

ORIGINAL ARTICLE

Polycyclic aromatic hydrocarbons exposure in humans and reproductive health outcomes: An umbrella review

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ABSTRACT

Background: Polycyclic aromatic hydrocarbons (PAHs) are a public health threat, but evidence linking PAHs exposure to adverse reproductive health outcomes remains unclear. **Methods:** PubMed, Embase, and Web of Science were searched from inception to April 17, 2024, for systematic reviews and meta-analyses of observational studies on PAHs exposure and reproductive outcomes. Methodological quality was assessed using A Measurement Tool to Assess Systematic Reviews (AMSTAR). Random-effects models generated pooled estimates, without conversion among beta coefficients (β), odds ratios (OR), and risk ratios (RR). Evidence credibility was evaluated using evidence-class criteria and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). **Results:** Five articles reporting 15 associations were included. Four (26.7%) were significant: bladder cancer in aluminum production workers (RR = 1.26, 95% CI = 1.16, 1.36) and iron and steel foundry workers (RR = 1.36, 95% CI = 1.14, 1.62), birth weight reduction associated with PAHs DNA-adducts (OR = 1.02, 95% CI = 1.01, 1.03), and offspring attention deficit hyperactivity disorder (ADHD) associated with prenatal PAHs exposure (RR = 1.73, 95% CI = 1.15, 2.58). Dietary PAHs were not associated with birth length (β = -0.04, 95% CI = -0.09, 0.01) or birth weight (β = -5.65, 95% CI = -16.35, 5.06). Overall, the certainty of evidence was generally low or very low. **Conclusion:** Occupational and prenatal PAHs exposures may be associated with adverse outcomes, but evidence was low or very low certainty, and most birth-size outcomes showed no significant pooled associations.

Keywords: meta-analysis, observational study, polycyclic aromatic hydrocarbons, pregnancy, reproductive health.

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INTRODUCTION

Polycyclic aromatic hydrocarbons (PAHs) constitute a class of volatile organic compounds primarily from the incomplete burning processes of various materials, including coal, petroleum products, wood, tobacco leaves, and organic polymers.^[1] Their chemical structure, characterized by fused aromatic rings, contributes to their persistence in the environment and tendency to bioaccumulate, posing significant ecological and health risks.^[2] PAHs are ubiquitous environmental pollutants, with occupational exposure predominantly occurring through inhalation and dermal contact, while dietary intake represents the primary exposure pathway for the general population.^[3]

Recently, epidemiological research has significantly emphasized the detrimental effects of PAHs on human health, encompassing carcinogenicity, teratogenicity, and mutagenicity.^[3,4] These previous studies have indicated that exposure to PAHs may lead to adverse reproductive health outcomes. Nevertheless, these studies often present contradictory and inconsistent findings. A systematic review encompassing 15 cohort studies revealed a significant link between prenatal PAHs exposure and attention deficit hyperactivity disorder (ADHD).^[5] However, a recently published umbrella review (UR), which outlined the relationships between PAHs and non-cancerous health outcomes, failed to find significant associations for ADHD of offspring.^[6] Notably, both this UR and previous literature reviews primarily relied on qualitative analysis without providing a clear and accurate hierarchy of evidence across the full spectrum of reproductive health outcomes.^[6–8] This absence of evaluation for the certainty of evidence hinders the overall interpretation of research findings and their translation into public health policies. Furthermore, despite the abundance of evidence, research has often focused on total PAHs or specific subsets of related diseases, leading to fragmented understanding regarding the overall health impact of PAHs.^[9,10] It is noteworthy that while the International Agency for Research on Cancer (IARC) supports carcinogenic potential of certain PAHs in animals, no comprehensive epidemiological data were available to the IARC Working Group.^[11] Given above, it is crucial to conduct a thorough review to classify and quantify the existing evidence on PAH-related reproductive health outcomes.

UR is a valuable approach for assessing the robustness and validity of evidence through integrating and synthesizing individual meta-analysis on specific topics, ultimately yielding high-level evidence resources and enhancing the efficiency of tackling issues.^[12,13] Therefore, we embarked on an exhaustive UR of systematic reviews with meta-analyses of observational studies to investigate

the relationships linking PAHs exposure to various reproductive health outcomes, while evaluating the robustness and reliability of the available evidence to establish a clear hierarchy, ultimately promoting greater public consciousness about the harmful effects of PAHs and intensifying efforts towards its mitigation.

METHODS

Protocol registration

The UR complied with established guidelines from the Preferred Reporting Items for Systematic Reviews,^[14] as well as the Meta-Analysis of Observational Studies in Epidemiology guideline (Supplementary Table 1 and 2).^[15] This UR was not prospectively registered in International Prospective Register of Systematic Reviews (PROSPERO) or a similar registry.

Search strategy

We performed a thorough literature search across the PubMed, Embase, and Web of Science research data sources spanning from all available literature up to April 17, 2024. We aimed to ascertain systematic reviews and meta-analyses that examined the reproductive health effects associated with PAHs exposure. Supplementary Table 3 presents the detailed search strategy. Additionally, the references of qualified systematic reviews and meta-analyses were manually scrutinized. Two researchers separately screened articles for potential inclusion, with any kind of disparities dealt with by a third reviewer.

Selection criteria

The inclusion criteria were specified using the PECOS framework, which encompasses population, exposure, comparison, outcome, and study design: (1) Population: encompassing both adult and pediatric participants; (2) Exposure: total PAHs, specific PAHs compounds or their metabolites (*e.g.*, dietary PAHs, 1-hydroxypyrene [1-OHP], and PAHs DNA-adducts *etc.*); (3) Comparison: high versus low/dose-response analysis; (4) Outcome: any reproductive health outcomes (*e.g.*, adverse reproductive outcomes, adverse birth outcomes, and offspring outcomes, *etc.*); and (5) Study design: systematic reviews or meta-analyses regarding observational studies.

We applied the following exclusion criteria: (1) Systematic reviews without quantitative analysis; (2) Meta-analyses incorporating less than three primary studies; (3) Studies focusing on animal studies and/or genetic polymorphisms; (4) Studies failing to present comprehensive data, such as beta coefficients (β), relative risk (RR), odd ratio (OR), 95% confidence intervals (CIs), *etc.*; or (5) Non-English articles, or conference abstracts.

In the presence of similar datasets, priority was given to

meta-analyses with the highest research quality.^[16] When several meta-analyses resolving the very same study question, preference was granted to those with the largest datasets.^[16] Additionally, our study incorporated all forms of comparisons, including high versus low analysis, dose-response analysis, and other relevant comparative metrics, for any given outcome.^[17]

Data extraction

Qualified articles were resolved through discussion with a third reviewer. The extracted information included the first author, publication year, exposure assessment, reproductive health outcome, study design, number of primary studies, number of participants, the original effect measure, pooled effect estimates, and 95% CIs. The original effect measure was retained for each association: β values were extracted or recalculated as β , whereas ORs and RRs were extracted or recalculated as the corresponding ORs and RRs. The model used for pooling was also recorded. Information required for heterogeneity, prediction intervals, small-study effects, excess significance bias, and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) assessment was also collected.

Quality assessment of evidence and methods

We independently applied A Measurement Tool to Assess Systematic Reviews (AMSTAR) assessment tool to evaluate the methodological rigor of eligible articles.^[18] This tool provided a robust and reliable means of evaluating the quality of these reviews, covering 11 domains that include literature search, study selection, data extraction, statistical analysis, and bias assessment.^[19] Two trained investigators independently assessed the methodological quality. A senior researcher fellow assisted in resolving differences.

Based on the strategies applied in previously published URs,^[20,21] the strength of each association was classified into five categories: convincing, highly suggestive, suggestive, weak (ranging from class I to class IV) or non-significant (NS) evidence. Full classification criteria are detailed in Table 1.

A team of two investigators applied the GRADE framework to evaluate the evidence credibility. Initially categorized as low-quality, observational studies underwent assessment for potential downgrading based on predefined criteria such as risk of bias, inconsistency, indirectness, imprecision, and publication bias.^[22] The final ratings classified evidence as either high, moderate, low or very low quality.^[23]

Data analysis

For each association identified in the eligible meta-analyses, we recalculated the pooled effect estimate and its

95% CI using random-effects models. The null value was 0 for β estimates and 1 for RRs and ORs.^[24] Heterogeneity was evaluated through the I^2 metric; an I^2 value exceeding 50% indicated substantial heterogeneity, and over 75% indicated very substantial heterogeneity.^[25] In addition, we calculated the 95% prediction intervals (PIs) for the summary random effect sizes. This approach considers both inter-study heterogeneity and effect uncertainty, thereby offering an anticipated range for the effect size in future research examining the same association.^[26]

To identify small-study effects, we utilized the regression asymmetry test. Such effects occur when smaller studies report disproportionately larger effect sizes than larger studies.^[27] Small-study effects were considered present if the largest study exhibited a more conservative effect size than the overall estimate, coupled with a regression asymmetry test P -value below 0.10.^[28]

We evaluated excess significance bias using a *chi-square* test, comparing observed (O) to expected (E) number of studies with statistically significant results ($P < 0.05$).^[29] The strength of the studies was gauged by the effect size of the largest study, identified by the smallest standard error. The E number of statistically significant studies was determined through an algorithm based on a non-central t -distribution.^[30] The test for excess significance bias was considered affirmative if both O exceeded E and the P -value was under 0.10.^[29]

Sensitivity analyses

To ensure our findings are robust and reliable, sensitivity analyses were performed to evaluate the consistency of the summary associations. For those involving various observational study designs, we reassessed the strength of the evidence solely using data from cohort studies.^[31] Additionally, a sensitivity analysis was conducted within the initially excluded associations due to overlap.^[32] All statistical analyses were carried out using Stata 17 and RStudio 3.6.2.

RESULTS

Literature review

Through the exhaustive search across the three electronic databases, 5095 records were identified in total. After eliminating duplicates, 4435 titles and abstracts underwent screening, with a subsequent evaluation of 48 full-text articles for eligibility. Applying predefined inclusion criteria resulted in the selection of five articles, encompassing 15 associations in our UR (Figure 1).

Summary findings

Supplementary Table 4 presents the characteristics and general results of the 15 associations which were pub-

Table 1: Criteria for categorizing the credibility of evidence in this umbrella review

Evidence classification	Criteria
Convincing (Class I)	• $P < 10^{-6}$ under the random-effects models • Number of participants $> 20,000$ • Heterogeneity (I^2) $< 50\%$ • $P < 0.05$ of the largest study in the meta-analysis • 95% prediction interval that excluded the null value • No evidence of small-study effects ($P > 0.1$) • No evidence of excess significance bias ($O < E$ or $P > 0.1$)
Highly suggestive (Class II)	• $P < 10^{-6}$ under the random-effects models • Number of participants $> 20,000$ • $P < 0.05$ of the largest study in the meta-analysis
Suggestive (Class III)	• $P < 10^{-3}$ under the random-effects models • Number of participants $> 20,000$
Weak (Class IV)	• $P < 0.05$ under the random-effects models
Not significant	• $P > 0.05$ under the random-effects models

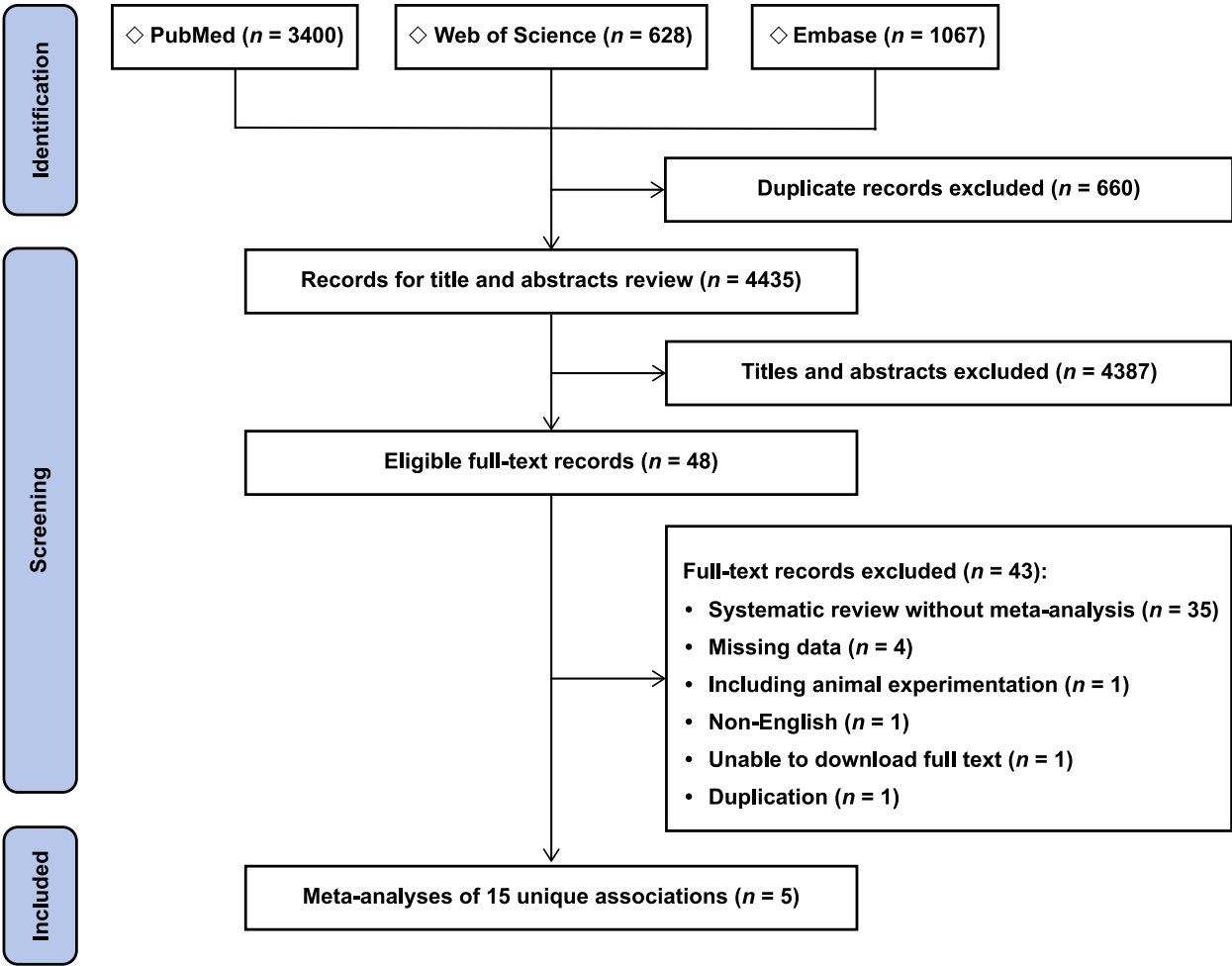


Figure 1. Flowchart of selection of studies for inclusion in umbrella review

lished from 2014 to 2024. For each association, the primary studies included ranged from 3 to 10. Additionally, the median number of participants across these studies was 2237 (range 837 to 604,950). Among the 15 associations, three (20.0%) focused on bladder cancer and 12 (80.0%) assessed birth outcomes. Additionally, eight (53.3%) and seven (46.7%) associations concentrated on total PAHs and PAH-metabolites, respectively.

According to the random-effects model, four (26.7%) associations reached statistical significance at $P < 0.05$. The remaining 11 (73.3%) associations were not statistically significant according to their pooled estimates and 95% CIs. Heterogeneity was low for 11 associations (73.3%) and high or very high for four (26.7%). The 95% PIs excluded the null value for two associations (13.3%). The effect estimates derived from the largest studies demonstrated nominal statistical significance in six (40.0%) associations. Moreover, excess significance bias was evident in one (6.7%) association, and no associations showed small-study effects.

Methodological quality

According to the AMSTAR criteria, three (60.0%) articles were evaluated as high quality (≥ 8 points), while two (40.0%) were deemed to be of moderate quality (4–7 points) (Figure 2). Generally, the key methodological limitations identified across the studies were the omission of excluded study lists and the failure to evaluate study quality or discuss individual study quality's influence on the overall results.

Strength and credibility of evidence

A total of 15 associations between PAHs exposure and health outcomes were summarized. Four associations (26.7%) reached statistical significance ($P < 0.05$). These included bladder cancer among aluminum production workers (RR = 1.26, 95% CI = 1.16, 1.36) and iron and steel foundry workers (RR = 1.36, 95% CI = 1.14, 1.62), birth-weight reduction in relation to PAHs DNA-adducts (OR = 1.02, 95% CI = 1.01, 1.03), and offspring ADHD in relation to prenatal PAHs exposure (RR = 1.73, 95% CI = 1.15, 2.58). The association between PAHs exposure and bladder cancer among carbon black production workers was not statistically significant (RR = 1.25, 95% CI = 0.87, 1.81).

For birth outcomes, dietary PAHs were not significantly associated with birth length ($\beta = -0.04$, 95% CI = -0.09, 0.01) or birth weight ($\beta = -5.65$, 95% CI = -16.35, 5.06). Similarly, no significant associations were observed between urinary 1-OHP and birth-weight reduction, newborn birth weight, birth length, head circumference, ponderal index, or cephalization index. The association between prenatal PAHs exposure and offspring ADHD was statistically significant, although the certainty of

evidence was rated as very low. Overall, most associations were supported by low or very low certainty evidence (Table 2).

Regarding the GRADE evidence, one association was rated as moderate certainty, three as low certainty, and 11 as very low certainty. The moderate-certainty evidence concerned urinary 1-OHP and birth-weight reduction, but the pooled association was not statistically significant. Most statistically significant associations, including the two occupational bladder cancer associations, PAHs DNA-adducts and birth-weight reduction, and prenatal PAHs exposure and offspring ADHD, were supported by very low-certainty evidence (Table 2 and Supplementary Table 5).

Sensitivity analyses

For two associations, which initially included various observational study designs, sensitivity analyses restricted to cohort studies produced results consistent with the primary analyses (Supplementary Table 6). Additionally, we excluded two associations from our UR owing to duplication, while the alterations in evidence quality were considered acceptable (Supplementary Table 7). Furthermore, findings from associations that were excluded due to insufficient data for quantitative synthesis were summarized in Supplementary Table 8, with results generally aligning with the main findings.

DISCUSSION

This UR synthesized 15 associations from five systematic reviews and meta-analyses examining PAHs exposure and reproductive health outcomes. Using random-effects models, four associations were statistically significant: occupational PAHs exposure and bladder cancer among aluminum production workers and iron and steel foundry workers, PAHs DNA-adducts and birth-weight reduction, and prenatal PAHs exposure and offspring ADHD. In contrast, pooled associations for most birth-size outcomes, including birth length, birth weight, head circumference, and related anthropometric indices, were not statistically significant. The certainty of evidence was generally low or very low, indicating that the observed associations should be interpreted cautiously.

Our findings support an association between occupational PAHs exposure and bladder cancer in aluminum production workers and iron and steel foundry workers. The association was not statistically significant among carbon black production workers, suggesting that occupational risk may vary according to the industrial process, exposure intensity, co-exposures, and workforce characteristics. The aluminum-worker association and the iron-and-steel association were classified as class IV, and both were rated as very low certainty by GRADE.

Table 2: Fifteen associations of PAHs and reproductive health outcomes

Outcomes	Exposure	Author, Year, Reference	Random effects	AMSTAR	Grade	Evidence class
Bladder cancer (aluminum production workers)	PAHs	Rota <i>et al.</i> , 2014 ^[33]	RR = 1.26 (1.16, 1.36)	6	Very low	IV
Bladder cancer (iron and steel foundry workers)	PAHs	Rota <i>et al.</i> , 2014 ^[33]	RR = 1.36 (1.14, 1.62)	6	Very low	IV
Bladder cancer (carbon black production workers)	PAHs	Rota <i>et al.</i> , 2014 ^[33]	RR = 1.25 (0.87, 1.81)	6	Very low	NS
Birth length	Dietary PAHs	Sewor <i>et al.</i> , 2024 ^[9]	β = -0.04 (-0.09, 0.01)	11	Very low	III
Birth weight	Dietary PAHs	Sewor <i>et al.</i> , 2024 ^[9]	β = -5.65 (-16.35, 5.06)	11	Very low	NS
Birth weight reduction	PAHs DNA-adducts	Yang <i>et al.</i> , 2020 ^[34]	OR = 1.02 (1.01, 1.03)	10	Very low	IV
Birth weight reduction	Urinary 1-OHP	Yang <i>et al.</i> , 2020 ^[34]	RR = 1.00 (0.96, 1.03)	10	Moderate	NS
Head circumference	Dietary PAHs	Sewor <i>et al.</i> , 2024 ^[9]	β = 0 (0, 0)	11	Low	NS
Low birth weight	PAHs	MoghaddamHosseini <i>et al.</i> , 2023 ^[35]	RR = 1.04 (0.97, 1.12)	9	Very low	NS
Newborn's birth weight	Urinary 1-OHP	MoghaddamHosseini <i>et al.</i> , 2023 ^[35]	β = -0.02 (-0.01, 0.07)	9	Very low	NS
Newborn's birth length	Urinary 1-OHP	MoghaddamHosseini <i>et al.</i> , 2023 ^[35]	β = -0.00 (-0.01, 0.01)	9	Very low	NS
Newborn's head circumference	Urinary 1-OHP	MoghaddamHosseini <i>et al.</i> , 2023 ^[35]	β = -0.11 (-0.34, 0.13)	9	Very low	NS
Newborn's ponderal index	Urinary 1-OHP	MoghaddamHosseini <i>et al.</i> , 2023 ^[35]	β = 0.00 (-0.01, 0.01)	9	Low	NS
Newborn's cephalization index	Urinary 1-OHP	MoghaddamHosseini <i>et al.</i> , 2023 ^[35]	β = 0.34 (-0.94, 1.63)	9	Low	NS
Offspring ADHD	Prenatal PAHs	Kaur <i>et al.</i> , 2023 ^[5]	RR = 1.73 (1.15, 2.58)	7	Very low	IV

ADHD, attention deficit hyperactivity disorder; AMSTAR, A Measurement Tool to Assess systematic Reviews; CI, confidence interval; DNA, deoxyribonucleic acid; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; NS, non-significant; PAHs, polycyclic aromatic hydrocarbons; 1-OHP, 1-hydroxypyrene. Evidence class of each meta-analysis was categorized into convincing, highly suggestive, suggestive, and weak, which was expressed as class I, II, III, and IV, respectively.

Therefore, these findings strengthen concern regarding occupational PAHs exposure but do not establish a high-certainty causal relationship. The results are consistent with the IARC classification of aluminum production as a Group 1 carcinogenic exposure circumstance^[11] and with previous evidence indicating elevated bladder cancer risk in several PAHs-exposed occupational groups.^[36] Future studies should use quantitative exposure assessment and sex-stratified analyses to clarify risks across specific industrial settings.

Contrary to previous studies, we found that the birth-outcome findings were heterogeneous and the conclusions were often not clear.^[37–41] Dietary PAHs were not significantly associated with birth length (β = -0.04, 95% CI = -0.09, 0.01) or birth weight (β = -5.65, 95% CI = -16.35, 5.06) in the pooled analyses. Although the birth-length association was categorized as class III according to the evidence-class criteria, its 95% CI included the null value; therefore, it should not be described as a statistically significant association. Similarly, no significant

associations were observed for urinary 1-OHP and the other newborn anthropometric outcomes. The association between PAHs DNA-adducts and birth-weight reduction was statistically significant (OR = 1.02, 95% CI = 1.01, 1.03), but its GRADE certainty was very low. Research showed that inter-racial genetic variation may influence susceptibility to prenatal PAHs exposures and subsequent birth outcomes.^[42] Hence, future investigations should prioritize examining the complex relationships between specific PAHs exposures and birth outcomes, while considering different PAHs sources and racial factors, to strengthen the attention given to vulnerable populations.

This UR represents a pioneering effort to comprehensively synthesize and update the current evidence linking PAHs exposure to various reproductive health outcomes, consolidating findings from meta-analyses and identifying the gaps and uncertainties systematically. In addition, it is noteworthy that our study stands out for its more comprehensive methodological approach and

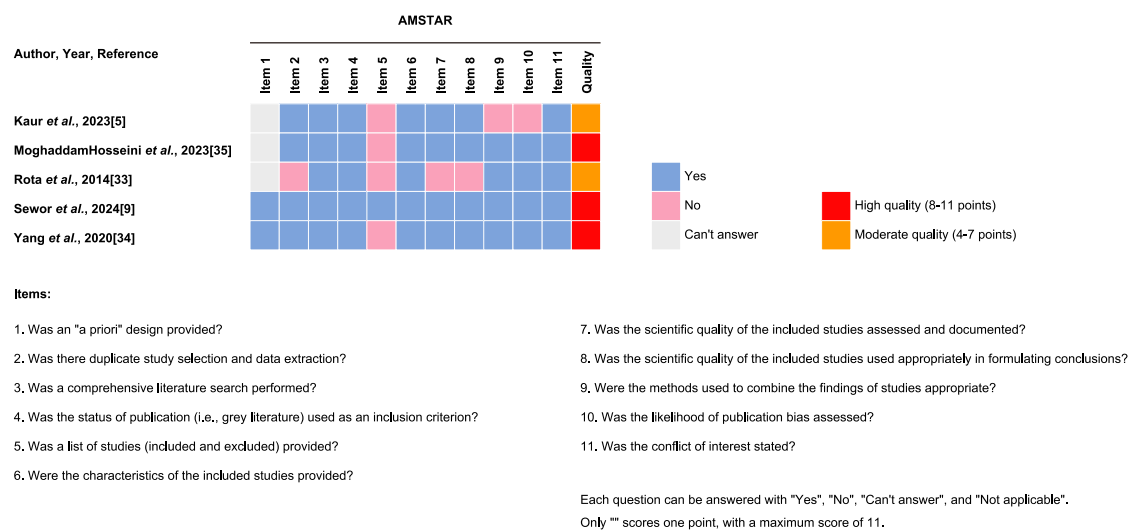


Figure 2. AMSTAR scores for each published meta-analysis. AMSTAR, A Measurement Tool to Assess systematic Reviews.

expanded scope compared to the work of Lee *et al.*^[6] Not only did we integrate both qualitative evaluations and quantitative analyses, but we also incorporated the assessments of both cancer and non-cancer outcomes while simultaneously focusing on general, vulnerable and occupational populations. Moreover, we implemented systematic methods, encompassing duplicate study selection and meticulous data extraction processes, coupled with rigorous evidence classification criteria and comprehensive GRADE assessments, which allowed us to thoroughly evaluate the credibility and quality of the available evidence. Furthermore, employing the AMSTAR tool to evaluate methodological rigor, we found that all included studies scored in the moderate-to-high range, with 60% rating as high quality, thereby ensuring the reliability of our findings. Additionally, we employed multiple sensitivity analyses to determine the stability of our results.

There are some limitations in this UR that should be acknowledged. Firstly, this UR was not prospectively registered in PROSPERO or a similar registry. Although we strictly adhered to PRISMA and MOOSE guidelines and prespecified the protocol a priori, the absence of registration may increase the risk of selective reporting bias and should be considered when interpreting the findings. Secondly, the exclusion of systematic reviews containing only qualitative analyses and meta-analyses lacking study-specific data, resulted in a potential for misestimation of true associations between PAH and the reproductive health outcomes. Nevertheless, we took the additional step of compiling the findings from excluded qualitative studies, and confirmed consistency in results. While it is plausible that some of the most recent primary studies may have been overlooked, the consistency observed in overlapping meta-analyses for

identical associations corroborates the reliability of our results. Furthermore, our UR exclusively focused on meta-analyses derived from observational studies, which inherently possess certain limitations (*e.g.*, selection and recall bias). However, given the ethical constraints surrounding this topic, randomized controlled trials are challenging to implement, making observational studies the most viable and appropriate approach. To address this concern regarding the robustness of findings from observational studies, we reanalyzed all the included associations using only cohort studies, which confirmed the consistency of our results. Thirdly, the GRADE system recommends starting the evaluation of observational studies at a low credibility threshold due to their inherent design limitations mentioned above. Consequently, the evidence in our UR was predominantly categorized as very low credibility. Fourthly, the variability in exposure assessment methods across primary studies poses a significant challenge. The precision and dependability of PAHs exposure estimates can vary considerably depending on the methodology employed, potentially biasing results.^[43] Although biomonitoring-based assessments could offer a more comprehensive evaluation of total human exposure, most biomonitoring studies have predominantly focused on measuring urinary PAHs metabolites, which primarily reflects recent exposure.^[44] Developing and validating accurate biomarkers of long-term PAHs exposure, such as fat tissue monitoring,^[45] should be a priority for future research to elucidate the impact of PAHs exposure across the life course. Fifthly, it is important to acknowledge that the complexity of PAHs mixtures and the limited set of PAHs typically measured,^[2,46] may result in an underestimation of the true health risks. More efficient PAHs measurement methods and more rigorous monitoring strategies are necessary for future studies. Notably, the PAHs analyzed

in our compiled associations were predominantly considered as a whole without distinguishing specific compounds, potentially obscuring important differences in physicochemical properties, toxicity, and exposure levels among individual PAHs.^[47,48] Future research should focus more on evaluating specific PAHs compounds to accurately assess their respective health risks and elucidate compound-specific effects.

CONCLUSION

This UR summarized 15 associations between PAHs exposure and reproductive health outcomes. Four associations were statistically significant: increased bladder cancer risk among aluminum production workers and iron and steel foundry workers, birth-weight reduction associated with PAHs DNA-adducts, and offspring ADHD associated with prenatal PAHs exposure. However, pooled associations for dietary PAHs and birth length or birth weight, as well as most urinary 1-OHP-related newborn anthropometric outcomes, were not statistically significant. The certainty of evidence was moderate for one non-significant association, low for three associations, and very low for 11 associations. These findings indicate that PAHs may pose important occupational and developmental health risks, but the current evidence remains insufficient to support strong causal conclusions. Future prospective studies should apply repeated and quantitative exposure measurements, harmonized outcome definitions, careful control of co-exposures and confounders, and sufficiently large samples to clarify the effects of specific PAHs and exposure biomarkers on reproductive health.

DECLARATIONS

Supplementary information

Supplementary materials are only available at the official site of the journal (<https://www.hksmp.com/journals/prm>).

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None.

Author contributions

Wang Y, Dong BH: Conceptualization, Writing—Original draft preparation, Writing—Reviewing and Editing. Wang Y, Chen YL, Chen LL, Dong BH : Conceptualization, Supervision. Wang Y, Chen YL, Chen LL, Dong BH: Supervision, Project administration.

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Ethical approval

Not applicable.

Informed consent

Not applicable.

Use of large language models, AI and machine learning tools

None declared.

Data availability statement

Processed datasets used in the analysis are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare no competing interest.

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