County-Level Associations Between Airborne Toxicant Emissions and Ewing Sarcoma Diagnosis in the United States

Amanda Perrotta MS, BHS(PA), BS, Kole Joachim BA, Adrian Lin BS, Brandon Gettleman MD, Christopher Hamad MD, Sumin Jeong BSN, Michael Fice MD, Lauren Wessel MD, Nicholas Bernthal MD, Alexander Christ MD

[1]David Geffen School of Medicine at UCLA, Department of Orthopaedic Surgery, Los Angeles, CA

aperrotta@mednet.ucla.edu

Disclosures: Nicholas M. Bernthal (3B-Biomet; 3B-Daiichi Sankyo; 3B-Deciphera; 4-National Institutes of Health [NIAMS & NICHD]; 3B-Onkos; 3B-Zimmer; 5-Trellis; 9-Musculoskeletal Tumor Society; 9-Orthopaedic Research and Education Foundation), Alexander B. Christ (3B-Onkos Surgical, Inc.; 3B-Smith & Nephew, Inc.; 3B-Zimmer Biomet Holdings, Inc.; 3B-Stryker; 3B-Daiichi Sankyo; 3B-Globus Medical, Inc.; 9-AAOS Hip & Knee Evaluation Committee; 9-MSTS Fellowship Committee; 9-ORS Implant Section President; 8-Arthroplasty Editorial Board).

INTRODUCTION: Ewing sarcoma, a rare pediatric bone cancer with unclear origins, has been hypothesized to link with environmental factors like airborne toxins, though population evidence remains scarce. This study investigates associations between industrial airborne chemical emissions and Ewing sarcoma incidence across U.S. counties.

METHODS: We conducted a cross-sectional ecological study using U.S. county-level data on Ewing sarcoma diagnoses the Surveillance, Epidemiology, and End Results (SEER) 2020 county population estimates derived from ZIP Code Tabulation Areas, and industrial airborne chemical emissions (EPA Toxics Release Inventory, 24 chemicals). Counties were categorized as “high” or “low” exposure for each chemical based on median emission thresholds. Ewing sarcoma incidence per 1,000,000 population was compared between groups using Mann-Whitney U tests.

RESULTS: Of 3,229 total U.S. counties, 1,090 had Ewing sarcoma data, and 656 had complete data on case counts, population, and chemical exposure. 17 chemicals met inclusion criteria with ≥10 counties per exposure group. Xylene (12.95 vs 7.63, p=0.001), ethylbenzene (13.56 vs 9.33, p=0.007), toluene (12.88 vs 7.35, p=0.01), naphthalene (13.56 vs 10.65, p=0.016), nickel compounds, (11.75 vs 9.41, p=0.019) and benzo[g,h,i]perylene (13.13 vs 10.84, p=0.005) was determined to be statistically significant in counties with high exposure levels (Figure 1).

DISCUSSION: Ewing sarcoma is a rare pediatric bone tumor driven by the EWS-FLI1 fusion protein, with traditionally minimal emphasis on environmental factors. Our study identifies a potential association between higher county-level exposure to specific airborne toxicants—including xylene, ethylbenzene, toluene, naphthalene, nickel compounds, and benzo[g,h,i]perylene—and increased Ewing sarcoma diagnosis rates. High-molecular weight polycyclic aromatic hydrocarbons and nickel compounds are known to induce DNA damage and genomic instability, suggesting plausible mechanisms for facilitating the chromosomal translocations underlying Ewing sarcoma oncogenesis. By leveraging chemical-level emission data from the EPA Toxics Release Inventory and SEER diagnosis rates, this study provides more precise environmental risk assessment than previous analyses using aggregate air quality metrics, highlighting the importance of specific pollutant exposures in pediatric cancer risk. While causality cannot be inferred, these findings support further investigation of environmental risk factors in Ewing sarcoma, particularly in high-emission geographic clusters.

SIGNIFICANCE/CLINICAL RELEVANCE: These findings suggest that targeted monitoring of airborne chemical exposures may inform pediatric cancer prevention strategies and environmental health policies. Clinically, recognition of high-risk geographic areas may support early detection efforts and guide future studies investigating mechanistic links between environmental toxins and Ewing sarcoma development.

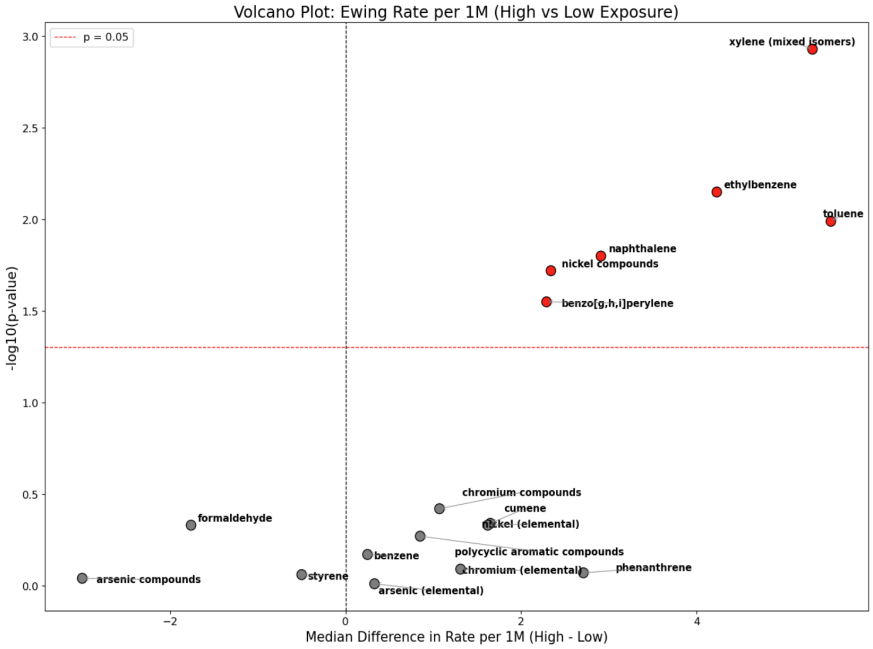

Figure 1. Volcano plot illustrating the association between chemical exposure classification and Ewing sarcoma incidence rates per million individuals. The x-axis represents the median difference in Ewing sarcoma incidence rates per million people between high and low exposure groups for each chemical. The y-axis shows the statistical significance of these differences as –log10(p-value). Chemicals that are both highly associated (i.e., large rate differences) and statistically significant (above the red horizontal threshold line) are labeled and highlighted in red. Xylene, ethylbenzene, toluene, naphthalene, nickel compounds, and benzo[g,h,i]perylene show the strongest association with increased Ewing sarcoma diagnosis incidence in high-exposure areas.