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Cross-sectional associations between selected EU priority chemicals acrylamide, pesticides and UV-filters and overweight/obesity among adults from the HBM4EU Aligned Studies

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1. Introduction

The global prevalence of overweight and obesity has increased dramatically over recent decades, with the World Health Organization reporting that worldwide obesity has nearly tripled since 1975 (NCD-Risk, 2017). While excessive caloric intake and sedentary lifestyles remain primary drivers of this epidemic, emerging evidence suggests that environmental chemical exposures may contribute to the development of obesity by disrupting metabolic, endocrine, and inflammatory pathways (Heindel et al., 2017; La Merrill et al., 2025). Understanding the bidirectional relationship between environmental pollutants and obesity has become a critical public health priority. Not only may chemical exposures contribute to obesity development through obesogenic mechanisms, but obesity itself may alter internal exposure and susceptibility to environmental chemicals through modified toxicokinetics, reduced metabolic clearance, and heightened inflammatory responses, potentially creating reinforcing cycles of metabolic dysfunction in populations facing ubiquitous chemical exposures (Cano-Sancho et al., 2020; Nadal et al., 2017). Several classes of environmental chemicals prioritized under the European HBM4EU initiative, an effort now continued in the Partnership for the Assessment of Risks from Chemicals (PARC) European project, have been identified as potential contributors to metabolic dysfunction and weight gain, including acrylamide, pesticides, and UV filters (Govarts et al., 2023).

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Acrylamide is a neurotoxic and potentially carcinogenic compound formed through the Maillard reaction during high-temperature cooking of carbohydrate-rich foods including fried potatoes, coffee, bread, and breakfast cereals (EFSA CONTAM Panel, 2015). Acrylamide is metabolized via two competing pathways: phase I CYP2E1-mediated epoxidation to the genotoxic metabolite glycidamide (GA), which forms adducts with hemoglobin and DNA; and phase II glutathione conjugation yielding the urinary mercapturic acids N-acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA) and N-acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine (GAMA), representing the predominant urinary metabolites in humans (Rietjens et al., 2018; Watzek et al., 2013). Animal studies have demonstrated that acrylamide can influence lipid metabolism, impair insulin signaling and promote weight gain (Lee and Pyo, 2019); however, findings in epidemiological studies are inconsistent (Huang et al., 2018; Mérida et al., 2024).

Benzophenones, particularly benzophenone-1 (BP-1) and benzophenone-3 (BP-3), are widely used as UV filters in sunscreens, cosmetics, and other personal care products, resulting in widespread human exposure with detection frequencies exceeding 80% in European biomonitoring studies (Govarts et al., 2023). In addition, BP-1 is also the major metabolite of BP-3, and thereby exposure to BP-3 is both excreted in urine as BP-3 itself and partly metabolized and excreted in urine as BP-1. These compounds have demonstrated endocrine-disrupting properties in vitro and in animal models, with evidence for estrogenic and anti-androgenic activities that may affect adipogenesis, metabolic homeostasis, and thyroid function (Mustieles et al., 2023). However, human epidemiological data linking benzophenone exposure to obesity in adults remain limited and inconsistent (Carwile and Michels, 2011; Jiang et al., 2026).

Pesticides constitute another major exposure category of concern. Pyrethroid insecticides, synthetic analogues of natural pyrethrins, are among the most widely used residential and agricultural pesticides globally, with common metabolites including 3-phenoxybenzoic acid (3-PBA), cis- and trans-dichlorovinyl carboxylic acids (cis-DCCA, trans-DCCA), and cis-dibromovinyl carboxylic acid (cis-DBCA) detected in the majority of the general EU population (Govarts et al., 2023). Animal studies have suggested that certain pyrethroids can disrupt glucose homeostasis, alter lipid metabolism, and affect thyroid hormone signaling (Ren et al., 2020), though human evidence for obesogenic effects remains inconclusive. Chlorpyrifos, an organophosphate insecticide, is metabolized to 3,5,6-trichloro-2-pyridinol (TCPY), which serves as a biomarker of exposure (Barr et al., 2004). While exposure to chlorpyrifos has been linked to metabolic disruption in some in vitro and animal studies, associations with obesity in adults are poorly characterized (Howell et al., 2016; Peris-Sampedro et al., 2015). Glyphosate, the world's most widely used herbicide, is primarily metabolized to aminomethylphosphonic acid (AMPA) (Benbrook, 2016). Despite widespread exposure and experimental evidence suggesting potential metabolic-disrupting properties (Feng et al., 2025; Haas et al., 2025; Rosolen et al., 2024; Tang et al., 2024), human epidemiological data on glyphosate and obesity are extremely limited (Otaru et al., 2025).

To address this knowledge gap, the present study leveraged harmonized biomonitoring data from HBM4EU-aligned studies to explore cross-sectional associations between urinary biomarkers of acrylamide metabolites (AAMA and GAMA), pesticide metabolites (pyrethroids, chlorpyrifos, and glyphosate), and benzophenones (BP-1, BP-3) with BMI and overweight/obesity prevalence in adults across eight aligned studies.

2. Materials and methods

2.1. Study population

Participants were recruited from nationally or regionally representative studies participating in the Human Biomonitoring for Europe (HBM4EU) initiative between 2014 and 2021. HBM4EU was established to generate harmonized biomonitoring data on human exposure to priority environmental chemicals across European populations, facilitating comparable exposure assessment across diverse geographic regions (Gilles et al., 2022; Govarts et al., 2023). The initiative encompassed 23 participating countries from all European geographic areas, with recruitment across three age groups: children (6–11 years), adolescents (12–18 years), and young adults (20–39 years). The present analysis was conducted as part of the PARC European project (Marx-Stoelting et al., 2023), and focused exclusively on the young-adult age group.

Eligible studies for inclusion in the HBM4EU-Aligned Studies framework were required to: (1) maintain biobanked urine specimens suitable for chemical analysis; (2) implement standardized HBM4EU protocols for data collection and harmonization (Pack et al., 2023); (3) recruit participants within the period 2014-2021 from general population samples rather than occupationally or clinically selected groups; (4) collect a core set of demographic, anthropometric, and lifestyle variables using harmonized questionnaire instruments; (5) obtain ethical approval from appropriate institutional review boards or ethics committees and informed consent from the participants; (6) adhere to the HBM4EU data management plan and data sharing policies; and (7) conduct biomarker analyses in laboratories that successfully completed HBM4EU quality assurance/quality control (QA/QC) programs and maintained compliance with established analytical protocols (Esteban López et al., 2021; Gilles et al., 2022; Govarts et al., 2023). These stringent quality requirements ensured analytical comparability and data reliability across the multi-study dataset.

Eight HBM4EU-Aligned Studies contributed data on urinary biomarkers of priority pollutants and anthropometric measurements in adults aged 20-39 years (Gilles et al., 2022; Govarts et al., 2023): RAVMABAT (National Health and Nutrition Survey, 2015-2016; Israel) (Berman et al., 2017), DIET-HBM (Diet and Human Biomonitoring Study, 2019-2020; Iceland) (Poteser et al., 2022), INSEF-ExpoQuim (Portuguese Health Examination Survey with Exposure to Chemicals Module, 2019-2020; Portugal) (Gaio et al., 2018), Oriscav-Lux2 (Observation of Cardiovascular Risk Factors in Luxembourg 2, 2016-2018; Luxembourg) (Backes et al., 2024), CPHmini/DYMS (parents from the Copenhagen Minipuberty Study (CPHmini) and men from the Danish Young Men Study (DYMS; Denmark) (Frederiksen et al., 2020, 2022), ESB (German Environmental Specimen Bank, 2015-2021; Germany) (Kolossa-Gehring et al., 2012), ESTEBAN (Étude de santé sur l'environnement, la biosurveillance, l'activité physique et la nutrition 2014-2016; France) (Balicco et al., 2017) and the HBM4EU Study in Switzerland (2020; Switzerland) (Gilles et al., 2022; Govarts et al., 2023). The resulting total study population was 2336 adults from across Europe and Israel, and the number of individuals with complete data was 1114 for acrylamide, 1152 for pyrethroids/-chlorpyrifos, 956 for benzophenones, and 419 for glyphosate (Fig. S1).

2.2. Outcome and covariate data

BMI (kg/m^2) derived from weight and height was available as a continuous outcome for all the sub-studies. We binarized BMI to assess the risk of overweight/obesity ($\geq 25\ kg/m^2$) compared to normal weight or underweight ($<25\ kg/m^2$). Anthropometric measures were self-reported or measured by a study nurse or physician depending on the cohort; the method used in each study is specified in Table 1. Covariates considered in the models included age at sampling (years), study, sex, creatinine (mg/L), smoking (no/yes), socioeconomic status (highest household education based on International Standard Classification of Education [ISCED], 8 levels). Fried potato and fruit and vegetable consumption were selected as dietary variables for the acrylamide and pesticide sensitivity analyses, respectively, as both represent principal dietary sources of these chemical families in European populations and are independently associated with adiposity through dietary intake patterns. Dietary variables were post-harmonized across contributing studies according to the HBM4EU Aligned Studies harmonized codebook

Table 1
Characteristics of the study population from the HBM4EU-Aligned Studies (n = 2336 adults) by study. Values are presented as median (interquartile range, Q1–Q3) for continuous variables and as count (percentage, %) for categorical variables. Percentages were calculated within each study (column) and may not sum to 100% due to rounding or to the presence of missing values, which are reported in dedicated rows where applicable.

	HBM4EU-Switzerland	ESB	ESTEBAN	RAVMABAT	DIET-HBM	INSEF-ExpoQuim	Oriscav-Lux2	CPHmini/DYMS
	N = 299	N = 683	N = 357	N = 82	N = 178	N = 257	N = 205	N = 275
Country	Switzerland (CH)	Germany (DE)	France (FR)	Israel (IL)	Iceland (IS)	Portugal (PT)	Luxembourg (LU)	Denmark (DK)
Study year	2020	2015-2021	2014-2016	2015-2016	2019-2020	2019-2020	2016-2018	2017-2019
Age (years)	31 (27 - 35)	23 (22 - 25)	33 (29 - 37)	35 (30 - 37)	30 (26 - 35)	35 (32 - 37)	34 (31 - 37)	31 (28 - 34)
Body mass index (kg/m^2)	23.7 (21.1 - 25.1)	22.2 (20.6 - 23.9)	23.0 (21.1 - 26.3)	24.8 (22.9 - 29.2)	25.5 (23.2 - 28.6)	24.6 (22.1 - 28.1)	24.1 (21.5 - 27.2)	23.6 (21.6 - 25.8)
Obesity/overweight (%)	80 (27%)	105 (15%)	112 (31%)	37 (45%)	98 (55%)	121 (47%)	85 (42%)	91 (33%)
Sex (female participants)	137 (46%)	344 (50%)	197 (55%)	47 (57%)	106 (60%)	152 (59%)	109 (53%)	112 (41%)
Creatinine (mg/L)	980 (620 - 1470)	658 (491 - 939)	1045 (630 - 1590)	1110 (695 - 1775)	1250 (803 - 1880)	1177 (837 - 1640)	1946 (1267 - 2557)	1473 (764 - 2118)
Urine sampling	UM	UD	UM	US	US	UM	US	US
ISCED								
Low	3 (1%)	0 (0%)	9 (3%)	6 (7%)	12 (7%)	52 (20%)	9 (4%)	32 (12%)
Medium	69 (23%)	0 (0%)	103 (29%)	65 (79%)	57 (32%)	89 (35%)	69 (34%)	65 (24%)
High	223 (75%)	683 (100%)	245 (69%)	11 (13%)	107 (60%)	116 (45%)	127 (62%)	173 (63%)
Missing	4 (1%)	0 (0%)	0 (0%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)	5 (2%)
Smoking	66 (22%)	43 (6%)	115 (32%)	21 (26%)	12 (7%)	66 (26%)	35 (17%)	26 (10%)
Missing	16 (5%)	0 (0%)	1 (0%)	0 (0%)	4 (2%)	0 (0%)	0 (0%)	3 (1%)
Anthropometric measurement								
Fieldwork measurement	57 (19%)	0 (0%)	357 (100%)	0 (0%)	0 (0%)	0 (0%)	205 (100%)	0 (0%)
Self-reported	242 (81%)	683 (100%)	0 (0%)	0 (0%)	178 (100%)	257 (100%)	0 (0%)	0 (0%)
Missing	0 (0%)	0 (0%)	0 (0%)	82 (100%)	0 (0%)	0 (0%)	0 (0%)	275 (100%)

Abbreviations: ISCED, Highest household education based on International Standard Classification of Education; UD, 24-h urine; UM, first morning urine; US, random spot urine.

(Gilles et al., 2022; Govarts et al., 2023), in which the frequency of consumption of food groups was originally coded as a six-level ordinal scale ranging from 'never' (0) to 'once a day or more' (5). To ensure adequate number of observations in each category and parsimony, the original six-level fried potato variable was collapsed into four ordinal categories ('never', 'less than once per month', '1–3 times per month', and 'once per week or more') and the fruit and vegetable variable was dichotomized into 'daily or more' versus 'less than daily'.

2.3. Laboratory analysis

First morning urine void, spot urine or 24-h-urine samples were collected for each study and analysed for chemical concentrations. Despite differences in collection and analytical methods, the comparability was generally guaranteed by the HBM4EU quality assurance/quality control (QA/QC) programme (Esteban López et al., 2021; Gilles et al., 2022; Govarts et al., 2023).

2.3.1. Acrylamide

The levels of AAMA and GAMA were quantified in urine samples (100 μL) from 5 studies ESB (DE), ESTEBAN (FR), DIET-HBM (IS), INSEF-ExpoQuim (PT) and Oriscav-Lux2 (LU) using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) system in the respective laboratories, details described elsewhere (Govarts et al., 2023; Poteser et al., 2022). For both metabolites, the limit of detection (LOD) ranged between 0.33 and 1.0 ng/mL and for the limit of quantification (LOQ) between 1 and 10 ng/mL, respectively. We also calculated the GAMA:AAMA ratio, which indicates the relative extent to which acrylamide is metabolized via the glycidamide formation pathway versus the direct conjugation pathway, and has been positively associated with increased cardiometabolic risk in adults (Wang et al., 2022).

2.3.2. Pesticides

Five metabolites of pyrethroid pesticides and the chlorpyrifos metabolite 3,5,6-trichloro-2-pyridinol (TCPY) were measured in urine from 5 studies HBM4EU-Switzerland (CH), ESB (DE), ESTEBAN (FR), RAVMABAT (IL) and DIET-HBM (IS) using GC- or LC-MS/MS. Pyrethroid metabolites included cis-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acid [cis-DBCA], cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid [cis-DCCA], trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid [trans-DCCA], 3-phenoxybenzoic acid [3-PBA] and cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid [CIFCA]. The LOQ ranged between 0.05 and 0.5 ng/mL for TCPY and between 0.015 and 0.7 ng/mL for the pyrethroid metabolites. The main metabolite of glyphosate AMPA was measured in two studies from Germany (ESB) and France (ESTEBAN), using gas chromatography (GC) and LC-MS/MS and LOQ of 0.1 and 0.05 ng/mL, respectively.

2.3.3. UV filters

Benzophenone 1 (BP-1) and 3 (BP-3) were measured in urine from ESB (DE), ESTEBAN (FR), Oriscav-Lux2 (LU) and CPHmini/DYMS (DK) using LC-MS/MS (Rigshospitalet, Region Hovedstaden, Denmark and Ruhr-Universität Bochum, Germany). The LOQs ranged between 0.01 and 0.5 ng/mL for BP-1 and 0.03-2 ng/mL for BP-3.

2.4. Adjustment of biomarkers for urine dilution

Urinary biomarker concentrations were adjusted for dilution using covariate-adjusted standardization (CAS) (O'Brien et al., 2016). Traditional creatinine standardization (simple ratio of biomarker to creatinine) may introduce bias when factors associated with both creatinine excretion and the health outcome are present. The CAS method addresses this by: (1) modeling log-transformed creatinine (Cr) as a function of the covariates (age and sex, BMI was excluded because it is also the main outcome); (2) calculating predicted creatinine values ($\hat{Cr}$) from

this model; and (3) estimating the dilution-adjusted biomarker concentration ($C_{adjusted}$) using the formula: $C_{adjusted} = C_{raw}/(Cr/\hat{C}r)$, where C_{raw} is observed biomarker concentration in urine. This standardization controls for the multiplicative effect of hydration on urinary concentration while accounting for chronic determinants of creatinine excretion. To evaluate the consistency of our primary findings to this methodological choice, we conducted a sensitivity analysis comparing other urinary dilution correction approaches: covariate-adjusted standardization based on age and sex (CAS, primary analysis), CAS with BMI additionally included in the creatinine prediction model (CAS + BMI), classical creatinine ratio standardization, inclusion of creatinine as a covariate in the outcome regression model, and the unadjusted (raw) biomarker concentration.

2.5. Statistical analysis

Chemical biomarkers were modelled as continuous variables when quantification frequencies (QF) exceeded 70% within each country-specific study, otherwise dichotomized or excluded. For chemicals modelled as continuous, observations below the limit of quantification were imputed by single random imputation from a truncated lognormal distribution (Lubin et al., 2004; Peeters et al., 2025), representing 0.6–9.4% of modelled observations. Studies below the thresholds were excluded for the analysis: TCPY (ESTEBAN, DIET-HBM), BP-1 and BP-3 (ESB). Chemicals with QF below 70% and above detection frequencies of 10% were dichotomized, excluded below that threshold. To make the contrast comparable across studies with differing analytical sensitivity, these biomarkers were dichotomized at a common concentration threshold, taken as the highest documented limit of quantification among the contributing studies (AMPA 0.1; cis-DCCA 0.2; CIFCA 0.2; cis-DBCA 0.7; trans-DCCA 0.3 ng/mL). Individuals without missing covariate and outcome data were considered in the final statistical analysis (Fig. S1).

Multivariable linear regression models were used to characterize the associations between chemical biomarkers and BMI, whereas multivariable robust Poisson regression models were used to explore the associations with overweight/obesity prevalence ratio. Minimally adjusted models included age, sex and study. The additional inclusion of smoking and ISCED had minimal impact on regression estimates for biomarkers, therefore these covariables were excluded from the main models. We assessed effect modification by sex and study through stratified analyses. Statistical significance of interactions was evaluated using Wald tests applied to models including multiplicative interaction terms (biomarker × sex; biomarker × study). A p-value < 0.1 for the Wald test was used as a threshold for significant heterogeneity of associations across strata. Model assumptions were assessed by examining linearity, homoscedasticity, and normality of residuals. Departures from linearity were explored using generalized additive models (GAMs) fitted with the 'mgcv' R package, estimating the smoothing parameters with the restricted maximum likelihood method and the approximate F-test for the smooth components.

Pairwise Spearman correlations between chemical biomarkers were computed on log-transformed, CAS-standardized biomarker concentrations within each study-specific analytical subpopulation to characterize the dependency structure of the mixtures and to inform the interpretation of component-level coefficients. To evaluate the joint association of co-occurring chemical exposures with BMI, we applied quantile g-computation ('qgcomp' R package), a mixture method that estimates the overall effect of a simultaneous one-quantile increase across all mixture components without imposing the directional homogeneity assumption required by weighted quantile sum regression (Keil et al., 2020). Three mixture models were defined a priori based on the joint availability of biomarker measurements at the individual level, i.e., subsets of participants for whom all components of a given mixture had been quantified in the same urine sample within the contributing studies: a pesticide-acrylamide mixture (3-PBA, trans-DCCA, GAMA, AAMA) in Germany, France and Iceland (n = 224); a benzophenones-acrylamide mixture (BP-1, BP-3, GAMA, AAMA) in Germany, France, and Luxembourg (n = 498); and a pesticide mixture (trans-DCCA, TCPY, 3-PBA) in Switzerland, Germany, Israel, and Iceland (n = 483). All exposures were quantile-scored into quartiles (q = 4) prior to analysis. Models were fitted assuming a Gaussian distribution for BMI and adjusted for sex, age and study. Cross-product interactions terms between biomarkers were manually selected and tested as covariates, and retained if they were statistically significant or improved the model fit based on AIC and likelihood ratio testing.

The overall mixture effect and individual exposure coefficients were extracted from the underlying generalized linear model to characterize both the joint and component-specific contributions to BMI, and mixture weights were computed to reflect the proportional contribution of each exposure to the positive or negative partial mixture effect.

Given the exploratory and hypothesis-generating nature of the analyses and the a priori selection of priority biomarkers under the HBM4EU framework, no formal correction for multiple comparisons was applied. All statistical analyses were conducted in R software (v.4.2.3).

3. Results

3.1. Study sample

Participant characteristics varied considerably across the eight countries included in this analysis (N = 2336). The German study population was notably younger (median age 23 years, IQR: 22-25) compared to other countries, where median ages ranged from 30 to 35 years. Body mass index distributions also differed by study, with the lowest median BMI and prevalence of overweight/obesity observed in Germany (22.2 kg/m^2 and 15%, respectively) and the highest in Iceland (25.5 kg/m^2 and 55%, respectively). Female participants comprised 41-60% of study-specific samples. Urinary creatinine concentrations, used for standardization of biomarker levels, showed marked variation across countries, with the lowest median values in Germany (658 mg/L) and the highest in Luxembourg (1946 mg/L). Educational attainment was predominantly high across most study populations, particularly in Germany (100%) and Switzerland (75%), while Portugal showed a more balanced distribution with 20% low, 35% medium, and 45% high household education. Smoking prevalence varied substantially, from 6% in Germany to 32% in France. Missing data were restricted to two covariates (ISCED and smoking) and were minimal across all countries, with the highest per-variable missingness reaching 5% for smoking in HBM4EU-Switzerland and <2% in all other study-variable combinations. Height and weight were measured at fieldwork in two studies (ESTEBAN, Oriscav-Lux2), self-reported in three (ESB, DIET-HBM, INSEF-ExpoQuim), obtained by both methods in one (HBM4EU-Switzerland, 57 and 242 participants respectively), and the method was not recorded in two (RAVMABAT, CPHmini/DYMS); overall 619 participants (27%) had measured, 1360 (58%) self-reported and 357 (15%) unrecorded anthropometry (Table 1). Because ISCED and smoking were evaluated only in sensitivity analyses and were not retained in the final adjusted models (see Statistical Methods), the analytical sample for the main exposure-outcome associations using complete-case analysis was unaffected by missingness in these variables. Participant's characteristics across different datasets were similar and representative of sampled population (Supplemental Tables S1–S4). Dietary consumption patterns showed expected variation across countries (Supplementary Table S5). Fried potato consumption was most commonly reported at moderate frequencies (1–3 times per month: 43%), with relatively few daily consumers (2%) and considerable variation in the 'never' category across countries (12% overall). Fruit and vegetable consumption was strongly left-skewed, with 77% of participants reporting daily intake and only 0.5% reporting consumption less than once per month; cross-study variation was notable in the proportion of daily consumers.

3.2. Exposure distributions

Urinary biomarker concentrations are presented as creatinine-standardized values (μg/g creatinine) throughout the descriptive analyses to facilitate direct comparison with previously published HBM4EU studies and the broader human biomonitoring literature. The results showed substantial variability across the participating countries, reflecting differences in exposure patterns, age, sampling period, dietary habits, and product use (Table 2). For pyrethroid and chlorpyrifos metabolites (n = 1152), quantification frequencies ranged from 1% to 100% depending on the metabolite and study, with median concentrations spanning 0.1-2.4 μg/g creatinine for individual metabolites. TCPY showed the highest concentrations in Israel (2.4 μg/g crt) and notably lower levels in France (0.1 μg/g crt) and Iceland (0.6 μg/g crt). 3-PBA demonstrated consistently high detection frequencies (>82%) across most countries with the highest concentrations measured in France and Israel, roughly double those of the other countries. Glyphosate metabolite AMPA (n = 419) was quantifiable in 34-76% of samples from France and Germany, with median concentrations of 0.1-0.2 μg/g creatinine. Acrylamide metabolites (n = 1114) were nearly ubiquitously detected (91-100%), with AAMA concentrations ranging from 28.8 μg/g creatinine in Luxembourg to 91.0 μg/g creatinine in France, and GAMA showing the highest levels in Portugal (25.4 μg/g crt). UV-filter benzophenones (n = 956) displayed high quantification frequencies (30-100%) in the four countries assessed, with BP-3 concentrations highest in Germany (7.9 μg/g crt) and lowest in Luxembourg (0.9 μg/g crt), indicating differential sunscreen use or exposure to other benzophenone-containing products across populations.

Pairwise Spearman rank correlations between the exposure biomarkers varied substantially across analytical data subsets (Supplementary Table S6). The two acrylamide metabolites AAMA and GAMA showed the highest correlation (ρ = 0.85–0.86), consistent with their shared origin as urinary phase II metabolites of acrylamide. The two pyrethroid metabolites 3-PBA and trans-DCCA were also moderately to strongly correlated (ρ = 0.63–0.70), as were the two benzophenones BP-1 and BP-3 (ρ = 0.78). Correlations between chemical classes were generally low to moderate (ρ ranging from 0.07 to 0.48), with the highest correlations observed between pyrethroid and acrylamide metabolites (3-PBA-AAMA ρ = 0.48; 3-PBA-GAMA ρ = 0.44).

3.3. Associations between priority chemicals and overweight/obesity prevalence ratio and body mass index

Using covariate-adjusted standardization to account for factors

Table 2
Distributions presented as median (interquartile range, Q1–Q3) and quantification frequencies (%) of chemical biomarkers in urine in the different HBM4EU aligned studies used in the present analysis datasets.

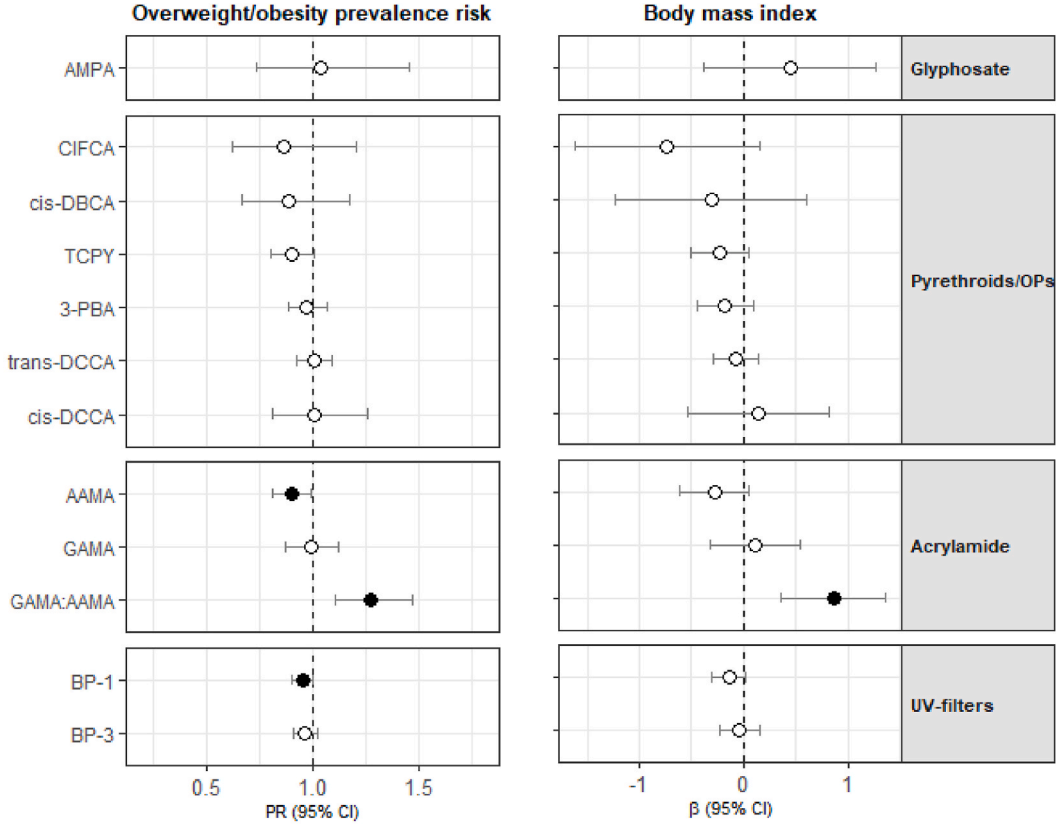
	HBM4EU-Switzerland	ESB	ESTEBAN	RAVMABAT	DIET-HBM	INSEF-ExpoQuim	Oriscav-Lux2	CPHmini/DYMS
Country	Switzerland (CH)	Germany (DE)	France (FR)	Israel (IL)	Iceland (IS)	Portugal (PT)	Luxembourg (LU)	Denmark (DK)
Dataset - Pyrethroids and chlorpyrifos (n=1152)								
	N= 299	**N=180**	**N=166**	**N=82**	**N=168**	**N=257**		
TCPY (μg/g crt)	1.00 (0.58 - 1.65)	1.66 (1.09 - 2.84)	0.08 (0.05 - 0.09)	2.41 (1.57 - 3.55)	0.65 (0.42 - 0.94)	1.64 (1.11 - 2.44)		
QF (%)	99	77	3	99	57	100		
cis-DBCA (μg/g crt)[a]	0.18 (0.11 - 0.34)	0.24 (0.17 - 0.51)	0.74 (0.39 - 1.75)	0.15 (0.09 - 0.27)	0.20 (0.12 - 0.44)			
QF (%)	66	50	99	56	67			
cis-DCCA (μg/g crt) [a]	0.18 (0.10 - 0.32)	0.21 (0.17 - 0.35)	0.30 (0.15 - 0.53)	0.22 (0.14 - 0.37)	0.11 (0.08 - 0.22)			
QF (%)	52	24	98	78	38			
trans-DCCA (μg/g crt)	0.28 (0.18 - 0.51)	0.31 (0.20 - 0.49)	0.21 (0.11 - 0.40)	0.36 (0.25 - 0.63)	0.16 (0.11 - 0.29)			
QF (%)	82	64	97	88	67			
3-PBA (μg/g crt)	0.41 (0.23 - 0.72)	0.35 (0.25 - 0.54)	0.79 (0.50 - 1.45)	0.73 (0.43 - 1.07)	0.29 (0.19 - 0.45)			
QF (%)	92	86	100	96	82			
CIFCA (μg/g crt) [a]	0.21 (0.16 - 0.25)	0.46 (0.29 - 0.58)	0.03 (0.01 - 0.07)	0.20 (0.20 - 0.20)	0.11 (0.07 - 0.30)			
QF (%)	1	4	25	6	2			
Dataset - Glyphosate (n=419) μg/g crt								
		N=250	**N= 169**					
AMPA (μg/g crt)		0.18 (0.13 - 0.29)	0.13 (0.08 - 0.22)					
QF (%)		34	76					
Dataset - Acrylamide (n=1114) μg/g crt								
		N= 180	**N= 298**		**N= 177**	**N= 255**	**N= 204**	
AAMA (μg/g crt)		36.30 (28.51 - 51.86)	91.02 (54.87 - 194.56)		45.94 (32.22 - 73.22)	72.37 (46.42 - 114.81)	28.78 (20.61 - 45.89)	
QF (%)		92	100		100	100	100	
GAMA (μg/g crt)		7.13 (5.49 - 8.87)	11.10 (7.22 - 20.56)		7.81 (5.80 - 10.30)	25.37 (18.81 - 33.51)	6.03 (4.74 - 8.17)	
QF (%)		99	100		91	100	100	
Dataset - Benzophenones (n=956) μg/g crt								
		N= 180	**N= 298**				**N= 203**	**N= 275**
BP-1 (μg/g crt)		2.03 (1.10 - 4.12)	0.60 (0.22 - 1.76)				0.37 (0.16 - 1.06)	0.93 (0.34 - 2.39)
QF (%)		30	97				100	89
BP-3 (μg/g crt)		7.99 (4.73 - 16.66)	1.34 (0.51 - 3.85)				0.94 (0.45 - 2.64)	2.44 (1.17 - 6.02)
QF (%)		30	99				100	100

Abbreviations: crt, creatinine; QF, quantification frequencies.
[a] Exposure variables dichotomized in the statistical models.

affecting creatinine excretion, our cross-sectional analysis revealed chemical-specific patterns of association with adiposity (Fig. 1 and Table S7). Among acrylamide metabolites, the GAMA:AAMA ratio showed significant positive associations with overweight/obesity (Prevalence Ratio [PR]: 1.27, 95%CI: 1.10, 1.47, $p < 0.001$) and BMI (β: 0.86, 95%CI: 0.40, 1.33, $p < 0.001$). Negative associations were found for AAMA with overweight/obesity (PR:0.90, 95%CI:0.81,1.00, $p = 0.04$), but not for BMI (β −0.28, $p = 0.079$). Neither the pesticide metabolites nor the glyphosate metabolite AMPA was associated with either outcome, with confidence intervals spanning the null throughout. Point estimates were nevertheless predominantly negative, most notably for TCPY with overweight/obesity (PR 0.90, 95% CI:0.80–1.01, $p = 0.06$) and 3-PBA with BMI (β: −0.23, 95% CI: −0.47, 0.01). Nominal inverse association was found between overweight/obesity and BP-1 (PR: 0.95, 95% CI: 0.90, 1.00, $p = 0.047$). Visual inspection and statistical testing revealed predominantly linear associations across most biomarkers (Figs. S2 and S3). Minor departures from linearity were observed for the ratio GAMA:AAMA, characterized by an inverted-U or slightly downward-curving shape. Because these non-linear patterns did not substantially affect effect estimates or alter conclusions regarding the magnitude or direction of the associations, linear models were used for the primary analyses to maintain consistency and interpretability across all chemical classes. Sensitivity analyses progressively adjusting for fried potato consumption (acrylamide models) and fruit and vegetable consumption (pesticide models) yielded estimates indistinguishable from the main models, supporting the consistency of the observed associations to dietary adjustment (Fig. S4). These results were also broadly consistent across creatinine adjustment methods (Fig. S5), with the exception of the CAS + BMI approach, which produced estimates that diverged more substantially for acrylamide metabolites than for other chemical families, particularly GAMA and changed the sign of the AAMA–BMI coefficient. The GAMA:AAMA ratio was unaffected by the choice of method, since dividing both metabolites by the same dilution factor leaves their ratio unchanged. This pattern is consistent with the higher correlation observed between creatinine and acrylamide metabolites (Spearman ρ ~ 0.5) compared with the rest of biomarkers (Spearman ρ ~ 0.3-0.4). Associations were also examined within groups of studies sharing a urine collection protocol (Fig. S6). Because each contributing study used a single matrix type, protocol is nested within study and cannot be separated from other study characteristics; estimates were nonetheless broadly consistent between first morning void and random spot collections, including the positive GAMA:AAMA–BMI association. The 24-h urine group comprises a single study with a narrow BMI distribution, and its divergent estimates are therefore interpreted as between-study heterogeneity rather than as an effect of collection protocol. Associations were not affected by the method of anthropometric ascertainment (Fig. S7). Restricted to the 502 participants with measured height and weight and available covariate data, the GAMA:AAMA ratio remained positively associated with both outcomes (β: 1.36, 95% CI: 0.46, 2.26; PR: 1.43, 95% CI: 1.08, 1.89) and AAMA remained inversely associated with overweight/obesity (PR: 0.83, 95% CI: 0.70, 0.98).

3.4. Sex-specific associations

Several sex-specific patterns were observed (Fig. 2). Among



Note: Abbreviations: OPs, organophosphate pesticides; PR, prevalence ratio.

Fig. 1. Forest plots depicting the associations between urinary biomarkers (CAS-standardized with sex and age) of acrylamide, pesticides and UV-filters and overweight/obesity prevalence ratio and body mass index, estimated using robust Poisson and linear regression, respectively. The models were adjusted for age, sex and study. Black circles indicate statistical significance (p-value <0.05). The biomarkers AMPA, CIFCA, cis-DBCA, cis-DCCA and trans-DCCA were modelled as dichotomous (detected/non-detected).
Note: Abbreviations: OPs, organophosphate pesticides; PR, prevalence ratio.

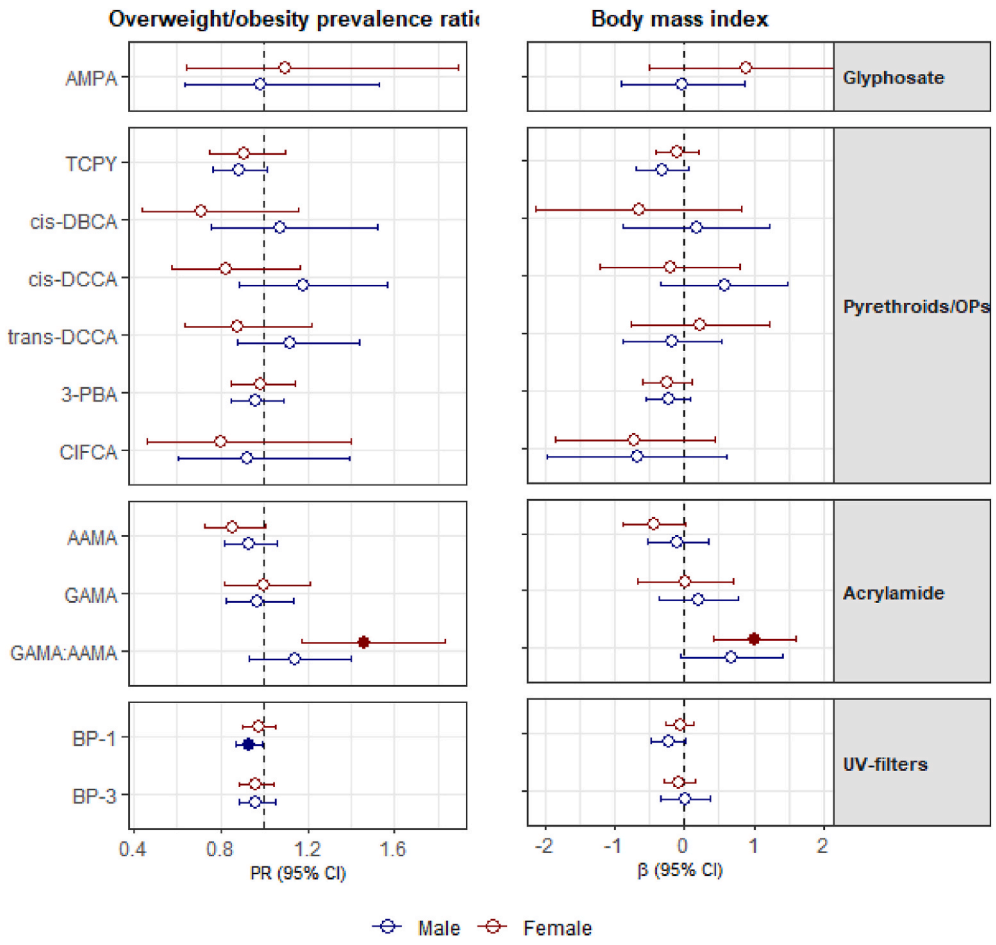


Fig. 2. Forest plots of associations between urinary biomarkers CAS-standardized with sex and age) of acrylamide, pesticides, and UV filters and overweight/obesity prevalence and body mass index (BMI), stratified by sex. Overweight/obesity prevalence ratios and BMI regression coefficients were estimated using robust Poisson and linear regression models, respectively, adjusted for age and study. Filled circles denote statistically significant associations ($p < 0.05$). The biomarkers AMPA, CIFCA, cis-DBCA, cis-DCCA and trans-DCCA were modelled as dichotomous (detected/non-detected).
Abbreviations: OPs, organophosphate pesticides; PR, prevalence ratio.

acrylamide metabolites, the positive association of the GAMA:AAMA ratio with overweight/obesity and BMI was apparent in females but not in males. Among UV-filter compounds, BP-1 showed a statistically significant negative association with overweight/obesity prevalence ratio in males only, while BP-3 showed null associations in both strata. Glyphosate (AMPA), pyrethroid and organophosphate (OP) metabolites yielded predominantly null associations in both sexes, with prevalence ratios spanning unity and β-coefficients centered near zero; no sex-discordant pattern of nominal significance was identified within these chemical classes. Despite these sex-specific significant findings, the corresponding interaction Wald tests did not reach statistical significance for any compound, indicating that heterogeneity of effect by sex could not be formally established.

3.5. Study-specific associations

Study-stratified analyses revealed variability in the magnitude of pollutant–BMI associations across the eight participating studies (Fig. 3). Formal interaction tests indicated heterogeneity for the GAMA:AAMA ratio ($p = 0.004$) and were non-significant for the remaining biomarkers. For the GAMA:AAMA ratio, positive associations with BMI were observed in ESTEBAN France (β = 2.09, 95% CI: 0.95, 3.24), DIET-HBM Iceland (2.15; 0.22, 4.08) and INSEF-ExpoQuim Portugal (1.05; 0.08, 2.02), with null estimates in ESB Germany (0.05; −0.39, 0.50) and Oriscav-Lux2 Luxembourg (0.58; −0.68, 1.83). The trend was also supported by the leave-one-study-out analyses (Fig. S8), excluding ESB raises the BMI β GAMA:AAMA ratio from 0.86 to 1.38. For the rest of chemicals, no single study altered the pooled estimates materially, indicating that the pooled associations were not driven by any individual study. Interaction tests were performed on BMI only: as the continuous form of the outcome it retains more information than the dichotomized overweight/obesity indicator and therefore provides the more sensitive test of between-study heterogeneity.

3.6. Mixture analysis

To assess whether the chemicals examined acted cumulatively, three mixtures were modelled by quantile g-computation (Fig. 4). In the pesticide-acrylamide mixture (France, Germany, and Iceland; n = 224; Fig. 4A–B), the overall mixture effect was negative but did not reach significance (ψ = −0.71, 95% CI: −1.48, 0.05; $p = 0.067$). The component weights opposed one another almost exactly, GAMA accounting for essentially all of the positive partial effect (weight 1.00) and AAMA for most of the negative one (−0.91), with 3-PBA (−0.09) and trans-DCCA (<0.01) contributing negligibly. In the benzophenones-acrylamide mixture (Germany, France, and Luxembourg; n = 498; Fig. 4C–D), and the pesticide-only mixture (Switzerland, Germany, Israel, and Iceland; n = 483; Fig. 4E–F), neither individual component coefficients nor the overall mixture effect reached statistical significance (ψ = −0.13, 95% CI: −0.69, 0.43 and ψ = −0.25, 95% CI: −0.69, 0.19, respectively). Globally, AAMA showed the most consistent negative association with BMI, as shown by single-pollutant models, with no evidence of

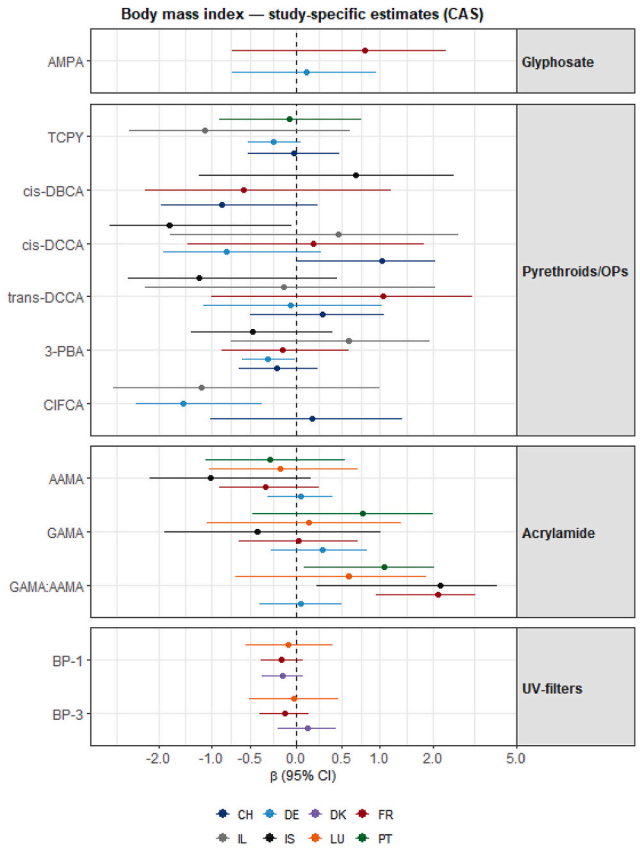


Fig. 3. Forest plot depicting the associations between urinary biomarkers (CAS-standardized with sex and age) of acrylamide, pesticides and UV-filters and body mass index stratified by study, estimated using linear regression. The models were adjusted for age and sex. The biomarkers AMPA, CIFCA, cis-DBCA, cis-DCCA and trans-DCCA were modelled as dichotomous (detected/non-detected).

Abbreviations: CH, HBM4EU-Switzerland (Switzerland); DE, ESB (Germany); DK, CPHmini/DYMS (Denmark); FR, ESTEBAN (France); IL, RAVMABAT (Israel); IS, DIET-HBM (Iceland); LU, Oriscav-Lux2 (Luxembourg); OPs, organophosphate pesticides; PR, prevalence ratio, PT, INSEF-ExpoQuim (Portugal).

cumulative effects nor interactions between chemicals in the three mixture models. Because AAMA and GAMA were highly correlated (Spearman $\rho = 0.86$ and 0.85 in the two acrylamide-containing mixtures), their component coefficients and weights are not separately identifiable, and the opposing weights should not be interpreted as independent effects acting in opposite directions. Replacing the two metabolites by their molar sum left the overall mixture effect essentially unchanged ($\psi = -0.70$, 95% CI: −1.47, 0.07), with the acrylamide term then carrying the largest negative weight (−0.78). Adding an AAMA × GAMA product term did not improve model fit in either mixture, providing no evidence of interaction.

4. Discussion

The present study examined cross-sectional associations between urinary biomarkers of acrylamide, pesticides, and UV-filter benzophenones and BMI and overweight/obesity prevalence in adults across eight countries, leveraging harmonized human biomonitoring data from HBM4EU-aligned studies. The most consistent and novel finding was the association between acrylamide exposure biomarkers and adiposity markers.

The inverse associations observed for AAMA with overweight/obesity and the positive association for GAMA:AAMA ratio with both adiposity markers represent one of the central findings of this study. Importantly, these results are not isolated, as converging evidence from US-based studies points in the same direction. Huang et al. reported in a large NHANES sample (2003–2006) that hemoglobin adducts of acrylamide (HbAA) were strongly and inversely associated with obesity, abdominal obesity, and overweight, with a dose-response trend across quartiles (p for trend <0.0001), and that the sum of HbAA and hemoglobin adducts of glycidamide (HbGA) was similarly inversely associated with all adiposity outcomes (Huang et al., 2018). This finding, based on long-term internal exposure biomarkers, substantially strengthens the plausibility of the inverse direction observed in our study using short-term urinary metabolites. A recent systematic review further consolidating this literature reported that across nine studies (eight of which used NHANES data) AAMA was associated with a 21% lower prevalence of both abdominal and general obesity, while HbAA was associated with a 64% lower prevalence of abdominal obesity (Mérida et al., 2024). However, the same review highlighted one NHANES study where HbGA and the HbGA/HbAA ratio were associated with higher abdominal obesity prevalence, which is consistent with our findings, where the GAMA:AAMA ratio was positively associated with adiposity markers (Wan et al., 2022). These findings suggest that the direction of association may depend on which metabolic pathway predominates, direct glutathione conjugation (reflected by AAMA and HbAA) versus epoxidation to glycidamide (reflected by GAMA and HbGA), a distinction with potential mechanistic implications for differential adiposity effects.

The mixture analyses using quantile g-computation were consistent with single-pollutant models but provided no evidence of a cumulative effect. In the pesticide-acrylamide mixture (France, Germany, Iceland; $n = 224$) the overall effect was the largest of the three but did not reach significance ($\psi = -0.71$, 95% CI: −1.48, 0.05; $p = 0.067$), and AAMA was the dominant negative contributor and GAMA accounted for the totality of positive weights (weight 1.00). The positive direction of the GAMA association is consistent with the positive HbGA-abdominal obesity association reported in NHANES-based studies where the glycidamide hemoglobin adduct was linked to higher adiposity (Mérida et al., 2024). However, this finding warrants cautious interpretation due to the modest magnitude of the associations and the high correlation between AAMA and GAMA, which can produce multicollinearity-related coefficient instability despite the partial robustness of the qgcomp framework to correlated exposures (Keil et al., 2020). Replacing the two highly correlated mercapturic acids by their molar sum, a reparametrisation that eliminates rather than accommodates the collinearity, left the joint effect unchanged ($\psi = -0.70$, 95% CI: −1.47, 0.07), with acrylamide carrying the largest negative weight (−0.78), indicating that the opposing component coefficients reflect correlation between the metabolites rather than independent effects in opposite directions. In the benzophenones-acrylamide mixture (Germany, France, Luxembourg; $n = 498$) and the pesticide-only mixture (Switzerland, Germany, Israel, Iceland; $n = 483$), no significant individual or joint effects on BMI were observed, consistent with the null single-pollutant findings for pyrethroid and organophosphate metabolites across most countries.

These results partially contrast with the emerging literature positioning acrylamide as a potential obesogen. Recent mechanistic reviews have proposed that acrylamide may promote adipogenesis and disrupt lipid and energy metabolism through activation of PPARγ-related pathways, AMPK signaling disruption, and altered adipocyte differentiation (Buyukdere and Akyol, 2023). However, experimental and epidemiological evidence in humans remains mixed and context-dependent. A key interpretive challenge in cross-sectional studies using urinary AAMA and GAMA as biomarkers is the substantial dietary confounding these biomarkers involve. The significance of the GAMA:AAMA ratio, reflecting individual metabolic conversion of acrylamide to its genotoxic epoxide glycidamide, may additionally capture inter-individual variability in CYP2E1 activity and glutathione conjugation capacity, which could themselves be influenced by

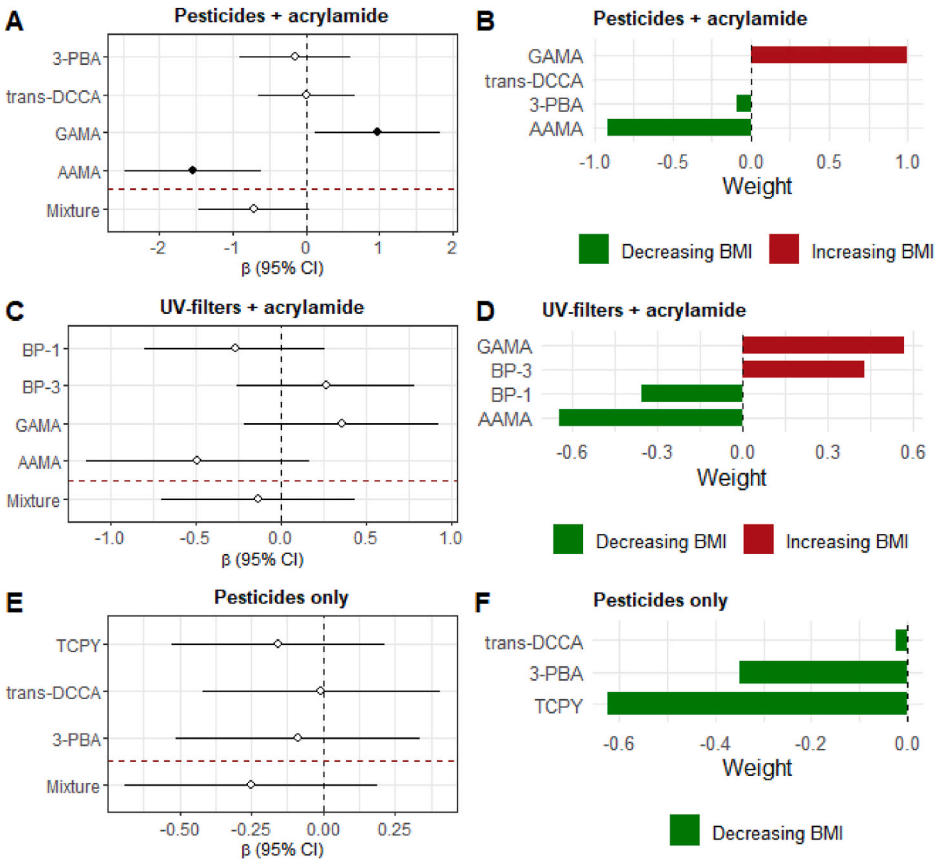


Fig. 4. Quantile g-computation mixture analyses of associations between CAS-standardized environmental chemical mixtures and body mass index in European adults. Left panels (A, C, E) display forest plots of individual exposure coefficients (β, 95% CI) per one quantile increase in each exposure, mutually adjusted for all other mixture components, and the overall mixture effect (below dashed horizontal line). Filled circles indicate statistically significant associations ($p < 0.05$); open circles indicate non-significant associations. Right panels (B, D, F) display the corresponding mixture weights, reflecting the proportional contribution of each component to the positive (red, increasing BMI) or negative (green, decreasing BMI) partial mixture effect. Results are shown for three mixture models: the pesticide-acrylamide mixture in adults from France, Germany, and Iceland (n = 224; panels A-B); the benzophenones-acrylamide mixture in adults from Germany, France, and Luxembourg (n = 498; panels C-D); and the pesticide mixture in adults from Switzerland, Germany, Israel, and Iceland (n = 483; panels E-F). All models were adjusted for sex, age and study. Exposures were quantile-scored into quartiles (q = 4) prior to analysis.

metabolic status and adiposity. These findings also warrant some caution given their sensitivity to the choice of urinary dilution adjustment for the individual metabolites. Our dataset did not allow adjusting dilution with creatinine-free measures (e.g. urine flow rate) which are generally considered a preferable reference and relied on creatinine-based approaches including the covariate-adjusted standardization (CAS), a method proposed to mitigate collider bias (O'Brien et al., 2016). In our data, CAS estimates for individual metabolites were substantially influenced by whether BMI was included in the creatinine prediction model, particularly for acrylamide metabolites. In the absence of an independent, creatinine-free benchmark, we cannot determine which specification more accurately reflects the true biomarker-obesity association, as was possible in a comparable arsenic-obesity analysis using urinary flow rate as a reference method (Bulka et al., 2017). Unlike the individual metabolites discussed above, the GAMA:AAMA ratio is exempt from this concern because both metabolites are measured in the same urine sample, any dilution factor applied to both cancels, indicating that its association with adiposity cannot be an artefact of dilution adjustment. Taken together, while the associations between acrylamide biomarkers and adiposity appear broadly concordant across US and European populations and across both short-term urinary and long-term hemoglobin biomarkers, they should be considered hypothesis-generating, given the cross-sectional design and the heterogeneous findings reported across biomarker matrices and adiposity outcomes in the prior literature. Prospective studies with repeated biomarker measurements and careful dietary and dilution adjustment are needed to disentangle these relationships.

The null associations observed for UV-filter benzophenones (BP-1, BP-3) and pyrethroid/organophosphate metabolites with BMI are broadly consistent with the limited existing literature. A comprehensive toxicological review of benzophenones confirmed their endocrine-disrupting properties, underpinning regulatory efforts to limit human exposure in Europe (Mustieles et al., 2023), yet epidemiological evidence specifically linking BP-3 and its major metabolite BP-1 to adiposity in adults remains sparse and inconsistent. A recent study using CAS standardization (adjusted for age, sex, and BMI) reported that BP-1 and BP-3 exposure was associated with increased odds of obesity in European male teenagers (Peinado et al., 2025), suggesting potential age- and sex-specific susceptibility windows not captured in our adult population. The sex-specific associations observed in our data, with BP-1 showing a significant negative association in males only, are intriguing but were not supported by formal interaction tests, limiting causal inference. For pyrethroids, the predominantly null associations with BMI are consistent with findings from HBM4EU risk assessments indicating low health concern at population-level exposure concentrations observed in European adults (Tarazona et al., 2022). However, some evidence from NHANES-based analyses suggests pyrethroid exposure, as measured by urinary 3-PBA, may be associated with glucose dysregulation, with insulin resistance more pronounced in obese participants (Liang et al., 2023), pointing to potential metabolic pathways that may not manifest at the level of BMI in our cross-sectional analysis.

5. Strengths, limitations, and public health implications

This study benefits from harmonized biomonitoring data across multiple European countries, biomarker-based internal exposure assessment, and the application of mixture methodology that accounted for co-exposures and their directional interactions. However, important limitations must be acknowledged. The cross-sectional design precludes causal inference, and reverse causality remains a plausible alternative explanation for the observed inverse associations with acrylamide metabolites and, as discussed above, for the positive association with the GAMA:AAMA ratio, a marker reflecting metabolic conversion as well as external exposure. However, irrespective of causal direction, a higher epoxidation fraction in individuals with greater adiposity would imply a larger internal dose of the genotoxic metabolite glycidamide per unit of acrylamide intake, which is relevant for risk assessment in populations with a high prevalence of overweight. The study-specific samples available for mixture analyses were relatively small ($n = 224–498$), limiting statistical power. Because each chemical family was measured in a different subset of the pooled population, depending on which studies ran which analytical panel, the magnitude of associations is not directly comparable across families. Some chemicals in the mixtures, like AAMA and GAMA, were also strongly correlated, hence mutually adjusted coefficients should not be interpreted as independent effects of each metabolite. Given the exploratory nature of the study, we did not apply formal correction for multiple comparisons; borderline associations should therefore be regarded as hypothesis-generating rather than confirmatory. Although sensitivity analyses adjusting for fried potato and fruit and vegetable consumption supported the consistency of the main associations to dietary adjustment, residual confounding by other dietary and lifestyle factors not captured in the post-harmonized HBM4EU codebook, including caloric intake, dietary quality, physical activity, and other acrylamide sources, cannot be excluded. Height and weight were self-reported for most participants, which tends to underestimate BMI and attenuate associations rather than inflate them. Within HBM4EU-Switzerland, the only study using both methods, BMI did not differ appreciably by ascertainment after adjustment for age and sex, and the analysis restricted to participants with measured values did not indicate influence on the results. Additionally, the use of spot urine samples may introduce exposure misclassification due to the short biological half-life of urinary acrylamide metabolites and pyrethroid metabolites which reflect short-term exposure and show day-to-day variability (Poteser et al., 2022), as repeated measurements were not available in this dataset, within-person variability and the reliability of a single spot sample could not be quantified, and the resulting misclassification is likely non-differential with respect to adiposity, tending to attenuate rather than inflate associations.

Despite these limitations, the consistency of the GAMA:AAMA ratio with both adiposity outcomes warrants further investigation, ideally in prospective designs with dietary adjustment and repeated biomarker measurements. From a regulatory perspective, the findings underscore the importance of monitoring acrylamide and other priority chemicals identified under the HBM4EU framework and support the integration of co-exposure assessment in future risk evaluations.

CRediT authorship contribution statement

German Cano-Sancho: Writing – original draft, Visualization, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Bianca Cox:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization. **Andrea Rodriguez-Carrillo:** Writing – review & editing, Methodology, Investigation. **Vicente Mustieles:** Writing – review & editing, Methodology. **Margaux Riou:** Writing – review & editing, Resources, Data curation. **Loïc Rambaud:** Writing – review & editing, Resources, Data curation. **Nicole Probst-Hensch:** Writing – review & editing, Resources, Data curation. **Medea Imboden:** Writing – review & editing, Resources, Data curation. **Nina Vogel:** Writing – review & editing, Resources, Data curation. **Till Weber:** Writing – review & editing, Resources, Data curation. **Tamar Berman:** Writing – review & editing, Resources, Data curation. **An van Nieuwenhuyse:** Writing – review & editing, Resources, Data curation. **Brice Appenzeller:** Writing – review & editing, Resources, Data curation. **Anders Juul:** Writing – review & editing, Resources, Data curation. **Hanne Frederiksen:** Writing – review & editing, Resources, Data curation. **Thorhallur I. Halldórsson:** Writing – review & editing, Resources, Data curation. **Kristín Ólafsdóttir:** Writing – original draft, Resources, Data curation. **Sonia Namorado:** Writing – review & editing, Resources, Data curation. **Bruno Le Bizec:** Writing – review & editing, Resources, Investigation, Funding acquisition. **Eva Govarts:** Writing – review & editing, Resources, Investigation, Funding acquisition, Conceptualization. **Jean-Philippe Antignac:** Writing – review & editing, Resources, Project administration, Investigation, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2026.126186.

Data availability

The authors do not have permission to share data.

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