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Supplemental Material

Association between Outdoor Air Pollution and Childhood Leukemia: A Systematic Review and Dose–Response Meta-Analysis

Tommaso Filippini, Elizabeth E. Hatch, Kenneth J. Rothman, Julia E. Heck, Andrew S. Park, Alessio Crippa, Nicola Orsini, and Marco Vinceti

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Table S1. Detailed PECOS statement used for identification of search strategies implemented on online databases.

Table S2. Newcastle - Ottawa quality assessment scale for included studies: details used for study score assignment. High quality choices are identified with a 'star' (i.e. asterisk). A maximum of one 'star' for each item within the 'Selection' and 'Exposure/Outcome' categories; maximum of two 'stars' for 'Comparability' can be identified.

Table S3. Newcastle - Ottawa quality assessment scale (NOS) for included studies: details of score assignment for each included study, divided according to case-control and cohort study design. S-1 through S-4 correspond to the 'Selection' questions, C-1 and C-2 correspond to the 'Comparability' questions, E-1 through E-3 correspond to the 'Exposure' questions, and O-1 through O-3 correspond to the 'Outcome' questions reported in Table S2. Letters stand for answers to each question reported in Table S2, and number in parenthesis indicate if the given answer identified a high (1) or low (0) quality rank. Total score is the sum of the score for each answer to the NOS scale. A high score indicates that the study is of high quality.

Table S4. Summary risk ratios (RR) of childhood leukemia in the highest exposure category versus the lowest one for traffic density, benzene and nitrogen dioxide (NO_2) exposure, for all studies and stratified by age at diagnosis, leukemia subtype, exposure timing, and region. Results of leave-one-out sensitivity analysis of range of summary RR ('min RR' and 'max RR') investigating the influence of each individual study on the overall meta-analysis summary estimates.

Table S5. Summary risk ratios (RR) for association of childhood leukemia with particulate matter ($PM_{2.5}$/PM_{10}) and 1,3-butadiene comparing the highest versus the lowest exposure categories for all studies, and stratified by age at diagnosis, leukemia subtype, exposure timing, and region. Results of leave-one-out sensitivity analysis of range of summary RR ('min RR' and 'max RR') investigating the influence of each individual study on the overall meta-analysis summary estimates.

Figure S1. Risk ratio (RR) of childhood leukemia from indicators of traffic exposure for all children: all studies (A); by leukemia subtype (B); by exposure window, i.e. residence at birth vs. at diagnosis (C); by region/continent (D). The area of each gray square is proportional to the inverse of the variance of the estimated log RR. Black diamonds represent point estimates of RR and horizontal lines represent their 95% confidence intervals (CIs). The open diamonds represent the combined RR for each subgroup and the overall RR for all studies. The solid line represents RR=1. The dash line represents the point estimate of overall RR for all studies.

Figure S2. Risk ratio (RR) of childhood leukemia and leukemia subtype from benzene exposure for all children: all studies (A); by leukemia subtype (B); by exposure window, i.e. residence at birth vs. at diagnosis (C); by region/continent (D). The area of each gray square is proportional to the inverse of the variance of the estimated log RR. Black diamonds represent point estimates of RR and horizontal lines represent their 95% confidence intervals (CIs). The open diamonds represent the combined RR for each subgroup and the overall RR for all studies. The solid line represents RR=1. The dash line represents the point estimate of overall RR for all studies.

Figure S3. Risk ratio (RR) of childhood leukemia and leukemia subtype from air NO_2 exposure for all children: all studies (A); by leukemia subtype (B); by exposure window, i.e. residence at birth vs. at diagnosis (C); by region/continent (D). The area of each gray square is proportional to the inverse of the variance of the estimated log RR. Black diamonds represent point estimates of RR and horizontal lines represent their 95% confidence intervals (CIs). The open diamonds represent the combined RR for each subgroup and the overall RR for all studies. The solid line represents RR=1. The dash line represents the point estimate of overall RR for all studies.

Figure S4. Risk ratio (RR) with 95% confidence interval (CI) of childhood leukemia from particulate matter ($PM_{2.5}$) for all children: all studies (A); by leukemia subtype (B); by exposure window, i.e. residence at birth vs. at diagnosis (C); by region/continent (D). The area of each gray square is proportional to the inverse of the variance of the estimated log RR. Black diamonds represent point estimates of RR and horizontal lines represent their 95% confidence intervals (CIs). The open diamonds represent the combined RR for each subgroup and the overall RR for all studies. The solid line represents RR=1. The dash line represents the point estimate of overall RR for all studies.

Figure S5. Risk ratio (RR) with 95% confidence interval (CI) of childhood leukemia from particulate matter (PM_{10}) for all children: all studies (A); by leukemia subtype (B); by exposure window, i.e. residence at birth vs. at diagnosis (C); by region/continent (D). The area of each gray square is proportional to the inverse of the variance of the estimated log RR. Black diamonds represent point estimates of RR and horizontal lines represent their 95% confidence intervals (CIs). The open diamonds represent the combined RR for each subgroup and the overall RR for all studies. The solid line represents RR=1. The dash line represents the point estimate of overall RR for all studies.

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Figure S21. Sensitivity analysis entering a ±15% value instead of ±20 in the dose-response meta-analysis of childhood leukemia risk from nitrogen dioxide exposure of all leukemia (A), acute lymphoblastic leukemia only (B), and acute myeloid leukemia only (C). Overall spline curve (black solid line) with 95% confidence limits (black dashed lines). RR: risk ratio.

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Additional File- Excel Document

References