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Correspondence

CORRESPONDENCE

Re: "Radiation Exposure From Pediatric CT Scans and Subsequent Cancer Risk in the Netherlands"

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Meulepas et al. (1) recently reported evidence for an increased dose-dependent risk of brain tumors related to previous pediatric computed tomography (CT) examinations in a cohort from the Netherlands (2). Results for CT-related leukemia risk were inconclusive. We argue that reverse causation, a potential methodological limitation (3) of retrospective CT studies (4–6), may have affected the primary analysis. Furthermore, some person-year results that are essential for the dose-response analysis seem peculiar.

The Dutch study contains data on pediatric CT scans from 1979 to 2014 (1). Cancer incidence was determined by linkage with the Netherlands Cancer Registry, which includes all malignancies since 1989. Childhood leukemia incidence before 1989 was ascertained through linkage with the Dutch Childhood Oncology Group, which is considered complete for ages 0–14 years since 1973 (7).

Person-time accrual for the analysis of leukemia started in 1981 and for the analysis of solid tumors in 1989. Clinical indications for CT scans were unavailable. To safeguard against reverse causation, an exclusion period was applied—for leukemia 2 years and for brain tumors 5 years—after each CT scan.

We worry that patients born before complete cancer registration with a cancer diagnosis prior to their first CT may have been included in the study, contrary to the exclusion criteria (2). Either a solid tumor diagnosed before 1989 may not have been retrospectively registered at all or may have been retrospectively registered during follow-up care with the date of diagnosis falsely set to the reporting date. The same argument applies to leukemia diagnoses before 1989 in patients aged 14–18 years, and before 1973 in patients of all ages. In such patients, CT scans may have been part of cancer diagnostics or follow-up care. Because cancer therapy can be carcinogenic, this creates a risk of reverse causation: a therapy-induced second neoplasm would appear as a CT-related primary cancer, thus biasing the estimated dose-response upwards. Other CT studies (4–6) are affected by the same problem.

The issue is mitigated in the sensitivity analysis for brain tumors without patients born before 1989, the start of complete registration for malignant tumors. Based on only 11 events, the results are not statistically significant and have large uncertainties.

Compared with the general population, Meulepas et al. (1) report elevated standardized incidence ratios for each individual cancer site. This may be an indication of reverse causation because 65% of scans were for head CT scans, and organ doses were probably too low for a plausible causal link.

The leukemia and brain cancer analyses in the Dutch study contain the same person-time in the two longest categories for time since first exposure (1) (Table 1 in the originalrticle). We would expect more person-time in at least the longest category for the leukemia analysis because its accrual of person-time started 8 years earlier and includes 16 943 person-years more before 1990.

Finally, the abstract notes that data on CT scans were collected until 2012 whereas the results report 2014 as the end of data collection. Table 6 (in the original article) lacks information on the category with 2–5 years of follow-up in the leukemia analysis.

Notes

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All authors declare no conflict of interest.

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