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BCPP.org (https://www.bcpp.org/)

Chemicals of Concern in Cosmetics

Our Red List is a resource for businesses to assess the safety of the ingredients in the personal care products they make and sell.

Download PDF: Red List (https://bit.ly/redlist2024)

For information on how to use our Red List, **contact us (https://www.safecosmetics.org/contact/).**

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Overview

The Campaign for Safe Cosmetics (CSC) developed the Red List of Chemicals of Concern in Cosmetics to serve as a resource and tool to help brands, companies, and retailers reduce their use of toxic chemicals in the beauty and personal care products they make and sell.

Adopting and making a list of prohibited (or "do not use") substances publicly available helps companies and consumers alike by advancing transparency, increasing customer trust, and guiding safer product formulations. It also establishes guidelines for suppliers of fragrance, raw materials, and finished products to ensure these entities are aware of and avoid the use of chemicals the company has pledged to eliminate.

What's On CSC's Red List

Background

In 2015, BCPP's Campaign for Safe Cosmetics developed a Red List of Chemicals of Concern (https://www.safecosmetics.org/wp-content/uploads/2016/04/RED-LIST.pdf) in cosmetics. The list included 102 chemicals found in personal care products that pose serious, chronic health concerns including cancer, hormone disruption

(https://www.bcpp.org/resource/hormone-disruption-and-breast-development/), and reproductive and developmental harm. In 2018, we then expanded the *Red List of Chemicals of Concern* to also include chemicals used in cleaning products and fragrances. The updated list included the original cosmetics Red List (https://www.safecosmetics.org/wp-content/uploads/2016/04/RED-LIST.pdf), fragrance ingredients found through product testing, as well as authoritative lists of hazardous chemicals compiled by colleague organizations, researchers, and reputable scientific organizations.

Your Action Helps

Together, we can make beauty safer for all.

Take Action Today!

(/take-action/)

The New Three-Tiered Red List

Our most recent iteration of the Red List of Chemicals of Concern, released in August 2022, expanded to **480 chemicals** used in beauty, personal care products, and/or as fragrance ingredients. The list includes:

- **241 Tier 1** chemicals of concern that should be prohibited from use in personal care products or as fragrance ingredients by manufacturers and retailers.
- **112 Tier 2** emerging chemicals of concern which should be avoided in products whenever possible.
- **127 Tier 3** asthmagens, allergens and irritants whose presence in products should be disclosed so people suffering from these adverse health effects can avoid these chemicals of concern.

More about the three tiers

- **Tier 1: Chemicals of concern that should not be used in personal care products or fragrances.**
    - Chemicals that are listed on an authoritative list (such as the International Agency for Research on Cancer (IARC), the National Toxicology Program

(NTP), California's Prop. 65 Program, etc.) as being harmful to human health are listed as Tier 1 chemicals and the relevant authoritative list is marked.
    - Chemicals that are not on authoritative lists but for which our literature review found multiple studies linking them with relevant human health effects are listed as Tier 1 chemicals and the citations are marked.
- **Tier 2: Emerging chemicals of concern that should be avoided in products if possible.**
    - Chemicals that have only a single study indicating a human health concern are listed as emerging chemicals of concern and placed on Tier 2.
    - Chemicals that have been designated as ecotoxicants by authoritative bodies are also placed on Tier 2.
- **Tier 3: Asthmagens, allergens and irritants whose presence in products should be disclosed as potential allergens.**
    - Chemicals that have been identified as asthmagens, allergens or irritants by the authoritative organizations that we cite in the Red List should be disclosed if they are present in products so that consumers with sensitivities can avoid them. If the chemical is also listed on Tier 2, they should be avoided in products if possible.

For a list of the authoritative governmental and scientific lists of hazardous chemicals used to build the Red List, and a discussion on chemicals of concern listed as Tier 1 chemicals because of special circumstances, see Appendix 1.

Chemicals of Concern in Black Beauty Products Added to the Red List

As a key part of CSC's Black Beauty Project (https://www.safecosmetics.org/black-beauty-project/), our third iteration of the Red List includes cosmetic chemicals of concern negatively impacting Black women's health (Tier 1 "Do Not Use" Chemicals of Greater Concern for Black Women (https://www.safecosmetics.org/wp-content/uploads/2022/08/BCPP-Red-List-for-Web_Tier-1_Black-Health-COC-_Key.pdf)).

To create this newest addition to the Red List, we worked with our Advisory Committee (https://www.safecosmetics.org/black-beauty-project/) made up of leading non-profit organizations and scientists working to improve Black women's health and conducted a scientific literature review to identify chemicals of concern in beauty products used by Black women that are linked to negative health outcomes. This project represents the first comprehensive effort to generate a list of chemicals of concern in Black beauty products that should be avoided by consumers, cosmetic manufacturers, and retailers.

Our Red List's Tier 1 "Do Not Use" Chemicals of Greater Concern for Black Women (https://www.safecosmetics.org/wp-content/uploads/2022/08/BCPP-Red-List-for-Web_Tier-1_Black-Health-COC-_Key.pdf) also attempts to address: 1) bias in scientific research on chemical exposures that does not adequately account for the unequal burden

Black women experience through their use of beauty products; and 2) inadequate capture of hazardous chemicals linked to negative health outcomes in Black women by governmental and scientific organizations that create authoritative lists of hazardous chemicals. Our goal was to identify and better understand chemicals negatively impacting Black women's health that are present in beauty and personal care products in order to address their unique health concerns.

In total, we reviewed 8,119 titles and 580 scientific papers. Through this review process, we identified 141 scientific studies that showed a significant association between chemicals in personal care products and health concerns for Black women. We then expanded the CSC's Red List to include the findings from these studies to have a more representative list of both the chemicals of concern in beauty and personal care products marketed to Black women and related negative health outcomes.

With this latest update, companies can use our Red List to avoid ingredients linked to health outcomes of greater concern to Black women.

APPENDIX 1: Authoritative Lists Used to Define Health Hazards in the BCPP Red List

Carcinogens

- Agents Classified by International Agency for Research on Cancer (IARC) Monographs (https://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf)
  - IARC Group 1: Known Human Carcinogen
  - IARC Group 2A: Probable Human Carcinogen
  - IARC Group 2B: Possible Human Carcinogen
- National Toxicology Program Report on Carcinogens (https://ntp.niehs.nih.gov/ntp/roc/content/listed_substances_508.pdf)
  - NTP Known: Known Human Carcinogen
  - NTP RA: Reasonably Anticipated to Be a Human Carcinogen
- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
- GHS H350: May Cause Cancer
- GHS H351: Suspected of Causing Cancer
- California Proposition 65 Listed Chemicals (https://oehha.ca.gov/media/downloads/proposition-65/p65122917_0.pdf)
  - Prop 65 Chemicals Known to the State of California to be Linked to Cancer

Mammary Gland Carcinogens

- Silent Spring Institute List of Chemicals Linked to Mammary Gland Tumors (http://sciencereview.silentspring.org/mamm_about.cfm)

Endocrine-Disrupting Compounds

- EU Strategy for Endocrine Disruptors (http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm)
  - EU ED Category 1: Substances for which endocrine activity has been documented in at least one study of a living organism. These substances are given the highest priority for further studies.
  - EU ED Category 2: Substances without sufficient evidence of endocrine activity, but with evidence of biological activity relating to endocrine disruption.
- EU Candidate List of Substances of Very High Concern for Authorization
- ChemSec SIN List (http://sinlist.chemsec.org/search/search?query=&healthenvironmentconcerns=1)
- The Endocrine Exchange List of Potential Endocrine Disruptors (https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list)

Reproductive and Developmental Toxicants

- California Proposition 65 Listed Chemicals (https://oehha.ca.gov/media/downloads/proposition-65/p65122917_0.pdf)
  - Prop 65: developmental
  - Prop 65-f: developmental — female
  - Prop 65-m: developmental — male
  - Prop 65-f,m: developmental — male, female
- Nominated for Study NIH (https://ntp.niehs.nih.gov/publications/abstracts/index.html)
  - NTP-R: Reproductive toxicity
  - NTP-D Developmental toxicity
- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
  - EU EC H361f: Suspected of damaging fertility
  - EU EC H361d: Suspected of damaging the fetus
- EU Candidate List of Substances of Very High Concern for Authorization (https://echa.europa.eu/candidate-list-table)
  - This list feeds into California DTSC list

Neurotoxic Chemicals

- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
  - GHS 336: May cause drowsiness or dizziness

Chronic Aquatic Toxicity

- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
  - GHS 410: Very toxic to aquatic life with long-lasting effects
  - GHS 411: Toxic to aquatic life with long-lasting effects
  - GHS H412: Harmful to aquatic life with long-lasting effects

Respiratory Toxicity/ Asthmagens

- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
  - EU EC H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
- Association of Occupational and Environmental Clinics (http://www.aoecdata.org/ExpCodeLookup.aspx)
  - AOEC R — Suspected Asthmagen
  - AOEC Rs— Asthmagen, Sensitizer
  - AOEC Rr— RADS: Reactive Airways Dysfunction Syndrome
  - AOEC G— Generally Accepted Asthmagen

Skin Irritation

- EU Fragrance Allergen: Established Contact Allergens in Humans (http://ec.europa.eu/health/scientific_committees/opinions_layman/perfume-allergies/en/figtableboxes/table-13-1.htm)
- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
  - EU EC H315: Causes skin irritation
  - EU EC H314: Causes severe skin burns and eye damage

Eye Irritation

- EU Globally Harmonized System (https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp)
- EU EC H318: Causes eye irritation

- EU EC H319: Causes eye irritation
- EU EC 6.4A: Causes eye irritation (Category 2)

Persistent, Bio-accumulative and Toxic

- OSPAR PBT: Chemicals for Priority Action (https://www.ospar.org/work-areas/hasec/hazardous-substances/priority-action)

APPENDIX 2: Bibliography

Annotated Bibliography of Scientific Journal Articles Referenced in the CSC's Red List of Tier 1 Prohibited Chemicals

This annotated bibliography provides a summary of – and full citations for – the approximately 110 scientific journal articles referenced in Tier 1 of the CSC Red List of Chemicals of Concern in Cosmetics. Each of these articles present links between one of more chemicals found in beauty products and negative health outcomes experienced by Black women.

This bibliography contains sources that range from 1989, when environmental exposures became a hot topic following the initiation of the Clean Air and Water Act, to 2021 when unsafe exposures via personal care products began to gain public attention. The studies within this list are categorized by health conditions, including diabetes, puberty, endometriosis, fertility, menopause, maternal health, obesity, cancer, preterm birth, polycystic ovarian syndrome, fibroids, and allergies. Within each group, the APA style source is listed, and directly under the source is a short synopsis about the goal and results of the study. Out of the 110 papers, 23 investigate diabetes, 6 investigate puberty, 4 investigate endometriosis, 11 investigate fertility, 4 investigate menopause, 43 investigate maternal health, 8 investigate obesity, 11 investigate cancer, 1 investigates PCOS, 7 investigate preterm birth, 5 investigate fibroids and 2 investigate allergies.

Download Bibliography PDF (https://www.safecosmetics.org/wp-content/uploads/2022/08/Red-List-Annotated-Bibliography.pdf)

Diabetes

Ashley-Martin, J., Dodds, L., Arbuckle, T. E., Bouchard, M. F., Shapiro, G. D., Fisher, M., Monnier, P., Morisset, A. S., & Ettinger, A. S. (2018). Association between maternal urinary speciated arsenic concentrations and gestational diabetes in a cohort of Canadian women.

Environment international, 121(Pt 1), 714–720. https://doi.org/10.1016/j.envint.2018.10.008 (https://doi.org/10.1016/j.envint.2018.10.008)

Ashley-Martin et al studied the association between arsenic and gestational diabetes using data from the maternal-infant research on environmental chemicals cohort. The group reported that a metabolite of arsenic, dimethylarsenic acid, was associated with gestational diabetes [1].

Grau-Perez, M., Kuo, C. C., Gribble, M. O., Balakrishnan, P., Jones Spratlen, M., Vaidya, D., Francesconi, K. A., Goessler, W., Guallar, E., Silbergeld, E. K., Umans, J. G., Best, L. G., Lee, E. T., Howard, B. V., Cole, S. A., & Navas-Acien, A. (2017). Association of Low-Moderate Arsenic Exposure and Arsenic Metabolism with Incident Diabetes and Insulin Resistance in the Strong Heart Family Study. Environmental health perspectives, 125(12), 127004. https://doi.org/10.1289/EHP2566 (https://doi.org/10.1289/EHP2566)

Grau-Perez et al evaluated the prospective association between arsenic exposure and metabolism in persons with type 2 diabetes and insulin resistance. The group reported that arsenic exposure was associated with incidence of diabetes [2].

Gribble, M. O., Howard, B. V., Umans, J. G., Shara, N. M., Francesconi, K. A., Goessler, W., Crainiceanu, C. M., Silbergeld, E. K., Guallar, E., & Navas-Acien, A. (2012). Arsenic exposure, diabetes prevalence, and diabetes control in the Strong Heart Study. American journal of epidemiology, 176(10), 865–874. https://doi.org/10.1093/aje/kws153 (https://doi.org/10.1093/aje/kws153)

Gribble et al conducted a study to evaluate the association between urinary arsenic and the prevalence of diabetes, glycated hemoglobin, and insulin resistance. The group reported that high levels of urinary arsenic were associated with poor diabetes control [3].

Hou, Y., Li, S., Xia, L., Yang, Q., Zhang, L., Zhang, X., Liu, H., Huo, R., Cao, G., Huang, C., Tian, X., Sun, L., Cao, D., Zhang, M., Zhang, Q., & Tang, N. (2021). Associations of urinary phenolic environmental estrogens exposure with blood glucose levels and gestational diabetes mellitus in Chinese pregnant women. The Science of the total environment, 754, 142085. https://doi.org/10.1016/j.scitotenv.2020.142085 (https://doi.org/10.1016/j.scitotenv.2020.142085)

Hou et al conducted a cross-sectional study using pregnant Chinese women to investigate the link between exposure to endocrine-disrupting chemicals and gestational diabetes. They found that exposure to 2-tert-octylphenol was associated with a higher risk of gestational diabetes, but exposure to nonylphenol was associated with a lower risk [4].

Jia, X., Zhang, L., Zhao, J., Ren, M., Li, Z., Wang, J., Wang, S., Liu, Y., An, H., Li, Y., Yan, L., Li, Z., Liu, X., Pan, B., & Ye, R. (2021). Associations between endocrine-disrupting heavy metals in maternal hair and gestational diabetes mellitus: A nested case-control study in China.

Environment international, 157, 106770. https://doi.org/10.1016/j.envint.2021.106770 (https://doi.org/10.1016/j.envint.2021.106770)

Jia et al investigated the association between endocrine-disrupting heavy metals in maternal hair and the risk of gestational diabetes. The group reported that high maternal levels of tin and mercury were associated with the development of gestational diabetes [5].

Liu, X., Zhang, L., Chen, L., Li, J., Wang, Y., Wang, J., Meng, G., Chi, M., Zhao, Y., Chen, H., & Wu, Y. (2019). Structure-based investigation on the association between perfluoroalkyl acids exposure and both gestational diabetes mellitus and glucose homeostasis in pregnant women. *Environment international*, *127*, 85–93. https://doi.org/10.1016/j.envint.2019.03.035 (https://doi.org/10.1016/j.envint.2019.03.035)

Liu et al conducted a prospective nested case-control study in China to determine if there is an association between exposure to perfluoroalkyl acids and gestational diabetes mellitus. The group found that exposure to short-chain perfluoroalkyl carboxylates was significantly associated with gestational diabetes mellitus. Exposure to these chemicals was also associated with higher postprandial glucose levels [6].

Liu, W., Zhang, B., Huang, Z., Pan, X., Chen, X., Hu, C., Liu, H., Jiang, Y., Sun, X., Peng, Y., Xia, W., Xu, S., & Li, Y. (2018). Cadmium Body Burden and Gestational Diabetes Mellitus: A Prospective Study. Environmental health perspectives, 126(2), 027006. https://doi.org/10.1289/EHP2716 (https://doi.org/10.1289/EHP2716)

Liu et al conducted a prospective study to examine the association between cadmium body burden in early pregnancy and the risk of gestational diabetes mellitus in Chinese women. The group reported an association between urinary cadmium levels and an increased risk of gestational diabetes mellitus [7].

Nam DJ, Kim Y, Yang EH, Lee HC, Ryoo JH. Relationship between urinary phthalate metabolites and diabetes: Korean National Environmental Health Survey (KoNEHS) cycle 3 (2015–2017). Ann Occup Environ Med. 2020 Jan;32(1):e34. https://doi.org/10.35371/aoem.2020.32.e34 (https://doi.org/10.35371/aoem.2020.32.e34)

Nam et al aimed to determine the relationship between diabetes and urinary phthalate metabolites using data from the Korean National Environmental Health Survey cycle 3. The group reported that higher urinary phthalate concentration was associated with a higher prevalence of diabetes [8].

Peng, S., Liu, L., Zhang, X., Heinrich, J., Zhang, J., Schramm, K. W., Huang, Q., Tian, M., Eqani, S. A., & Shen, H. (2015). A nested case-control study indicating heavy metal residues in meconium associate with maternal gestational diabetes mellitus risk. *Environmental health : a global access science source*, *14*, 19. https://doi.org/10.1186/s12940-015-0004-0 (https://doi.org/10.1186/s12940-015-0004-0)

Peng et al conducted a retrospective case-control nested study within a cohort of pregnant women to investigate the association between heavy metal exposure and gestational diabetes. The group reported that higher concentrations of arsenic, mercury, chromium, and cadmium were associated with gestational diabetes in a dose-dependent manner [9].

Rahman, M. L., Zhang, C., Smarr, M. M., Lee, S., Honda, M., Kannan, K., Tekola-Ayele, F., & Buck Louis, G. M. (2019). Persistent organic pollutants and gestational diabetes: A multi-center prospective cohort study of healthy US women. Environment international, 124, 249–258. https://doi.org/10.1016/j.envint.2019.01.027 (https://doi.org/10.1016/j.envint.2019.01.027)

Rahman et al prospectively evaluated the association of POPs measured in early pregnancy with gestational diabetes risk. The group reported that environmentally relevant levels of heavily chlorinated PCBs and some PFAs and PBDEs were positively associated with gestational diabetes [10].

Shapiro, G. D., Dodds, L., Arbuckle, T. E., Ashley-Martin, J., Fraser, W., Fisher, M., Taback, S., Keely, E., Bouchard, M. F., Monnier, P., Dallaire, R., Morisset, A., & Ettinger, A. S. (2015). Exposure to phthalates, bisphenol A and metals in pregnancy and the association with impaired glucose tolerance and gestational diabetes mellitus: The MIREC study. Environment international, 83, 63–71. https://doi.org/10.1016/j.envint.2015.05.016 (https://doi.org/10.1016/j.envint.2015.05.016)

Shapiro et al conducted a study using data from the maternal-infant research on environmental chemicals cohort to determine the associations between plasticizers/metals and impaired glucose tolerance/gestational diabetes. Their findings supported the role of maternal arsenic exposure in the development of gestational diabetes [11].

Soomro, M. H., Baiz, N., Huel, G., Yazbeck, C., Botton, J., Heude, B., Bornehag, C. G., Annesi-Maesano, I., & EDEN mother-child cohort study group (2019). Exposure to heavy metals during pregnancy related to gestational diabetes mellitus in diabetes-free mothers. The Science of the total environment, 656, 870–876. https://doi.org/10.1016/j.scitotenv.2018.11.422 (https://doi.org/10.1016/j.scitotenv.2018.11.422)

Soomro et al investigated the role of heavy metal exposure and the development of gestational diabetes mellitus and impaired glucose tolerance. The group reported that cadmium exposure was statistically relevant to having a diagnosis of gestational diabetes mellitus or glucose intolerance. Additionally, exposure to lead was associated with similar outcomes [12].

Sun, Q., Zong, G., Valvi, D., Nielsen, F., Coull, B., & Grandjean, P. (2018). Plasma Concentrations of Perfluoroalkyl Substances and Risk of Type 2 Diabetes: A Prospective Investigation among U.S. Women. Environmental health perspectives, 126(3), 037001. https://doi.org/10.1289/EHP2619 (https://doi.org/10.1289/EHP2619)

Sun et al examined the association between PFAS exposures and the incidence of type 2 diabetes using the Nurses' Health Study II. The group reported that background exposures to PFASs in the late 1990s were associated with a higher risk of type 2 diabetes [13].

Wang, X., Mukherjee, B., Karvonen-Gutierrez, C. A., Herman, W. H., Batterman, S., Harlow, S. D., & Park, S. K. (2020). Urinary metal mixtures and longitudinal changes in glucose homeostasis: The Study of Women's Health Across the Nation (SWAN). Environment international, 145, 106109. https://doi.org/10.1016/j.envint.2020.106109 (https://doi.org/10.1016/j.envint.2020.106109)

Wang et al conducted a longitudinal cohort study to assess the association between exposure to metal mixtures and insulin resistance/beta-cell function. The group reported that high levels of urinary zinc were associated with insulin resistance and lower beta-cell activity [14].

Wang, Y., Zhang, P., Chen, X., Wu, W., Feng, Y., Yang, H., Li, M., Xie, B., Guo, P., Warren, J. L., Shi, X., Wang, S., & Zhang, Y. (2019). Multiple metal concentrations and gestational diabetes mellitus in Taiyuan, China. Chemosphere, 237, 124412. https://doi.org/10.1016/j.chemosphere.2019.124412 (https://doi.org/10.1016/j.chemosphere.2019.124412)

Wang et al conducted a study to observe the association between multiple metal concentrations and gestational diabetes using 776 women with or without gestational diabetes. The group reported that gestational diabetes was associated with increased blood levels of arsenic and mercury [15].

Wang, H., Yang, J., Du, H., Xu, L., Liu, S., Yi, J., Qian, X., Chen, Y., Jiang, Q., & He, G. (2018). Perfluoroalkyl substances, glucose homeostasis, and gestational diabetes mellitus in Chinese pregnant women: A repeat measurement-based prospective study. Environment international, 114, 12–20. https://doi.org/10.1016/j.envint.2018.01.027 (https://doi.org/10.1016/j.envint.2018.01.027)

Wang et al conducted a study that aimed to expose the associations between exposure to perfluoroalkyl substances and glucose homeostasis. The group reported that exposure to PFAS may influence glucose homeostasis in Chinese pregnant women [16].

Wang, X., Gao, D., Zhang, G., Zhang, X., Li, Q., Gao, Q., Chen, R., Xu, S., Huang, L., Zhang, Y., Lin, L., Zhong, C., Chen, X., Sun, G., Song, Y., Yang, X., Hao, L., Yang, H., Yang, L., & Yang, N. (2020). Exposure to multiple metals in early pregnancy and gestational diabetes mellitus: A prospective cohort study. *Environment international*, *135*, 105370. https://doi.org/10.1016/j.envint.2019.105370 (https://doi.org/10.1016/j.envint.2019.105370)

Wang et al aimed to investigate the association between urinary nickel, arsenic, cadmium, antimony, cobalt, and vanadium in early pregnancy and the risk of diabetes. The group reported that increasing concentrations of nickel (individually or in a mixture of chemicals) in early pregnancy increased the risk of gestational diabetes [17].

Xia, X., Liang, C., Sheng, J., Yan, S., Huang, K., Li, Z., Pan, W., Tao, R., Hao, J., Zhu, B., Tong, S., & Tao, F. (2018). Association between serum arsenic levels and gestational diabetes mellitus: A population-based birth cohort study. Environmental pollution (Barking, Essex : 1987), 235, 850–856. https://doi.org/10.1016/j.envpol.2018.01.016 (https://doi.org/10.1016/j.envpol.2018.01.016)

Xia et al used a population-based birth cohort to examine the association between arsenic exposure and gestational diabetes. The group reported that the incidence of gestational diabetes gradually increased with increasing quartiles of arsenic levels during the first trimester of pregnancy [18].

Xie, X., Lu, C., Wu, M., Liang, J., Ying, Y., Liu, K., Huang, X., Zheng, S., Du, X., Liu, D., Wen, Z., Hao, G., Yang, G., Feng, L., & Jing, C. (2020). Association between triclocarban and triclosan exposures and the risks of type 2 diabetes mellitus and impaired glucose tolerance in the National Health and Nutrition Examination Survey (NHANES 2013-2014). *Environment International*, *136*, 105445. https://doi.org/10.1016/j.envint.2019.105445 (https://doi.org/10.1016/j.envint.2019.105445)

Xie et al aimed to explore if triclocarban or triclosan exposure was associated with an increased risk of impaired glucose tolerance and type 2 diabetes using data from the U.S. National Health and Nutrition Examination Survey. The group reported that triclocarban exposure may increase the risk of type 2 diabetes in women [19].

Xing, Y., Xia, W., Zhang, B., Zhou, A., Huang, Z., Zhang, H., Liu, H., Jiang, Y., Hu, C., Chen, X., Xu, S., & Li, Y. (2018). Relation between cadmium exposure and gestational diabetes mellitus. Environment international, 113, 300–305. https://doi.org/10.1016/j.envint.2018.01.001 (https://doi.org/10.1016/j.envint.2018.01.001)

Xing et al measured the urinary cadmium concentration of pregnant Chinese women to investigate whether cadmium exposure during pregnancy was associated with gestational diabetes mellitus. The group reported that a 3-fold increase in cadmium levels was associated with an increased risk of gestational diabetes. Risk factors such as obesity or being overweight further increased the risk of gestational diabetes associated with exposure to cadmium [20].

Xu, H., Zhou, Q., Zhang, J., Chen, X., Zhao, H., Lu, H., Ma, B., Wang, Z., Wu, C., Ying, C., Xiong, Y., Zhou, Z., & Li, X. (2020). Exposure to elevated per- and polyfluoroalkyl substances in early pregnancy is related to increased risk of gestational diabetes mellitus: A nested case-

control study in Shanghai, China. Environment international, 143, 105952. https://doi.org/10.1016/j.envint.2020.105952 (https://doi.org/10.1016/j.envint.2020.105952)

Xu et al conducted a nested case-control study to investigate the relationship between gestational diabetes and exposure to poly-fluoroalkyl substances and their short-chain alternatives among Chinese women. The group found that high levels of perfluorobutane sulfonic acid and perflourododecanoic acid were found in the serum of pregnant women with gestational diabetes [21].

Zhang, Y., Chen, T., Zhang, Y., Hu, Q., Wang, X., Chang, H., Mao, J. H., Snijders, A. M., & Xia, Y. (2021). Contribution of trace element exposure to gestational diabetes mellitus through disturbing the gut microbiome. Environment international, 153, 106520. https://doi.org/10.1016/j.envint.2021.106520 (https://doi.org/10.1016/j.envint.2021.106520)

Zhang et al conducted a prospective cohort study using pregnant women to assess the relationship between trace element exposure, the gut microbiome, and gestational diabetes mellitus. They reported that there was no association between trace metals and the development of diabetes. However, exposure to trace elements altered the gut microbiome and this change was associated with the development of diabetes [22].

Zhang, C., Sundaram, R., Maisog, J., Calafat, A. M., Barr, D. B., & Buck Louis, G. M. (2015). A prospective study of prepregnancy serum concentrations of perfluorochemicals and the risk of gestational diabetes. Fertility and sterility, 103(1), 184–189. https://doi.org/10.1016/j.fertnstert.2014.10.001 (https://doi.org/10.1016/j.fertnstert.2014.10.001)

Zhang et al aimed to examine preconception serum concentrations of PFOA and PFCs in relation to gestational diabetes. The group reported that higher environmentally relevant concentrations of PFOA were significantly associated with an increased risk of gestational diabetes. [23].

Puberty

Ashrap, P., Sánchez, B. N., Téllez-Rojo, M. M., Basu, N., Tamayo-Ortiz, M., Peterson, K. E., Meeker, J. D., & Watkins, D. J. (2019). In utero and peripubertal metals exposure in relation to reproductive hormones and sexual maturation and progression among girls in Mexico City. Environmental research, 177, 108630. https://doi.org/10.1016/j.envres.2019.108630 (https://doi.org/10.1016/j.envres.2019.108630)

Ashrap et al aimed to investigate measures of in utero and peripubertal metal exposure in relation to reproductive hormone levels and sexual maturation among girls from the early life exposure in Mexico to environmental toxicants cohorts. The group reported that female

reproductive development may be vulnerable to the effects of metal exposure including slower progression of breast development and altered testosterone levels [24].

Binder, A.M., Corvalan, C., Calafat, A.M. *et al.* Childhood and adolescent phenol and phthalate exposure and the age of menarche in Latina girls. *Environ Health* **17,** 32 (2018). https://doi.org/10.1186/s12940-018-0376-z (https://doi.org/10.1186/s12940-018-0376-z)

Binder et al conducted a longitudinal cohort study to investigate the relationship between chemical biomarkers associated with the age of menarche among Chilean girls. The group reported that an increased concentration of the di(2-Ethylhexyl) phthalate biomarker was associated with later menarche. However, increased concentration of 2,5-dichlrophenol and benzophenone-3 was associated with early menarche [25].

Chen, A., Chung, E., DeFranco, E. A., Pinney, S. M., & Dietrich, K. N. (2011). Serum PBDEs and age at menarche in adolescent girls: analysis of the National Health and Nutrition Examination Survey 2003-2004. *Environmental research*, *111*(6), 831–837. https://doi.org/10.1016/j.envres.2011.05.016

Chen et al analyzed the National Health and Nutrition Examination Survey to observe associations between serum PBDE levels and age on menarche. The group reported that the median total serum PBDE concentration was 44.7ng/g. Higher levels of PBDE were associated with slightly earlier ages at menarche [26].

Harley, K. G., Berger, K. P., Kogut, K., Parra, K., Lustig, R. H., Greenspan, L. C., Calafat, A. M., Ye, X., & Eskenazi, B. (2019). Association of phthalates, parabens and phenols found in personal care products with pubertal timing in girls and boys. Human reproduction (Oxford, England), 34(1), 109–117. https://doi.org/10.1093/humrep/dey337 (https://doi.org/10.1093/humrep/dey337)

Harley et al analyzed the data from the Center for Health Assessment of Mothers and Children of Salinas longitudinal cohort. They used members of this cohort to determine the relationship between exposure to phthalates and the onset of puberty. The group reported that prenatal exposure to monoethyl phthalate was associated with the early onset of pubic hair development in girls. In boys, prenatal exposure to propyl paraben was associated with earlier genital development [27].

Jurewicz, J., & Hanke, W. (2011). Exposure to phthalates: reproductive outcome and children health. A review of epidemiological studies. International journal of occupational medicine and environmental health, 24(2), 115–141. https://doi.org/10.2478/s13382-011-0022-2 (https://doi.org/10.2478/s13382-011-0022-2)

Jurewicz et al discussed the relationship between exposure to phthalates and human health concerns in a literature review. The group highlighted multiple negative effects that phthalate exposure has on human health. This includes but is not limited to impaired

sperm quality, gestational age, head circumference, thyroid function, gynecomastia, and puberty [28].

Schlumpf, M., Schmid, P., Durrer, S., Conscience, M., Maerkel, K., Henseler, M., Gruetter, M., Herzog, I., Reolon, S., Ceccatelli, R., Faass, O., Stutz, E., Jarry, H., Wuttke, W., & Lichtensteiger, W. (2004). Endocrine activity and developmental toxicity of cosmetic UV filters–an update. Toxicology, 205(1-2), 113–122. https://doi.org/10.1016/j.tox.2004.06.043 (https://doi.org/10.1016/j.tox.2004.06.043)

Schlumpf et al used long Evans rats to observe the developmental toxicity of 4-MBC, a UV filter. The group reported that exposure to this chemical was associated with weight gain in pregnant rats, increased postnatal thymic weight, and delayed male puberty—associated with alterations in the weight of reproductive organs as an adult [29].

Endometriosis

Jackson, L. W., Zullo, M. D., & Goldberg, J. M. (2008). The association between heavy metals, endometriosis and uterine myomas among premenopausal women: National Health and Nutrition Examination Survey 1999-2002. Human reproduction (Oxford, England), 23(3), 679–687. https://doi.org/10.1093/humrep/dem394 (https://doi.org/10.1093/humrep/dem394)

Jackson et al investigated the association between heavy metals and the risk of endometriosis and uterine myomas via a cross-sectional study using data from the National Health and Nutrition Examination Survey. The group reported that a dose-dependent response was associated with exposure to cadmium and the observation of endometriosis [30].

Kunisue, T., Chen, Z., Buck Louis, G. M., Sundaram, R., Hediger, M. L., Sun, L., & Kannan, K. (2012). Urinary concentrations of benzophenone-type UV filters in U.S. women and their association with endometriosis. *Environmental science & technology*, *46*(8), 4624–4632. https://doi.org/10.1021/es204415a (https://doi.org/10.1021/es204415a)

Kunisue et al aimed to determine the concentrations of 5 benzophenones in women residing in Utah and California. The group reported an association between the diagnosis of endometriosis and increasing urinary concentrations of benzophenone derivatives. Overall, the group speculated that exposure to elevated levels of 2,4,OH-BP was associated with endometriosis [31].

Louis, G. M., Peterson, C. M., Chen, Z., Hediger, M. L., Croughan, M. S., Sundaram, R., Stanford, J. B., Fujimoto, V. Y., Varner, M. W., Giudice, L. C., Kennedy, A., Sun, L., Wu, Q., & Kannan, K. (2012). Perfluorochemicals and endometriosis: the ENDO study. Epidemiology (Cambridge, Mass.), 23(6), 799–805. https://doi.org/10.1097/EDE.0b013e31826cc0cf (https://doi.org/10.1097/EDE.0b013e31826cc0cf)

Louis et al examined the possible role of PFCs in the incidence of endometriosis. The group reported that serum PFOA was associated with endometriosis. Additionally, exposure to PFSA was associated with increased odds of moderate/severe endometriosis [32].

Peinado, F. M., Ocón-Hernández, O., Iribarne-Durán, L. M., Vela-Soria, F., Ubiña, A., Padilla, C., Mora, J. C., Cardona, J., León, J., Fernández, M. F., Olea, N., & Artacho-Cordón, F. (2021). Cosmetic and personal care product use, urinary levels of parabens and benzophenones, and risk of endometriosis: results from the EndEA study. Environmental research, 196, 110342. https://doi.org/10.1016/j.envres.2020.110342 (https://doi.org/10.1016/j.envres.2020.110342)

Peinado et al conducted a case-control study to examine the relationship between urinary concentrations of benzophenones and parabens in persons who use personal care products and how this relationship impacts the risk of endometriosis. The group reported that the frequency of personal care product use was significantly associated with urinary concentrations of benzophenones and parabens. Additionally, urinary concentrations of these chemicals were associated with an increased risk of endometriosis [33].

Fertility

Alviggi, C., Guadagni, R., Conforti, A., Coppola, G., Picarelli, S., De Rosa, P., Vallone, R., Strina, I., Pagano, T., Mollo, A., Acampora, A., & De Placido, G. (2014). Association between intrafollicular concentration of benzene and outcome of controlled ovarian stimulation in IVF/ICSI cycles: a pilot study. Journal of ovarian research, 7, 67. https://doi.org/10.1186/1757-2215-7-67 (https://doi.org/10.1186/1757-2215-7-67)

Alviggi et al performed an observational prospective pilot study to evaluate if levels of benzene in follicular fluid were correlated with response to controlled ovarian stimulation. The group reported that ovarian response to endogenous and exogenous gonadotrophins was influenced by intra-follicular benzene levels [34].

Arya, S., Dwivedi, A. K., Alvarado, L., & Kupesic-Plavsic, S. (2020). Exposure of U.S. population to endocrine disruptive chemicals (Parabens, Benzophenone-3, Bisphenol-A and Triclosan) and their associations with female infertility. *Environmental pollution (Barking, Essex : 1987)*, *265*(Pt A), 114763. https://doi.org/10.1016/j.envpol.2020.114763 (https://doi.org/10.1016/j.envpol.2020.114763)

Ayra et al conducted a cross-sectional study to investigate the relationship between exposure to endocrine-disrupting chemicals and infertility among women in the United States using the National Health and Nutrition Examination Surveys. The group found that self-reported infertility was associated with increased concentrations of mixtures of benzophenones as well as triclosan and butyl parabens [35].

Buck Louis G. M. (2014). Persistent environmental pollutants and couple fecundity: an overview. *Reproduction (Cambridge, England)*, *147*(4), R97–R104. https://doi.org/10.1530/REP-13-0472

A review discussing the association between exposure to persistent environmental chemicals and reproductive outcomes. The review also discusses ways to improve studies that investigate the impact that environmental exposures have on women's reproductive health outcomes [36].

Green, M. P., Harvey, A. J., Finger, B. J., & Tarulli, G. A. (2021). Endocrine disrupting chemicals: Impacts on human fertility and fecundity during the peri-conception period. Environmental research, 194, 110694. https://doi.org/10.1016/j.envres.2020.110694 (https://doi.org/10.1016/j.envres.2020.110694)

This review discussed the current understanding that exposure to endocrine-disrupting chemicals has on reproductive health. Specifically, this review discussed the relationship between environmental exposures and male/female reproductivity during the periconception period and how this impacts sex/embryo characteristics and pregnancy outcomes [37].

Hua, R., Zhou, Y., Wu, B., Huang, Z., Zhu, Y., Song, Y., Yu, Y., Li, H., & Quan, S. (2017). Urinary triclosan concentrations and early outcomes of in vitro fertilization-embryo transfer. Reproduction (Cambridge, England), 153(3), 319–325. https://doi.org/10.1530/REP-16-0501 (https://doi.org/10.1530/REP-16-0501)

Hua et al performed a prospective cohort study to investigate whether high urinary triclosan concentration is adversely associated with early reproductive outcomes in women undergoing in vitro fertilization-embryo transfer. The group reported that high levels of urinary triclosan were associated with a significant decrease in top-quality embryo formation and implantation rate [38].

Lei, H. L., Wei, H. J., Ho, H. Y., Liao, K. W., & Chien, L. C. (2015). Relationship between risk factors for infertility in women and lead, cadmium, and arsenic blood levels: a cross-sectional study from Taiwan. BMC public health, 15, 1220. https://doi.org/10.1186/s12889-015-2564-x (https://doi.org/10.1186/s12889-015-2564-x)

Lei et al conducted a cross-sectional study to investigate the association between blood lead, cadmium, and arsenic in infertile women. The group reported that blood levels of lead, arsenic, and cadmium were significantly higher in infertile women, but exercising may reduce the accumulation of lead [39].

Smith, K. W., Souter, I., Dimitriadis, I., Ehrlich, S., Williams, P. L., Calafat, A. M., & Hauser, R. (2013). Urinary paraben concentrations and ovarian aging among women from a fertility center. Environmental health perspectives, 121(11-12), 1299–1305. https://doi.org/10.1289/ehp.1205350 (https://doi.org/10.1289/ehp.1205350)

Smith et al analyzed the urine and ovarian reserve of a cohort of women seeking fertility treatment to determine if paraben exposure is associated with characteristics of fertility. The group found that exposure to propylparaben may be associated with a diminished ovarian reserve [40].

Radwan, P., Wielgomas, B., Radwan, M., Krasiński, R., Klimowska, A., Zajdel, R., Kaleta, D., & Jurewicz, J. (2021). Triclosan exposure and in vitro fertilization treatment outcomes in women undergoing in vitro fertilization. Environmental science and pollution research international, 28(10), 12993–12999. https://doi.org/10.1007/s11356-020-11287-w (https://doi.org/10.1007/s11356-020-11287-w)

Radwan et al examined the association between urinary levels of triclosan and in vitro reproductive outcomes. The group reported that urinary triclosan concentrations were associated with decreased implantation rate, but not other aspects of invitro fertilization [41].

Tanrıkut, E., Karaer, A., Celik, O., Celik, E., Otlu, B., Yilmaz, E., & Ozgul, O. (2014). Role of endometrial concentrations of heavy metals (cadmium, lead, mercury and arsenic) in the aetiology of unexplained infertility. *European journal of obstetrics, gynecology, and reproductive biology*, *179*, 187–190. https://doi.org/10.1016/j.ejogrb.2014.05.039 (https://doi.org/10.1016/j.ejogrb.2014.05.039)

Tanrikut et al collected endometrial biopsies from 32 fertile and 33 infertile women to determine the role of endometrial concentrations of heavy metals on unexplained infertility. The group reported that cadmium was detected in over 90% of the women who experienced unexplained infertility, compared to 34% of fertile women. Additionally, lead was detected in 15% of infertile women versus only 3% of fertile women [42].

Tulić, L., Vidaković, S., Tulić, I., Ćurčić, M., & Bulat, Z. (2019). Toxic Metal and Trace Element Concentrations in Blood and Outcome of In Vitro Fertilization in Women. Biological trace element research, 188(2), 284–294. https://doi.org/10.1007/s12011-018-1421-z (https://doi.org/10.1007/s12011-018-1421-z)

Tulic et al aimed to investigate the association between blood levels of trace elements and toxic metal concentrations and the outcome of in vitro fertilization. They reported that there was a significant correlation between the negative outcome of IVF with higher concentrations of lead and cadmium. Additionally, pregnant women had lower levels of manganese, arsenic, and lead. It should be noted that patients with a smoking history had significantly higher levels of lead and slightly higher levels of arsenic and mercury[43].

Zhang, C., Sundaram, R., Maisog, J., Calafat, A. M., Barr, D. B., & Buck Louis, G. M. (2015). A prospective study of prepregnancy serum concentrations of perfluorochemicals and the risk of gestational diabetes. Fertility and sterility, 103(1), 184–189. https://doi.org/10.1016/j.fertnstert.2014.10.001 (https://doi.org/10.1016/j.fertnstert.2014.10.001)

Zhang et al aimed to examine preconception serum concentrations of PFOA and PFCs in relation to gestational diabetes. The group reported that higher environmentally relevant concentrations of PFOA were significantly associated with an increased risk of gestational diabetes. [23].

Menopause

Chen, X., Zhu, G., & Jin, T. (2017). Effects of Cadmium Exposure on Age of Menarche and Menopause. Toxics, 6(1), 6. https://doi.org/10.3390/toxics6010006 (https://doi.org/10.3390/toxics6010006)

Chen et al conducted a study using women who either did not live in cadmium-polluted areas to determine if there was an association between cadmium exposure and menarche. The group reported that women who lived in cadmium-polluted environments started menarche at a significantly younger age than women who lived in unpolluted environments. However, this geographic locale did not impact menopause [44].

Ding, N., Harlow, S. D., Randolph, J. F., Calafat, A. M., Mukherjee, B., Batterman, S., Gold, E. B., & Park, S. K. (2020). Associations of Perfluoroalkyl Substances with Incident Natural Menopause: The Study of Women's Health Across the Nation. The Journal of clinical endocrinology and metabolism, 105(9), e3169–e3182. https://doi.org/10.1210/clinem/dgaa303 (https://doi.org/10.1210/clinem/dgaa303)

Ding et al aimed to investigate associations between perfluoroalkyl substances and the incidence of natural menopause. The group reported that selected PFAS serum concentrations are associated with earlier natural menopause [45].

Wang, X., Ding, N., Harlow, S. D., Randolph, J. F., Jr, Mukherjee, B., Gold, E. B., & Park, S. K. (2021). Urinary metals and metal mixtures and timing of natural menopause in midlife women: The Study of Women's Health Across the Nation. Environment international, 157, 106781. https://doi.org/10.1016/j.envint.2021.106781 (https://doi.org/10.1016/j.envint.2021.106781)

Wang et al investigated the association between urinary metal and mixture combinations and natural menopause. The group reported that arsenic, lead and metal mixtures are associated with earlier natural menopause [46].

Wang, W., Craig, Z. R., Basavarajappa, M. S., Hafner, K. S., & Flaws, J. A. (2012). Mono-(2-ethylhexyl) phthalate induces oxidative stress and inhibits growth of mouse ovarian antral follicles. *Biology of reproduction*, *87*(6), 152. https://doi.org/10.1095/biolreprod.112.102467 (https://doi.org/10.1095/biolreprod.112.102467)

Wang et al used a murine model to observe if exposure to MEHP affects ovarian antral follicles and identify potential mechanisms associated with this effect. The group reported that MEHP exposure increased reactive oxygen species which inhibits follicle growth in antral follicles [47].

Maternal Health

Ashley-Martin, J., Dodds, L., Arbuckle, T. E., Bouchard, M. F., Shapiro, G. D., Fisher, M., Monnier, P., Morisset, A. S., & Ettinger, A. S. (2018). Association between maternal urinary speciated arsenic concentrations and gestational diabetes in a cohort of Canadian women. Environment international, 121(Pt 1), 714–720. https://doi.org/10.1016/j.envint.2018.10.008 (https://doi.org/10.1016/j.envint.2018.10.008)

Ashley-Martin et al studied the association between arsenic and gestational diabetes using data from the maternal-infant research on environmental chemicals. The group reported that a metabolite of arsenic, dimethylarsenic acid, was associated with gestational diabetes [1].

Ashrap, P., Watkins, D. J., Mukherjee, B., Boss, J., Richards, M. J., Rosario, Z., Vélez-Vega, C. M., Alshawabkeh, A., Cordero, J. F., & Meeker, J. D. (2020). Maternal blood metal and metalloid concentrations in association with birth outcomes in Northern Puerto Rico. Environment international, 138, 105606. https://doi.org/10.1016/j.envint.2020.105606 (https://doi.org/10.1016/j.envint.2020.105606)

Ashrap et al conducted a study using the Puerto Rico Test site for Exploring Contamination Threats cohort to observe the effects of metals and metalloids on birth outcomes. The group reported that metal was associated with a higher odds of preterm birth and shorter gestational age. To a smaller extent, manganese, zinc, mercury, and nickel were associated with similar outcomes [48].

Baker, B. H., Wu, H., Laue, H. E., Boivin, A., Gillet, V., Langlois, M. F., Bellenger, J. P., Baccarelli, A. A., & Takser, L. (2020). Methylparaben in meconium and risk of maternal thyroid dysfunction, adverse birth outcomes, and Attention-Deficit Hyperactivity Disorder (ADHD). Environment international, 139, 105716. https://doi.org/10.1016/j.envint.2020.105716 (https://doi.org/10.1016/j.envint.2020.105716)

Baker et al used data from the GESTation and the Environment (GESTE) prospective observational pregnancy cohort to determine if there is a relationship between prenatal exposure to methylparaben and adverse health outcomes. The group reported that the presence of methylparaben in meconium samples was associated with the onset of preterm birth, decreased gestational age, attention-deficit hyperactivity disorder, and more [49].

Bayat, F., Akbari, S. A., Dabirioskoei, A., Nasiri, M., & Mellati, A. (2016). The Relationship Between Blood Lead Level and Preeclampsia. Electronic physician, 8(12), 3450–3455. https://doi.org/10.19082/3450 (https://doi.org/10.19082/3450)

Bayat et al conducted a case-control study to determine the relationship between maternal blood lead levels and preeclampsia. The group reported a significant relationship between blood lead levels and preeclampsia [50].

Bloom, M. S., Wenzel, A. G., Brock, J. W., Kucklick, J. R., Wineland, R. J., Cruze, L., Unal, E. R., Yucel, R. M., Jiyessova, A., & Newman, R. B. (2019). Racial disparity in maternal phthalates exposure; Association with racial disparity in fetal growth and birth outcomes. Environment international, 127, 473–486. https://doi.org/10.1016/j.envint.2019.04.005 (https://doi.org/10.1016/j.envint.2019.04.005)

Bloom et al conducted an observational study of southeastern women in the United States to determine racial differences in maternal phthalate exposure, fetal growth, and birth outcomes. The group reported that high levels of MEHP were associated with small gestational age in whites, but not blacks. However, higher levels of MiBP were associated with preterm birth in blacks, but not whites. Overall, higher levels of MEP were associated with low birth weight in males but not females, independent of race [51].

Bloom, M. S., Fujimoto, V. Y., Steuerwald, A. J., Cheng, G., Browne, R. W., & Parsons, P. J. (2012). Background exposure to toxic metals in women adversely influences pregnancy during in vitro fertilization (IVF). Reproductive toxicology (Elmsford, N.Y.), 34(3), 471–481. https://doi.org/10.1016/j.reprotox.2012.06.002 (https://doi.org/10.1016/j.reprotox.2012.06.002)

Bloom et al aimed to generate a hypothesis concerning associations between background exposure to heavy metals and pregnancy outcomes. The group reported that increases in blood cadmium levels are associated with decreases in clinical and biochemical pregnancies. Increases in blood mercury and lead were also associated with a decrease in clinical and biochemical pregnancies [52].

Cherry, N., Shaikh, K., McDonald, C., & Chowdhury, Z. (2008). Stillbirth in rural Bangladesh: arsenic exposure and other etiological factors: a report from Gonoshasthaya Kendra. Bulletin of the World Health Organization, 86(3), 172–177. https://doi.org/10.2471/blt.07.043083 (https://doi.org/10.2471/blt.07.043083)

Cherry et al aimed to describe the epidemiological patterns of still birth and arsenic contamination of hand-pump wells in Bangladesh. The group reported that there was an increased risk of stillbirth associated with increasing arsenic contamination [53].

Chan, M., Mita, C., Bellavia, A., Parker, M., & James-Todd, T. (2021). Racial/Ethnic Disparities in Pregnancy and Prenatal Exposure to Endocrine-Disrupting Chemicals Commonly Used in Personal Care Products. Current environmental health reports, 8(2), 98–

112. https://doi.org/10.1007/s40572-021-00317-5 (https://doi.org/10.1007/s40572-021-00317-5)

Chan et al reviewed the literature for studies that investigated the relationship between exposure to endocrine-disrupting chemicals during pregnancy and adverse maternal/child health outcomes. Specifically, the group investigated this relationship as it pertains to the use of personal care products. They reported that few studies investigated this link, but they found that black and Hispanic women had high levels of phthalates as phenols, whereas white women had high levels of benzophenone-3 [54].

Disha, Sharma, S., Goyal, M., Kumar, P. K., Ghosh, R., & Sharma, P. (2019). Association of raised blood lead levels in pregnant women with preeclampsia: A study at tertiary centre. Taiwanese journal of obstetrics & gynecology, 58(1), 60–63. https://doi.org/10.1016/j.tjog.2018.11.011 (https://doi.org/10.1016/j.tjog.2018.11.011)

Disha et al aimed to measure the blood lead levels in pregnant women and their association with pre-eclampsia. The group reported that higher blood lead levels are associated with an increased risk of preeclampsia [55].

El-Badry, A., Rezk, M., & El-Sayed, H. (2018). Mercury-induced Oxidative Stress May Adversely Affect Pregnancy Outcome among Dental Staff: A Cohort Study. The international journal of occupational and environmental medicine, 9(3), 113–119. https://doi.org/10.15171/ijoem.2018.1181 (https://doi.org/10.15171/ijoem.2018.1181)

El-Brady et al investigated the obstetric outcome among dental staff and oxidative stress induced by mercury exposure. The group reported that women who were exposed to mercury had higher incidences of spontaneous abortion and pre-eclampsia. Additionally, babies born to exposed women tended to be smaller for gestational age [56].

Elongi Moyene, J. P., Scheers, H., Tandu-Umba, B., Haufroid, V., Buassa-Bu-Tsumbu, B., Verdonck, F., Spitz, B., & Nemery, B. (2016). Preeclampsia and toxic metals: a case-control study in Kinshasa, DR Congo. Environmental health: a global access science source, 15, 48. https://doi.org/10.1186/s12940-016-0132-1 (https://doi.org/10.1186/s12940-016-0132-1)

Elongi et al used a case-control design to observe if preeclampsia was associated with exposure to environmental metals within the Democratic Republic of Congo. The group found that women with preeclampsia have higher levels of several toxic metals (especially lead) than control women[57].

Ettinger, A. S., Zota, A. R., Amarasiriwardena, C. J., Hopkins, M. R., Schwartz, J., Hu, H., & Wright, R. O. (2009). Maternal arsenic exposure and impaired glucose tolerance during pregnancy. *Environmental health perspectives*, *117*(7), 1059–1064. https://doi.org/10.1289/ehp0800533 (https://doi.org/10.1289/ehp0800533)

Ettinger et al conducted a study to investigate whether arsenic exposure is associated with impaired glucose tolerance during pregnancy. The group reported that women in the highest quartile of arsenic exposure have higher odds of impaired glucose tolerance tests compared to women in the lowest quartile of exposure [58].

Etzel, T. M., Calafat, A. M., Ye, X., Chen, A., Lanphear, B. P., Savitz, D. A., Yolton, K., & Braun, J. M. (2017). Urinary triclosan concentrations during pregnancy and birth outcomes. Environmental research, 156, 505–511. https://doi.org/10.1016/j.envres.2017.04.015 (https://doi.org/10.1016/j.envres.2017.04.015)

Etzel et al investigated the relationship between prenatal exposure to triclosan exposure, birth anthropometry, and gestational duration. The group reported that maternal urinary triclosan concentrations were inversely associated with infants' birth weight, length, head circumference and gestational age [59].

Erinc, A., Davis, M. B., Padmanabhan, V., Langen, E., & Goodrich, J. M. (2021). Considering environmental exposures to per- and polyfluoroalkyl substances (PFAS) as risk factors for hypertensive disorders of pregnancy. Environmental research, 197, 111113. https://doi.org/10.1016/j.envres.2021.111113 (https://doi.org/10.1016/j.envres.2021.111113)

Erinc et al wrote a review article that presented epidemiological and mechanistic evidence for the link between PFAs and hypertensive disorders of pregnancy. The group also offered prevention efforts. Overall, they discussed that pregnant women may be vulnerable to PFAS exposure and policymakers should consider setting limits on exposure to PFAS [60].

Fei, C., McLaughlin, J. K., Lipworth, L., & Olsen, J. (2009). Maternal levels of perfluorinated chemicals and subfecundity. Human reproduction (Oxford, England), 24(5), 1200–1205. https://doi.org/10.1093/humrep/den490 (https://doi.org/10.1093/humrep/den490)

Fei et al examined whether exposure to PFOA or PFOS decreases fecundity in humans. The group reported that a longer time to pregnancy was associated with higher maternal plasma levels of PFOA and PFOS [61].

Gokoel, A. R., Zijlmans, W., Covert, H. H., Abdoel Wahid, F., Shankar, A., MacDonald-Ottevanger, M. S., Hindori-Mohangoo, A. D., Wickliffe, J. K., Lichtveld, M. Y., & Harville, E. W. (2020). Influence of Prenatal Exposure to Mercury, Perceived Stress, and Depression on Birth Outcomes in Suriname: Results from the MeKiTamara Study. International journal of environmental research and public health, 17(12), 4444. https://doi.org/10.3390/ijerph17124444 (https://doi.org/10.3390/ijerph17124444)

Gokoel aimed to assess the influence of prenatal mercury exposure, perceived stress, and depression on adverse birth outcomes in Surinamese women within the Caribbean Consortium for Research in Environmental and Occupational Health prospective cohort.

They reported associations between mercury exposure and preterm birth and perceived stress. However, depression was not associated with any birth outcomes [62].

Harris, S. M., Jin, Y., Loch-Caruso, R., Padilla, I. Y., Meeker, J. D., & Bakulski, K. M. (2020). Identification of environmental chemicals targeting miscarriage genes and pathways using the comparative toxicogenomics database. Environmental research, 184, 109259. https://doi.org/10.1016/j.envres.2020.109259 (https://doi.org/10.1016/j.envres.2020.109259)

Harris et al reported that environmental exposure to chemicals such as parathion, cadmium, and arsenic are associated with miscarriage in humans, mice, and rats. Specifically, exposure to environmental contaminants can influence the expression of genes involved in miscarriage. Exposure to such chemicals altered the expression of genes involved in pregnancy complications, such as vasculature development and inflammatory response [63].

Jia, X., Zhang, L., Zhao, J., Ren, M., Li, Z., Wang, J., Wang, S., Liu, Y., An, H., Li, Y., Yan, L., Li, Z., Liu, X., Pan, B., & Ye, R. (2021). Associations between endocrine-disrupting heavy metals in maternal hair and gestational diabetes mellitus: A nested case-control study in China. Environment international, 157, 106770. https://doi.org/10.1016/j.envint.2021.106770 (https://doi.org/10.1016/j.envint.2021.106770)

Jia et al investigated the association between endocrine-disrupting heavy metals in maternal hair and the risk of gestational diabetes. The group reported that high maternal levels of tin and mercury were associated with the development of gestational diabetes [5].

Kile, M. L., Cardenas, A., Rodrigues, E., Mazumdar, M., Dobson, C., Golam, M., Quamruzzaman, Q., Rahman, M., & Christiani, D. C. (2016). Estimating Effects of Arsenic Exposure During Pregnancy on Perinatal Outcomes in a Bangladeshi Cohort. Epidemiology (Cambridge, Mass.), 27(2), 173–181. https://doi.org/10.1097/EDE.0000000000000416 (https://doi.org/10.1097/EDE.0000000000000416)

Kile et al conducted a prospective cohort study of pregnant women to evaluate the causal relationship between prenatal exposure to arsenic and birthweight. The group reported that arsenic exposure during pregnancy was associated with lower birth weight. They also reported that this association is mediated through gestational age [64].

Kolusari, A., Kurdoglu, M., Yildizhan, R., Adali, E., Edirne, T., Cebi, A., Demir, H., & Yoruk, I. H. (2008). Catalase activity, serum trace element and heavy metal concentrations, and vitamin A, D and E levels in pre-eclampsia. *The Journal of international medical research*, *36*(6), 1335–1341. https://doi.org/10.1177/147323000803600622 (https://doi.org/10.1177/147323000803600622)

Kolusari et al conducted a study to observe the relationship between catalase activity, heavy metal, vitamin concentrations, and preeclampsia. The group reported that women with preeclampsia had lower levels of catalase, vitamin A, D, E, and cobalt. Women with preeclampsia also had higher levels of copper, iron, and cadmium [65].

Laine, J. E., Ray, P., Bodnar, W., Cable, P. H., Boggess, K., Offenbacher, S., & Fry, R. C. (2015). Placental Cadmium Levels Are Associated with Increased Preeclampsia Risk. PloS one, 10(9), e0139341. https://doi.org/10.1371/journal.pone.0139341 (https://doi.org/10.1371/journal.pone.0139341)

Laine et al conducted a study that aimed to identify the association between heavy metals in the placenta and the odds of preeclampsia in a nested case-control design. The group reported that increased levels of placental cadmium were associated with an increased risk of preeclampsia. Additionally, lower levels of placental zinc were associated with preeclampsia [66].

Lauritzen, H.B., Larose, T.L., Øien, T. et al. Prenatal exposure to persistent organic pollutants and child overweight/obesity at 5-year follow-up: a prospective cohort study. Environ Health 17, 9 (2018). https://doi.org/10.1186/s12940-017-0338-x (https://doi.org/10.1186/s12940-017-0338-x)

Lauritzen et al aimed to investigate the relationship between prenatal exposure to persistent organic pollutants and offspring weight gain. The group reported that maternal serum PFAS concentrations were positively associated with child overweight/obesity trends at the 5-year follow-up [67].

Liew, Z., Luo, J., Nohr, E. A., Bech, B. H., Bossi, R., Arah, O. A., & Olsen, J. (2020). Maternal Plasma Perfluoroalkyl Substances and Miscarriage: A Nested Case-Control Study in the Danish National Birth Cohort. Environmental health perspectives, 128(4), 47007. https://doi.org/10.1289/EHP6202 (https://doi.org/10.1289/EHP6202)

Liew et al sought to examine the relationship between PFAS exposures and the risk of miscarriage in humans. The group reported that maternal exposure to high levels of PFOA, PFHpS and PFAS mixtures were associated with the risk of miscarriage [68].

Mullin, A. M., Amarasiriwardena, C., Cantoral-Preciado, A., Claus Henn, B., Leon Hsu, H. H., Sanders, A. P., Svensson, K., Tamayo-Ortiz, M., Téllez-Rojo, M. M., Wright, R. O., & Burris, H. H. (2019). Maternal blood arsenic levels and associations with birth weight-for-gestational age. Environmental research, 177, 108603. https://doi.org/10.1016/j.envres.2019.108603 (https://doi.org/10.1016/j.envres.2019.108603)

Mullin et al analyzed mother-infant dyads within the PROGRESS cohort to investigate the association of blood arsenic levels with birth weight-for-gestational age. The group reported that higher maternal blood arsenic levels at delivery were associated with higher odds of small for gestational age and large-for-gestational-age among infants [69].

Ng, T. P., Foo, S. C., & Yoong, T. (1992). Risk of spontaneous abortion in workers exposed to toluene. *British journal of industrial medicine*, *49*(11), 804–808. https://doi.org/10.1136/oem.49.11.804 (https://doi.org/10.1136/oem.49.11.804)

Ng et al interviewed women to observe the relationship between toluene exposure and the rate of spontaneous abortion. The group reported that exposure to toluene was associated with an increased risk of fetal loss in a majority of women who did not smoke or drink [70].

Nyanza, E. C., Dewey, D., Manyama, M., Martin, J. W., Hatfield, J., & Bernier, F. P. (2020). Maternal exposure to arsenic and mercury and associated risk of adverse birth outcomes in small-scale gold mining communities in Northern Tanzania. Environment international, 137, 105450. https://doi.org/10.1016/j.envint.2019.105450 (https://doi.org/10.1016/j.envint.2019.105450)

Nyanza et al conducted a longitudinal prospective study to examine the association between prenatal and maternal exposure to arsenic and mercury exposure and birth outcomes in mining communities. The group reported that women living in mining communities had higher blood levels of mercury than women who did not live in mining communities. Additionally, high levels of arsenic were associated with spontaneous abortion, stillbirth, and preterm birth, whereas mercury exposure was associated with stillbirth solely [71].

Park, N. Y., Cho, Y. H., Choi, K., Lee, E. H., Kim, Y. J., Kim, J. H., & Kho, Y. (2019). Parabens in breast milk and possible sources of exposure among lactating women in Korea. *Environmental pollution (Barking, Essex : 1987)*, *255*(Pt 2), 113142. https://doi.org/10.1016/j.envpol.2019.113142 (https://doi.org/10.1016/j.envpol.2019.113142)

Park et al measured the paraben concentration in the breastmilk of lactating mothers to determine the baseline concentration of parabens in breastmilk and identify possible sources of exposure. The group reported that ethyl paraben was detected at the highest levels in breastmilk samples, followed by other major parabens. The authors also noted that increased levels of parabens in breastmilk were associated with pre-pregnancy BMI, use of skincare products, use of cosmetics, canned beverage use, and milk consumption [72].

Peng, S., Liu, L., Zhang, X., Heinrich, J., Zhang, J., Schramm, K. W., Huang, Q., Tian, M., Eqani, S. A., & Shen, H. (2015). A nested case-control study indicating heavy metal residues in meconium associate with maternal gestational diabetes mellitus risk. *Environmental health : a global access science source*, *14*, 19. https://doi.org/10.1186/s12940-015-0004-0 (https://doi.org/10.1186/s12940-015-0004-0)

Peng et al conducted a retrospective case-control nested study within a cohort of pregnant women to investigate the association between heavy metal exposure and gestational diabetes. The group reported that higher concentrations of arsenic, mercury,

chromium, and cadmium were associated with gestational diabetes in a dose-dependent manner [9].

Quinn, A. L., Regan, J. M., Tobin, J. M., Marinik, B. J., McMahon, J. M., McNett, D. A., Sushynski, C. M., Crofoot, S. D., Jean, P. A., & Plotzke, K. P. (2007). In vitro and in vivo evaluation of the estrogenic, androgenic, and progestagenic potential of two cyclic siloxanes. Toxicological sciences : an official journal of the Society of Toxicology, 96(1), 145–153. https://doi.org/10.1093/toxsci/kfl185 (https://doi.org/10.1093/toxsci/kfl185)

Quinn et al aimed to determine the potential estrogenic, androgenic and progestogenic activity of two cyclic siloxanes. The group reported that D4 exhibited a low affinity for ER-alpha in vitro and a weak estrogenic response in vivo [73].

Rahman, A., Persson, L. Å., Nermell, B., El Arifeen, S., Ekström, E. C., Smith, A. H., & Vahter, M. (2010). Arsenic exposure and risk of spontaneous abortion, stillbirth, and infant mortality. Epidemiology (Cambridge, Mass.), 21(6), 797–804. https://doi.org/10.1097/EDE.0b013e3181f56a0d (https://doi.org/10.1097/EDE.0b013e3181f56a0d)

Rahman et al conducted a population-based prospective cohort study to assess the association between arsenic exposure and adverse pregnancy outcomes. They reported that spontaneous abortion and infant mortality was associated with arsenic exposure as well [74].

Santos, D., & Nascimento, L. (2019). Maternal exposure to benzene and toluene and preterm birth. A longitudinal study. Sao Paulo medical journal = Revista paulista de medicina, 137(6), 486–490. https://doi.org/10.1590/1516-3180.2019.0224170919 (https://doi.org/10.1590/1516-3180.2019.0224170919)

Santos et al investigated whether exposure to benzene and toluene among pregnant women contributes to preterm delivery. The group found that maternal exposure to benzene and toluene had an acute effect on preterm delivery [75].

Shapiro, G. D., Dodds, L., Arbuckle, T. E., Ashley-Martin, J., Fraser, W., Fisher, M., Taback, S., Keely, E., Bouchard, M. F., Monnier, P., Dallaire, R., Morisset, A., & Ettinger, A. S. (2015). Exposure to phthalates, bisphenol A and metals in pregnancy and the association with impaired glucose tolerance and gestational diabetes mellitus: The MIREC study. Environment international, 83, 63–71. https://doi.org/10.1016/j.envint.2015.05.016 (https://doi.org/10.1016/j.envint.2015.05.016)

Sharpio et al conducted a study using data from the maternal-infant research on environmental chemicals cohort to determine the associations between plasticizers/metals and impaired glucose tolerance/gestational diabetes. Their findings supported the role of maternal arsenic exposure in the development of gestational diabetes [11].

Smarr, M. M., Mirzaei Salehabadi, S., Boyd Barr, D., Buck Louis, G. M., & Sundaram, R. (2021). A multi-pollutant assessment of preconception persistent endocrine disrupting chemicals and incident pregnancy loss. Environment international, 157, 106788. https://doi.org/10.1016/j.envint.2021.106788 (https://doi.org/10.1016/j.envint.2021.106788)

Smarr et al followed a prospective cohort using 501 couples to determine if there was an association between exposure to a mixture of endocrine-disrupting chemicals and human gonadotrophin chorionic pregnancy loss. The group reported that preconception exposure to polybrominated ether 28 and cadmium in females was positively associated with human gonadotrophin pregnancy loss [76].

Sohel, N., Vahter, M., Ali, M. et al. Spatial patterns of fetal loss and infant death in an arsenic-affected area in Bangladesh. Int J Health Geogr 9, 53 (2010). https://doi.org/10.1186/1476-072X-9-53 (https://doi.org/10.1186/1476-072X-9-53)

Sohel et al conducted a study using pregnant women to identify spatial and spatiotemporal clustering of fetal loss and infant death and clusters of arsenic concentrations in tube-well water [77]. The group reported that geographical variation in tube-well water arsenic contamination is associated with higher fetal loss and infant death [77].

Tabacova, S., & Balabaeva, L. (1993). Environmental pollutants in relation to complications of pregnancy. Environmental health perspectives, 101 Suppl 2(Suppl 2), 27–31. https://doi.org/10.1289/ehp.93101s227 (https://doi.org/10.1289/ehp.93101s227)

Tabacova et al discussed how certain maternal environmental exposures can negatively impact pregnancy outcomes. Women who were exposed to lead or aromatic hydrocarbons were at risk of poor pregnancy outcomes. These outcomes included spontaneous abortion, anemia, and toxemia [78].

Thomas, S., Arbuckle, T. E., Fisher, M., Fraser, W. D., Ettinger, A., & King, W. (2015). Metals exposure and risk of small-for-gestational age birth in a Canadian birth cohort: The MIREC study. Environmental research, 140, 430–439. https://doi.org/10.1016/j.envres.2015.04.018 (https://doi.org/10.1016/j.envres.2015.04.018)

Thomas et al conducted a study to examine the relationship between exposure to heavy metals during pregnancy and risk of small for gestational age. The group reported that there was no association between blood levels of lead, cadmium, and arsenic. However, increased blood mercury levels were associated with an increased risk of small for gestational age [79].

Tsuji, M., Shibata, E., Askew, D. J., Morokuma, S., Aiko, Y., Senju, A., Araki, S., Sanefuji, M., Ishihara, Y., Tanaka, R., Kusuhara, K., Kawamoto, T., & Japan Environment and Children's Study Group (2019). Associations between metal concentrations in whole blood and

placenta previa and placenta accreta: the Japan Environment and Children's Study (JECS). *Environmental health and preventive medicine*, *24*(1), 40. https://doi.org/10.1186/s12199-019-0795-7 (https://doi.org/10.1186/s12199-019-0795-7)

Tsuji et al administered a questionnaire to women with singleton pregnancies to determine if metal exposure is associated with placenta previa and placenta accrete. The group divided the subjects into 4 quartiles of exposure and found that Q4 cadmium was associated with placenta previa, but Q2 lead was associated with placenta previa [80].

Vélez, M. P., Arbuckle, T. E., & Fraser, W. D. (2015). Maternal exposure to perfluorinated chemicals and reduced fecundity: the MIREC study. Human reproduction (Oxford, England), 30(3), 701–709. https://doi.org/10.1093/humrep/deu350 (https://doi.org/10.1093/humrep/deu350)

Velez et al observed if maternal exposure to PFOS, PFOA, and PFHxS affected female fecundity using the maternal-infant research on environmental chemicals cohort. The group reported that their data supported evidence that suggests exposure to PFOA and PFHxS may reduce fecundability [81].

Vigeh, M., Yokoyama, K., Ramezanzadeh, F., Dahaghin, M., Sakai, T., Morita, Y., Kitamura, F., Sato, H., & Kobayashi, Y. (2006). Lead and other trace metals in preeclampsia: a case-control study in Tehran, Iran. Environmental research, 100(2), 268–275. https://doi.org/10.1016/j.envres.2005.05.005 (https://doi.org/10.1016/j.envres.2005.05.005)

Vigeh et al assessed the effects of environmental exposures to trace metals on the incidence of preeclampsia. The group reported that environmental exposure to lead, antimony, and manganese may increase the risk of preeclampsia in women without occupational exposure. Additionally, metal concentration in umbilical cord blood may be a sensitive indicator for maternal toxicity, as compared to whole blood samples [82].

Wei, L., Qiao, P., Shi, Y., Ruan, Y., Yin, J., Wu, Q., & Shao, B. (2017). Triclosan/triclocarban levels in maternal and umbilical blood samples and their association with fetal malformation. Clinica chimica acta; international journal of clinical chemistry, 466, 133–137. https://doi.org/10.1016/j.cca.2016.12.024 (https://doi.org/10.1016/j.cca.2016.12.024)

Wei et al investigated the potential impact of exposure to triclosan and triclocarban on fetal abnormalities in Beijing. The group reported that significantly increased levels of these chemicals in maternal sera were associated with abnormal birth and fetal malformations [83].

Wikström, S., Hussein, G., Lingroth Karlsson, A., Lindh, C. H., & Bornehag, C. G. (2021). Exposure to perfluoroalkyl substances in early pregnancy and risk of sporadic first trimester miscarriage. Scientific reports, 11(1), 3568. https://doi.org/10.1038/s41598-021-82748-6 (https://doi.org/10.1038/s41598-021-82748-6)

Wilkstrom et al used the Sweedish SELMA pregnancy cohort to study if levels of PFAs in early pregnancy are associated with spontaneous abortion/miscarriage in the first trimester. The group found that a doubling of PFOA exposure was associated with miscarriage. A similar but not significant trend was observed following exposure to PFNA as well [84].

Xu, W., Zhang, W., Zhang, X., Dong, T., Zeng, H., & Fan, Q. (2017). Association between formaldehyde exposure and miscarriage in Chinese women. Medicine, 96(26), e7146. https://doi.org/10.1097/MD.0000000000007146 (https://doi.org/10.1097/MD.0000000000007146)

Xu et al conducted a case-control study aimed to assess whether higher plasma formaldehyde levels existed in women diagnosed with miscarriage and if this contributed to a higher risk of miscarriage among Chinese women [85]. The group found that plasma levels of formaldehyde were significantly higher in women who were diagnosed with miscarriage than those who delivered at term. Additionally, higher levels of formaldehyde were an independent risk factor for miscarriage, with higher levels being associated with a higher risk [85].

Xu, X., Chiung, Y. M., Lu, F., Qiu, S., Ji, M., & Huo, X. (2015). Associations of cadmium, bisphenol A and polychlorinated biphenyl co-exposure in utero with placental gene expression and neonatal outcomes. Reproductive toxicology (Elmsford, N.Y.), 52, 62–70. https://doi.org/10.1016/j.reprotox.2015.02.004 (https://doi.org/10.1016/j.reprotox.2015.02.004)

Xu et al studied the effects of in utero exposure to cadmium, bisphenol A and polychlorinated biphenyls on master regulatory genes using a cohort of pregnant women. The group reported that exposure to those chemicals may be associated with higher KISS1 gene expression [86].

▲ Obesity

Karakis, I., Baumfeld, Y., Landau, D., Gat, R., Shemesh, N., Yitshak-Sade, M., Tirosh, O., Sarov, B., & Novack, L. (2021). Exposure to metals and morbidity at eight years follow-up in women of childbearing age. Scientific reports, 11(1), 11429. https://doi.org/10.1038/s41598-021-90904-1 (https://doi.org/10.1038/s41598-021-90904-1)

Karakis et al conducted an exploratory study aimed to investigate the link between toxic metal content in women's urine and their morbidity. The group reported that increased levels of cadmium were linked to cancer, but increased levels of lead were associated with cardiovascular outcomes and obesity [87].

Kim, S. H., & Park, M. J. (2014). Phthalate exposure and childhood obesity. Annals of pediatric endocrinology & metabolism, 19(2), 69–75. https://doi.org/10.6065/apem.2014.19.2.69 (https://doi.org/10.6065/apem.2014.19.2.69)

Kim et al searched the literature for in vivo and in vitro studies that investigated the relationship between phthalate exposure and obesity. Within this review, they discussed possible biological mechanisms by which phthalate exposure could lead to obesity in humans and animals [88].

Lauritzen, H.B., Larose, T.L., Øien, T. et al. Prenatal exposure to persistent organic pollutants and child overweight/obesity at 5-year follow-up: a prospective cohort study. Environ Health 17, 9 (2018). https://doi.org/10.1186/s12940-017-0338-x (https://doi.org/10.1186/s12940-017-0338-x)

Lauritzen et al aimed to investigate the relationship between prenatal exposure to persistent organic pollutants and offspring weight gain. The group reported that maternal serum PFAS concentrations were positively associated with child overweight/obesity trends at the 5-year follow-up [67].

Lee K. (2018). Blood mercury concentration in relation to metabolic and weight phenotypes using the KNHANES 2011-2013 data. International archives of occupational and environmental health, 91(2), 185–193. https://doi.org/10.1007/s00420-017-1269-0 (https://doi.org/10.1007/s00420-017-1269-0)

Lee examined the association of blood mercury levels with metabolic and weight phenotypes. Lee reported that blood mercury concentration was associated with both metabolic syndrome and obesity. This association occurred in a dose-dependent manner [89].

Shin, J. C., Lee, E., An, S., Jin, S. H., Ha, J., Choi, W. J., & Noh, M. (2020). Benzophenone-3 and benzophenone-8 exhibit obesogenic activity via peroxisome proliferator-activated receptor γ pathway. *Toxicology in vitro: an international journal published in association with BIBRA*, *67*, 104886. https://doi.org/10.1016/j.tiv.2020.104886 (https://doi.org/10.1016/j.tiv.2020.104886)

Shin et al used a cell-based study to demonstrate that benzophenone-3 and benzophenone-8 are obesogenic environmental chemicals. This means that these chemicals may increase the risk of obesity. These chemicals are commonly used in products such as sunscreen because they can filter ultraviolet rays of light [90].

Tian, Y. P., Zeng, X. W., Bloom, M. S., Lin, S., Wang, S. Q., Yim, S., Yang, M., Chu, C., Gurram, N., Hu, L. W., Liu, K. K., Yang, B. Y., Feng, D., Liu, R. Q., Nian, M., & Dong, G. H. (2019). Isomers of perfluoroalkyl substances and overweight status among Chinese by sex status: Isomers of C8 Health Project in China. Environment international, 124, 130–138. https://doi.org/10.1016/j.envint.2019.01.006 (https://doi.org/10.1016/j.envint.2019.01.006)

Tian et al conducted a study using Chinese women to identify a relationship between obesity and serum isomers of PFOS, PFOA, and other PFASs. The group reported that PFASs and their isomers are positively associated with being overweight or having an increased waist circumference in women primarily [91].

Uche, U. I., & King, C. C. (2022). Age, gender, and racial/ethnic differences in the association of triclocarban with adulthood obesity using NHANES 2013-2016. Archives of environmental & occupational health, 77(1), 68–75. https://doi.org/10.1080/19338244.2020.1853016 (https://doi.org/10.1080/19338244.2020.1853016)

Uche and King examined the association between triclocarban and obesity among US adults. The group reported that triclocarban was associated with obesity. The risk of obesity increased with older age. The group also reported racial differences in this association [92].

Xing, Y., Xia, W., Zhang, B., Zhou, A., Huang, Z., Zhang, H., Liu, H., Jiang, Y., Hu, C., Chen, X., Xu, S., & Li, Y. (2018). Relation between cadmium exposure and gestational diabetes mellitus. Environment international, 113, 300–305. https://doi.org/10.1016/j.envint.2018.01.001 (https://doi.org/10.1016/j.envint.2018.01.001)

Xing et al measured the urinary cadmium concentration of pregnant Chinese women to investigate whether cadmium exposure during pregnancy was associated with gestational diabetes mellitus. The group reported that a 3-fold increase in cadmium levels was associated with an increased risk of gestational diabetes. Risk factors such as obesity or being overweight further increased the risk of gestational diabetes associated with exposure to cadmium [20].

Cancer

Cramer, D. W., Vitonis, A. F., Terry, K. L., Welch, W. R., & Titus, L. J. (2016). The Association Between Talc Use and Ovarian Cancer: A Retrospective Case-Control Study in Two US States. Epidemiology (Cambridge, Mass.), 27(3), 334–346. https://doi.org/10.1097/EDE.0000000000000434 (https://doi.org/10.1097/EDE.0000000000000434)

Cramer et al investigated the association between ovarian cancer and the genital use of talc. The group reported that the risk for epithelial ovarian cancer from genital talc use varies by histologic subtype, menopausal status, hormone therapy use, weight, and smoking history [93].

Duong, A., Steinmaus, C., McHale, C. M., Vaughan, C. P., & Zhang, L. (2011). Reproductive and developmental toxicity of formaldehyde: a systematic review. Mutation research, 728(3), 118–138. https://doi.org/10.1016/j.mrrev.2011.07.003 (https://doi.org/10.1016/j.mrrev.2011.07.003)

Duong et al systematically evaluated evidence of an association between formaldehyde exposure and adverse reproductive and developmental effects in human populations and animal studies. The group discussed animal and human studies that supported this association and offered potential mechanisms [94].

Gabriel, I. M., Vitonis, A. F., Welch, W. R., Titus, L., & Cramer, D. W. (2019). Douching, Talc Use, and Risk for Ovarian Cancer and Conditions Related to Genital Tract Inflammation. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 28(11), 1835–1844. https://doi.org/10.1158/1055-9965.EPI-19-0375 (https://doi.org/10.1158/1055-9965.EPI-19-0375)

Gabriel et al investigated the relationship between douching and inflammatory genital conditions, in combination with genital talc use and epithelial ovarian cancer. The group reported that douching is not an independent risk factor for ovarian cancer; however, the combination of talc use and store-bought douches may increase the risk for epithelial ovarian cancer [95].

Gates, M. A., Tworoger, S. S., Terry, K. L., Titus-Ernstoff, L., Rosner, B., De Vivo, I., Cramer, D. W., & Hankinson, S. E. (2008). Talc use, variants of the GSTM1, GSTT1, and NAT2 genes, and risk of epithelial ovarian cancer. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 17(9), 2436–2444. https://doi.org/10.1158/1055-9965.EPI-08-0399 (https://doi.org/10.1158/1055-9965.EPI-08-0399)

Gates et al analyzed interactions between talc use and genes in detoxification pathways. The group reported that women with certain genetic variants may have a higher risk of ovarian cancer associated with genital use of talc. Risk of disease varied by differences in phenotype between GSTT1 and GSTM1 [96].

Gong, L., Luo, Z., Tang, H., Tan, X., Xie, L., Lei, Y., He, C., Ma, J., & Han, S. (2020). Integrative, genome-wide association study identifies chemicals associated with common women's malignancies. Genomics, 112(6), 5029–5036. https://doi.org/10.1016/j.ygeno.2020.09.011 (https://doi.org/10.1016/j.ygeno.2020.09.011)

Gong et al performed a transcriptome-wide association study and a gene enrichment analysis to identify correlations between chemical exposure and altered gene expression using a United Kingdom biobank and comparative toxicogenomic database. They found that 5 chemicals (NSC668394, glafenine, methylnitronitrosoguanidine, fenofibrate, and methylparaben) were associated with an increased incidence of both breast and cervical cancer [97].

Gonzalez, N. L., O'Brien, K. M., D'Aloisio, A. A., Sandler, D. P., & Weinberg, C. R. (2016). Douching, Talc Use, and Risk of Ovarian Cancer. Epidemiology (Cambridge, Mass.), 27(6), 797–802. https://doi.org/10.1097/EDE.0000000000000528

(https://doi.org/10.1097/EDE.0000000000000528)

Gonzalez et al used data from the Sister cohort to identify an association between vaginal douching and ovarian cancer. The group reported that douching, but not talc use was associated with an increased risk of ovarian cancer [98].

Harlow, B. L., & Weiss, N. S. (1989). A case-control study of borderline ovarian tumors: the influence of perineal exposure to talc. American journal of epidemiology, 130(2), 390–394. https://doi.org/10.1093/oxfordjournals.aje.a115345 (https://doi.org/10.1093/oxfordjournals.aje.a115345)

Harlow et al conducted a case-control study to determine the association between ovarian tumors and the use of hygienic powders in Washington State. The group reported that women who use deodorized powders alone or in combination with talc-containing powders had 2.8 times the risk of ovarian tumors [99].

Karakis, I., Baumfeld, Y., Landau, D., Gat, R., Shemesh, N., Yitshak-Sade, M., Tirosh, O., Sarov, B., & Novack, L. (2021). Exposure to metals and morbidity at eight years follow-up in women of childbearing age. Scientific reports, 11(1), 11429. https://doi.org/10.1038/s41598-021-90904-1 (https://doi.org/10.1038/s41598-021-90904-1)

Karakis et al conducted an exploratory study aimed to investigate the link between toxic metal content in women's urine and their morbidity. The group reported that increased levels of cadmium were linked to cancer, but increased levels of lead were associated with cardiovascular outcomes and obesity [87].

Merritt, M. A., Green, A. C., Nagle, C. M., Webb, P. M., Australian Cancer Study (Ovarian Cancer), & Australian Ovarian Cancer Study Group (2008). Talcum powder, chronic pelvic inflammation and NSAIDs in relation to risk of epithelial ovarian cancer. International journal of cancer, 122(1), 170–176. https://doi.org/10.1002/ijc.23017 (https://doi.org/10.1002/ijc.23017)

Merritt et al evaluated the potential role of chronic local ovarian inflammation in the development of the major subtypes of epithelial ovarian cancer. The group confirmed that talc use was associated with ovarian cancer, but regular use of aspirin was inversely associated with the risk of low malignant potential mucinous ovarian tumors [100].

Mills, P. K., Riordan, D. G., Cress, R. D., & Young, H. A. (2004). Perineal talc exposure and epithelial ovarian cancer risk in the Central Valley of California. International journal of cancer, 112(3), 458–464. https://doi.org/10.1002/ijc.20434 (https://doi.org/10.1002/ijc.20434)

Mills et al performed a population-based epidemiologic case-control study to determine if perineal talc use was associated with ovarian cancer. The group found that talc use was commonly used in women with serious invasive tumors [101].

Terry, K. L., Karageorgi, S., Shvetsov, Y. B., Merritt, M. A., Lurie, G., Thompson, P. J., Carney, M. E., Weber, R. P., Akushevich, L., Lo-Ciganic, W. H., Cushing-Haugen, K., Sieh, W., Moysich, K., Doherty, J. A., Nagle, C. M., Berchuck, A., Pearce, C. L., Pike, M., Ness, R. B., Webb, P. M., … Ovarian Cancer Association Consortium (2013). Genital powder use and risk of ovarian cancer: a pooled analysis of 8,525 cases and 9,859 controls. Cancer prevention research (Philadelphia, Pa.), 6(8), 811–821. https://doi.org/10.1158/1940-6207.CAPR-13-0037 (https://doi.org/10.1158/1940-6207.CAPR-13-0037)

Terry et al estimated the association between self-reported genital powder use and epithelial ovarian cancer risk in eight population-based case-control studies. The group reported that genital powder is a modifiable exposure associated with small-to-moderate increases in the risk of most histologic subtypes of epithelial ovarian cancer [102].

Polycystic Ovarian Syndrome

Vagi, S.J., Azziz-Baumgartner, E., Sjödin, A. et al. Exploring the potential association between brominated diphenyl ethers, polychlorinated biphenyls, organochlorine pesticides, perfluorinated compounds, phthalates, and bisphenol a in polycystic ovary syndrome: a case–control study. BMC Endocr Disord 14, 86 (2014). https://doi.org/10.1186/1472-6823-14-86 (https://doi.org/10.1186/1472-6823-14-86)

Vagi et al conducted a case-control pilot study to determine whether women with PCOS have higher concentrations of specific environmental contaminants. The group reported that women with PCOS had higher serum concentrations of two PFCs, PFOA and PFOS. However, these women had lower urinary concentrations of mBP and mBzP [103].

Preterm Birth

Ashrap, P., Watkins, D. J., Mukherjee, B., Boss, J., Richards, M. J., Rosario, Z., Vélez-Vega, C. M., Alshawabkeh, A., Cordero, J. F., & Meeker, J. D. (2020). Maternal blood metal and metalloid concentrations in association with birth outcomes in Northern Puerto Rico. Environment international, 138, 105606. https://doi.org/10.1016/j.envint.2020.105606 (https://doi.org/10.1016/j.envint.2020.105606)

Ashrap et al conducted a study using the Puerto Rico Test site for Exploring Contamination Threats cohort to observe the effects of metals and metalloids on birth outcomes. The group reported that lead exposure was associated with a higher odd of preterm birth and shorter gestational age. To a smaller extent, manganese, zinc, mercury, and nickel were associated with similar outcomes [48].

Baker, B. H., Wu, H., Laue, H. E., Boivin, A., Gillet, V., Langlois, M. F., Bellenger, J. P., Baccarelli, A. A., & Takser, L. (2020). Methylparaben in meconium and risk of maternal thyroid dysfunction, adverse birth outcomes, and Attention-Deficit Hyperactivity Disorder (ADHD).

Environment international, 139, 105716. https://doi.org/10.1016/j.envint.2020.105716 (https://doi.org/10.1016/j.envint.2020.105716)

Baker et al used data from the GESTation and the Environment (GESTE) prospective observational pregnancy cohort to determine if there is a relationship between prenatal exposure to methylparaben and adverse health outcomes. The group reported that the presence of methylparaben in meconium samples was associated with the onset of preterm birth, decreased gestational age, attention-deficit hyperactivity disorder, and more [49].

Bloom, M. S., Wenzel, A. G., Brock, J. W., Kucklick, J. R., Wineland, R. J., Cruze, L., Unal, E. R., Yucel, R. M., Jiyessova, A., & Newman, R. B. (2019). Racial disparity in maternal phthalates exposure; Association with racial disparity in fetal growth and birth outcomes. Environment international, 127, 473–486. https://doi.org/10.1016/j.envint.2019.04.005 (https://doi.org/10.1016/j.envint.2019.04.005)

Bloom et al conducted an observational study of southeastern women in the United States to determine racial differences in maternal phthalate exposure, fetal growth, and birth outcomes. The group reported that high levels of MEHP were associated with small gestational age in whites, but not blacks. However, higher levels of MiBP were associated with preterm birth in blacks, but not whites. Overall, higher levels of MEP were associated with low birth weight in males but not females, independent of race [51].

Gokoel, A. R., Zijlmans, W., Covert, H. H., Abdoel Wahid, F., Shankar, A., MacDonald-Ottevanger, M. S., Hindori-Mohangoo, A. D., Wickliffe, J. K., Lichtveld, M. Y., & Harville, E. W. (2020). Influence of Prenatal Exposure to Mercury, Perceived Stress, and Depression on Birth Outcomes in Suriname: Results from the MeKiTamara Study. International journal of environmental research and public health, 17(12), 4444. https://doi.org/10.3390/ijerph17124444 (https://doi.org/10.3390/ijerph17124444)

Gokoel aimed to assess the influence of prenatal mercury exposure, perceived stress, and depression on adverse birth outcomes in Surinamese women within the Caribbean Consortium for Research in Environmental and Occupational Health prospective cohort. They reported associations between mercury exposure and preterm birth and perceived stress. However, depression was not associated with any birth outcomes [62].

Nyanza, E. C., Dewey, D., Manyama, M., Martin, J. W., Hatfield, J., & Bernier, F. P. (2020). Maternal exposure to arsenic and mercury and associated risk of adverse birth outcomes in small-scale gold mining communities in Northern Tanzania. Environment international, 137, 105450. https://doi.org/10.1016/j.envint.2019.105450 (https://doi.org/10.1016/j.envint.2019.105450)

Nyanza et al conducted a longitudinal prospective study to examine the association between prenatal and maternal exposure to arsenic/mercury exposure and birth outcomes in mining communities. The group reported that women living in mining

communities had higher blood levels of mercury than women who did not live in mining communities. Additionally, high levels of arsenic were associated with spontaneous abortion, stillbirth, and preterm birth, whereas mercury exposure was associated with stillbirth solely [71].

Rowland, A. S., Baird, D. D., Shore, D. L., Darden, B., & Wilcox, A. J. (1996). Ethylene oxide exposure may increase the risk of spontaneous abortion, preterm birth, and postterm birth. Epidemiology (Cambridge, Mass.), 7(4), 363–368. https://doi.org/10.1097/00001648-199607000-00005 (https://doi.org/10.1097/00001648-199607000-00005)

Rowland et al used a questionnaire to determine if exposure to ethylene oxide was associated with poor pregnancy outcomes. The group reported that exposure to this chemical may be associated with spontaneous abortion and preterm birth [104].

Santos, D., & Nascimento, L. (2019). Maternal exposure to benzene and toluene and preterm birth. A longitudinal study. Sao Paulo medical journal = Revista paulista de medicina, 137(6), 486–490. https://doi.org/10.1590/1516-3180.2019.0224170919 (https://doi.org/10.1590/1516-3180.2019.0224170919)

Santos et al investigated whether exposure to benzene and toluene among pregnant women contributes to preterm delivery. The group found that maternal exposure to benzene and toluene had an acute effect on preterm delivery [75].

▲ Fibroids

Jackson, L. W., Zullo, M. D., & Goldberg, J. M. (2008). The association between heavy metals, endometriosis and uterine myomas among premenopausal women: National Health and Nutrition Examination Survey 1999-2002. Human reproduction (Oxford, England), 23(3), 679–687. https://doi.org/10.1093/humrep/dem394 (https://doi.org/10.1093/humrep/dem394)

Jackson et al investigated the association between heavy metals and the risk of endometriosis and uterine myomas via a cross-sectional study using data from the National Health and Nutrition Examination Survey. The group reported that a dose-dependent response was associated with exposure to cadmium and the observation of endometriosis [30]

Johnstone, E. B., Louis, G. M., Parsons, P. J., Steuerwald, A. J., Palmer, C. D., Chen, Z., Sun, L., Hammoud, A. O., Dorais, J., & Peterson, C. M. (2014). Increased urinary cobalt and whole blood concentrations of cadmium and lead in women with uterine leiomyomata: Findings from the ENDO Study. Reproductive toxicology (Elmsford, N.Y.), 49, 27–32. https://doi.org/10.1016/j.reprotox.2014.06.007 (https://doi.org/10.1016/j.reprotox.2014.06.007)

Johnstone et al used a cohort of 473 women to identify an association between uterine fibroids and blood/urinary levels of heavy metals and trace elements. The odds of fibroid diagnosis were associated with higher levels of cadmium in whole blood, but not urinary samples. Overall, increased exposure to trace elements may promote fibroid growth/diagnosis [105]

Shen, Y., Dong, Y. M., Lu, Q., Xu, J., Wu, Y. T., Yun, S. S., & Ren, M. L. (2016). Phenolic environmental estrogens in urine and blood plasma from women with uterine leiomyoma: Epidemiological survey. *The journal of obstetrics and gynaecology research*, *42*(4), 440–445. https://doi.org/10.1111/jog.12928 (https://doi.org/10.1111/jog.12928)

Shen et al explored the effect of phenolic environmental estrogens on women with uterine leiomyoma using blood and urine sample from patients at Zhongda Hospital. The group reported that octylphenol concentrations in urine and blood were significantly higher in women with uterine leiomyomas. However, there were no significant differences between the levels of bisphenol A or nonylphenol [106].

Shen, Y., Xu, Q., Ren, M., Feng, X., Cai, Y., & Gao, Y. (2013). Measurement of phenolic environmental estrogens in women with uterine leiomyoma. *PloS one*, *8*(11), e79838. https://doi.org/10.1371/journal.pone.0079838 (https://doi.org/10.1371/journal.pone.0079838)

Shen et al investigated the effect of phenolic environmental estrogens on uterine leiomyomas from a perspective using the plasma samples of women living in China. The group reported that exposure to phenolic environmental estrogens (BPA, OP, and NP) in humans were related to leiomyoma tumorigenesis [107].

Ye, S., Chung, H. W., Jeong, K., Sung, Y. A., Lee, H., Park, S. Y., Kim, H., & Ha, E. H. (2017). Blood cadmium and volume of uterine fibroids in premenopausal women. *Annals of occupational and environmental medicine*, *29*, 22. https://doi.org/10.1186/s40557-017-0178-8 (https://doi.org/10.1186/s40557-017-0178-8)

Ye et al conducted a cross-sectional study using premenopausal women in Seoul to demonstrate the relationship between blood heavy metal concentrations and uterine fibroids. The group reported that there was no connection between the two factors. However, the odds of women having uterine fibroids increased with higher exposure to 3 metals [108].

Allergies

Deleo, V. A., Alexis, A., Warshaw, E. M., Sasseville, D., Maibach, H. I., DeKoven, J., Zug, K. A., Belsito, D. V., Fowler, J. F., Jr, Marks, J. G., Mathias, C. G., Pratt, M. D., Rietschel, R. L., Storrs, F. J., Taylor, J. S., & Zirwas, M. (2016). The Association of Race/Ethnicity and Patch Test Results:

North American Contact Dermatitis Group, 1998-2006. Dermatitis : contact, atopic, occupational, drug, 27(5), 288–292. https://doi.org/10.1097/DER.0000000000000220 (https://doi.org/10.1097/DER.0000000000000220)

Deleo aimed to identify differences in reactive dermatitis between races using the North American contact dermatitis group patch testing results. The group reported that blacks reacted more frequently to phenylenediamine compared to white [109].

Thürmann, L., Herberth, G., Seiwert, B., Schlittenbauer, L., Rolle-Kampczyk, U., Röder, S., Sack, U., Borte, M., von Bergen, M., Trump, S., Reemtsma, T., & Lehmann, I. (2021). Prenatal paraben exposure and atopic dermatitis-related outcomes among children. Allergy, 76(10), 3122–3132. https://doi.org/10.1111/all.14890 (https://doi.org/10.1111/all.14890)

Thurmann et al used members of the German mother-child study LINA, to determine if prenatal exposure to parabens was associated with an increased risk of atopic dermatitis in children. The group reported that prenatal exposure to ethylparaben and n-butylparaben increased children's risk of developing persistent atopic dermatitis at a very early age [110].

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