted an exposure-driven approach, highlighting compounds frequently detected in biomonitoring programs across populations. The framework generated quantitative ranges of compound concentrations in biological samples, predicted blood concentrations, and external intake values, which can be compared with in vitro toxicity benchmarks such as half-maximal activity concentration (AC50).
Results show that incorporating human exposure data substantially influences chemical prioritization. This framework provides a practical pathway for embedding exposome data into NGRA workflows, thereby strengthening human-relevant risk assessments and informing future chemical safety evaluations.
https://doi.org/10.1016/j.envint.2026.110110

****

Meng, D. H., Wan, X. Z., Zhang, L. E., Tian, Y. M., Jia, W., Song, X. R.*, et al.*
Association of exposure to selected chemical contaminants with diabetes mellitus in Chinese adults : Mixture associations and metabolic mediation in the PNFS study.
Journal of Hazardous Materials, Vol. 501, (2026) 140853.

Despite existing research on the adverse association of individual chemical contaminants and diabetes mellitus (DM), the joint effects of co-exposure to multiple contaminants remain largely unclear.
This study investigated the associations between urinary biomarkers of four common chemical contaminants, including acrylamide, 3-monochloropropane-1,2-diol, glycidol, and thiocyanate, and DM prevalence in a Chinese population, as well as potential mediation by plasma metabolites. Bayesian kernel machine regression (BKMR) and quantile gcomputation analyses demonstrated a significant joint effect of the contaminant mixture on DM prevalence. BKMR with hierarchical variable selection identified thiocyanate as the key contributor to this joint effect. We observed a nonlinear relationship between thiocyanate exposure and DM prevalence. Metabolomics analysis revealed significant associations between thiocyanate exposure and 11 plasma metabolites. Mediation analysis identified acrylic acid and glucose as the most important mediators, accounting for 36.19 % and 35.22 % of the association of thiocyanate exposure with DM prevalence, respectively.
Our findings provide novel insights into the complex relationships between exposure to chemical contaminant mixtures, metabolic alterations, and DM prevalence, highlighting the importance of considering mixture effects in environmental health research and suggesting potential targets for diabetes prevention strategies.
https://doi.org/10.1016/j.jhazmat.2025.140853

****

Rehman, M. U., Sehar, N., Elboughdiri, N., Nisar, B., Naqash, N., Sheikh, W. M.*, et al.*
Analytical advances in pesticide toxicology : Integrating omics, biosensors, microfluidics and exposome-based monitoring for risk assessment.
Microchemical Journal, Vol. 220, (2026), p. 116373.

Pesticide toxicology and risk assessment have undergone significant advancements in recent years, driven by the urgent need to understand and mitigate the health risks associated with pesticide exposure. As pesticides continue to be widely used in agriculture and public health, concerns regarding their long-term biological effects have increased. Traditional risk assessment approaches, which primarily depend on animal models and limited exposure data, are now being complemented by integrative methods that provide a more accurate and comprehensive understanding of human health outcomes. Recent developments include high-throughput screening, omics-based technologies, human biomonitoring (HBM), and computational modeling, all of which are improving the ability to link external pesticide exposure to internal biological responses. Additionally, the adoption of exposome frameworks, wastewater-based epidemiology, and wearable biosensors is enabling realtime, population-level monitoring and personalized exposure assessments.
These innovations are enhancing our ability to detect early biomarkers of effect, understand mechanisms of toxicity, and assess cumulative and mixture risks.
This review highlights the progress made in pesticide toxicology and risk assessment, emphasizing interdisciplinary approaches that bridge the gap between exposure science and toxicological outcomes. Ultimately, these advancements support more informed decision-making and effective policy development to protect both environmental and public health.
https://doi.org/10.1016/j.microc.2025.116373

****

Yang, Y., Liu, Q., Filippidis, F. T., Lu, P., Guo, Y.
Association and biological pathways between lifetime occupational exposure to workplace hazards and incident chronic obstructive pulmonary disease and cardiovascular disease in middle-aged and older adults.
Journal of Hazardous Materials, Vol., (2026) 141188.

The long-term impact of lifetime occupational exposure (LOE) on chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD) risk remains unclear. This study examined associations between LOE and the risks of COPD and CVD in middle-aged and older adults. A prospective cohort study was conducted using UK Biobank data, including demographic, lifestyle, and genetic information. Cox proportional hazard models assessed associations of one-hazard (OLOE) and total-hazards LOE (TLOE) with cardiopulmonary outcomes. Mediation analyses explored the role of biomarkers and metabolites. Over a median 12.5-year follow-up, 2.4% (2,426/103,176) developed COPD and 20.6% (18,035/87,419) developed CVD. All OLOEs, except pesticide, were associated with elevated risks for both diseases. Higher TLOE was linked to increased COPD (HR: 1.21, 95% CI: 1.15–1.26) and CVD (HR: 1.05, 95% CI: 1.03–1.06) risks per exposure level increase. Clear dose-response relationships were observed. Inflammatory markers, such as white blood cell count, neutrophil count, and C-reactive protein, partially mediated these associations. Moreover, TLOE was significantly associated with the onset of a single cardiopulmonary disease and its progression to comorbidity. Our findings underscored the potential long-term cardiopulmonary burden of occupational hazards and supported the need for workplace hazard reduction to promote healthy aging.
https://doi.org/10.1016/j.jhazmat.2026.141188

****

Zhou, Y.-Y., Li, M.-L., Wang, X.-D., Xu, H.-B., Liang, J.
A comparative study of urinary mycotoxin biomarkers co-occurrence patterns and cumulative risk assessment in population from three typical areas in China.
Journal of Exposure Science and Environmental Epidemiology, (2025). https://doi.org/10.1038/s41370-025-00830-x

BACKGROUND: This biomonitoring study investigated levels of multi-mycotoxin biomarkers in the urine of subjects living in three different geographic locations and dietary patterns in China.
OBJECTIVE: This study provides a comprehensive understanding of the inner-exposure characteristics to multiple mycotoxins within the Chinese population.
METHODS: The study involved a total of 311 healthy volunteers, with 103 from Anhui Province, 102 from Henan Province, and 106from Sichuan Province. UHPLC-MS/MS was employed to analyze seven mycotoxin biomarkers [total deoxynivalenol (DONt),beta-zearalenol (beta-ZEL), nivalenol (NIV),alpha-zearalenol (alpha-ZEL), diacetoxy cyclohexenol (DAS), zearalenone (ZEN), aflatoxin M1(AFM1)] in urine samples. Urinary biomarker concentrations were used to estimate probable daily intake (PDI), further calculate hazard quotient (HQ), and hazard index (HI).
RESULTS: In the study population, DON was the most prevalent (100%) with a mean concentration of 90.77 ng/ml, followed by beta-ZEL (27.97%), NIV (24.76%),alpha-ZEL (24.12%), DAS (12.86%), ZEN (6.11%) and AFM1(10.96%) in urine samples. The mean PDI for DONt, ZENt and NIV in the total population were 3.02 mu g/kg bw/d, 0.01 mu g/kg bw/d and 0.79 mu g/kg bw/d, respectively. There were 61.09%of the total population with an HQ > 1 for DONt, while 0.96% and 10.93% had an HQ > 1 for ZENt and NIV, respectively. Moreover, approximately 64.31% of urine samples exhibited the co-occurrence of two or more mycotoxins. The most common binary andternary combinations were DONt-ZENt (46.34%) and DONt-ZENt-NIV (19.02%). The percentages of HI > 1 for DONt-ZENt and DONt-ZENt-NIV were 61.09% and 69.77% respectively.
IMPACT: In the present study, the co-occurrence pattern and cumulative risk of the metabolite biomarkers of multi-mycotoxinswerefirstly revealed in three typical areas with different climate types and dietary patterns. This study helps assess the health risksof mycotoxin exposure under different environmental and dietary conditions, reveals the relationship between diet and mycotoxinexposure, and provides scientific support for mitigating the harmful effects of mycotoxins on human health.
https://doi.org/10.1038/s41370-025-00830-x

****

3. Approches métabolomiques

Haalck, I., Krauss, M., Brack, W., Huber, C.
Exploring Domestic Discharge Patterns in Wastewater through LC-HRMS Screening and Temporal Clustering.
Environ Sci Technol, 2025, Vol. 59 (29), p. 15375-15384

Wastewater influent contains valuable epidemiological information, but the complexity of the wastewater matrix poses challenges for data interpretation and linking signals to human exposure.
This study aims to analyze daily discharge patterns in influent wastewater to identify recurring patterns for trace organic compounds, particularly those from domestic sources, providing insights into discharge dynamics originating from population chemical consumption and exposure. Over three 24-h periods, hourly composite influent samples from a wastewater treatment plant were analyzed using liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS).
Target and non-target screening revealed over 72,000 features, with 402 target compounds annotated. Temporal k-means clustering of target compounds identified five distinct daily patterns, with two clusters linked to domestic use : one correlated with wastewater flow, representing general daily population activities, and another showing a morning peak, likely associated with morning urine. Based on these patterns, cluster predictions were applied to the non-targeted feature list, prioritizing features with similar temporal trends. This led to 70 additional features associated with the morning peak pattern, with four compounds exemplarily identified. The findings highlight the value of combining targeted and non-targeted analyzes with clustering methods to improve the interpretation of complex wastewater data and unravel chemical discharge patterns linked to population exposure.
https://doi.org/10.1021/acs.est.5c02486

****

Kolawole, O., Elzein, A., Marczylo, T.
Exposomics as a discovery engine for emerging contaminants and hidden biological risks.
Emerging Contaminants 2026, Vol. 12 (1). 100619

Over the past decade, exposome science has evolved from a conceptual framework into a practical discovery engine for environmental health. By combining high-resolution mass spectrometry, nontargeted analysis, multi-omics integration, wearable sensors, and computational tools, exposomics can capture the complexity of real-world chemical mixtures and uncover exposures missed by conventional monitoring. We conducted a scoping review following PRISMA-ScR guidelines to map how exposomic approaches have been applied to the detection and characterisation of under-regulated or previously unknown contaminants.
Searches of four bibliographic databases and targeted grey literature (2015-2025) yielded 67 eligible studies, of which 42 were charted quantitatively. The evidence was heavily concentrated in high-income countries and focused on pesticides, PFAS, and heavy metals, with metabolic, developmental, and epigenetic outcomes most frequently reported. Across this landscape, 17 priority compounds emerged where exposomics revealed either new detections or novel biological effects, including halobenzoquinones, GenX, bisphenol S, microplastics, tungsten, and 3hydroxyoctanedioic acid. These case exemplars illustrate how exposomics can expand hazard characterisation and provide early warning of risks that are invisible to targeted surveillance. At the same time, critical gaps persist, particularly in geographic coverage, longitudinal cohorts, data infrastructures, and mixture analysis tools. Scaling exposomics through harmonised biomonitoring systems and embedding it within One Health frameworks will be essential to accelerate discovery and to translate emerging evidence into more proactive and equitable chemical risk governance.

ncnd/4.0/).
https://doi.org/10.1016/j.emcon.2025.100619

****

Liu, C., Liu, L., Ran, B. Q., Wu, Y. J., Wang, F.
Linking the metals to metabolism in recurrent pregnancy loss through untargeted metabolomics and machine learning.
Frontiers in Endocrinology, Vol. 16, (2025)

The association between recurrent pregnancy loss (RPL) and environmental exposure has attracted increasing attention. However, associations between RPL and metal exposure in northwestern China remained unclear.
Methods: This case-control study (318 RPL women, 326 controls) investigated associations between serum metal concentrations and RPL. Five machine learning algorithms identified significant variables. Bayesian kernel machine regression (BKMR) and quartile g-computation (Qgcomp) models assessed the combined effects of metal mixtures on RPL risk. Untargeted metabolomics integrated with metal exposure data explored potential mechanisms underlying metal-induced disruption.
Results: Compared to controls, RPL women exhibited higher BMI ($P<0.001$) and elevated serum Ti, Cu, and Se levels ($P<0.05$), while controls had higher Li, V, Cr, Sr, Pb, Ni, Zn, and Fe ($P<0.05$). Machine learning algorithms (AUC = 0.99-1.0) identified V, Li, Cr, Ti, and Ni as top five discriminative metals. Mixture analyses (BKMR/Qgcomp) revealed a significantly increased RPL risk with mixed metals (beta=0.37, 95% CI: 0.31-0.42). Ti contributed positively to this risk, whereas V contributed negatively after adjusted for confounders. Metabolomic analysis in a subset (n=100) linked these metals primarily to perturbations in purine metabolism, pantothenate and CoA biosynthesis, retinol metabolism, and ubiquinone/terpenoid-quinone biosynthesis.
Conclusion : Our study provides valuable insights into the metabolic and environmental factors associated with RPL.
https://doi.org/10.3389/fendo.2025.1679190

****

Peng, L., Yan, H., Cai, Z.
Metabolomics in environmental analysis : Applications, advances, and emerging challenges.
Trac-Trends in Analytical Chemistry, Vol. 195, (2026), 118556.

The growing complexity and ubiquity of environmental contaminants demands sensitive, mechanistically informative tools for exposure science. Metabolomics, capturing system-wide metabolic perturbations from chemical exposures, offers a transformative platform for linking molecular disruptions to organismal and population-level outcomes.
This review highlights recent advances in environmental metabolomics, focusing on three key domains: (1) ecological biomonitoring, enhancing early biological effect detection and causality assessment with effect-directed analysis (EDA); (2) mechanistic toxicology, informing Adverse Outcome Pathway (AOP) and quantitative AOP development by bridging multi-scale models from in vivo and in vitro studies; and (3) environmental epidemiology, driving biomarker discovery and pathway inference via metabolome-wide association studies (MWAS), meet-in-the-middle (MITM) frameworks, and advanced statistical, AI computational approaches. By synthesizing methodologies and innovations, this review positions metabolomics as a cornerstone of next-generation environmental health research, advancing predictive, mechanistic chemical risk assessments aligned with New Approach Methodologies (NAMs) in complex scenarios.
https://doi.org/10.1016/j.trac.2025.118556

****

Singh, V.
Current Advancements in Untargeted Metabolomics Analysis and Testing Driven by Machine Learning : Prospects for Artificial Intelligence in Patient-Centric Healthcare Transformation.
Applied Biochemistry and Biotechnology, 2025, doi.org/10.1007/s12010-025-05458-z

Metabolomics is a high-throughput methodology that measures various metabolites in biological fluids. An advantage of an untargeted approach for analyzing metabolomics, which involves an impartial examination of the metabolome, lies in its ability to identify crucial metabolites that contribute to, or serve as indicators of, human health and disease.
This review discusses the significance of artificial intelligence and machine learning in advancing disease diagnosis and small molecule detection using untargeted metabolomics, providing an updated and integrative perspective on their recent impact in this field. The discussion focuses on how artificial intelligence and machine learning have contributed to the evolution of high-resolution mass spectrometry. This approach involves unbiased detection of endogenous and exogenous biochemical compounds and metabolites in biological tissue. It enables the characterization of exposures linked to disease outcomes by providing context for the applications of artificial intelligence and machine learning and exploring their roles in enhancing the precision and efficiency of disease exposure assessments.
While several review articles address the application of artificial intelligence and machine learning in metabolomics, this article aims to highlight recent opportunities for leveraging these technologies specifically in untargeted metabolomics, covering improvements in data quality, methodological rigor, sensitivity in detection, and precise compound identification. The novelty holds transformative potential that artificial intelligence and machine learning bring to metabolomics, paving the way for more robust and insightful investigations.
https://doi.org/10.1007/s12010-025-05458-z

****

4. Modèles d'analyse, outils, méthodes

Cot, S., Bernard, N., Martin, B., Gauthier-Manuel, H., Pujol, S., Mauny, F.*, et al.*
How to Better Assess the Real Role of the Environment in Pregnancy, From Past to Future : A Relational Open Data Infrastructure Covering 30,000 Births.
Health Sci Rep 2026, Vol. 9 (2), (2026), e71668.

BACKGROUND AND AIMS: One of today's challenges in terms of understanding the real impact of the environment on pregnancy and its complications is the ability to work with real-life data that are correctly and extensively connected to data on the contamination of living environments and individualized exposures. We present a solution based on a data infrastructure that is directly usable for research. We describe (i) the methodological characteristics of the infrastructure, (ii) the geographical territory and environmental exposures covered by the infrastructure, and (iii) the initial description of the real-life health data of the included population.
METHODS: The infrastructure is a relational database that integrates routine obstetric care data from CHUB with individual environmental exposure data linked via home addresses. The infrastructure includes all deliveries at Besancon University Hospital (CHUB) from January 1, 2010, to December 31, 2021.
RESULTS: Our infrastructure included information on 20,376 women, 28,344 pregnancies, and 29,190 births. The infrastructure described includes 20% of deliveries in an administrative region of more than 1.5 million inhabitants. The quality of the data is linked to highly contrasted exposure of living areas within this region and temporal coverage of more than 10 years of obstetrical events. This infrastructure is a research tool with the capacity to incorporate data in the future.
CONCLUSION: This infrastructure can be used to address a wide range of questions aimed at describing the phenomena of environmental exposure during pregnancy, multiple exposures and their cumulative effects, particularly the phenomena of mediation, interaction, or confusion.
https://doi.org/10.1002/hsr2.71668

****

Hughes, L., Cops, J., Geerts, L., De Brouwere, K., Sangion, A., Li, L.*, et al.*
Integrating Monitoring and Biomonitoring Data with Mechanistic Models to Better Estimate and Characterize Aggregate Human Exposures to Semivolatile Organic Chemicals.
Environmental Science & Technology, Vol. 59 (49), (2025), 26362-26372.

Humans are exposed to many chemicals from multiple sources through various pathways. Many semivolatile organic chemicals (SVOCs) are ubiquitous in indoor environments, but the extent of exposure and relative importance of different pathways (near-field or far-field) are uncertain.
Here, 37 SVOCs with measured concentrations in indoor media are used in conjunction with a mass balance indoor fate, exposure, and toxicokinetic model to 1) estimate exposures from indoor environments, 2) incorporate measured dietary (far-field) exposures, 3) evaluate modeled biological concentrations in blood and urine against previously published human biomonitoring (HBM) estimates, 4) calculate the relative importance of different exposure pathways, and 5) demonstrate the value of using models and monitoring data to estimate aggregate exposure for human health assessment. All model calculated blood and urine concentrations are within 2 orders of magnitude of HBM values, and 73% are within 1 order of magnitude. The method explicitly considers uncertainty in measured indoor concentrations and mouthing-mediated ingestion (MMI). When median measured chemical concentrations in dust and MMI are used for modeling, far-field dietary intake is determined to be the dominant contributor to the overall exposure for almost all investigated SVOCs. However, when modeling with higher (third quartile reported) measured chemical concentrations in dust and similar to 3x higher dust ingestion rates, near-field sources result in exposures for some SVOCs that are comparable to or exceed contributions from far-field exposure pathways. The model also addresses measurement data gaps and, combined with the monitoring data, provides a method to estimate chemical emission rates.
https://doi.org/10.1021/acs.est.5c08964

****

Domingo, J. L.
Mixture toxicity revisited : A translational review of experimental evidence from animal models to human health risk assessment.
Toxicology, Vol. 520, (2025), 154372.

This review examines research investigating how simultaneous exposure to multiple chemicals affects biological systems, highlighting deficiencies in conventional single-substance risk evaluation frameworks. Living organisms in their natural habitats face continuous exposure to diverse chemical combinations, which frequently result in interactive effects, including synergism and antagonism, that diverge from the straightforward additive outcomes anticipated by traditional toxicological approaches. Research using animal and aquatic experimental models has shown that these exposures depend on numerous variables, such as the specific chemicals involved, their dose relationships, duration of contact, measured biological outcomes, and underlying mechanistic processes.
This review examines fundamental methodological frameworks, particularly concentration addition (CA) and independent action (IA) models, used for predicting mixture toxicity, with most mixture effects falling within a two-fold range of additivity predictions though important deviations occur. Additional complicating factors include the timing of exposure and the specific biological traits of test species.
The present review also addresses difficulties in applying findings from animal research to human populations, given differences in toxicokinetic processes and genetic makeup across species. To navigate these complexities, this review supports the adoption of mechanism-based frameworks incorporating high-throughput omics technologies, computational approaches, and standardized protocols for evaluating environmentally realistic mixtures. The review advocates for implementing tiered, cumulative risk-assessment methodologies that accurately represent real-world exposure conditions and emphasize protection of susceptible populations. This transformation is vital for advancing predictive toxicology and

strengthening protections for public and environmental health.
Ultimately, the review argues for moving beyond the obsolete single-substance paradigm toward comprehensive, evidence-driven approaches equipped to handle the multifaceted nature of chemical exposures. This review critically evaluates experimental animal studies in chemical mixture toxicology, emphasizing the complexities and prospects of applying animal findings to human health risk assessment. It identifies key gaps linking controlled experiments with epidemiological data and proposes research directions to advance risk evaluation and management of real-world chemical co-exposures.
https://doi.org/10.1016/j.tox.2025.154372

****

Gao, P.
The human airborne exposome.
Nature Health, Vol. 1, (2026), 26-34

Environmental health research has historically focused on associations between criteria air pollutants—particularly particulate matter—and health outcomes. Although these studies have established critical links between regulated pollutants and adverse effects, they fail to capture the multidimensional nature of the human airborne exposome. The air comprises thousands of organic compounds, dozens of inorganic substances and millions of microorganisms that are breathed in, leading to personalized exposure profiles. This current paradigm has three limitations: statistical challenges in analysing multi-pollutant data; inadequacies in exposure assessment; and knowledge gaps in biological mechanisms. Here a new research framework is proposed, which integrates mixture-based analytical approaches, advanced personal monitoring technologies and multi-omics methods. This framework would illuminate the aetiology of complex diseases with multifactorial environmental components, such as cancers, neurological disorders and immune dysregulation. By better characterizing individual-level exposures and biological responses, this approach could enable precision interventions that protect vulnerable populations with unprecedented specificity.
https://doi.org/10.1038/s44360-025-00026-5

****

Jian, Z., Jinting, Z., Wang, L., Zhenjie, Y., Jingying, L., Shuang, W*., et al.*
Machine learning-based prediction of occupational exposure risks among oral healthcare workers.
Front Public Health, Vol. 13, (2025), 1713841

OBJECTIVE: This study aims to identify the key risk factors for occupational exposure among oral healthcare workers and develop a predictive model using machine learning algorithms to lay the foundation for early screening of high-risk populations and the formulation of preemptive intervention plans.
METHODS: A multicenter cross-sectional study was conducted among 367 oral healthcare workers in 27 hospitals in Tianjin, China, from January 2025 to June 2025. Data were collected via an online questionnaire, encompassing demographic information, Work Preference Inventory, Organizational Climates, resilience, and other relevant factors. Logistic regression, random forest, decision tree, and XGBoost algorithms were employed to construct predictive models. The models were evaluated based on the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, specificity, and F1 score.
RESULTS: The incidence rates of occupational exposure in the modeling and validation groups were 15.5% and 16.5%, respectively. Univariate analysis revealed significant differences between the exposed and non-exposed groups in terms of Work Preference Inventory, Organizational Climates, resilience, professional title, hospital level, age, and gender. Multivariate analysis using logistic regression indicated that Work Preference Inventory, resilience, Organizational Climates, professional title, hospital level, and gender were independent risk factors for occupational exposure. The random forest model exhibited the best predictive performance, with an AUC of 0.755, accuracy of 89.2%, sensitivity of 56.3%, specificity of 94.7%, and F1 score of 0.600.
CONCLUSION: This study successfully identified the key risk factors for occupational exposure among oral healthcare workers and developed a predictive model using the random forest algorithm. These findings

can guide the development of targeted interventions to mitigate the risks of occupational exposure. Future research should focus on validating the model with larger and more diverse datasets.
https://doi.org/10.3389/fpubh.2025.1713841

****

Liu, Y., Ma, F., Zhong, Z., Liu, X., Liu, M., Lou, K.
The Impact of High-Resolution LC-MS/MS Detected Environmental Exposures on Obesity: A Study of Cumulative Effects Through Statistical Modeling.
Diabetes, Metabolic Syndrome and Obesity, Vol. 19, (2026), 1-11

Background: Obesity is a major and escalating public health challenge worldwide. Growing evidence implicates environmental chemicals, especially organophosphate flame retardants (OFRs) and per- and polyfluoroalkyl substances (PFAS), as potential obesogens due to their ability to disrupt endocrine function and lipid metabolism. However, data on the association between these chemical mixtures and overweight in Chinese populations—particularly in industrialized regions—are scarce, representing a critical knowledge gap.
Methods: We conducted a matched case–control study of 214 adults from northern China, including 107 overweight individuals (body mass index [BMI] ≥ 24 kg/m2) and 107 normal-weight controls (BMI < 24 kg/m2), pair-matched by age and sex. Using high-resolution liquid chromatography–tandem mass spectrometry (LC-MS/MS), we quantified serum concentrations of 202 environmental exposures. Multivariable logistic regression, Weighted Quantile Sum (WQS) regression, and Bayesian Kernel Machine Regression (BKMR) models were employed to assess individual and cumulative associations with overweight, adjusting for key metabolic covariates (eg, blood pressure, lipids, and fasting glucose).
Results: Thirteen chemicals showed significant differences between groups (|log2 fold change| ≥ 1). Ten were elevated in the overweight group, most notably tris(2-butoxyethyl) phosphate (TBOEP; adjusted odds ratio [OR] = 2.40, 95% confidence interval [CI]: 1.79– 3.33), 1,3,5-triazine-2,4,6-trione tris(2,3-dibromopropyl) ester (TBC), perfluorooctanoic acid (PFOA), and perfluorobutane sulfonic acid (PFBS). The WQS index reflecting the combined effect of these 13 chemicals was strongly associated with higher odds of overweight (OR = 2.33, 95% CI: 1.77– 3.07). BKMR analysis further revealed a non-linear cumulative exposure–response relationship, with maximal risk observed at moderate exposure levels.
Conclusion: This study provides robust epidemiological evidence that circulating levels of specific environmental pollutants—particularly TBOEP, PFOA, PFBS, and TBC—are significantly associated with increased likelihood of overweight in a northern Chinese adult population. Our findings highlight the potential contribution of complex chemical mixtures to obesity etiology in rapidly industrializing settings and underscore the need for targeted environmental health interventions.
https://doi.org/10.2147/dmso.S558970

****

Recoules, C., Audebert, M.
Set up of a human 3D liver multicellular model for chemical high-throughput toxic hazard assessment.
NAM Journal, Vol. 2, (2026) 100075.

Despite progress, many drugs fail because toxicity is missed during preclinical testing. In vitro liver cell models are therefore continuously evolving in order to investigate hepatic functions and assess drug-induced liver toxicity more efficiently. Three-dimensional (3D) cell models have recently emerged as superior to 2D systems.
Here, we present a human multicellular liver spheroid comprising hepatocytes, cholangiocytes, stellate cells, and immune cells. This model was designed to closely mimic liver physiology for toxicological studies. It was characterized using biomarkers targeting key toxicological endpoints, such as hepatotoxicity, genotoxicity, oxidative stress, inflammation, and lipid accumulation. High-resolution confocal imaging was performed at the cellular level with four uniform spheroids per well. A dedicated workflow was developed for analyzing 3D-reconstructed images, enabling robust biomarker assessment.
This advanced 3D liver model is a promising tool for identifying hepatotoxic compounds and their mode of

action in a human-relevant context.
https://doi.org/10.1016/j.namjnl.2025.100075

****

Gonzalez Combarros, R., Gonzalez-Garcia, M., Blanco-Diaz, G. D., Segovia Bravo, K., Reino Moya, J. L., Lopez-Sanchez, J. I.
Risk Assessment of Chemical Mixtures in Foods: A Comprehensive Methodological and Regulatory Review.
Foods (Basel, Switzerland), Vol. 15 (2), (2026), p.

Over the last 15 years, mixture risk assessment for food xenobiotics has evolved from conceptual discussions and simple screening tools, such as the Hazard Index (HI), towards operational, component-based and probabilistic frameworks embedded in major food-safety institutions. This review synthesizes methodological and regulatory advances in cumulative risk assessment for dietary "cocktails" of pesticides, contaminants and other xenobiotics, with a specific focus on food-relevant exposure scenarios. At the toxicological level, the field is now anchored in concentration/dose addition as the default model for similarly acting chemicals, supported by extensive experimental evidence that most environmental mixtures behave approximately dose-additively at low effect levels. Building on this paradigm, a portfolio of quantitative metrics has been developed to operationalize component-based mixture assessment: HI as a conservative screening anchor; Relative Potency Factors (RPF) and Toxic Equivalents (TEQ) to express doses within cumulative assessment groups; the Maximum Cumulative Ratio (MCR) to diagnose whether risk is dominated by one or several components; and the combined Margin of Exposure (MOET) as a point-of-departure-based integrator that avoids compounding uncertainty factors. Regulatory frameworks developed by EFSA, the U.S. EPA and FAO/WHO converge on tiered assessment schemes, biologically informed grouping of chemicals and dose addition as the default model for similarly acting substances, while differing in scope, data infrastructure and legal embedding. Implementation in food safety critically depends on robust exposure data streams. Total Diet Studies provide population-level, "as eaten" exposure estimates through harmonized food-list construction, home-style preparation and composite sampling, and are increasingly combined with conventional monitoring. In parallel, human biomonitoring quantifies internal exposure to diet-related xenobiotics such as PFAS, phthalates, bisphenols and mycotoxins, embedding mixture assessment within a dietary-exposome perspective. Across these developments, structured uncertainty analysis and decision-oriented communication have become indispensable. By integrating advances in toxicology, exposure science and regulatory practice, this review outlines a coherent, tiered and uncertainty-aware framework for assessing real-world dietary mixtures of xenobiotics, and identifies priorities for future work, including mechanistically and data-driven grouping strategies, expanded use of physiologically based pharmacokinetic modelling and refined mixture-sensitive indicators to support public-health decision-making.
https://doi.org/10.3390/foods15020244

****

5. Co-expositions aux métaux lourds

Bieck, C., Koopmann, K., Alberts, A., Buder, V., Schedlbauer, G., Nienhaus, A.*, et al.*
Nickel and Cobalt Release From Hairdressing Tools in German Barbershops.
Contact Dermatitis, Vol. 93 (6), (2025), 499-506.

La libération de nickel et de cobalt par les outils a récemment été mise en évidence dans les salons de coiffure allemands. Aucune donnée comparable n'était disponible pour les salons de barbiers allemands. Cent quarante et un outils ont été testés dans six salons de barbiers situés en Basse-Saxe, en Allemagne.

Un test ponctuel pour le nickel et un test ponctuel pour le cobalt ont été utilisés. Au total, 35 des 141 outils (24,8 %) ont libéré du nickel et 3 des 141 outils (2,1 %) ont libéré du cobalt. La libération de nickel a été constatée dans 10 des 57 tondeuses à cheveux, 9 des 13 pinces à épiler, 8 des 11 pinces à cheveux, 3 des 14 rasoirs droits, 2 des 32 ciseaux, 2 des 4 peignes à queue et 1 des 2 blaireaux. La libération de cobalt a été détectée dans 2 des 14 rasoirs droits et 1 des 11 pinces à cheveux. Les outils utilisés dans les salons de barbiers allemands ont été identifiés comme des sources professionnelles d'exposition au nickel et au cobalt. La libération de nickel a été observée plus fréquemment. Il est donc recommandé de respecter plus strictement la réglementation européenne sur le nickel. En outre, l'importance des mesures de prévention de la peau au travail devrait être communiquée aux coiffeurs, par exemple dans le cadre de mesures pédagogiques en matière de santé.
Référence INRS-Biblio : 751434
https://doi.org/10.1111/cod.70031

****

G. V. P. Husodho, I. M. P., A. D. A. Kumalasari, T. A. Listiyanti, R. H. Setiawan, and S. Bakri.
Prenatal–Postnatal Heavy Metal Exposure in Relation to Neurodevelopmental Disorder and ADHD : A Systematic Review.
Diponegoro International Medical Journal, Vol. 6 (2), (2025), 32-39.

Introduction: Susceptibility to environmental insults during fetal brain development has been linked to an increased risk of neurodevelopmental disorders, including attention-deficit/hyperactivity disorder (ADHD). ADHD is a prevalent neurodevelopmental disorder in children and is influenced not only by genetics, but also by environmental factors, particularly prenatal exposure to heavy metals. Heavy metals, such as lead, mercury, cadmium, and arsenic, are known neurotoxins that can disrupt fetal brain development; however, evidence regarding their role in ADHD remains inconsistent.
Methods: This systematic review followed PRISMA guidelines to evaluate the association between prenatal heavy metal exposure and the risk of ADHD in children. The PECO framework was used to define population, exposure, comparators, and outcomes. A comprehensive literature search was conducted across PubMed, ScienceDirect, and ProQuest, using relevant keywords. Eligible studies included human observational research (cohort, case-control, cross-sectional) between 2021 and 2025 assessing prenatal exposure to heavy metals, neurodevelopmental outcomes, and ADHD.
Results: Several studies have reported that elevated prenatal levels of cadmium, lead, and manganese are associated with increased ADHD symptoms and reduced cognitive performance. The findings on mercury were mixed, potentially due to confounding factors, including fish intake and maternal nutrition. Selenium and copper demonstrate dual effects, being essential at low levels but harmful at high concentrations. Thallium exposure in the third trimester significantly impaired cognitive and psychomotor development. Some studies have highlighted sex-specific and nonlinear dose-response effects.
Conclusion: Heavy metals have an inconsistent impact on neurodevelopment. While some studies have associated prenatal exposure to cadmium and lead with neurodevelopmental issues, others have not found such links. Both prenatal and postnatal exposure to heavy metals, particularly cadmium, mercury, and lead, are associated with childhood ADHD.
https://www.researchgate.net/publication/399754225_Prenatal_and_Postnatal_Heavy_Metal_Exposure_in_Relation_to_Neurodevelopmental_Disorder_and_ADHD_A_Systematic_Review#:~:text=Conclusion%3A%20Heavy%20metals%20affect%20neurodevelopment,is%20linked%20to%20childhood%20ADHD.
https://doi.org/10.14710/dimj.v6i2.29755

****

Gonzalez-Villalva, A., Rojas-Lemus, M., López-Valdez, N., Cervantes-Valencia, M. E., Guerrero-Palomo, G., Casarrubias-Tabarez, B.*, et al.*
Metal Pollution in the Air and Its Effects on Vulnerable Populations : A Narrative Review.
International Journal of Molecular Sciences, 2026. Vol. 27 (2), 720.

Particulate atmospheric pollution poses a global threat to human health. Metals enter the body through inhalation attached to these particles. Certain vulnerable groups are more susceptible to toxicity because of age, physiological changes, and chronic and metabolic diseases and also workers because of high and cumulative exposure to metals. A narrative review was conducted to examine the effects of key metals—arsenic, cadmium, chromium, copper, lead, mercury, manganese, nickel, vanadium, and zinc—on vulnerable populations, analyzing articles published over the past decade. Some of these metals are essential for humans; however, excessive levels are toxic. Other non-essential metals are highly toxic. Shared mechanisms of toxicity include competing with other minerals, oxidative stress and inflammation, and interacting with proteins and enzymes. Prenatal and childhood exposures are particularly concerning because they can interfere with neurodevelopment and have been associated with epigenetic changes that have long-term effects. Occupational exposure has been studied, but current exposure limits for specific metals appear dangerous, emphasizing the need to revise these standards. Older adults, pregnant women, and individuals with metabolic diseases are among the least studied groups in this review, underscoring the need for more research to understand these populations better and create effective public health policies.
https://doi.org/10.3390/ijms27020720

****

Guo, X., Gao, F., Li, M., Pan, B., Gao, F., Wang, S.*, et al.*
Association between plasma metal element profiles and cognitive impairment in occupationally aluminum-exposed workers at a large aluminum plant in northern China.
J Prev Alzheimers Dis, (2026), 100470 p.

This study explored the association between plasma levels of multiple metals and cognitive impairment (CI) in 455 aluminum electrolysis workers from a northern Chinese plant, divided into CI (256) and control (199) groups by MoCA scores. Using inductively coupled plasma mass spectrometry, 11 metals were measured, with analyses via conditional logistic regression, generalized linear models (GLM), Bayesian kernel machine regression (BKMR), and age stratification (40 years). Plasma aluminum (Al), lead (Pb), lithium (Li), manganese, cobalt, and copper were significantly higher in the CI group (all $P < 0.05$), while zinc showed no difference. Single-element analysis found Al, Pb, and Li negatively correlated with MoCA total and subscores (e.g., visuospatial function; $P < 0.05$), and zinc positively correlated with attention (beta = 1.10, $P < 0.05$). BKMR confirmed metal mixtures above the 25th percentile reduced MoCA scores (beta = -0.875, 95 % CI: -1.379 to -0.371), with Al, Pb, and Li as key contributors (PIP > 0.6). Subgroup analysis showed Al primarily affected those <40, while Pb had greater impact in those >40. Findings indicate elevated Al, Pb, and Li associate with higher CI risk, metal mixtures synergistically exacerbate impairment, and age modifies these effects, aiding occupational cognitive impairment prevention.
https://doi.org/10.1016/j.tjpad.2025.100470

****

Huang, Z. X., Li, Y. L., Peng, J. C., Ho, T. T., Huang, H., Aschner, M.*, et al.*
The Effects of Lead, Cadmium and Arsenic Exposure Alone or in Combination on Neurotoxicity Through Neural Signaling Pathways.
Biol Trace Elem Res, Vol., (2025).

Environmental toxic heavy metals seldom exist in isolation. Lead (Pb), cadmium (Cd), and arsenic (As) often co-occur as complex pollutant mixtures, resulting in prolonged combined human exposure through multiple pathways. While traditional toxicological research has largely focused on the effects of individual metals, accumulating evidence indicates that the neurotoxicity induced by co-exposure is not necessarily additive. Indeed, it often manifests as synergistic or antagonistic, involving complex mechanisms that disrupt neural signaling pathways. Thus, investigating their combined effects is essential for achieving more realistic and accurate health risk assessments.
This review systematically elucidates the mechanisms by which Pb, Cd, and As both individually and in combination disrupt key signaling pathways in the central nervous system (CNS). Although these metals

exert distinct properties, they all induce oxidative stress, disrupt intracellular calcium homeostasis, cause mitochondrial dysfunction, and trigger neuroinflammation to impair neural signaling. Taken together, given the complexity of real-world human exposure scenarios, transitioning from single-metal studies to combined exposure research represents both an urgent need and an inevitable trend in environmental toxicology. Deepening our understanding of the mechanisms underlying their combined toxicity will not only enable more accurate health risk assessment but also provide a critical foundation for the development of science-based public health interventions and the identification of effective neuroprotective targets.
https://doi.org/10.1007/s12011-025-04943-0

****

Kan, H., Jiang, Z., Chen, M., Yin, T., Pan, M., Zheng, M.*, et al.*
Accelerated biological aging underlies the link between heavy metal mixture exposure and depression : A multi-omics study.
Environ Pollut, Vol. 391, (2025), 127611.

Growing evidence implicates accelerated biological aging in environmentally induced psychiatric disorders, yet its role in metal-associated depression remains unclear. Using NHANES data, we evaluated associations between heavy metal mixtures and depression. Bidirectional mediation analysis was used to assess reciprocal pathways linking heavy metals, biological aging, and depression. Simultaneously, candidate genes linking heavy metal exposure to depression and biological aging were identified by mining the Comparative Toxicogenomics Database, analyzing differentially expressed genes (DEGs) from the Gene Expression Omnibus, and integrating the resulting evidence within a toxicogenomic framework to explore potential molecular mechanisms. The prevalence of depression among participants was 8.66 %. Metal mixtures significantly increased depression risk. Notably, cadmium and antimony increased the risk of depression (OR: 1.52, 95 % CI: 1.19, 1.94 and OR: 1.54, 95 % CI: 1.22, 1.93). Both metals have low thresholds (0.227 mug/L and 0.053 mug/L, respectively). Additionally, lead, cobalt, and molybdenum showed positive associations in specific models. Although population-level exposure to heavy metals declined from 1999 to 2020, concentrations remained sufficient to elevate depression risk. Our correlation analysis also identified a strong correlation between PhenoAge and chronological age ($r = 0.84$, $P < 0.001$). Mechanistically, we found that accelerated PhenoAge partially mediated the associations of several metals with depression risk, including monomethylarsonic acid (beta = 0.004; 95 %CI: 0.003,0.006), cadmium (beta = 0.006; 95 %CI: 0.003, 0.010), lead (beta = 0.009; 95 %CI: 0.006, 0.011), cobalt (beta = 0.010; 95 %CI: 0.006, 0.013), molybdenum (beta = 0.009; 95 %CI: 0.006, 0.011), and antimony (beta = 0.008; 95 %CI: 0.005, 0.011). Pathway analysis and DEGs implicated the contribution of neurodegeneration-multiple diseases pathway, with core molecular targets centering on BDNF, IL6, GSK3B, PTGS2, and SOD1. These findings, which imply biological aging as a potential link between metal exposure and depression, call for revised safety thresholds and pinpoint molecular targets for intervention.

https://doi.org/10.1016/j.envpol.2025.127611

****

Lee, J. E., Baek, J. Y., Park, J. D., Chang, J. Y., Choi, B. S.
Co-exposure to environmental cadmium and arsenic leads to kidney damage even at lower concentrations.
J Expo Sci Environ Epidemiol, Vol., (2025).

BACKGROUND: While many studies have examined the effects of single heavy metal exposure, the impact of combined exposure to multiple heavy metals on kidney health remains underexplored.
OBJECTIVE: This study aims to assess the risk of kidney damage associated with relatively low concentrations of Cd and As, below established reference levels, and to investigate whether simultaneous exposure leads to synergistic or additive harmful effects.
METHODS: In this cross-sectional study of 1948 non-occupationally exposed individuals, we explored the

relationship between environmental exposure to heavy metals at sub-occupational levels and the prevalence of kidney damage in this population.
RESULTS: The risk of kidney damage was increased proportionally to urinary cadmium (uCd) and urinary arsenic (uAs) levels. Co-exposure to Cd and As at Co3 (both metals were above the 3rd tertile) resulted in a 2.65-fold increase in beta2-microglobulin (MG) and a 4.41-fold increase in urinary total protein compared to those at Co1 (both metals were below the 3rd tertile). N-acetyl-beta-D-glucosaminidase (NAG) level was 7.42-fold higher at Co3 than at Co1. Subgroup analysis showed that the odds ratio of NAG level elevation increased by 2.74 folds when uCd level was >0.96 mug/g Creatinine (Cr) and uAs level was >8.17 mug/g Cr, and by 3.04-fold when uCd level was >1.86 mug/g Cr (3rd tertile) and uAs level was >4.71 mug/g Cr (2nd tertile). This suggests that co-exposure to both metals can cause kidney damage at concentrations lower than the reference level and even lower than the single metal concentration (uCd 1.86 mug/g Cr) that caused kidney damage.
SIGNIFICANCE: In this study, combined exposure to cadmium and arsenic causes kidney damage even at levels below reference thresholds. The findings highlight synergistic effects, with significant increases in biomarkers like beta2-microglobulin and NAG.
IMPACT: This study demonstrates that environmental cadmium and arsenic exposure can lead to kidney damage in the general population, even at levels significantly below established reference thresholds. These findings highlight the need to reconsider and potentially lower the biological exposure index for combined heavy metal exposure. Additionally, NAG was identified as a highly sensitive biomarker for detecting kidney damage caused by low-level exposure to heavy metals. Unlike previous studies, this research provides specific concentration thresholds, offering a clearer understanding of exposure risks and advancing the assessment of combined heavy metal toxicity on kidney health.
https://doi.org/10.1038/s41370-025-00828-5

****

Merutka, I. R., Ettinger, K. M., Chernick, M., Kolli, R. T., De Silva, M. C. S., Drummond, I. A.*, et al.*
Chronic exposure to low levels of glyphosate and metals induces kidney dysfunction.
Toxicological sciences : an official journal of the Society of Toxicology, Vol., (2026), kfag007.

Chronic kidney disease (CKD) affects 15% of U.S. adults and over 840 million people worldwide. Environmental contaminants, including pesticides and metals, are increasingly recognized as disease contributors, yet mechanisms and consequences of long-term, low-level mixture exposures remain poorly defined.
Our prior work identified glyphosate and metals (cadmium, arsenic, lead, vanadium) in drinking water from agricultural regions with high CKD prevalence and showed that early-life co-exposures disrupt kidney development. Here, using adult zebrafish as a mechanistic model, we tested whether chronic, low-level exposure to glyphosate, metals, and their combination impairs kidney function and structure. We exposed zebrafish for 10 and 60days to glyphosate (10ppb), metals (2ppb Cd, 4ppb As, 5ppb Pb, 15V), or glyphosate + metals and evaluated low-molecular weight proteinuria, histopathology, metabolomics, mitochondrial function, mitochondrial copy number, and mitophagy in the kidney. Chronic exposure to glyphosate and metals produced distinct yet overlapping kidney toxicity signatures, including tubular injury, altered metabolism, and impaired mitochondrial function. Co-exposures generated the most severe effects, with mitochondrial beta oxidation, respiration, and mitophagy as sensitive targets.
These findings demonstrate that glyphosate and metals at levels found in drinking water damage kidney function over time, with co-exposure worsening outcomes compared to individual chemicals. Our study identifies mitochondria-rich proximal tubules as critical targets of chronic glyphosate-metal exposure, providing mechanistic insight into how environmental contaminants contribute to CKD risk. This work advances understanding of disease etiology in environmental nephropathies and highlights environmental factors as important drivers of kidney health.
https://doi.org/10.1093/toxsci/kfag007

****

Trivedi, A., Trivedi, S. P., Saxena, V., Arya, N., Bakhasha, J.
Brass-Derived Copper and Zinc Induce Oxidative Stress and Autophagy-Mediated Nephrotoxicity in Channa punctatus.
J Appl Toxicol, Vol., (2025), p.

Brass toxicity has emerged as a pressing environmental concern, with its dual-metal burden of copper (Cu) and zinc (Zn) from industrial discharges continuing to jeopardize aquatic ecosystem health. This study investigates the effects of environmentally relevant concentrations (ERC) and 10% and 20% elevated levels of Cu (0.85, 0.935, and 1.02 mg/L) and Zn (1.2, 1.32, and 1.44 mg/L) on the kidney of Channa punctatus during a 60-day exposure, with sampling conducted at 15-day intervals under controlled laboratory conditions. Results revealed significant ($p < 0.05$), dose- and time-dependent accumulation of Cu and Zn in renal tissues, accompanied by elevated reactive oxygen species (ROS) and lipid peroxidation (LPO) levels, and increased superoxide dismutase (SOD) and catalase (CAT) activities, whereas reduced glutathione (GSH) content declined markedly. qRT-PCR analysis demonstrated pronounced upregulation of atg5, beclin1, lc3, and ulk1b with concomitant downregulation of mTOR, suggesting activation of the autophagic pathway in response to oxidative stress. Histopathological examination confirmed progressive renal degeneration, including glomerular degenerative cells, vacuolization, and epithelial disorganization, especially at higher concentrations. Principal component analysis (PCA) indicated a strong association among ROS, antioxidant enzymes, LPO, and autophagy genes, emphasizing redox-autophagy coupling in metal-induced stress responses. Collectively, these findings identify brass as a key driver of nephrotoxicity, where chronic Cu-Zn release disrupts redox balance and induces cytotoxic autophagy, with autophagy-related genes serving as sensitive biomarkers of brass toxicity in freshwater ecosystems.
https://doi.org/10.1002/jat.70021

****

Xu, Z., Zhong, J., Yang, T., Liu, L., Lei, T., Cheng, S.*, et al.*
Urinary zinc-lead and strontium-iron combinations affect renal function via serum uric acid: A cross-sectional study in Chinese adults.
Environ Pollut, Vol. 392, (2026), 127630 p.

The relationships between urinary metal mixture exposures and CKD, as well as the mediating role of serum uric acid (SUA), remain unexplored. The study analyzed baseline data from the China Multi-Ethnic Cohort (CMEC) of 14,806 adults.
Urinary concentrations of 21 metals were quantified using inductively coupled plasma mass spectrometry. Least absolute shrinkage and selection operator (LASSO) regression was used to identify key metals, and their associations with CKD were assessed using logistic regression and restricted cubic splines. To comprehensively assess all possible combinations of the selected metals, Mixture effects were analyzed through Qgcomp and WQS regression.
Significant metal combinations and their interactions were further assessed, while the mediating role of SUA was evaluated using generalized linear models. Multiple sensitivity analyses were used to ensure robustness. LASSO regression identified six primary urinary metals (Zn, Sr, Mo, Pb, B, and Fe) from a total of 21 metals analyzed. In the single-metal models, Sr and Fe exhibited inverse associations with CKD, though causality requires further investigation given potential confounding by altered renal excretion. Conversely, Zn indicated a significant positive association with CKD. In mixture analyses, the qgcomp revealed significant heterogeneity across all 63 combinations, and the directional consistency with single-metal models was maintained. WQS confirmed stability in the weight directions.
Among 63 metal combinations. Zn + Pb exhibited risk-enhancing effects through a synergistic interaction, while Sr + Fe demonstrated the strongest inverse association without significant multiplicative interaction. Uric acid mediated 24.9 % and 22.7 % of the Sr + Fe-CKD and Zn + Pb-CKD effects, respectively. This study highlights the individual or combined effects of six urinary metals (Zn, Sr, Mo, Pb, B, and Fe) on CKD, focusing on the specific urinary metal combinations (Zn + Pb and Sr + Fe) mediated by SUA, providing novel insights into the associations of metal with CKD.
https://doi.org/10.1016/j.envpol.2025.127630

****

Zhang, S., Tang, H., Pan, L., Zhou, M.
Association of metal and metalloid exposure with cardiovascular-kidney-metabolic syndrome : mediation by inflammation, oxidative stress, and aging.
BMC public health, Vol., 26, 222 (2026).

BACKGROUND: Metal and metalloid exposure has been linked to various health impairments; however, its association with Cardiovascular-Kidney-Metabolic (CKM) syndrome has not been systematically investigated. This study aims to evaluate this relationship.
METHODS: This cross-sectional study analyzed data from the National Health and Nutrition Examination Survey (NHANES) spanning 1999-2018. Urinary concentrations of nine metal and metalloid species (barium, cadmium, cobalt, cesium, molybdenum, lead, antimony, thallium, and tungsten) were examined. Weighted multinomial logistic regression was used to assess associations between individual metals and CKM syndrome stages. Additionally, mixture models including quantile g-computation (Qgcomp), weighted quantile sum (WQS), and Bayesian kernel machine regression (BKMR) were applied to evaluate combined effects of metals and metalloids. Mediation analyses explored whether inflammation, oxidative stress, and biological aging may partially mediate these associations. Subgroup analyses were conducted by sex, age, and race. Sensitivity analyses including urinary arsenic were also conducted (2003-2018 NHANES cycles).
RESULTS: After applying exclusion criteria, a total of 6,650 participants were included (3,358 men and 3,292 women; mean age 47.3 years, SD=16.5). CKM syndrome exhibited a high prevalence in the U.S.
POPULATION: Except for lead, higher CKM stages were generally associated with higher urinary metal levels. Multiple statistical models consistently indicated significant positive associations between exposure to several metals and CKM syndrome. Barium, thallium, and antimony were significantly associated with the overall odds of CKM syndrome, as well as with the risks of Stage 1 and Stage 2 CKM, with barium showing the highest weight. For advanced CKM stages, antimony had the greatest contribution, followed by tungsten and cobalt. Significant variations were observed by sex, age, and race. Mediation analyses suggested that inflammation, oxidative stress, and biological aging may partially explain the observed associations between metal co-exposure and CKM syndrome. In the sensitivity analysis, inorganic arsenic showed the strongest positive association with CKM syndrome and contributed most prominently in the mixture models.
CONCLUSIONS: Exposure to metal and metalloid species is closely associated with the prevalence of CKM syndrome at different stages. Inflammation, oxidative stress, and biological aging may play partial mediating roles in these associations. As NHANES reflects exposure patterns in the U.S. general population, the findings are most applicable to community-level environmental exposures and should not be directly extrapolated to high-exposure occupational groups. Further validation in prospective cohort studies and mechanistic research is warranted.
https://doi.org/10.1186/s12889-025-25894-0

****

6. Multi-expositions aux pesticides, VOCs, polluants ambiants

Zhu, Y., Ju, Y., Wang, M., Hong, G., Wu, R.
Mediating effect of sleep duration and depressive symptoms on the association of volatile organic compounds with cardiovascular disease in the general population.
Atmospheric Pollution Research, Vol. 17 (2), (2026), p.

Cardiovascular disease (CVD) is a leading global cause of mortality, with air pollution increasingly implicated as a risk factor. Volatile organic compounds (VOCs), widespread ambient pollutants, pose significant health risks; however, their specific association with CVD risk remains insufficiently explored. This study

investigated associations between VOC exposure and CVD risk and evaluated the mediating roles of sleep duration and depressive symptoms.
We analyzed data from 2918 U.S. adults in the National Health and Nutrition Examination Survey. Associations of six VOCs with CVD risk were assessed using weighted logistic regression, weighted quantile sum (WQS) regression, and quantile-based g-computation (QGC). Mediation analyses examined the contributions of sleep duration and depressive symptoms. After full covariate adjustment, benzene, styrene, and toluene were significantly associated with elevated CVD risk (odds ratios [ORs] = 1.77-2.09). Mixed-exposure analyses confirmed positive associations, with styrene contributing the highest weights (WQS: OR = 1.56, 95 % CI: 1.05, 2.30; QGC: OR = 1.62, 95 % CI: 1.25, 2.10). Subgroup analyses indicated stronger associations among women and smokers. Sleep duration and depressive symptoms partially mediated the relationships between individual VOCs (benzene, styrene, toluene), combined VOC exposure, and CVD risk, explaining 6.39 %-22.78 % of the total effect. Furthermore, a serial mediation pathway (sleep duration -> depressive symptoms) mediated these associations (proportion mediated: 2.44 %-2.63 %). These findings suggest that VOC exposure may increase CVD risk, partly through adverse effects on sleep and mental health. Addressing sleep deficits and depressive symptoms in exposed populations could be critical for mitigating CVD burden and improving public health outcomes.
https://doi.org/10.1016/j.apr.2025.102737

****

Iversen, A. P., Bruun, J., Lund, L. C., Andreasen, S. B. M., Halldorsson Thorn, I., Juul, A.*, et al.*
Prenatal exposure to the pesticides chlorpyrifos and 2,4-Dichlorophenoxyacetic acid is associated with circulating levels of reproductive hormones in healthy infant girls.
Reprod Toxicol, Vol. 139, (2026), 109112.

BACKGROUND: Pesticides are widespread in the environment and suspected endocrine disruptors that may interfere with sex hormones. Following the chlorpyrifos ban in 2020, use of alternative pesticides has increased; 2,4-Dichlorophenoxyacetic acid (2,4-D) remains widely used. This study examined the association between maternal pesticide exposure and pituitary, gonadal, and adrenal hormones in offspring during infancy.
METHODS: We recruited pregnant women from 2010 to 2012 in the Odense Child Cohort, including 489 mother-child pairs. Maternal urinary concentrations of the generic pyrethroid metabolite 3-phenoxybenzoic acid (3-PBA), the chlorpyrifos metabolite 3,5,6-trichloro-2-pyridinol (TCPY), and the herbicide 2,4-D were measured at gestational week 28. Serum concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone (T), estrone (E1), estradiol (E2), 17-hydroxyprogesterone (17-OHP), Androstenedione (Adione), and Dehydroepiandrosterone sulfate (DHEAS) were assessed in infancy. Associations between prenatal pesticide exposure and offspring reproductive hormones (expressed as age- and sex-specific standard deviation (SD) scores) were assessed using multivariate linear regression.
RESULTS: In girls, higher maternal urinary TCPY and 2,4-D concentrations were associated with lower LH (-0.07 SD, 95 % CI: - 0.13; - 0.01 and - 0.06 SD, 95 % CI: - 0.11; - 0.02, per 1 microg/L increase, respectively); there were trends towards associations between 3-PBA, TCPY, 2,4-D and lower LH, FSH, E1 and E2, respectively. No associations were seen in boys.
CONCLUSION: In this low-exposed cohort, prenatal exposure to chlorpyrifos and 2,4-D may affect the reproductive hormones in girls, but not boys, during minipuberty, which may have long-term implications. This is of public health concern given the fact that > 90 % of participants were exposed.
https://doi.org/10.1016/j.reprotox.2025.109112

****

Montiel-Mora, J. R., Pérez-Rojas, G., Brenes-Alfaro, L., Rodríguez-Rodríguez, C. E.
Multiple exposure pathways to pesticide residues in tropical agroecosystems: A human health risk assessment in Costa Rica.
Environmental Monitoring and Assessment, Vol. 198 (1), (2025), p.

Pesticide use in intensive agricultural systems poses a growing concern for human and environmental health. In Costa Rica, large-scale pineapple cultivation involves frequent agrochemical applications, increasing the potential for contamination of groundwater and agricultural products. This study evaluated human health risks associated with pesticide residues detected in groundwater and pineapples from the Northern Region of Costa Rica, where intensive pineapple production takes place. Concentration data from ten groundwater sources and 30 pineapple samples collected between 2015 and 2018 were analyzed. Non-carcinogenic risk (estimated as a hazard quotient, HQ) and carcinogenic risk were determined for adults and children using U.S. EPA reference doses and cancer slope factors. Nine pesticides were detected in groundwater and nine in pineapples, with bromacil (up to 3.8 mu g/L) being the most frequent compound in water and carbendazim (up to 0.027 mg/kg) in the fruit. All hazard quotients (HQ < 1) indicated no non-carcinogenic risk for either exposure route. Carcinogenic risks were only assessed for imazalil and diuron, with values for imazalil in groundwater ranging from 2.4 x 10(-)(7) to 3.3 x 10(-)(6), slightly exceeding the reference threshold (1 x 10(-)(6)) in children. Risk values from pineapple consumption were lower (<= 10(-)(7)) compared to those from groundwater intake, suggesting minimal concern. Although overall risks remain low, the detection of residues in both water and fruit reveals multiple exposure pathways and highlights the need for cumulative risk assessments. Strengthening environmental monitoring and promoting integrated pesticide management are essential to safeguard public health in regions under intensive agricultural production.
https://doi.org/10.1007/s10661-025-14869-8

****

Xu, C., Qiu, Y., Chen, W., Liu, N., Yang, X.
Non-Targeted and Targeted Analysis of Organic Micropollutants in Agricultural Soils Across China: Occurrence and Risk Evaluation.
Toxics, Vol. 14 (1), (2025).

Organic micropollutants in agricultural soils pose significant ecological and health risks. This study conducted the first large-scale, integrated non-targeted screening and targeted analysis across China's major food-producing regions. Using high-resolution mass spectrometry, 498 micropollutants were identified, including pesticides, industrial chemicals, pharmaceuticals, personal care products, food additives, natural products, and emerging contaminants. Spatial analysis revealed strong correlations in pesticide detections between Henan and Hebei, as well as between Hebei and Shandong, indicating pronounced regional similarities in pesticide occurrence patterns. Concentrations of 50 quantified micropollutants showed clear spatial variability, which was associated with precipitation, water use, and agricultural output, reflecting climate–agriculture–socioeconomic synergies. Greenhouse soils accumulated higher micropollutant levels than open fields, driven by intensive agrochemical inputs, plastic-film confinement, and reduced phototransformation. Co-occurrence patterns indicated similar pathways for personal care products, industrial chemicals, and pesticides, whereas natural products and pharmaceuticals showed lower levels of co-occurrence due to crop-specific exudates, fertilization, and rainfall-driven leaching. Among cropping systems, orchard soils had the highest micropollutant accumulation, followed by paddy and vegetable soils, consistent with frequent pesticide use and minimal tillage. Risk quotients indicated moderate-to-high ecological risks at over half of the sites. These results reveal complex soil pollution patterns and highlight the need for dynamic inventories and spatially differentiated, crop- and system-specific mitigation strategies.
https://doi.org/10.3390/toxics14010025

****

Angeli, K., Cavelier, A., Coja, T., Crivellente, F., Lanzoni, A., Mohimont, L.*, et al.*
Specific effects on the reproductive function including fertility relevant for cumulative risk assessment of pesticide residues.
Efsa Journal, Vol. 23 (12), (2025).

According to the 'EFSA-SANTE Action Plan on Cumulative Risk Assessment for pesticides residues', EFSA, with the support of a working group, undertook the identification of specific effects on male and female reproductive function, including fertility, that are considered relevant for grouping pesticide residues and for assessing retrospectively the cumulative risk (CRA) deriving from consumers' dietary exposure. In this first report, two specific effects leading to two correspondent cumulative assessment groups (CAGs) were identified for male reproduction, namely, (1) altered mating performance and (2) decreased fertility. Four distinct CAGs were proposed for grouping chemicals affecting female reproduction: (1) altered mating performance, (2) decreased fertility, (3) altered gestation and (4) altered parturition. EFSA also defined the list of indicators (i.e. toxicological endpoints measurable in regulatory studies) describing each specific effect. Qualitative and quantitative information on these indicators will be collected from the toxicological assessment reports on individual pesticide active substances: indicators will be used to determine the inclusion of prioritised active substances and their metabolites into the respective CAG and to estimate the no observed adverse effect level (NOAEL) and lowest observed adverse effect level (LOAEL) of each chemical in relation to the given specific effect. Additional endpoints (named ancillary findings), not sufficiently informative to define a specific effect but contributing to the overall evidence, will be collected for a limited number of substances identified as risk drivers, based on hazard and exposure considerations, to support the estimation of CAG-membership probabilities. Additional criteria for including active substances into CAGs, the hazard characterisation methodology and the lines of evidence for assessing CAG-membership probabilities are detailed in this report, which was sent for public consultation. The process of data extraction and actual establishment of the CAGs are instead beyond the scope of this report. This part of the CRA process was outsourced and will be dealt with in a separate report.
https://doi.org/10.2903/j.efsa.2025.9809

****

Li, S., Lv, Y., Tan, Z., Liu, Q., Zhu, C., Long, Z.*, et al.*
Lipid dysregulation as a mediator of genotoxicity from benzene, toluene, and xylene co-exposure: Insights from a longitudinal study of petrochemical workers and network toxicology analysis.
Environmental Chemistry and Ecotoxicology, Vol. **8**, (2026), p :708-719.

Benzene, toluene, and xylene (BTX) are pervasive in industrial settings. However, how their shared lipophilicity and lipid dysregulation synergistically contribute to genotoxicity at low dose exposures remain unclear, limiting the development of targeted preventive measures. In a longitudinal cohort of 736 petrochemical workers (523 followed for 5 years), with cumulative exposure doses derived from workplace monitoring. Blood lipids [total cholesterol (TC), triglycerides (TG), low−/high-density lipoprotein cholesterol (LDL-C/HDL-C)] and genotoxicity markers [olive tail moment (OTM), Tail DNA%, Tail moment, 8-hydroxy-2'-deoxyguanosine (8-OHdG)] were measured. Generalized linear and log-binomial regression models evaluated baseline and longitudinal associations, while generalized weighted quantile sum (gWQS) regression captured mixture effects. Mediation models assessed lipid-driven genotoxicity. BTX co-exposure was associated with increased TC, LDL-C, and HDL-C at baseline, and elevated risks of hypercholesterolemia (RR = 1.64, 95 % CI: 1.05, 2.58) and high LDL-C (RR = 1.32, 95 % CI: 1.01, 1.71) during follow-up. Workers with baseline hyperlipidemia showed stronger lipid responses and greater DNA damage under exposure (P-interaction < 0.05). Longitudinal analyses showed that benzene and toluene exposure elevated higher follow-up 8-OHdG levels among hypercholesterolemic workers (Pinteraction < 0.05) supporting oxidative damage as a downstream mechanism. Total cholesterol mediated 8.22 % of BTX-related genotoxicity (P < 0.05). Consistently, network toxicology highlighted lipid metabolism as key pathway linking BTX exposure to DNA damage. These findings demonstrate that BTX co-exposure disrupts lipid homeostasis and that toluene and xylene contribute significantly to this dysregulation, which in turn exacerbates benzene-initiated genotoxicity. The study highlights lipid metabolism as a critical mediator and amplifier of BTX mixture toxicity, underscoring the necessity of incorporating metabolic pathways and mixture effects into

occupational risk assessments.
https://doi.org/10.1016/j.enceco.2025.12.019

****

Wang, D., Ma, R., Xiao, M., Zhang, Z., Yang, H., Lv, Y.*, et al.*
BTEXS metabolites and lung dysfunction in petrochemical workers: Dose-response relationships and the mediation of oxidative stress.
Atmospheric Pollution Research, Vol., (2026), 102885.

Co-exposure to benzene, toluene, ethylbenzene, xylenes, and styrene (BTEXS) is implicated in pulmonary dysfunction, yet the oxidative stress-mediation underlying mixture effects remains mechanistically unclear. Thus, the goal of this study was to estimate the association between urinary BTEXS metabolites and lung function parameters and the potential role of oxidative stress in this association. We investigated 635 petrochemical workers in southern China, quantifying eight urinary BTEXS metabolites, four oxidative stress indices, and spirometry-measured lung function parameters. Bayesian Kernel Machine Regression (BKMR) models demonstrated that BTEXS mixtures induced dose-dependent reductions in forced vital capacity and increased odds of lung ventilation dysfunction (LVD), with xylenes metabolites exerting the greatest influence. BTEXS exposure was associated with decreased SOD and increased MDA and 8-OHdG levels. Mediation analysis revealed the SOD and MDA mediated LVD at low BTES exposure levels (5th to 50th percentile; natural indirect effects: 1.49 [95 % CI: 1.09, 2.25] and 1.48 [95 % CI: 1.11, 2.46]), but not at higher exposures. These findings establish oxidative stress as a critical pathway for BTEXS-induced lung injury under specific co-exposure patterns and support prioritizing xylenes control in occupational guidelines.
https://doi.org/10.1016/j.apr.2026.102885

****

Shad, N. A., Li, W., Yu, Y., He, Y., Shi, S., Lu, M.*, et al.*
Maternal exposure to volatile organic compounds and the risk of congenital anomalies: A systematic review and meta-analysis.
Ecotoxicology and Environmental Safety, Vol. 309, January 2026, 119656

Volatile organic compounds (VOCs) are widespread environmental and occupational pollutants with potential teratogenic effects. Growing evidence indicates that maternal exposure to VOCs during pregnancy may increase the risk of congenital anomalies in offspring. This systematic review aims to evaluate and synthesize the association between maternal exposure to benzene, toluene, xylene, and formaldehyde during pregnancy and the occurrence of congenital anomalies, including neural tube defects (NTDs), congenital heart defects (CHDs), and cleft lip and/or palate (CL/P). A systematic search was conducted across six electronic databases and grey literature for studies published between January 1, 2002, and January 1, 2025. We used a random-effects models to assess the associations. Sensitivity and publication bias analyses were also conducted. Nineteen studies met the inclusion criteria. Meta-analysis revealed a significant association between prenatal VOCs exposure and increased risk of NTDs (pooled OR = 1.63, 95 % CI: 1.32–1.95) and CHDs (pooled OR = 1.33, 95 % CI: 1.09–1.56). Studies using objective exposure assessment methods such as biomonitoring, residential GIS modelling, and environmental air measurements reported more consistent and robust associations. Maternal exposure to VOCs during pregnancy is associated with an increased risk of NTDs and CHDs. These findings highlight the importance of environmental health interventions, regulatory oversight, and prenatal risk mitigation strategies. Further prospective studies using standardized exposure assessments are needed to strengthen causal inference.
https://doi.org/10.1016/j.ecoenv.2025.119656

****

Jo, S. B., Ahn, S. T., Oh, M. M., Shim, S. H., Ahn, C. M., Oh, S. G.*, et al.*
Breathing-Zone Exposure to Aromatic Volatile Organic Compounds in Surgical Smoke During Transurethral Resection of Bladder Tumor: A Prospective Paired Monitoring Study.
Toxics, Vol. **14** n°(2), (2026), 130.

(1) Background: Energy-based transurethral resection of bladder tumor (TURBT) generates surgical smoke that may contain hazardous volatile organic compounds (VOCs), yet surgeon breathing-zone exposure during transurethral surgery remains insufficiently characterized.
(2) Methods: We conducted a prospective paired-exposure study during 28 TURBT procedures over 10 operating days using personal sampling at the surgeon's breathing zone and simultaneous intraoperative background sampling at three predefined locations (~1.5 m from the surgeon). VOCs were measured by active sampling onto Tenax TA sorbent tubes followed by thermal desorption Gas Chromatography–Mass Spectrometry (GC–MS), and formaldehyde was measured by 2,4-dinitrophenylhydrazine (DNPH) cartridges with high-performance liquid chromatography/ultraviolet detection (HPLC/UV). Breathing-zone versus background contrasts were summarized as paired geometric mean ratios (GMRs), and a dose index was calculated as concentration × operative time (µg·h/m3).
(3) Results: Breathing-zone concentrations consistently exceeded background levels, including total VOCs (GMR 4.31; 95% CI 2.92–6.38), ΣBTEXS (sum of benzene, toluene, ethylbenzene, xylenes, and styrene; GMR 2.10; 1.69–2.60), and styrene (GMR 8.51; 6.25–11.60); formaldehyde showed a smaller but significant elevation (GMR 1.20; 1.07–1.35). ΣBTEXS dose increased with operative time (Spearman ρ = 0.80, p < 0.001) and resection mass where available (ρ = 0.62, p = 0.0038; n = 20) and scaled with operative time (β = 0.86; R2 = 0.69; n = 28).
(4) Conclusions: TURBT is associated with marked enrichment of aromatic VOCs in the surgeon's breathing zone, supporting routine implementation of effective source-level smoke evacuation and filtration to reduce occupational exposure.
https://doi.org/10.3390/toxics14020130

****