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Collegium Ramazzini Statement

# Need to Enhance Research and Strengthen Policy for Prevention of Childhood Cancer

*The Collegium Ramazzini is an independent, international scientific academy comprised of 180 physicians and scientists from 45 countries. Its mission is to increase scientific knowledge of the environmental and occupational causes of disease and to transmit this knowledge to decision- makers, the media and the global public in order to prevent disease, promote good health and save lives. The Collegium Ramazzini is independent of commercial interests. It advances scientifically based solutions to global problems in occupational and environmental health.*

Each year, about 400,000 children and adolescents worldwide develop cancer. There are improvements in treatment and reductions in mortality, but incidence rates of many childhood cancers are on the rise, and overall incidence has increased by about 1% per year on average in the U.S.,[1] Europe,[2] and Latin America[3] over the past several decades.

These increases are too rapid to be solely of genetic origin, nor do they reflect improvements in diagnosis.[4]

Many pediatric cancers are associated with hazardous exposures in the environment [**Table**]. Therefore, these cancers are preventable. A growing literature links increased risk for childhood cancer to a range of chemical exposures during preconception, pregnancy, and early childhood. Prenatal exposures appear to be the most dangerous. Tobacco, benzene, and ionizing radiation are among the prenatal exposures linked to pediatric cancer.[5] A growing body of evidence suggests that exposures to pesticides and outdoor air pollution are additional risk factors for pediatric cancer. Breastfeeding and prenatal folic acid use are protective against pediatric cancer.

Other factors, such as genetic predisposition, birth characteristics, and infections, as well as parental factors such as alcohol intake, diet, and maternal medical history have been associated with pediatric cancer onset with varying levels of evidence.[6] Although these factors are important, our focus here is on the subset of environmental factors that have the potential for scalable interventions.[7]

At present, almost all research funding in pediatric cancer is dedicated to treatment, and there is relatively little investment into discovery and elucidation of the possible environmental causes of pediatric cancer. In the face of current, inadequately explained increases in pediatric cancer, such research is urgently needed to guide primary prevention of childhood cancer and to strengthen public policy to reduce children's exposures to environmental carcinogens. Already today, public health professionals can encourage

prenatal folic acid supplements and take steps to reduce exposure, especially prenatal, associated with increased incidence of pediatric cancer.

The international community of pediatric clinicians and public health professionals should adopt a new paradigm for prevention of pediatric cancer. The risks for pediatric cancer can be reduced by focusing on prevention in public policies and enhancing efforts to reduce children's exposures associated with increased incidence of pediatric cancer.

We call on the World Health Organization to adopt the following action items as the core of a new policy towards preventing pediatric cancer. Further, the WHO Collaborating Centers in Children's Environmental Health, as well as international and national professional societies in the fields of pediatric environmental health should adopt a preventive approach to pediatric cancer.

**Recommendations**

1. **Reduce children's exposures to carcinogenic chemicals in air, water and food.**

   Target chemicals that are associated with increased incidence of pediatric cancer for broad exposure reduction efforts and regulate them as carcinogens. Base targeting on hazard assessment rather than on risk assessment. Include in this effort all substances / exposures with evidence of carcinogenicity in humans or experimental animals, even if direct evidence on pediatric cancer is still missing. Three specific recommendations:

   a. Mandate toxicity testing of all chemicals in commerce.[8]

   b. Encourage reduced reliance on coal-fired electrical power generation and reduced reliance on motor vehicles with internal combustion engines, especially in urban or congested areas, given the large population exposed.

    c. Promote adherence to the WHO Air Quality Guidelines.

2. **Reduce children's exposure to tobacco**. Ban all sales of tobacco products to children and adolescents. Promote strict smoke-free policies in indoor environments, including cars. Strictly implement the Framework Convention on Tobacco Control and the Tobacco Free Initiative.
3. **Reduce children's exposure to radiation.** Educate medical staff about judicious use of CT in children and when radiological diagnostics are necessary use the best technology available to reduce radiation exposure. Ban access of children and adolescents to tanning salons. Promote home radon testing and remediation programs.
4. **Highlight opportunities for prevention of childhood cancer during pregnancy**. Mandate the addition of folic acid to all refined grain products (wheat, rice, corn). Promote the health benefits of prolonged breastfeeding (6 months or longer). Educate clinicians about the importance of teaching patients about how to reduce exposures to toxic substances before and during pregnancy and early childhood.
5. **Increase funding for prevention research in pediatric cancer** to better characterize the role of environmental exposures in the development of pediatric cancer. Conduct research on interventions to reduce pediatric cancer to guide primary prevention efforts.

Table. Established and suggested risk and protective factors for cancer in children and adolescents (ages 0-19)

| Cancer Type | Risk & Protective Factors | References |
| --- | --- | --- |
| Lymphoid leukemia | Ionizing radiation; prenatal exposure to tobacco smoke; painting in the home (solvents); parental and maternal pesticide exposures and paternal smoking; air pollution; inverse association with breastfeeding and maternal folic acid intake | 7, 9, 10, 11, 17, 19, 23, 25, 29, 38, 44-46, 49-51 |
| Acute myeloid leukemia | Benzene; 1,3-butadiene; parental occupational exposures such as benzene and pesticides; paternal smoking; traffic-related benzene exposure; residential proximity to repair garages or petrol stations; inverse association with breastfeeding and maternal folic acid intake | 17, 24, 27-28, 30-33, 34, 44-46, 49 |
| Non-Hodgkin lymphoma | Prenatal exposure to tobacco smoke | 26 |
| All CNS tumors (malignant) | Ionizing radiation; prenatal exposure to tobacco smoke; pesticides; parental occupation in agriculture; traffic-related air pollution; inverse association with breastfeeding and maternal folic acid intake | 9, 14-16, 18, 36, 48, 52, 53 |
| Neuroblastoma | Prenatal exposure to tobacco smoke; Pesticide exposures; inverse association with maternal folic acid intake | 9, 14 |
| Hepatoblastoma | Prenatal exposure to tobacco | 21, 22 |
| Nephroblastoma/Wilms tumor | Prenatal exposure to tobacco smoke; pesticides; traffic-related air pollution; Father employed as a welder or mechanic; pesticide exposures; inverse association with breastfeeding | 9, 12, 13, 35, 49, 54 |
| Rhabdomyosarcoma | Inverse association with breastfeeding | 47 |
| Thyroid carcinoma | Ionizing radiation | 39, 40 |
| Melanoma | Ultraviolet radiation from sun, artificial sources (tanning salons), sunburns in childhood/adolescence | 42, 43 |

**References**

1. Sultan I, Alfaar AS, Sultan Y, Salman Z, Qaddoumi I. Trends in childhood cancer: Incidence and survival analysis over 45 years of SEER data. PLoS One. 2025;20(1):e0314592. doi: 10.1371/journal.pone.0314592.
2. Steliarova-Foucher E, Fidler MM, Colombet M, Lacour B, Kaatsch P, Piñeros M, Soerjomataram I, Bray F, Coebergh JW, Peris-Bonet R, Stiller CA; ACCIS contributors. Changing geographical patterns and trends in cancer incidence in children and adolescents in Europe, 1991-2010 (Automated Childhood Cancer Information System): a population-based study. Lancet Oncol. 2018;19(9):1159-1169. doi: 10.1016/S1470-2045(18)30423-6.
3. de Paula Silva N, Colombet M, Moreno F, Erdmann F, Dolya A, Piñeros M, Stiller CA, Steliarova-Foucher E; IICC-3 contributors. Incidence of childhood cancer in Latin America and the Caribbean: coverage, patterns, and time trends. Rev Panam Salud Publica. 2024;48:e11. doi: 10.26633/RPSP.2024.11.
4. Schechter CB. Re: Brain and other central nervous system cancers: recent trends in incidence and mortality. J Natl Cancer Inst. 1999;91(23):2050-1. doi: 10.1093/jnci/91.23.2050.
5. Straif K. Environmental carcinogens and childhood cancer. In: Textbook of Children's Environmental Health, 2nd Ed. edited by Ruth A. Etzel and Philip J. Landrigan. New York: Oxford University Press, 2024.
6. Ricci AM, Emeny RT, Bagley PJ, et al. Causes of Childhood Cancer: A Review of the Recent Literature: Part I-Childhood Factors. Cancers (Basel) 2024;16(7) doi: 10.3390/cancers16071297
7. Benítez L, Castro-Barquero S, Crispi F, Youssef L, Crovetto F, Fischer U, Kameri E, Bueno C, Camos M, Menéndez P, Heinäniemi M, Borkhardt A, Gratacós E. Maternal Lifestyle and Prenatal Risk Factors for Childhood Leukemia: A Review of the Existing Evidence. Fetal Diagn Ther. 2024;51(4):395-410. doi: 10.1159/000539141.
8. The Consortium For Children's Environmental Health, Wirth DA, Cropper M, Axelrad DA, Bald C, Bhatnagar A, Birnbaum LS, Burke TA, Chiles TC, Geiser K, Griffin C, Kumar P, Mandrioli D, Park Y, Raps H, Roger A, Smith TR, States JC, Straif K, Tickner JA, Wagner W, Wang Z, Whitman EM, Woodruff TJ, Yousuf A, Landrigan PJ. Manufactured Chemicals and Children's Health - The Need for New Law. N Engl J Med. 2025;392(3):299-305. doi: 10.1056/NEJMms2409092.
9. Navarrete-Meneses MDP, Salas-Labadia C, Gomez-Chavez F, et al. Environmental Pollution and Risk of Childhood Cancer: A Scoping Review of Evidence from the Last Decade. Int J Mol Sci 2024;25(6) doi: 10.3390/ijms25063284
10. Karalexi MA, Tagkas CF, Markozannes G, et al. Exposure to pesticides and childhood leukemia risk: A systematic review and meta-analysis. Environ Pollut 2021;285:117376. doi: 10.1016/j.envpol.2021.117376
11. Ferreira JD, Couto AC, Pombo-de-Oliveira MS, et al. In utero pesticide exposure and leukemia in Brazilian children < 2 years of age. Environ Health Perspect 2013;121(2):269-75. doi: 10.1289/ehp.1103942

12. Chu A, Heck JE, Ribeiro KB, et al. Wilms' tumour: a systematic review of risk factors and meta-analysis. Paediatr Perinat Epidemiol 2010;24(5):449-69. doi: 10.1111/j.1365-3016.2010.01133.x
13. Rios P, Bauer H, Schleiermacher G, et al. Environmental exposures related to parental habits in the perinatal period and the risk of Wilms' tumor in children. Cancer Epidemiol 2020;66:101706. doi: 10.1016/j.canep.2020.101706
14. Khan A, Feulefack J, Sergi CM. Pre-conceptional and prenatal exposure to pesticides and pediatric neuroblastoma. A meta-analysis of nine studies. Environ Toxicol Pharmacol 2022;90:103790. doi: 10.1016/j.etap.2021.103790
15. Onyije FM, Dolatkhah R, Olsson A, et al. Risk factors for childhood brain tumours: A systematic review and meta-analysis of observational studies from 1976 to 2022. Cancer Epidemiol 2024;88:102510. doi: 10.1016/j.canep.2023.102510
16. Van Maele-Fabry G, Gamet-Payrastre L, Lison D. Residential exposure to pesticides as risk factor for childhood and young adult brain tumors: A systematic review and meta-analysis. Environ Int 2017;106:69-90. doi: 10.1016/j.envint.2017.05.018
17. Carlos-Wallace FM, Zhang L, Smith MT, et al. Parental, In Utero, and Early-Life Exposure to Benzene and the Risk of Childhood Leukemia: A Meta-Analysis. Am J Epidemiol 2016;183(1):1-14. doi: 10.1093/aje/kwv120
18. Peters S, Glass DC, Greenop KR, et al. Childhood brain tumours: associations with parental occupational exposure to solvents. British Journal of Cancer 2014;111(5):998-1003. doi: 10.1038/bjc.2014.358
19. Bailey HD, Metayer C, Milne E, Petridou ET, Infante-Rivard C, Spector LG, Clavel J, Dockerty JD, Zhang L, Armstrong BK, Rudant J, Fritschi L, Amigou A, Hatzipantelis E, Kang AY, Stiakaki E, Schüz J. Home paint exposures and risk of childhood acute lymphoblastic leukemia: findings from the Childhood Leukemia International Consortium. Cancer Causes Control. 2015;26(9):1257-70. doi: 10.1007/s10552-015-0618-0.
20. Secretan B, Straif K, Baan R, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V; WHO International Agency for Research on Cancer Monograph Working Group. A review of human carcinogens--Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. Lancet Oncol. 2009;10(11):1033-4. doi: 10.1016/s1470-2045(09)70326-2.
21. McLaughlin CC, Baptiste MS, Schymura MJ, et al. Maternal and infant birth characteristics and hepatoblastoma. Am J Epidemiol 2006;163(9):818-28. doi: 10.1093/aje/kwj104
22. Sorahan T, Lancashire RJ. Parental cigarette smoking and childhood risks of hepatoblastoma: OSCC data. Br J Cancer 2004;90(5):1016-8. doi: 10.1038/sj.bjc.6601651
23. Lee KM, Ward MH, Han S, et al. Paternal smoking, genetic polymorphisms in CYP1A1 and childhood leukemia risk. Leuk Res 2009;33(2):250-8. doi: 10.1016/j.leukres.2008.06.031
24. Metayer C, Petridou E, Arangure JM, et al. Parental Tobacco Smoking and Acute Myeloid Leukemia: The Childhood Leukemia International Consortium. Am J Epidemiol 2016;184(4):261-73. doi: 10.1093/aje/kww018

25. Lee KM, Ward MH, Han S, Ahn HS, Kang HJ, Choi HS, Shin HY, Koo HH, Seo JJ, Choi JE, Ahn YO, Kang D. Paternal smoking, genetic polymorphisms in CYP1A1 and childhood leukemia risk. Leuk Res. 2009 Feb;33(2):250-8. doi: 10.1016/j.leukres.2008.06.031.
26. Antonopoulos CN, Sergentanis TN, Papadopoulou C, Andrie E, Dessypris N, Panagopoulou P, Polychronopoulou S, Pourtsidis A, Athanasiadou-Piperopoulou F, Kalmanti M, Sidi V, Moschovi M, Petridou ET. Maternal smoking during pregnancy and childhood lymphoma: a meta-analysis. Int J Cancer. 2011 Dec 1;129(11):2694-703. doi: 10.1002/ijc.25929.
27. Boothe VL, Boehmer TK, Wendel AM, et al. Residential traffic exposure and childhood leukemia: a systematic review and meta-analysis. Am J Prev Med 2014;46(4):413-22. doi: 10.1016/j.amepre.2013.11.004
28. Filippini T, Hatch EE, Rothman KJ, et al. Association between Outdoor Air Pollution and Childhood Leukemia: A Systematic Review and Dose-Response Meta-Analysis. Environ Health Perspect 2019;127(4):46002. doi: 10.1289/EHP4381
29. Zhong C, Wang R, Morimoto LM, et al. Outdoor artificial light at night, air pollution, and risk of childhood acute lymphoblastic leukemia in the California Linkage Study of Early-Onset Cancers. Sci Rep 2023;13(1):583. doi: 10.1038/s41598-022-23682-z
30. Wheeler DC, Boyle J, Carli M, et al. Neighborhood Deprivation, Indoor Chemical Concentrations, and Spatial Risk for Childhood Leukemia. Int J Environ Res Public Health 2023;20(4) doi: 10.3390/ijerph20043582
31. Wei T, Jiao R, Nakyeyune R, et al. Exposure to outdoor air pollution at different periods and the risk of leukemia: a meta-analysis. Environ Sci Pollut Res Int 2021;28(27):35376-91. doi: 10.1007/s11356-021-14053-8
32. Khabarova O, Pinaev SK, Chakov VV, et al. Trends in childhood leukemia incidence in urban countries and their relation to environmental factors, including space weather. Front Public Health 2024;12:1295643. doi: 10.3389/fpubh.2024.1295643
33. Williams LA, Haynes D, Sample JM, et al. $PM_{2.5}$, vegetation density, and childhood cancer: a case-control registry-based study from Texas 1995-2011. J Natl Cancer Inst 2024;116(6):876-84. doi: 10.1093/jnci/djae035
34. Malavolti M, Malagoli C, Filippini T, Wise LA, Bellelli A, Palazzi G, Cellini M, Costanzini S, Teggi S, Vinceti M. Residential proximity to petrol stations and risk of childhood leukemia. Eur J Epidemiol. 2023;38(7):771-782. doi: 10.1007/s10654-023-01009-0.
35. Shrestha A, Ritz B, Wilhelm M, Qiu J, Cockburn M, Heck JE. Prenatal exposure to air toxics and risk of Wilms' tumor in 0- to 5-year-old children. J Occup Environ Med. 2014 Jun;56(6):573-8. doi: 10.1097/JOM.0000000000000167.
36. von Ehrenstein OS, Heck JE, Park AS, Cockburn M, Escobedo L, Ritz B. In Utero and Early-Life Exposure to Ambient Air Toxics and Childhood Brain Tumors: A Population-Based Case-Control Study in California, USA. Environ Health Perspect. 2016;124(7):1093-9. doi: 10.1289/ehp.1408582.
37. El Ghissassi F, Baan R, Straif K, Grosse Y, Secretan B, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V; WHO International Agency for Research on Cancer Monograph Working Group. A review of human carcinogens--

part D: radiation. Lancet Oncol. 2009;10(8):751-2. doi: 10.1016/s1470-2045(09)70213-x.
38. Abalo KD, Rage E, Leuraud K, et al. Early life ionizing radiation exposure and cancer risks: systematic review and meta-analysis. Pediatric Radiology 2021;51(1):45-56. doi: 10.1007/s00247-020-04803-0
39. Smith-Bindman R, Alber SA, Kwan ML, Pequeno P, Bolch WE, Bowles EJA, Greenlee RT, Stout NK, Weinmann S, Moy LM, Stewart C, Francisco M, Kofler C, Duncan JR, Ducore J, Mahendra M, Pole JD, Miglioretti DL. Medical Imaging and Pediatric and Adolescent Hematologic Cancer Risk. N Engl J Med. 2025;393(13):1269-1278. doi: 10.1056/NEJMoa2502098.
40. Brenner AV, Tronko MD, Hatch M, Bogdanova TI, Oliynik VA, Lubin JH, Zablotska LB, Tereschenko VP, McConnell RJ, Zamotaeva GA, O'Kane P, Bouville AC, Chaykovskaya LV, Greenebaum E, Paster IP, Shpak VM, Ron E. I-131 dose response for incident thyroid cancers in Ukraine related to the Chernobyl accident. Environ Health Perspect. 2011;119(7):933-9. doi: 10.1289/ehp.1002674.
41. Ngoc LTN, Park D, Lee YC. Human Health Impacts of Residential Radon Exposure: Updated Systematic Review and Meta-Analysis of Case-Control Studies. Int J Environ Res Public Health 2022;20(1) doi: 10.3390/ijerph20010097
42. Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P, et al. Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. Eur J Cancer 2005; 41: 45–60
43. Boniol M, Autier P, Boyle P, Gandini S. Cutaneous melanoma attributable to sunbed use: systematic review and metaanalysis. BMJ 2012; 345: e4757.
44. Masi AC, Stewart CJ. Role of breastfeeding in disease prevention. Microb Biotechnol 2024;17(7):e14520. doi: 10.1111/1751-7915.14520
45. Su Q, Sun X, Zhu L, et al. Breastfeeding and the risk of childhood cancer: a systematic review and dose-response meta-analysis. BMC Med 2021;19(1):90. doi: 10.1186/s12916-021-01950-5
46. Schraw JM, Bailey HD, Bonaventure A, et al. Infant feeding practices and childhood acute leukemia: Findings from the Childhood Cancer & Leukemia International Consortium. Int J Cancer 2022;151(7):1013-23. doi: 10.1002/ijc.34062
47. Soegaard SH, Andersen MM, Rostgaard K, et al. Exclusive Breastfeeding Duration and Risk of Childhood Cancers. JAMA Netw Open 2024;7(3):e243115. doi: 10.1001/jamanetworkopen.2024.3115
48. Schraw JM, Petridou ET, Bonaventure A, et al. Breastfeeding and risk of childhood brain tumors: a report from the Childhood Cancer and Leukemia International Consortium. Cancer Causes Control 2023;34(11):1005-15. doi: 10.1007/s10552-023-01746-3
49. Dessypris N, Karalexi MA, Ntouvelis E, et al. Association of maternal and index child's diet with subsequent leukemia risk: A systematic review and meta analysis. Cancer Epidemiol 2017;47:64-75. doi: 10.1016/j.canep.2017.01.003
50. Metayer C, Milne E, Dockerty JD, et al. Maternal supplementation with folic acid and other vitamins and risk of leukemia in offspring: a Childhood Leukemia International

Consortium study. Epidemiology 2014;25(6):811-22. doi: 10.1097/EDE.0000000000000141
51. Singer AW, Carmichael SL, Selvin S, et al. Maternal diet quality before pregnancy and risk of childhood leukaemia. Br J Nutr 2016;116(8):1469-78. doi: 10.1017/S0007114516003469
52. Chiavarini M, Naldini G, Fabiani R. Maternal Folate Intake and Risk of Childhood Brain and Spinal Cord Tumors: A Systematic Review and Meta-Analysis. Neuroepidemiology 2018;51(1-2):82-95. doi: 10.1159/000490249
53. Greenop KR, Miller M, Bailey HD, et al. Childhood folate, $B_6$, $B_{12}$, and food group intake and the risk of childhood brain tumors: results from an Australian case-control study. Cancer Causes Control 2015;26(6):871-9. doi: 10.1007/s10552-015-0562-z
54. Linabery AM, Johnson KJ, Ross JA. Childhood cancer incidence trends in association with US folic acid fortification (1986-2008). Pediatrics 2012;129(6):1125-33. doi: 10.1542/peds.2011-3418