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Supplemental Material

Linking Prenatal Environmental Exposures to Lifetime Health with Epigenome-Wide Association Studies: State-of-the-Science Review and Future Recommendations

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Prenatal environmental epigenome-wide association studies (EWAS) were identified through Pubmed, Web of Science, and Embase searches with the following terms.

PubMed

Web of Science All Databases

Embase

Figure S1. Inclusion and exclusion of studies for consideration in systemic review. Using the search terms described in the Supplementary Methods, we conducted a systemic review of epigenome-wide association studies. We excluded studies which were not epigenome-wide association studies (n=199) and studies which evaluated non-external exposures (n=27). We review in depth only studies that either performed replication in an independent sample or conducted a meta-analysis. We retained only EWAS of external exposures (n=134), excluding studies with only global or candidate methylation positions or examining non-exogenous exposures. We included studies using array or sequencing-based methods to measure methylation; 128 of the 134 exogenous exposure EWAS used the Illumina450K or EPIC arrays.

Table S1. Summary statistics on sample sizes of epigenome wide association studies.

Table S2. Complete data used to create Figure 2 from 134 epigenome wide association studies of external exposures. Please note not all rows included as data points in all facets of Figure 2, Figure 2 footnote explains exclusions.

Supplementary Methods

Prenatal environmental epigenome-wide association studies (EWAS) were identified through Pubmed, Web of Science, and Embase searches with the following terms.

PubMed

("Air Pollution"[Mesh] OR "Particulate Matter"[Mesh] OR "Vehicle Emissions"[Mesh] OR "Fossil Fuels"[Mesh] OR “Air Pollutants" [Pharmacological Action] OR "Air Pollutants, Occupational" [Pharmacological Action] OR "Volatile Organic Compounds"[Mesh] OR "Heating"[Mesh] OR "Cooking"[Mesh] OR "Dust"[Mesh:NoExp] OR "Radon"[Mesh] OR particulate-matter[tiab] OR smog[tiab] OR soot[tiab] OR PM2.5[tiab] OR "PM(2.5)"[tiab] OR PM10[tiab] OR "PM(10)"[tiab] OR carbon-black[tiab] OR black-carbon[tiab] OR elemental-carbon[tiab] OR ((air[tiab] OR airborne[tiab] OR coarse[tiab] OR ultrafine[tiab] OR fine[tiab]) AND (particle*[tiab] OR particulate*[tiab])) OR ((vehicle[tiab] OR vehicles[tiab] OR vehicular[tiab] OR auto[tiab] OR automobile[tiab] OR motor*[tiab] OR bus[tiab] OR buses[tiab] OR car[tiab] OR truck*[tiab] OR taxi[tiab] OR taxis[tiab] OR motorcycle*[tiab] OR engine*[tiab] OR traffic[tiab] OR road*[tiab] OR street*[tiab] OR highway*[tiab] OR interstate*[tiab] OR transport*[tiab] OR factory[tiab] OR factories[tiab] OR industr*[tiab] OR manufactur*[tiab]) AND (emission*[tiab] OR exhaust[tiab] OR fume*[tiab])) OR sulfur-dioxide[tiab] OR S02[tiab] OR ozone[tiab] OR O3[tiab] OR hydrogen-sulfide[tiab] OR H2S[tiab] OR carbon-monoxide[tiab] OR nitric-oxide[tiab] OR nitrogen-oxide[tiab] OR nitrogen-oxides[tiab] OR nitrogen-dioxide[tiab] OR NOx[tiab] OR "NO(x)"[tiab] OR NO2[tiab] OR volatile-organic-compound*[tiab] OR VOCs[tiab] OR gasoline*[tiab] OR diesel[tiab] OR petrol*[tiab] OR burn-pit*[tiab] OR ((wood[mesh] OR wood[tiab] OR firewood[tiab] OR biomass* OR charcoal[tiab] OR fuel[tiab] OR fuels[tiab] OR gas[tiab] OR gasoline[tiab] OR kerosene[tiab] OR dung[tiab] OR manure[tiab]) AND (smoke[mesh] OR combust*[tiab] OR burn*[tiab] OR burning[tiab])) OR cooker*[tiab] OR cooking[tiab] OR stove*[tiab] OR oven*[tiab] OR cookstove*[tiab] OR cook-stove*[tiab] OR woodstove*[tiab] OR heater*[tiab] OR fireplace*[tiab] OR woodsmoke[tiab] OR dust[tiab] OR radon[tiab] OR "Allergens"[Mesh] OR "Pollen"[Mesh:NoExp] OR "Dander"[Mesh] OR "Mites"[Mesh] OR allerg*[tiab] OR aeroallergen*[tiab] OR dander[tiab] OR dustmite*[tiab] OR mite[tiab] OR mites[tiab] OR cockroach*[tiab] OR pollen[tiab] OR mold[tiab] OR housedust[tiab] OR "Diet, Food, and Nutrition"[Mesh] OR "Dietary Exposure"[Mesh] OR "Food Contamination"[Mesh:NoExp] OR "Aflatoxins"[Mesh] OR "Fluorides"[Mesh] OR "Mycotoxins"[Mesh] OR "Isoflavones"[Mesh] OR "Polybrominated Biphenyls"[Mesh] OR "Micronutrients"[Mesh] OR "Trace Elements"[Mesh] OR "Micronutrients" [Pharmacological Action] OR "Trace Elements" [Pharmacological Action] OR "Food Additives" [Pharmacological Action] OR "Antioxidants" [Pharmacological Action] OR "Malnutrition"[Mesh] OR "Fetal Alcohol Spectrum Disorders"[Mesh] OR "Drinking Water"[Mesh] OR "Antioxidants"[Mesh] OR "Iodine"[Mesh] OR "Sulfur"[Mesh] OR "Riboflavin"[Mesh] OR "Thiamine"[Mesh] OR "Folic Acid"[Mesh] OR "Ascorbic Acid"[Mesh] OR "Vitamin D"[Mesh] OR "Vitamin B Complex"[Mesh] OR "Vitamin A"[Mesh] OR "Vitamins" [Pharmacological Action] OR "Dietary Fats"[Mesh] OR "Flavonoids"[Mesh] OR "Alcoholic Beverages"[Mesh] OR "Alcohol-Related Disorders"[Mesh] OR diet[tiab] OR diets[tiab] OR dietary[tiab] OR breast-feeding[tiab] OR breast-fed[tiab] OR fasting[tiab] OR nutrition*[tiab] caloric[tiab] OR calorie*[tiab] OR nutrient*[tiab] OR micronutrient*[tiab] OR macronutrient*[tiab] OR trace elements[tiab] OR Food-additive*[tiab] OR total-fat[tiab] OR total-sugar*[tiab] OR carbohydrate*[tiab] OR fiber[tiab] OR folic-acid[tiab] OR folate[tiab] OR vitamin*[tiab] OR ascorbic-acid[tiab] OR beta-carotene[tiab] OR biotin[tiab] OR calcium-ascorbate[tiab] OR choline[tiab] OR niacin[tiab] OR niacinamide[tiab] OR riboflavin[tiab] OR thiamine[tiab] OR sodium[tiab] OR iron[tiab] OR iodine[tiab] OR zinc[tiab] OR added-sugar*[tiab] OR sucrose[tiab] OR glucose[tiab] OR fructose[tiab] OR lactose[tiab] OR maltose[tiab] OR galactose[tiab] OR starch[tiab] OR calcium[tiab] OR magnesium[tiab] OR phosphorus[tiab] OR potassium[tiab] OR copper[tiab] OR manganese[tiab] OR selenium[tiab] OR pantothenic-acid[tiab] OR betaine[tiab] OR retinol[tiab] OR beta-cryptoxanthin[tiab] OR lycopene[tiab] OR tocopherol[tiab] OR dihydrophylloquinone[tiab] OR menaquinone[tiab] OR fish[tiab] OR seafood[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR LCPUFA[tiab] OR LCPUFAs[tiab] OR trans fat*[tiab] OR saturated fat*[tiab] OR monosaturated fat*[tiab] OR fatty acid*[tiab] OR mehg[tiab] OR omega-3[tiab] OR omega-6[tiab] OR methanol[tiab] OR "dietary sulfur"[tiab] OR antioxidant*[tiab] OR multivitamin*[tiab] OR mineral*[tiab] OR flavinoids[tiab] OR Hydroxyvitamin-D[tiab] OR caffeine[tiab] OR Chromium[tiab] OR eating[tiab] OR eat[tiab] OR eats[tiab] OR food[tiab] OR alcohol*[tiab] OR liquor[tiab] OR liquors[tiab] OR beer[tiab] OR wine[tiab] OR spirits[tiab] OR ((food[tiab] OR drinking water[tiab])

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OR 4-tertiary-octylphenol[tiab] OR "p-(1,1,3,3-tetramethylbutyl)-phenol"[tiab] OR triclocarban[tiab] OR trichlorocarbanilide[tiab] OR trichlorcarban[tiab] OR Triclosan[tiab] OR butylparaben[tiab] OR hydroxybenzoate[tiab] OR ethylparaben[tiab] OR methylparaben[tiab] OR polychlorinated biphenyl*[tiab] OR PCB[tiab] OR PCBs[tiab] OR Tetrachlorobiphenyl[tiab] OR pentachlorobiphenyl[tiab] OR hexachlorobiphenyl[tiab] OR Heptachlorobiphenyl[tiab] OR trichlorobiphenyl[tiab] OR Octachlorobiphenyl[tiab] OR Nonachlorobiphenyl[tiab] OR Decachlorobiphenyl[tiab] OR diethylstilbestrol[tiab] OR stilbestrol[tiab] OR stilbene-estrogen[tiab] OR xenoestrogen*[tiab] OR tributylin[tiab] OR nonylphenol[tiab] OR ethynylestradiol*[tiab] OR "Electronic Waste"[Mesh] OR electronic-waste*[tiab] OR electronics-waste* OR electronic-scrap*[tiab] OR Electronics-recycling[tiab] OR e-scrap*[tiab] OR e-waste*[tiab] OR EWRSs[tiab] OR Scrap-computer*[tiab] OR waste-electronic*[tiab] OR WEEE[tiab] OR ((electronic*[tiab] OR 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responder*[tiab] OR firefighter*[tiab] OR occupational[tiab] OR ethnic*[tiab] OR race[tiab] OR races[tiab] OR racial[tiab] OR racially[tiab] OR minorit*[tiab] OR nonwhite*[tiab] OR non-white*[tiab] OR people of color[tiab] OR women of color[tiab] OR black*[tiab] OR african-american*[tiab] OR afro-american*[tiab] OR asian-american*[tiab] OR Chinese-american*[tiab] OR Korean-american*[tiab] OR Japanese-american*[tiab] OR filipino[tiab] OR filipina[tiab] OR arab-american*[tiab] OR native-hawaiian*[tiab] OR pacific-islander*[tiab] OR native-american*[tiab] OR american-indian*[tiab] OR alaska-native*[tiab] OR first people*[tiab] OR caribbean-american*[tiab] OR caribbean-islander*[tiab] OR Spanish-american*[tiab] OR hispanic*[tiab] OR latina*[tiab] OR latino*[tiab] OR latinx[tiab] OR Mexican-american*[tiab] OR tejano[tiab] OR meso-american*[tiab] OR mestizo[tiab] OR puerto-rican*[tiab] OR Cuban*[tiab] OR Dominican*[tiab] OR criollo[tiab] OR "adverse childhood"[tiab] OR adverse experience*[tiab] OR adversity[tiab] OR adversities[tiab] OR abuse[tiab] OR violence[tiab] OR "traumatic childhood"[tiab] OR traumatic experience*[tiab] OR "traumatic early life"[tiab] OR "childhood trauma"[tiab] OR "early life trauma"[tiab] OR "violent childhood"[tiab] OR "troubled childhood"[tiab] OR "childhood maltreatment"[tiab] OR "child maltreatment"[tiab] OR "childhood mistreatment"[tiab] OR "child mistreatment"[tiab] OR "early life adverse"[tiab] OR "early adverse life"[tiab] OR "early life stress"[tiab] OR "childhood neglect"[tiab] OR "child neglect"[tiab] OR psychological trauma[tiab]) AND ("DNA Methylation"[Mesh] OR ("DNA"[Mesh] AND "Methylation"[Mesh]) OR "Epigenesis, Genetic"[Mesh] OR "Epigenome"[Mesh] OR "Epigenomics"[Mesh] OR "Genome-Wide Association Study"[Mesh] OR EWAS[tiab] OR 450k[tiab] OR 450 k[tiab] OR HM450K[tiab] OR HumanMethylation450K[tiab] OR Illumina450K[tiab] OR 850k[tiab] OR 850 k[tiab] OR HM850K[tiab] OR Illumina[tiab] OR 450-beadchip[tiab] OR EPIC BeadChip[tiab] OR Infinium MethylationEPIC[tiab] OR methylome-wide[tiab] OR epigenome-wide[tiab] OR EWA stud*[tiab] OR epigenom*[tiab] OR epigene*[tiab] OR methylat*[tiab] OR DNAm[tiab] OR DNAme[tiab] OR DNA-m[tiab] OR DNA-me[tiab] OR DMRs[tiab] OR differently-methylated[tiab] OR differential methylation[tiab] OR hypomethylation*[tiab] OR hypermethylation*[tiab] OR CPGs[tiab] OR CPG[tiab] OR CPGs[tiab] OR methylation-array[tiab] OR Methylome*[tiab] OR genome-wide[tiab] OR genomewide[tiab] OR epigenomewide[tiab] OR GWAS[tiab] OR GWA stud*[tiab] OR ExWAS[tiab]) AND ("Pregnancy"[Mesh] OR "Fetus"[Mesh] OR "Prenatal Exposure Delayed Effects"[Mesh] OR "Maternal Exposure"[Mesh] OR in utero[tiab] OR prenatal[tiab] OR pre-natal[tiab] OR foetal[tiab] OR foetus*[tiab] OR fetal[tiab] OR fetus*[tiab] OR maternal exposure*[tiab] OR maternal serum[tiab] OR pregnancy exposure*[tiab] OR exposure during pregnancy[tiab] OR exposures during pregnancy[tiab] OR developmental exposure*[tiab] OR early life exposure*[tiab] OR developmental origins of health[tiab] OR DOHaD[tiab]) AND ("Infant"[Mesh] OR infant*[tiab] OR newborn*[tiab] OR neonate*[tiab] OR placenta*[tiab] OR cord blood[tiab] OR dried blood spot*[tiab] OR buccal[tiab])

Web of Science All Databases

(TS=(EWAS OR 450k OR “450 K” OR HM450K OR HumanMethylation450* OR Illumina450K OR 850k OR “850 K” OR HM850K OR HumanMethylation850* OR Illumina OR 450-beadchip OR “EPIC BeadChip” OR MethylationEPIC OR methylome-wide OR epigenome-wide OR “EWA stud*” OR epigenomewide) OR TI=(epigenom* OR epigene* OR methylat* OR DNAm OR DNAme OR DNA-m OR DNA-me OR DMRs OR differently-methylated OR “differential methylation” OR hypomethylat* OR hypermethylat* OR methylation-array OR Methylome* OR genome-wide OR genomewide)) AND TS=((“in utero” OR prenatal OR pre-natal OR foetal OR foetus* OR fetal OR fetus* OR “maternal serum” OR ((pregnancy OR gestation* OR developmental OR maternal) NEAR/2 (exposure*)) OR “developmental origins of health” OR DOHaD OR mother-child OR mother-infant OR mother-offspring) AND (infant* OR newborn* OR neonat* OR progeny OR offspring OR placenta* OR “cord blood” OR “dried blood spot*” OR “dried bloodspot*” OR buccal)) AND TS=(particulate-matter OR smog OR soot OR PM2.5 OR "PM(2.5)" OR PM10 OR "PM(10)" OR carbon-black OR black-carbon OR elemental-carbon OR ((air OR airborne OR coarse OR ultrafine OR fine) NEAR/1 (particle* OR particulate*)) OR ((vehicle OR vehicles OR vehicular OR auto OR automobile OR motor* OR bus OR buses OR car OR truck* OR taxi OR taxis OR motorcycle* OR engine* OR traffic OR road* OR street* OR highway* OR interstate* OR transport* OR factory OR factories OR industr* OR manufactur*) NEAR/2 (emission* OR exhaust OR fume*)) OR sulfur-dioxide OR S02 OR ozone OR O3 OR hydrogen-sulfide OR H2S OR carbon-monoxide OR nitric-oxide OR nitrogen-oxide OR nitrogen-oxides OR nitrogen-dioxide OR NOx OR "NO(x)" OR NO2 OR volatile-organic-compound* OR VOCs OR gasoline* OR diesel OR petrol* OR burn-pit* OR ((wood OR firewood OR biomass* OR charcoal OR fuel OR fuels OR gas OR gasoline OR kerosene OR dung OR manure) NEAR/2 (combust* OR burn* OR burning)) OR cooker* OR cooking OR stove* OR oven* OR cookstove* OR cook-stove* OR woodstove* OR heater* OR fireplace* OR woodsmoke OR dust OR radon OR allerg* OR aeroallergen* OR dander OR dustmite* OR mite OR mites OR cockroach* OR pollen OR housedust OR “dietary exposure*” OR ((food OR “drinking water”) NEAR/1 (contamination OR contaminant*)) OR “food additive*” OR selenium OR mycotoxin* OR isoflavone* OR isoflavonoid* OR genistein OR phytoestrogen* OR phytochemical* OR “trace elements” OR micronutrient* OR macronutrient* OR nutrient* OR fluoride OR calcium OR nutrition* OR seafood OR PUFA OR PUFAs OR LCPUFA OR LCPUFAs OR "polyunsaturated fatty acids" OR “trans fat*” OR “saturated fat*” OR “monosaturated fat*” OR mehg OR omega-3 OR omega-6 OR methanol OR "dietary sulfur" OR antioxidant* OR vitamin* OR multivitamin* OR mineral* OR "trace elements" OR flavinoids OR iodine OR riboflavin OR thiamine OR folate OR "folic acid" OR choline OR betaine OR Hydroxyvitamin-D OR sugar* OR caffeine OR Zinc OR copper OR manganese OR iron OR Chromium OR biotin OR niacin OR “Pantothenic acid” OR dioxane* OR dioxin* OR furan OR furans OR dibenzofuran* OR heptachlorodibenzodioxin OR HpCDD OR HCDD OR hexachlorodibenzodioxin OR HxCDD OR PeCDD OR dibenzodioxin* OR PCDD OR Tetrachlorodibenzodioxin OR TCDD OR Heptachlorodibenzofuran OR Hexachlorodibenzofuran OR Octachlorodibenzofuran OR pentachlorodibenzofuran OR tetrachlorodibenzofuran OR TCDF OR (endocrine AND disrupt*) OR bisphenol OR BPA OR dinitrobisphenol OR tetrabromobisphenol OR "2,2-bis(4-hydroxyphenyl)propane" OR 4-tert-octylphenol OR p-tert-octylphenol OR 4-tertiary-octylphenol OR "p-(1,1,3,3-tetramethylbutyl)-phenol" OR triclocarban OR trichlorocarbanilide OR trichlorcarban OR Triclosan OR butylparaben OR hydroxybenzoate OR ethylparaben OR methylparaben OR “polychlorinated biphenyl*” OR PCB* OR Tetrachlorobiphenyl OR pentachlorobiphenyl OR hexachlorobiphenyl OR Heptachlorobiphenyl OR trichlorobiphenyl OR Octachlorobiphenyl OR Nonachlorobiphenyl OR Decachlorobiphenyl OR diethylstilbestrol OR stilbestrol OR stilbene-estrogen OR xenoestrogen* OR tributylin OR nonylphenol OR ethynylestradiol* OR “electronic waste*” OR “electronics waste*” OR “electronic scrap*” OR “Electronics recycling” OR e-scrap* OR e-waste* OR EWRSs OR “Scrap computer*” OR “waste electronic*” OR WEEE OR ((electronic* OR cell phone OR cellular phone OR mobile phone* OR computer OR television* OR "TV" OR "TVs" OR laptop* OR tablet* OR mobile-device* OR MP3-player* OR CD-player* OR DVD-player* OR sound-system OR home-entertainment* OR camera* OR game-console* OR calculator* OR circuit-board* OR mother-board* OR motherboard* OR crt-funnel-glass OR liquid-crystal OR amoled OR LCD OR cathode-ray-tube* OR battery OR batteries) AND (waste OR recycle* OR disposal* OR scrap OR scrapped OR scraps)) OR “fire retard*” OR “flame retard*” OR “fire proofing” OR ((halogenated OR chlorinated OR brominated OR polybrominated) NEAR/1 (diphenyl-ether*)) OR PBDE* OR PCDE* OR BDE OR BDEs OR “tribrominated diphenyl ether” OR “tribromodiphenyl ether” OR “tetrabromodiphenyl ether” OR “brominated diphenyl ether” OR tetraBDE OR “tetrabrominated diphenyl ether” OR “pentabromodiphenyl ether” OR pentaBDE OR “hexabromodiphenyl ether” OR hexabromodiphenyl OR hexaBDE OR “heptabromodiphenyl ether” OR HeptaBDE OR hexabromocyclododecane OR HBCD OR 345-HBB OR 245-HBB OR PBB-153 OR PBB153 OR asbestos OR TDBPP OR “Environmental-agent*” OR “environmental chemical*” OR

“environmental compound*” OR “environmental contaminant*” OR “environmental determinant*” OR “environmental estrogen*” OR “environmental exposure*” OR carcinogen* OR teratogen* OR mutagen* OR epimutagen* OR pollut* OR cardiotox* OR ecotox* OR epitox* OR toxicoepi* OR toxicant* OR toxin* OR xenobiotic* OR xenochemical* OR “chemical exposure*” OR “occupational exposure*” OR “household exposure*” OR “chemical mixture*” OR “chemical product*” OR “chemical hazard*” OR “hazardous compound*” OR “hazardous exposure*” OR “hazardous mixture*” OR “hazardous material*” OR “hazardous product*” OR “hazardous substance*” OR “industrial compound*” OR “industrial chemical*” OR biohazard* OR “personal product*” OR cosmetics OR “cosmetic product*” OR “care product*” OR “consumer product*” OR “commercial product*” OR “cleaning product*” OR “household product*” OR “consumer goods” OR makeup OR make-up OR “hair product*” OR “beauty product*” OR toys OR “plastic container*” OR “food container*” OR “heavy metal*” OR “toxic metal*” OR “synthetic metal*” OR arsenic OR arsenical* OR arsenite* OR arsenate* OR ((Titanium OR Vanadium OR Chromium OR Manganese OR Iron OR Cobalt OR Nickel OR Copper OR Zinc OR Gallium OR Germanium OR Zirconium OR Niobium OR Molybdenum OR Technetium OR Ruthenium OR Rhodium OR Palladium OR Silver OR Cadmium OR Indium OR Tin OR Tellurium OR Lutetium OR Hafnium OR Tantalum OR Tungsten OR Rhenium OR Osmium OR Iridium OR Platinum OR Gold OR Mercury OR Methylmercury OR Thallium OR Bismuth OR Polonium OR Astatine OR Lanthanum OR Cerium OR Praseodymium OR Neodymium OR Promethium OR Samarium OR Europium OR Gadolinium OR Terbium OR Dysprosium OR Holmium OR Erbium OR Thulium OR Ytterbium OR Actinium OR Thorium OR Protactinium OR Uranium OR Neptunium OR Plutonium OR Americium OR Curium OR Berkelium OR Californium OR Einsteinium OR Fermium OR Nobelium OR Radium OR Lawrencium OR Rutherfordium OR Dubnium OR Seaborgium OR Bohrium OR Hassium OR Meitnerium OR Darmstadtium OR Roentgenium OR Copernicium) AND (poison* OR exposure* OR exposed OR contaminat* OR dietary OR blood OR serum OR urine OR urinary)) OR “blood lead” OR (lead AND PB) OR “lead exposure*” OR “dietary lead” OR “lead poisoning” OR “lead level*” OR “polycyclic aromatic hydrocarbons” OR PAHs OR fumonisin OR benzopyrene OR benzo-a-pyrene OR "3,4-benzopyrene" OR hydroxypyrene OR benzene OR toluene OR xylene OR Pesticid* OR fungicide* OR herbicide* OR insecticide* OR insect-repellent* OR rodenticide* OR acaricide* OR algicide* OR biopesticide* OR fumigant* OR molluscicide* OR nematicide* OR weed-killer* OR pest control OR organochlorin* OR organic-chlorine OR chlorinated-hydrocarbon* OR aldrin OR chlordan OR chlordane OR chlordecone OR chlorobenzene* OR chlorofluorocarbon* OR dichlorodiphenyltrichloroethane* OR DDT OR Dichlorodiphenyldichloroethylene OR DDE OR dieldrin OR endrin OR heptachlor OR hexachlorobenzene OR hexachlorocyclohexane OR alpha-HCH OR beta-HCH OR lindane OR hexachlorocyclohexane OR methoxychlor OR mirex OR polychlorinated-biphenyl* OR "polychlorinated biphenyls" OR polychlorobiphenyl OR PCBs OR tetrachloroethylene OR trichloroethane* OR vinyl-chloride OR agent-orange OR Amitraz OR atrazine OR avermectin OR captan OR carbaryl OR carbofuran OR chlorfenvinphos OR chlorpyrifos OR coumaphos OR deet OR "N,N-diethyltoluamide" OR diazinon OR dichlorvos OR "dimethyl phthalate" OR endosulfan* OR linalool OR malathion OR paraquat OR parathion OR pentachlorobenzene OR PeCB OR pentachlorophenol OR permethrin OR pyrethrin* OR rotenone OR vinclozolin OR omethoate OR dichlorophenol OR “2,5-DCP” OR dichlorophenol OR “2,4-DCP” OR trichlorophenol OR “2,4,5-TCP” OR trichlorophenol OR “2,4,6-TCP” OR phthalate* OR butylbenzenesulfonamide OR plasticizers OR MEOHP OR MEHP OR DEHP OR “Bis(2-ethylhexyl)phthalate” OR fluorocarbon* OR “fluorinated organic compound*” OR PFAS OR PFASs OR GenX OR Gen-X OR PFAA OR perfluoroalkyl OR polyfluoroalkyl OR perfluorinated OR PFCs OR PFC OR PFOS OR perfluorobutanesulfonic OR perfluorodecanoic OR perfluoro-n-decanoic OR nonadecafluoro-n-decanoic OR perfluorododecanoic OR PFDoA OR perfluoroheptanoic OR PFHpA OR perfluorohexanesulfonic OR PFHS OR perfluorohexanesulfonate OR “Perfluorohexane sulfonate” OR PFHxS OR “perfluorononanoic acid” OR “perfluorooctanoic acid” OR pentadecafluorooctanoic OR “perfluorooctanoyl chloride” OR PFOA OR “sodium perfluorooctanoate” OR perfluorooctanoate OR ammonium-perfluorooctanoate OR "APFO" OR “perfluorooctane sulfonic acid” OR “perfluorooctanesulfonic acid” OR PFOSA OR “perfluorooctanyl sulfonate” OR Perfluorooctanesulfonate OR “perfluorooctane-sulfonate” OR perfluorooctanesulfonamide OR perfluoroundecanoic OR solvents OR “organic solvent*” OR "2-bromopropane" OR "2-propanol" OR acetone OR tetrachloroethylene OR toluene OR trichloroethylene OR "secondhand smoke" OR "second hand smoke" OR "passive smoke" OR cotinine OR nicotine OR smoking OR smoker* OR cigarette* OR tobacco OR cigar OR vaping OR “social stress*” OR “financial stress*” OR psychosocial OR socioeconomic OR “social determinant*” OR “social factors” OR “sociological factors” OR disparities OR “minority health” OR discrimination OR discriminated OR discriminatory OR segregat* OR prejudice* OR racism OR racist OR sexism OR sexist OR ableism OR ableist OR homophob* OR agist OR agism OR classism OR classist OR xenophobi* OR Marginalize* OR stigma OR stigmatize* OR Microaggress*

OR micro-aggress* OR sedentary OR exercise* OR screen-time OR “life choices” OR lifestyle* OR life-style* OR neighborhood* OR neighbourhood* OR “light pollut*” OR “noise pollut*” OR ALAN OR “light at night” OR greenspace* OR “green space*” OR "health equity" OR "health inequalities" OR "health inequality" OR "health justice" OR "health injustices" OR “vulnerable population*” OR “sensitive population*” OR “underserved population*” OR “special population*” OR indigent* OR homeless* OR squatter* OR migrant* OR “disaster victim*” OR poverty* OR deprived OR deprivation OR “working poor” OR disadvantage* OR out-of-work OR jobless OR unemploy* OR foreclosure OR foreclosed OR home-owner* OR refugee* OR displaced OR farmer* OR agricultural-worker* OR farm-hand* OR laborer* OR worker* OR miner* OR police* OR military OR first responder* OR firefighter* OR occupational OR ethnic* OR race OR races OR racial* OR minorit* OR nonwhite* OR non-white* OR “people of color” OR “person* of color” OR “women of color” OR black* OR african-american* OR afro-american* OR asian-american* OR Chinese-american* OR Korean-american* OR Japanese-american* OR filipino OR filipina OR arab-american* OR native-hawaiian* OR pacific-islander* OR native-american* OR american-indian* OR alaska-native* OR first people* OR caribbean-american* OR caribbean-islander* OR Spanish-american* OR hispanic* OR latina* OR latino* OR latinx OR Mexican-american* OR tejano OR meso-american* OR mestizo OR puerto-rican* OR Cuban* OR acculturat* OR Dominican* OR criollo OR "adverse childhood" OR “adverse experience*” OR adversity OR adversities OR abuse OR violence OR "traumatic childhood" OR “traumatic experience*” OR "traumatic early life" OR "childhood trauma" OR "early life trauma" OR "violent childhood" OR "troubled childhood" OR "childhood maltreatment" OR "child maltreatment" OR "childhood mistreatment" OR "child mistreatment" OR "early life adverse" OR "early adverse life" OR "early life stress" OR "childhood neglect" OR "child neglect" OR “psychological trauma” OR “war expose*” OR “war exposure*” OR “war trauma” OR roadway* OR highway* OR ((hot OR cold OR extreme OR winter OR summer OR heat OR freezing OR high OR low) NEAR/1 (weather OR temperature*)) OR "extreme heat" OR "extreme cold" OR “cold spell*” OR “heat wave*” OR heatwave* OR “cold snap*” OR “ambient temperature*” OR “outdoor temperature*” OR “air conditioning” OR “outdoor heat” OR “environmental temperature*” OR meteorologic* OR "heat stress” OR “cold stress” OR “cold exposure” OR “heat exposure” OR “severe weather” OR “extreme weather” OR disaster* OR hurricane* OR tornado* OR tsunami* OR typhoon* OR earthquake* OR wildfire* OR “wild fire*” OR flood OR flooding OR drought OR famine OR terrorism OR “terror attack*” OR terrorist* OR bombing OR “9/11” OR “twin towers” OR “nuclear accident*”) NOT (TI=(“global methylation” OR “global DNA methylation” OR paternal OR sperm OR mice OR mouse OR rat OR rats) OR AB=(pyrosequenc* OR 27K OR methylation27* OR “candidate gene*”))

Embase

Limit to: Human studies

('environmental exposure'/exp OR 'environmental exposure' OR 'environmental chemical'/exp OR 'environmental chemical' OR 'environmental factor'/exp OR 'environmental factor' OR 'indoor environment'/exp OR 'indoor environment' OR 'work environment'/exp OR 'work environment' OR 'pollution'/exp OR 'pollution' OR 'environmental stress'/exp OR 'environmental stress' OR 'polycyclic aromatic hydrocarbon'/exp OR 'polycyclic aromatic hydrocarbon' OR ‘PAHs’ OR ‘particulate matter’ OR smog OR soot OR PM2.5 OR ‘PM(2.5)’ OR PM10 OR ‘PM(10)’ OR ‘volatile organic compound*’ OR ‘VOCs’ OR 'pollutant'/exp OR 'pollutant*' OR ‘pollution’ OR 'toxic substance'/exp OR 'toxic substance*' OR ‘toxicant*’ OR 'dangerous goods'/exp OR 'dangerous goods' OR 'radiation exposure'/exp OR 'radiation exposure' OR 'tobacco use'/exp OR ‘smoking’ OR ‘tobacco’ OR ‘cotinine’ OR ‘nicotine’ OR 'allergen'/exp OR 'allergen*' OR 'body mass'/exp OR 'body mass' OR 'obesity'/exp OR 'obesity' OR ‘obese’ OR 'gestational weight gain'/exp OR 'gestational weight gain' OR 'overnutrition'/exp OR 'overnutrition' OR 'nutrition'/exp OR 'nutrition' OR 'vitamin'/exp OR 'vitamin*' OR 'trace element'/exp OR 'trace element*' OR 'dietary intake'/exp OR 'dietary intake*' OR ‘fluoride’ OR ‘calcium’ OR ‘nutrition*’ OR ‘seafood’ OR ‘PUFA’ OR ‘PUFAs’ OR ‘LCPUFA’ OR ‘LCPUFAs’ OR ‘polyunsaturated fatty acids’ OR ‘trans fat*’ OR ‘saturated fat*’ OR ‘monosaturated fat*’ OR ‘mehg’ OR ‘omega-3’ OR ‘omega-6’ OR ‘dietary sulfur’ OR ‘antioxidant*’ OR ‘vitamin*’ OR ‘multivitamin*’ OR ‘trace elements’ OR ‘flavinoids’ OR ‘iodine’ OR ‘riboflavin’ OR ‘thiamine’ OR ‘folate’ OR ‘folic acid’ OR ‘choline’ OR ‘betaine’ OR ‘Hydroxyvitamin-D’ OR ‘sugar*’ OR ‘caffeine’ OR 'dioxin'/exp OR 'dioxin*' OR 'furan'/exp OR 'furan*' OR 'endocrine disruptor'/exp OR 'endocrine disruptor' OR '4,4` isopropylidenediphenol'/exp OR '4,4` isopropylidenediphenol' OR 'phenol derivative'/exp OR 'phenol derivative' OR 'organochlorine derivative'/exp OR 'organochlorine' OR 'triclosan'/exp OR 'triclosan' OR 'organic solvent'/exp OR 'organic solvent*' OR 'diethylstilbestrol derivative'/exp OR 'diethylstilbestrol' OR 'xenoestrogen'/exp OR 'xenoestrogen*' OR 'flame retardant'/exp OR 'flame retardant*' OR ‘fire retardant*’ OR ((‘halogenated’ OR ‘chlorinated’ OR ‘brominated’ OR ‘polybrominated’) NEAR/1

(‘diphenyl-ether*’)) OR ‘PBDE*’ OR ‘PCDE*’ OR ‘BDE’ OR ‘BDEs’ OR ‘tribrominated diphenyl ether’ OR ‘tribromodiphenyl ether’ OR ‘tetrabromodiphenyl ether’ OR ‘brominated diphenyl ether’ OR ‘tetraBDE’ OR ‘tetrabrominated diphenyl ether’ OR ‘pentabromodiphenyl ether’ OR pentaBDE OR ‘hexabromodiphenyl ether’ OR ‘hexabromodiphenyl’ OR ‘hexaBDE’ OR ‘heptabromodiphenyl ether’ OR ‘HeptaBDE’ OR ‘hexabromocyclododecane’ OR ‘HBCD’ OR ‘asbestos’ OR ‘TDBPP’ OR ‘Pesticide*’ OR ‘aldrin’ OR ‘chlordan’ OR ‘chlordane’ OR ‘chlordecone’ OR ‘chlorobenzene*’ OR ‘chlorofluorocarbon*’ OR ‘dichlorodiphenyltrichloroethane*’ OR ‘DDT’ OR ‘Dichlorodiphenyldichloroethylene’ OR ‘DDE’ OR ‘dieldrin’ OR ‘endrin’ OR ‘heptachlor’ OR ‘hexachlorobenzene’ OR ‘hexachlorocyclohexane’ OR ‘alpha-HCH’ OR ‘beta-HCH’ OR ‘lindane’ OR ‘hexachlorocyclohexane’ OR ‘methoxychlor’ OR ‘mirex’ OR ‘tetrachloroethylene’ OR ‘trichloroethane*’ OR ‘vinyl-chloride’ OR ‘Amitraz’ OR ‘atrazine’ OR ‘avermectin’ OR ‘captan’ OR ‘carbaryl’ OR ‘carbofuran’ OR ‘chlorfenvinphos’ OR ‘chlorpyrifos’ OR ‘coumaphos’ OR ‘deet’ OR ‘N,N-diethyltoluamide’ OR ‘diazinon’ OR ‘dichlorvos’ OR ‘dimethyl phthalate’ OR ‘endosulfan*’ OR ‘linalool’ OR ‘malathion’ OR ‘paraquat’ OR ‘parathion’ OR ‘pentachlorobenzene’ OR ‘PeCB’ OR ‘pentachlorophenol’ OR ‘permethrin’ OR ‘pyrethrin*’ OR ‘rotenone’ OR ‘vinclozolin’ OR ‘omethoate’ OR ‘dichlorophenol’ OR 'benzene derivative'/exp OR ‘plasticizers’ OR ‘phthalates’ OR 'cosmetic'/exp OR 'cosmetics' OR 'personal care product'/exp OR 'care product*' OR 'heavy metal'/exp OR 'heavy metal*' OR 'heavy metal poisoning'/exp OR 'heavy metal poisoning' OR ‘lead poisoning’ OR ‘mercury’ OR ‘arsenic’ OR ‘arsenical*’ OR ‘arsenite*’ OR ‘arsenate*’ OR ‘methylmercury’ OR ‘cadmium’ OR ‘chromium’ OR ‘manganese’ OR ‘zinc’ OR ‘iron’ OR 'heavy metal pollution'/exp OR 'heavy metal pollution' OR 'xylene'/exp OR 'xylene' OR 'benzene'/exp OR 'benzene*' OR ‘psychosocial stress*’ OR 'social problem'/exp OR 'social problem*' OR 'social aspects and related phenomena'/exp OR 'social stress*' OR ‘social determinant*’ OR 'minority group'/exp OR 'minority group*' OR 'lifestyle and related phenomena'/exp OR 'lifestyle*' OR 'sleep'/exp OR 'sleep*' OR 'insomnia'/exp OR 'insomnia' OR 'social environment'/exp OR 'social environment' OR psychosocial OR socioeconomic OR ‘social determinant*’ OR ‘social factors’ OR ‘sociological factors’ OR ‘minority health’ OR discrimination OR discriminated OR discriminatory OR segregat* OR prejudice* OR racism OR racist OR sexism OR sexist OR ableism OR ableist OR homophob* OR agist OR agism OR classism OR classist OR xenophobi* OR Marginalize* OR stigma OR stigmatize* OR Microaggress* OR micro-aggress* OR sedentary OR exercise* OR screen-time OR ‘life choices’ OR lifestyle* OR life-style* OR neighborhood* OR neighbourhood* OR ‘light pollut*’ OR ‘noise pollut*’ OR ALAN OR ‘light at night’ OR greenspace* OR ‘green space*’ OR ‘health equity’ OR ‘health inequalities’ OR ‘health inequality’ OR ‘health justice’ OR ‘health injustices’ OR ‘vulnerable population*’ OR ‘sensitive population*’ OR ‘underserved population*’ OR ‘special population*’ OR indigent* OR homeless* OR squatter* OR migrant* OR ‘disaster victim*’ OR poverty* OR deprived OR deprivation OR ‘working poor’ OR disadvantage* OR out-of-work OR jobless OR unemploy* OR foreclosure OR foreclosed OR home-owner* OR refugee* OR displaced OR farmer* OR agricultural-worker* OR farm-hand* OR laborer* OR worker* OR miner* OR police* OR military OR first responder* OR firefighter* OR occupational OR ethnic* OR race OR races OR racial* OR minorit* OR nonwhite* OR non-white* OR ‘people of color’ OR ‘person* of color’ OR ‘women of color’ OR black* OR african-american* OR afro-american* OR asian-american* OR Chinese-american* OR Korean-american* OR Japanese-american* OR filipino OR filipina OR arab-american* OR native-hawaiian* OR pacific-islander* OR native-american* OR american-indian* OR alaska-native* OR first people* OR caribbean-american* OR caribbean-islander* OR Spanish-american* OR hispanic* OR latina* OR latino* OR latinx OR Mexican-american* OR tejano OR meso-american* OR mestizo OR puerto-rican* OR Cuban* OR acculturat* OR Dominican* OR criollo OR ‘adverse childhood’ OR ‘adverse experience*’ OR adversity OR adversities OR abuse OR violence OR ‘traumatic childhood’ OR ‘traumatic experience*’ OR ‘traumatic early life’ OR ‘childhood trauma’ OR ‘early life trauma’ OR ‘violent childhood’ OR ‘troubled childhood’ OR ‘childhood maltreatment’ OR ‘child maltreatment’ OR ‘childhood mistreatment’ OR ‘child mistreatment’ OR ‘early life adverse’ OR ‘early adverse life’ OR ‘early life stress’ OR ‘childhood neglect’ OR ‘child neglect’ OR ‘psychological trauma’ OR ‘war expose*’ OR ‘war exposure*’ OR ‘war trauma’ OR 'meteorological phenomena'/exp OR 'meteorological phenomena' OR ‘heat wave*’ OR ‘heatwave*’ OR ‘severe weather’ OR ‘disaster*’ OR ‘ambient temperature*’ OR ‘outdoor temperature*’ OR ‘air conditioning’ OR ‘outdoor heat’ OR ‘environmental temperature*’ OR 'occupational exposure'/exp OR 'occupational exposure*' OR 'military phenomena'/exp OR 'military' OR 'perfluoroalkanoic acid'/exp OR 'perfluoroalkanoic acid' OR 'fluorocarbon'/exp OR 'fluorocarbon' OR ‘fluorocarbon*’ OR ‘fluorinated organic compound*’ OR ‘PFAS*’ OR ‘GenX’ OR ‘Gen-X’ OR ‘PFAA’ OR ‘perfluoroalkyl’ OR ‘polyfluoroalkyl’ OR ‘perfluorinated’ OR ‘PFCs’ OR ‘PFC’ OR ‘PFOS’ OR ‘perfluorobutanesulfonic’ OR ‘perfluorodecanoic’ OR ‘perfluoro-n-decanoic’ OR ‘nonadecafluoro-n-decanoic’ OR ‘perfluorododecanoic’ OR ‘PFDoA’ OR ‘perfluoroheptanoic’ OR ‘PFHpA’ OR ‘perfluorohexanesulfonic’ OR ‘PFHS’ OR ‘perfluorohexanesulfonate’ OR ‘Perfluorohexane sulfonate’ OR ‘PFHxS’ OR ‘perfluorononanoic

acid’ OR ‘perfluorooctanoic acid’ OR ‘pentadecafluorooctanoic’ OR ‘perfluorooctanoyl chloride’ OR ‘PFOA’ OR ‘sodium perfluorooctanoate’ OR ‘perfluorooctanoate’ OR ‘ammonium perfluorooctanoate’ OR ‘APFO’ OR ‘perfluorooctane sulfonic acid’ OR ‘perfluorooctanesulfonic acid’ OR ‘PFOSA’ OR ‘perfluorooctanyl sulfonate’ OR ‘Perfluorooctanesulfonate’ OR ‘perfluorooctane-sulfonate’ OR ‘perfluorooctanesulfonamide’ OR ‘perfluoroundecanoic’) AND ('prenatal exposure'/exp OR 'prenatal exposure' OR 'maternal exposure'/exp OR 'maternal exposure' OR 'pregnancy'/exp OR 'pregnancy') AND ('newborn'/exp OR 'newborn' OR 'infant'/exp OR 'infant' OR 'blood spot*' OR 'bloodspot*' OR 'placenta'/exp OR placenta OR placental OR buccal OR 'cord blood'/exp OR 'cord blood') AND ('epigenome wide association study'/exp OR 'epigenome wide association study' OR 'epigenetics'/exp OR 'epigenetics' OR 'epigen*':ti OR 'epigenome'/exp OR 'epigenome' OR 'dna methylation'/exp OR 'dna methylation' OR 'dna methylation':ti OR ewas OR hm450* OR methylation450* OR 450k OR ‘450 k’ OR hm850* OR methylation850* OR 850k OR ‘850 k’ OR 'epic beadchip' OR (methylation NEAR/1 epic)) NOT (pyrosequenc* OR 27k OR methylation27*)

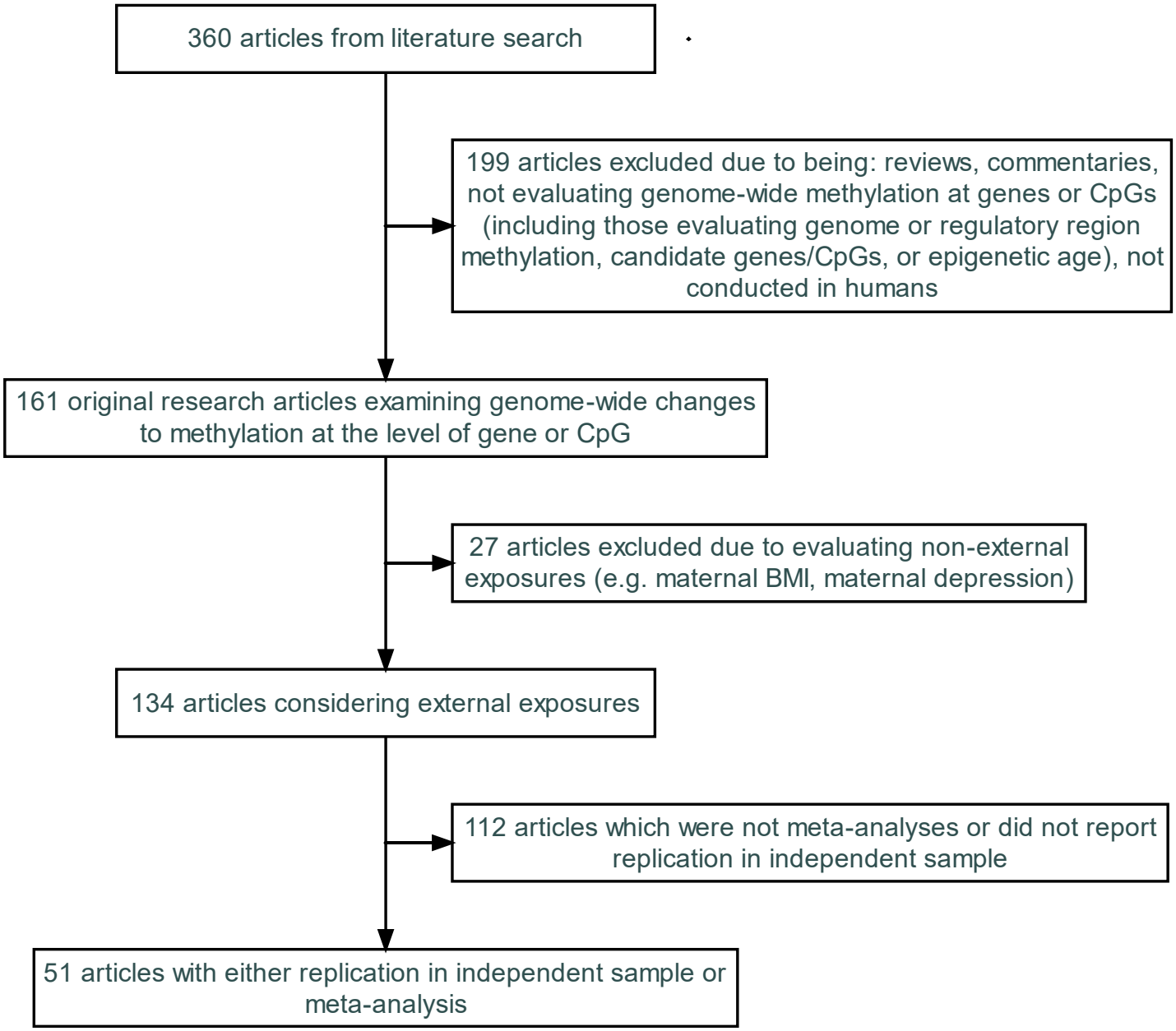

Figure S1: Inclusion and exclusion of studies for consideration in systemic review. Using the search terms described in the Supplementary Methods, we conducted a systemic review of epigenome-wide association studies. We excluded studies which were not epigenome-wide association studies (n=199) and studies which evaluated non-external exposures (n=27). We review in depth only studies that either performed replication in an independent sample or conducted a meta-analysis. We retained only EWAS of external exposures (n=134), excluding studies with only global or candidate methylation positions or examining non-exogenous exposures. We included studies using array or sequencing-based methods to measure methylation; 128 of the 134 exogenous exposure EWAS used the Illumina450K or EPIC arrays.

Table S1: Summary statistics on sample sizes of epigenome wide association studies

Exposure category	M (N)*	min	lower whisker[1]	Q25[2]	median	Q75[2]	upper whisker[1]	max
Stress	8 (8)	24	24	193	373	492	691	973
Other chemical	26 (28)	16	16	71	162	263	408	1033
Metal	36 (49)	17	17	61	202	361	484	1462
Air pollution	12 (14)	22	22	191	428	1093	1949	1949
Other	4 (4)	96	96	96	557	1424	2644	2644
Diet	29 (38)	13	13	70	176	378	709	2802
Alcohol	3 (3)	149	149	584	1018	2046	3075	3075
Smoking	19 (19)	20	20	213	568	1084	1700	6685

*M = number of sample size data points included N = number of unique studies. M and N are not always the same as some epigenome wide association study publications had >1 exposure included and different sample sizes for each exposure.

[1]Lower whisker is the smallest sample size that is greater than or equal to the 25% – 1.5*interquartile range. Upper whisker is the largest sample size that is less than or equal to the 75% + 1.5*interquartile range.

[2]25% and 75% respectively

Table S2: Complete data used to create Figure 2 from 134 epigenome wide association studies of external exposures. Please note not all rows included as data points in all facets of Figure 2, Figure 2 footnote explains exclusions.

DOI	Study Type	Significance criteria	Epigenetic measurement	Ancestry	Exposure	Exposure category	Sample size	Significant DMPs
https://doi.org/10.1093/aje/kwz184	No replication or meta-analysis	Bonferroni	EPIC	European	Prenatal maternal smoking	Smoking	441	71
https://doi.org/10.4161/15592294.2014.971593	No replication or meta-analysis	FDR<0.05	450K	Not described	Prenatal maternal smoking	Smoking	85	0
10.1038/s41467-021-24558-y	Meta-analysis	Bonferroni	450K	multi - primarily European	Maternal smoking	Smoking	1700	443
https://doi.org/10.1098/rstb.2018.0120	Meta-analysis	Bonferroni	450K	European	Prenatal maternal smoking	Smoking	1263	110
https://doi.org/10.1289/ehp3398	Replication	FDR<0.05	WGBS	European	Maternal prenatal smoking	Smoking	20	10381
https://doi.org/10.1186/s12967-015-0384-5	No replication or meta-analysis	FDR<0.05	450K	European	Maternal prenatal smoking	Smoking	20	31
https://doi.org/10.1289/ehp.1205412	Replication	Bonferroni	450K	multi - primarily European	Maternal prenatal smoking	Smoking	1062	26
https://doi.org/10.1016/j.ajhg.2016.02.019	Meta-analysis	Bonferroni	450K	multi - primarily European	Maternal prenatal smoking	Smoking	6685	6073
https://doi.org/10.1093/ije/dyv048	Meta-analysis	FDR<0.05	450K	European	Maternal prenatal smoking	Smoking	255	35
https://doi.org/10.1289/ehp.1307892	Replication	FDR<0.05	450K	European	Prenatal maternal smoking	Smoking	889	185
https://doi.org/10.1038/s41598-018-23772-x	No replication or meta-analysis	FDR<0.05	450K	Asian	Maternal smoking	Smoking	247	121
https://doi.org/10.1093/ije/dyw196	Replication	FDR<0.05	450K	European	maternal prenatal smoking	Smoking	179	50
https://doi.org/10.1186/s12864-016-3310-1	Replication	Bonferroni	450K	European	prenatal maternal smoking	Smoking	1062	27
https://doi.org/10.1186/s12916-020-01736-1	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	prenatal maternal smoking	Smoking	568	242

https://doi.org/10.1186/s13148-021-01161-y	Replication	FDR<0.05	EPIC	multi - primarily European	smoking	Smoking	59	726
https://doi.org/10.2217/epi-2019-0066	Meta-analysis	FDR<0.05	450K	multi - primarily European	prenatal maternal smoking	Smoking	5648	5547
https://doi.org/10.1186/s12916-020-01686-8	Replication	FDR<0.05	450K	multi - primarily European	Maternal prenatal smoking	Smoking	1105	41
https://doi.org/10.1186/s13148-021-01032-6	No replication or meta-analysis	FDR<0.05	EPIC	multi	prenatal maternal smoking	Smoking	954	38
https://doi.org/10.1080/15592294.2018.1475978	No replication or meta-analysis	FDR<0.05	450K	African	Maternal prenatal smoking	Smoking	379	12
https://doi.org/10.2217/epi-2021-0285	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	prenatal alcohol exposure	Alcohol	149	0
https://doi.org/10.2217/epi-2017-0095	Meta-analysis	FDR<0.05	450K	multi - primarily European	maternal alcohol	Alcohol	3075	0
https://doi.org/10.1002/ijc.32203	No replication or meta-analysis	FDR<0.05	450K	European	alcohol	Alcohol	1018	192
https://doi.org/10.4161/15592294.2014.983366	No replication or meta-analysis	FDR<0.05	450K	European	n-3 PUFA	Diet	70	0
https://doi.org/10.1096/fj.13-249029	Replication		450K	European	folate	Diet	23	N/A
https://doi.org/10.1089/bfm.2017.0231	No replication or meta-analysis	p<0.05 (no correction)	450K	multi - primarily European	Vitamin D	Diet	13	0
https://doi.org/10.3390/ijerph17249190	No replication or meta-analysis	Bonferroni	450K	multi - primarily European	Prenatal vitamin	Diet	130	0
https://doi.org/10.3389/fgene.2019.01050	No replication or meta-analysis	p<0.05 (no correction)	450K	European	n-3 PUFAS (polyunsaturated fatty acids)	Diet	118	0
https://doi.org/10.1093/hmg/ddx164	Replication	FDR<0.05	450K	European	B12	Diet	641	3
https://doi.org/10.3390/nu10040455	Replication	FDR<0.05	EPIC	European	Low glycemic index dietary intervention	Diet	60	0

https://doi.org/10.1080/15592294.2015.1117889	Replication	Permutation-based P values test	450K	multi - primarily European	Folate	Diet	343	4
https://doi.org/10.3390/nu12113309	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	breastfeeding	Diet	709	1
https://doi.org/10.1186/s13148-021-01115-4	No replication or meta-analysis	FDR<0.10	EPIC	European	*Lactobacillus reuteri* only vs placebo	Diet	63	1246
https://doi.org/10.1186/s13148-021-01115-4	No replication or meta-analysis	FDR<0.10	EPIC	European	ω-3 fatty acid supplementation vs placebo	Diet	63	984
https://doi.org/10.1186/s13148-021-01115-4	No replication or meta-analysis	FDR<0.10	EPIC	European	*Lactobacillus reuteri* and ω-3 fatty acid supplementation vs placebo	Diet	63	1659
https://doi.org/10.1038/ncomms10577	Meta-analysis	Bonferroni	450K	European	Folate	Diet	1988	48
https://doi.org/10.1038/s41598-018-35111-1	No replication or meta-analysis	FDR<0.05	450K	multi	One carbon	Diet	24	1
https://doi.org/10.1080/15592294.2022.2038412	Meta-analysis	FDR<0.05	450K	multi - primarily European	Mediterranean diet	Diet	2802	1
https://doi.org/10.1080/15592294.2021.1957575	No replication or meta-analysis	Bonferroni	450K	European	maternal diet pattern	Diet	557	0
https://doi.org/10.3390/nu13010099	No replication or meta-analysis	FDR<0.05	450K & EPIC	European	Breastfeeding	Diet	201	87
https://doi.org/10.1016/j.jnutbio.2022.108938	No replication or meta-analysis	FDR<0.05	EPIC	multi - primarily European	one-carbon metabolites - maternal trimester 3 SAH	Diet	89	272
https://doi.org/10.1016/j.jnutbio.2022.108938	No replication or meta-analysis	FDR<0.05	EPIC	multi - primarily European	one-carbon metabolites - cord blood SAH	Diet	89	81
https://doi.org/10.1016/j.jnutbio.2022.108938	No replication or meta-analysis	FDR<0.05	EPIC	multi - primarily European	one-carbon metabolites - cord blood betaine	Diet	89	2
https://doi.org/10.1016/j.jnutbio.2022.108938	No replication or meta-analysis	FDR<0.05	EPIC	multi - primarily European	one-carbon metabolites - cord blood methionine	Diet	89	1

https://doi.org/10.1093/ajcn/nqab348	No replication or meta-analysis	FDR<0.05	EPIC	European	caffeine metabolites - caffeine	Diet	378	0
https://doi.org/10.1093/ajcn/nqab348	No replication or meta-analysis	FDR<0.05	EPIC	European	caffeine metabolites - theobromine	Diet	378	1
https://doi.org/10.1093/ajcn/nqab348	No replication or meta-analysis	FDR<0.05	EPIC	European	caffeine metabolites - preconception self-report caffeine	Diet	378	1
https://doi.org/10.1186/s13148-022-01276-w	Meta-analysis	FDR<0.05	450K	European	Iron	Diet	1286	3
https://doi.org/10.1093/ajcn/nqz311	No replication or meta-analysis	FDR<0.05	EPIC	European	maternal fatty acids - PUFA	Diet	374	6
https://doi.org/10.1093/ajcn/nqz311	No replication or meta-analysis	FDR<0.05	EPIC	European	maternal fatty acids - SFA	Diet	374	4
https://doi.org/10.1093/ajcn/nqz311	No replication or meta-analysis	FDR<0.05	EPIC	European	maternal fatty acids - trans FA	Diet	374	7
https://doi.org/10.3390/ijerph17103569	No replication or meta-analysis	FDR<0.05	EPIC	European	breastfeeding	Diet	181	2
https://doi.org/10.1186/s13148-021-01161-y	No replication or meta-analysis	FDR<0.05	EPIC	multi - primarily European	vitamin C supplementation in smokers	Diet	72	1
https://doi.org/10.1038/s41598-018-27391-4	Replication	Bonferroni	450K	European	Iron supplement	Diet	1062	0
https://doi.org/10.1016/j.jsbmb.2016.03.005	Meta-analysis	FDR<0.05	450K	European	25-hydroxyvitamin D	Diet	1416	0
https://doi.org/10.1002/ijc.32203	No replication or meta-analysis	FDR<0.05	450K	European	caffeine	Diet	1018	66
https://doi.org/10.1093/eep/dvz004	No replication or meta-analysis	FDR<0.05	450K	Admixed/ Latino	maternal lipid metabolites	Diet	81	6
https://doi.org/10.1002/dev.22088	No replication or meta-analysis	FDR<0.05	450K	multi - primarily Admixed/ Latino	maternal sugar intake	Diet	170	0
https://doi.org/10.1186/s13148-016-0281-7	No replication or meta-analysis	FDR<0.05	450K	European	DHA fish oil	Diet	369	1

https://doi.org/10.1186/s12263-019-0634-x	Replication	FDR<0.05	450K	Asian	maternal glycemic index dietary intervention	Diet	24	365
https://doi.org/10.1016/j.envres.2021.112186	No replication or meta-analysis	p<0.0001	EPIC	Asian	long-chain n-3 polyunsaturated fatty acids	Diet	40	20
https://doi.org/10.1093/humrep/deab137	Meta-analysis	FDR<0.05	450K	European	medically assisted reproduction	Other	2644	5
https://doi.org/10.1038/s41435-021-00151-7	No replication or meta-analysis	FDR<0.05	EPIC	Not described	pet ownership	Other	96	113
https://doi.org/10.1016/j.ygeno.2021.03.006	No replication or meta-analysis	FDR<0.05	EPIC	European	opioid exposure	Other	96	1125
https://doi.org/10.1002/ijc.32203	No replication or meta-analysis	FDR<0.05	450K	European	radiation	Other	1018	288
https://doi.org/10.1016/j.envint.2018.05.007	No replication or meta-analysis	FDR<0.05	450K	European	NO2; PM10; temperature; humidity	Air pollution	668	6
https://doi.org/10.1093/eep/dvw005	Replication	FDR<0.15	450K	multi - primarily European	Air pollution PM	Air pollution	240	31
https://doi.org/10.1039/c6em00074f	No replication or meta-analysis	FDR<0.10	450K	African	HIV and air pollution	Air pollution	22	0
https://doi.org/10.1289/ehp36	Meta-analysis	FDR<0.05	450K	multi - primarily European	NO2	Air pollution	1508	3
https://doi.org/10.1289/ehp4522	Meta-analysis	FDR<0.05	450K	multi - primarily European	PM10	Air pollution	1949	6
https://doi.org/10.1289/ehp4522	Meta-analysis	FDR<0.05	450K	multi - primarily European	PM2.5	Air pollution	1949	14
https://doi.org/10.1016/j.envres.2022.112717	Replication	FDR<0.05	EPIC	European	PM10	Air pollution	384	284
https://doi.org/10.1016/j.envint.2016.03.020	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Proximity to roads	Air pollution	471	7
https://doi.org/10.1016/j.envint.2019.02.028	No replication or meta-analysis	FWER<0.05	450K	multi	NO(2)	Air pollution	175	N/A

https://doi.org/10.1016/j.envint.2019.02.028	No replication or meta-analysis	FWER<0.05	450K	multi	O(3)	Air pollution	175	N/A
https://doi.org/10.1289/ehp2034	Replication	FDR<0.05	450K	multi - primarily European	proximity to roadways	Air pollution	482	4
https://doi.org/10.1021/acs.est.7b06447	Meta-analysis	FDR<0.05	450K	multi - primarily European	PM	Air pollution	1235	1
https://doi.org/10.3390/ijerph19063292	No replication or meta-analysis	FDR<0.05	EPIC	Asian	PM10 & NO2	Air pollution	383	7
https://doi.org/10.1016/j.anai.2020.09.008	No replication or meta-analysis	P<0.05	EPIC	Asian	PM2.5	Air pollution	48	0
https://doi.org/10.1093/ije/dyv032	Replication	FDR<0.10	CHARM 2.0	multi - primarily African	Mercury	Metal	141	N/A
https://doi.org/10.1080/15592294.2018.1516453	Replication	p<1x10e-6	450K	Asian	Arsenic	Metal	44	380
10.1186/s12940-021-00754-7	Meta-analysis	FDR<0.05	EPIC & 450K	Asian & admixed/Latino	Arsenic	Metal	108	3
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Manganese (Mn)	Metal	361	1
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Copper (Cu)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Selenium (Se)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Magnesium (Mg)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Arsenic (As)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Cadmium (Cd)	Metal	361	0

https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Lead (Pb)	Metal	361	1
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	mercury (Hg)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Zinc (Zn)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Barium (ba)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Chromium (Cr)	Metal	361	0
https://doi.org/10.1186/s13148-021-01198-z	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Cesium (Cs)	Metal	361	0
https://doi.org/10.1017/s2040174414000221	No replication or meta-analysis	FDR<0.05	450K	Asian	Arsenic	Metal	127	3
https://doi.org/10.1080/15592294.2015.1046026	No replication or meta-analysis	Bonferroni	450K	European	Arsenic; Mercury	Metal	138	0
https://doi.org/10.1080/15592294.2015.1105424	No replication or meta-analysis	Bonferroni	450K	Asian	Arsenic	Metal	45	4
https://doi.org/10.1038/s41598-017-00384-5	No replication or meta-analysis	Bonferroni	450K	multi - primarily European	Mercury	Metal	321	1
https://doi.org/10.1289/EHP2085	No replication or meta-analysis		WGBS	multi	Cadmium	Metal	19	N/A
https://doi.org/10.1093/eep/dvv007	No replication or meta-analysis	FDR<0.05	450K	Asian	Lead	Metal	127	9
https://doi.org/10.1289/ehp2192	Meta-analysis	FDR<0.05	450K	multi - primarily European	Cadmium	Metal	484	3
https://doi.org/10.1289/ehp.1510437	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Aresnic	Metal	343	163
https://doi.org/10.1093/eep/dvaa014	No replication or meta-analysis	FDR<0.05	EPIC	Admixed/ Latino	Lead	Metal	420	0

https://doi.org/10.1186/s12940-017-0262-0	Replication	FDR<0.05	450K	Asian	Arsenic	Metal	64	579
https://doi.org/10.1080/15592294.2019.1661211	Meta-analysis	Bonferroni	450K	European	Copper	Metal	447	0
https://doi.org/10.4161/epi.28153	No replication or meta-analysis	FDR<0.05	450K	Asian	Arsenic	Metal	44	1
https://doi.org/10.4161/epi.24401	No replication or meta-analysis	FDR<0.05	450K	Asian	Cadmium	Metal	127	0
https://doi.org/10.1289/ehp.1205925	No replication or meta-analysis	FDR<0.05	450K	European	Arsenic	Metal	134	0
https://doi.org/10.3390/nano11112871	No replication or meta-analysis	p<0.00001	EPIC	Asian	heavy metals - maternal lead	Metal	367	11
https://doi.org/10.3390/nano11112871	No replication or meta-analysis	p<0.00001	EPIC	Asian	heavy metals - maternal cadmium	Metal	367	4
https://doi.org/10.3390/nano11112871	No replication or meta-analysis	p<0.00001	EPIC	Asian	heavy metals - prenatal lead	Metal	367	46
https://doi.org/10.1016/j.envres.2021.112093	Meta-analysis	FDR<0.10	450K and EPIC	multi - primarily European	prenatal methylmercury	Metal	1462	2
https://doi.org/10.1289/ehp.1408561	No replication or meta-analysis	omnibus p = 0.017 and __ > 0.125	450K	multi - primarily European	Mercury	Metal	41	0
https://doi.org/10.1016/j.reprotox.2015.05.002	No replication or meta-analysis	Bonferroni	450K	multi - primarily European	Manganese	Metal	61	5
https://doi.org/10.1016/j.envres.2015.02.004	No replication or meta-analysis	FDR<0.10	450K	multi - primarily European	Cadmium	Metal	24	3
https://doi.org/10.3390/ijerph17186775	No replication or meta-analysis	FDR<0.2	EPIC	multi - primarily European	Lead	Metal	96	33
https://doi.org/10.1016/j.envres.2021.110767	Meta-analysis	FDR<0.05	EPIC	Asian	Lead	Metal	364	111
https://doi.org/10.1016/j.envres.2022.113268	Meta-analysis	FDR<0.05	EPIC	Asian	Cadmium	Metal	202	2
https://doi.org/10.1016/j.envint.2022.107188	Replication	FDR<0.05	450K	Asian	Cadmium	Metal	71	458

https://doi.org/10.1021/acs.chemrestox.7b00221	No replication or meta-analysis	FDR<0.05	450K	Admixed/ Latino	inorganic arsenic	Metal	59	3493
https://doi.org/10.1093/toxsci/kfu210	No replication or meta-analysis	FDR<0.05	450K	Admixed/ Latino	Arsenic	Metal	38	4771
https://doi.org/10.1177/2516865720938669	No replication or meta-analysis	FDR<0.05	EPIC	Admixed/ Latino	lead	Metal	89	3
https://doi.org/10.4161/epi.26798	No replication or meta-analysis	P<0.05	MIRA	multi - primarily African	Cadmium	Metal	17	0
https://doi.org/10.1038/srep14466	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	lead	Metal	35	183
https://doi.org/10.1080/15592294.2015.1050172	No replication or meta-analysis	FDR<0.05	450K - modified for 5hmc	Admixed/ Latino	lead	Metal	48	N/A
https://doi.org/10.1016/j.envint.2020.105508	Meta-analysis	FDR<0.05	450K	multi - primarily European	Selenium	Metal	484	5
https://doi.org/10.1289/ehp1246	Replication	FDR<0.05	450K	multi - primarily European	lead	Metal	268	4
https://doi.org/10.1016/j.envres.2019.01.007	Replication	P<0.05	450K	Asian	e-waste exposure (heavy metals)	Metal	24	0
https://doi.org/10.1016/j.envres.2018.01.009	No replication or meta-analysis	FDR<0.05	450K	Asian	phthalate	Other chemical	64	25
https://doi.org/10.3390/ijerph16152786	No replication or meta-analysis	FDR<0.10	EPIC	Asian	polychlorinated biphenyls	Other chemical	75	6
https://doi.org/10.1186/s13148-018-0510-3	No replication or meta-analysis	Bonferroni	450K	European	Artificial reproductive technology	Other chemical	64	0
https://doi.org/10.1038/s41598-018-24505-w	No replication or meta-analysis	nominal p-value of 0.005	EPIC	multi - primarily European	Phthalate	Other chemical	16	0
https://doi.org/10.1093/ije/dyv027	No replication or meta-analysis	FDR<0.05	450K	African	aflatoxin	Other chemical	115	71
https://doi.org/10.1016/j.envpol.2021.118024	No replication or meta-analysis	FDR<0.05	450K	European	Phenols	Other chemical	202	596

https://doi.org/10.1016/j.envint.2021.107054	No replication or meta-analysis	FDR<0.05	450K	European	Phthalate metabolites (MEHP)	Other chemical	202	1
https://doi.org/10.1186/s13148-018-0478-z	No replication or meta-analysis	Bonferroni	450K	European	BPA	Other chemical	408	2
https://doi.org/10.1016/j.envres.2017.06.013	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	PFOA	Other chemical	44	0
https://doi.org/10.1080/15592294.2018.1445901	No replication or meta-analysis	FDR<0.05	450K	European	Chemical mixtures - PCB105	Other chemical	72	214
https://doi.org/10.1080/15592294.2018.1445901	No replication or meta-analysis	FDR<0.05	450K	European	Chemical mixtures - ppDDT	Other chemical	72	18
https://doi.org/10.1080/15592294.2018.1445901	No replication or meta-analysis	FDR<0.05	450K	European	Chemical mixtures - PCB101	Other chemical	72	10
https://doi.org/10.1289/ehp10118	Replication	FDR<0.05	EPIC	multi - primarily European	PFAS	Other chemical	266	435
https://doi.org/10.1080/15592294.2021.1975917	No replication or meta-analysis	FDR<0.05	EPIC	European	prenatal exposure to PCBs/PCDD/Fs	Other chemical	142	32
https://doi.org/10.1093/eep/dvaa021	Replication	FDR<0.05	EPIC	multi - primarily European	maternal BPA exposure	Other chemical	69	38
https://doi.org/10.1016/j.envint.2018.03.004	Replication	FDR<0.05	450K	Asian	PFOS PFOA	Other chemical	190	4
https://doi.org/10.1038/s41598-019-48916-5	Replication	FDR<0.05	450K	Asian	BPA	Other chemical	277	27
https://doi.org/10.1016/j.scitotenv.2021.147035	Replication	FDR<0.05	450K	Asian	di-2-ethylhexyl phthalate	Other chemical	203	2
https://doi.org/10.1186/s13148-020-00894-6	No replication or meta-analysis	FDR<0.05	450K	multi	persistent organic pollutants	Other chemical	260	214
https://doi.org/10.3389/fgene.2022.793278	No replication or meta-analysis	FDR<0.2	EPIC	multi - primarily European	Phthalates	Other chemical	262	0
https://doi.org/10.1016/j.envint.2022.107183	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	Phthalates	Other chemical	78	12

https://doi.org/10.1016/j.envres.2020.110668	No replication or meta-analysis	FDR<0.05	EPIC	multi - primarily European	PFOA/PFOS	Other chemical	597	3
https://doi.org/10.1016/j.envint.2018.12.017	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	swimming in pools	Other chemical	1033	0
https://doi.org/10.1002/em.22095	No replication or meta-analysis	FDR<0.05	450K	Admixed/ Latino	phthalate	Other chemical	336	5
https://doi.org/10.1289/ehp6888	No replication or meta-analysis	FDR<0.05	450K	multi	PFAS	Other chemical	583	1
https://doi.org/10.2217/epi.15.91	Replication	FDR<0.05	450K	European	xenoestrogens	Other chemical	181	0
https://doi.org/10.1016/j.envint.2020.106148	No replication or meta-analysis	FDR<0.05	EPIC	European	PFAS	Other chemical	59	248
https://doi.org/10.1016/j.lfs.2018.03.030	Replication	P<0.05	450K	Asian	DDT pesticide	Other chemical	24	0
https://doi.org/10.1093/ije/dyy259	Replication	FDR<0.05	450K	European	Socioeconomic position	Stress	973	20
https://doi.org/10.1371/journal.pone.0215745	No replication or meta-analysis	Bonferroni	450K	multi - primarily European	Circadian disruptions	Stress	237	57
https://doi.org/10.13110/humanbiology.91.2.04	No replication or meta-analysis	Bonferroni	450K	African	Maternal stress	Stress	24	0
https://doi.org/10.1016/j.biopsych.2018.12.023	No replication or meta-analysis	Bonferroni	450K	European	childhood adversity	Stress	691	38
https://doi.org/10.2217/epi-2019-0040	No replication or meta-analysis	FDR<0.05	450K	multi - primarily European	SES	Stress	422	29
https://doi.org/10.1080/15592294.2019.1614743	No replication or meta-analysis	FDR < 0.1.	EPIC	multi - primarily European	maternal SES	Stress	426	33
https://doi.org/10.1038/ncomms6592	No replication or meta-analysis	FDR<0.05	RRBS	European	famine	Stress	60	N/A
https://doi.org/10.1038/srep28616	No replication or meta-analysis	DMRs, ≥3 consecutive CpGs, Δmeth >10%, t > +/− 4.5	WGBS followed by MassARRAY	European	maternal stress	Stress	324	N/A

DMP: Differentially methylated positions. DMRs: Differentially methylated regions. SES: Socioeconomic status. RRBs: reduced representation bisulfite sequencing. WGBS: whole-genome bisulfite sequencing

Some studies represented >1 time as multiple exposures were measured.

Rows with N/A for Significant DMPs represent studies which did not report significance testing at position level (e.g. reported DMRs, external genomic annotations)