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Benzoyl Peroxide and Malignancy Risk: A Systematic Review and Meta-analysis of Over 4 Million Patients

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Dear Editor,

Benzoyl peroxide (BPO) is a widely used agent in the treatment of acne vulgaris (AV). Recently, concerns have emerged regarding the safety of BPO products, as they have been reported to degrade into benzene, particularly when exposed to elevated temperatures (37°C). Benzene exposure has been associated with an increased risk of several malignancies, particularly hematologic malignancies and internal malignancies, especially lung cancer.[1,2] Given the critical role of BPO in acne management and the potential safety concerns, we conducted a systematic review and meta-analysis to evaluate the association between BPO use for acne and the risk of developing malignancies.

A systematic search was conducted in PubMed, Embase, and Web of Science following PRISMA guidelines.[3] Inclusion criteria were: (1) Human participants with a diagnosis of AV or who were using BPO; (2) A clearly defined comparator group not exposed to BPO (eg, acne patients without BPO use, or non-acne controls). The search strategy was ('Benzoyl peroxide' OR BPO) AND ('hematologic malignancies' OR 'hematologic malignancy' OR 'blood cancer' OR leukemia OR lymphoma OR 'multiple myeloma' OR 'myelodysplastic syndrome' OR 'lung cancer'). Statistical analyses were performed using R version 4.3.2. A random-effects model was performed to determine the proportion with a 95% confidence interval (CI). Heterogeneity was assessed using the I^2 statistic.

Four studies were included (1, 2, 4, 5), encompassing a total of 4,062,218 patients. Three of these studies reported baseline characteristics; among them, the mean age was 20.3 years, 64.1% were female, and 63.0% were White. Additional baseline characteristics are presented in Table 1. Risk of leukemia was reported in all studies, and the pooled analysis (Figure 1A) showed no statistically significant association between patients using BPO and those who were not (RR 0.91; 95% CI 0.68, 1.21; P=0.5; I^2 = 69.7%). Three studies specifically reported on the risk of acute myeloid leukemia (AML), and the pooled analysis (Figure 1B) also did not demonstrate a statistically significant difference between the two groups (RR 0.98; 95% CI 0.67, 1.43; P=0.9; I^2 = 77.3%). Two studies reported on the risk of lymphoma (Figure 1C) and any hematologic malignancy (Figure 1D); neither analysis showed a statistically significant increase in risk, lymphoma (RR 0.99; 95% CI 0.70, 1.41; P=0.9; I^2=79.0%) and any hematologic malignancy (RR 0.99; 95% CI 0.92, 1.06; P=0.7; I^2 = 0%). Internal malignancy was reported by one study, which also found no significant difference in risk between BPO users and non-users. One study reported the risk of lung cancer, likewise finding no statistically significant difference.

Our pooled analyses of more than four million patients consistently demonstrated no statistically significant association between BPO use and the risk of leukemia, acute myeloid leukemia, lymphoma, or any hematologic malignancies. These results suggest no significant association between BPO use and malignancy risk.

TABLE 1.

Baseline Characteristics of Included Studies

Study	Study design	Patients, n	Age at index, y§	Female, %	White, %	Hispanic or latino, %	Tobacco use, %	Alcohol, %
CHAN 2024	Retrospective cohort	410,997‡ 410,997†	22.2 (11.6)‡ 22.1 (11.7 †	63.1‡ 63.0†	52.5‡ 52.7†	14.1‡ 14.2†	N/A	N/A
GARATE 2024	Retrospective cohort	91,055‡ 91,055†	22.24 (7.4)‡ 22.25 (7.5)†	61.8‡ 62.4†	65.8‡ 66.6†	9.1‡ 8.6†	1.6‡ 1.7†	0.4‡ 0.4†
VEENSTRA 2024	Cross-sectional analysis	668,756‡ 1,583,316†	N/A	N/A	N/A	N/A	N/A	N/A
VEENSTRA 2025	Retrospective cohort	115,257‡ 690,785†	18.4 (5.0)‡ 18.1 (5.0)†	65.5‡ 65.7†	72.0‡ 73.0†	9.9‡ 9.5†	13‡ 12.3†	4.1‡ 3.8†

‡ Intervention; † Control; § Mean (SD).

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FIGURE 1A. Forest plot on risk of leukemia.

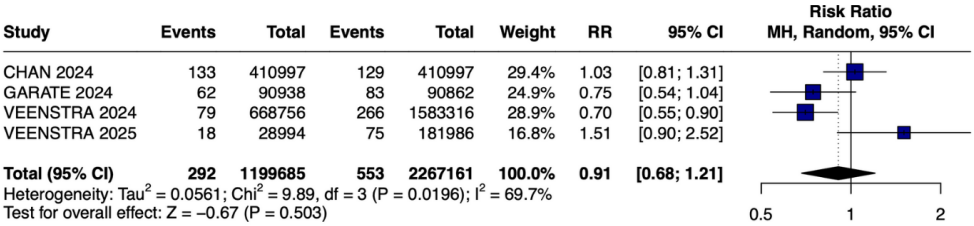


FIGURE 1B. Forest plot on risk of acute myeloid leukemia.

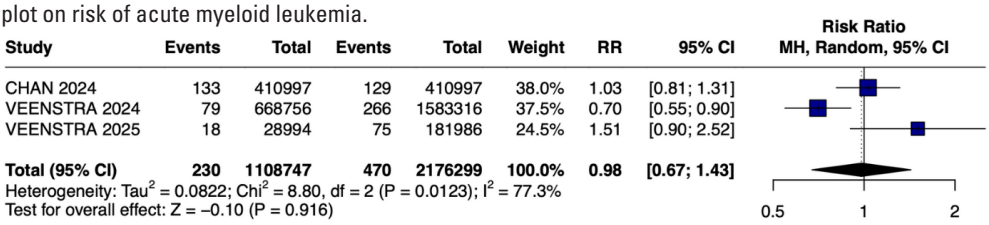


FIGURE 1C. Forest plot on risk of lymphoma.

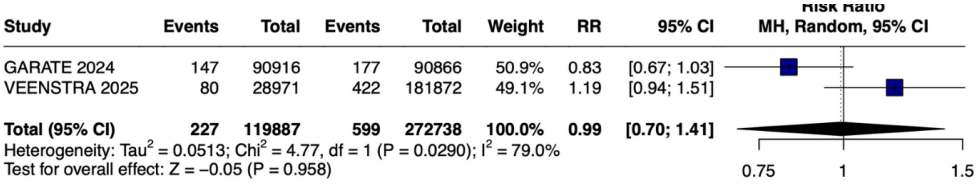
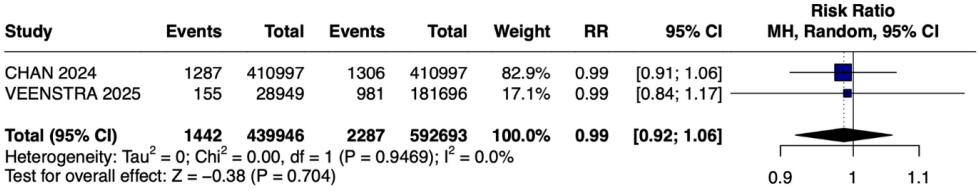


FIGURE 1D. Forest plot on risk of any hematologic malignancy.



Recent commentaries, such as that by Del Rosso,[6] have emphasized the uncertainty and 'many unanswered questions' surrounding benzoyl peroxide's safety profile in the context of benzene formation. Our findings are in line with those of Czyz et al[7] reported that despite raising concerns about benzene formation, they likewise concluded that available evidence does not support an elevated risk of hematologic malignancies with BPO use in pediatric populations. Study limitations include potential exposure misclassification due to reliance on prescription records or diagnostic codes and insufficient detailed exposure data (dosage, duration, cumulative use) across studies, hindering dose-response analysis.

Our findings suggest that the use of BPO for acne does not significantly increase the risk of benzene-related cancers

DISCLOSURES

The authors have no conflicts of interest or financial relationships to disclose relevant to the content of this article.

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