Epidemiologic Evidence for Air Pollution and Childhood Cancer

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The degree to which exposure to ambient air pollution may influence the risk of cancers in children has been a topic of some interest. In the United States, as well as most Westernized nations, motor vehicle emissions are a major source of many air constituents that are known or probable carcinogens such as benzene, 1,3-butadiene and diesel particulate matter (United States Environmental Protection Agency, 2002; Alexis *et al.*, 2004). Because benzene is an established leukemogen in adults, much of the research in this area has focused on the most common cancers in children, the leukaemias.

To date, fifteen epidemiologic studies on air quality and childhood cancer that bear directly on this topic have been published in the peer-reviewed literature (Raaschou-Nielsen and Reynolds, 2004). Approximately half (eight) of these are from the United States (Wertheimer and Leeper, 1979; Savitz and Feingold, 1989; Pearson *et al.*, 2000; Reynolds *et al.*, 2001; Reynolds *et al.*, 2002; Langholz *et al.*, 2002; Reynolds *et al.*, 2003; Reynolds *et al.*, 2004), three are from Great Britain (Alexander *et al.*, 1996; Knox and Gilman, 1997; Harrison *et al.*, 1999), two are from Sweden (Nordlinder and Jarvholm, 1997; Feychting *et al.*, 1998), one is from Denmark (Raaschou-Nielsen *et al.*, 2001) and one is from Italy (Crosignani *et al.*, 2004). The majority of these studies focus on risks associated with residential traffic-associated exposures.

The earliest studies on traffic and childhood cancer were conducted in Denver, Colorado, USA, in conjunction with studies of electric and magnetic field (EMF) exposures, largely in response to concerns for potential confounding effects. The observation that children living in close proximity to heavy traffic routes were more likely to have died from childhood cancer than control children in the earliest study of EMF (Wertheimer and Leeper, 1979) stimulated analyses in a subsequent case-control study of childhood cancer incidence in the Denver area. The striking risk associations in the incidence study for highest compared to lowest traffic volume at the residence at diagnosis for all sites combined (OR 3.1, 95% CI: 1.2–8.0), as well as for the leukaemias (OR 4.7, 95% CI: 1.6–13.5) were based on small numbers (18 and 8 cases respectively in the high risk categories), but were nonetheless provocative (Savitz and Feingold, 1989). In a more recent analysis of the data from this study, using a more comprehensive estimate of traffic exposure, similarly high risk estimates were noted (Pearson *et al.*, 2000). A small Swedish case-control study (142 cases) of modeled peak concentrations of NO_2 (based primarily on traffic volume) for children living within 300 meters of high voltage power lines suggested similarly elevated point estimates, but with extremely wide confidence intervals which included 1.0 (Feychting *et al.*, 1998). A very recent small case-control study from Italy (120 cases) which relied on modeled benzene concentrations (based on traffic density and weather conditions) reported a nearly four-fold excess of leukemia cases at the highest exposure measures (Crosignani *et al.*, 2004).

Alternatively, the largest and more recent case-control studies have tended to find no association between traffic metrics and childhood cancer. These include three studies from California, including some of the most traffic-intensive areas of the United States (Reynolds *et al.*, 2001; Langholz *et al.*, 2002; Reynolds *et al.*, 2004). One of the most comprehensive assessments of traffic-associated risks comes from a large population-based study spanning 24 years in Denmark (Raaschou-Nielsen *et al.*, 2001). This is the only study to assess both traffic density measures and modeled NO_2 concentrations for the full lifetime residential histories of study children. No elevated risk associations were observed in this study for all cancers combined, nor for the leukaemias.

Ecologic approaches to the assessment of air quality and childhood cancer incidence have utilized a number of different less direct and less spatially and temporally proximal measures of traffic exposure. In a large cancer mortality study in England and Wales, modestly elevated risks were noted in proximity to a number of potential environmental hazards, although not near benzene emitters (Knox and Gilman, 1997). Equally modest, but non-significant elevated leukemia incidence risks were suggested for children living within 100 meters of a main road or petrol station in the UK (Harrison *et al.*, 1999). With the exception of the rare subtype of acute mylogenous leukemia, childhood leukemia incidence rates were not higher in Swedish municipalities with higher car density (Nordlinder and Jarvholm, 1997). Neither childhood cancer nor childhood leukemia rates were higher in high traffic density California neighborhoods (block groups), even with adjustment for area differences in urbanization and socioeconomic status (Reynolds *et al.*, 2002). Similarly, a California study of childhood cancer incidence rate differences using modeled hazardous air pollutant (HAP) estimates by census tract noted higher rates associated with higher point-source emissions, but not with mobile source emissions (Reynolds *et al.*, 2003).

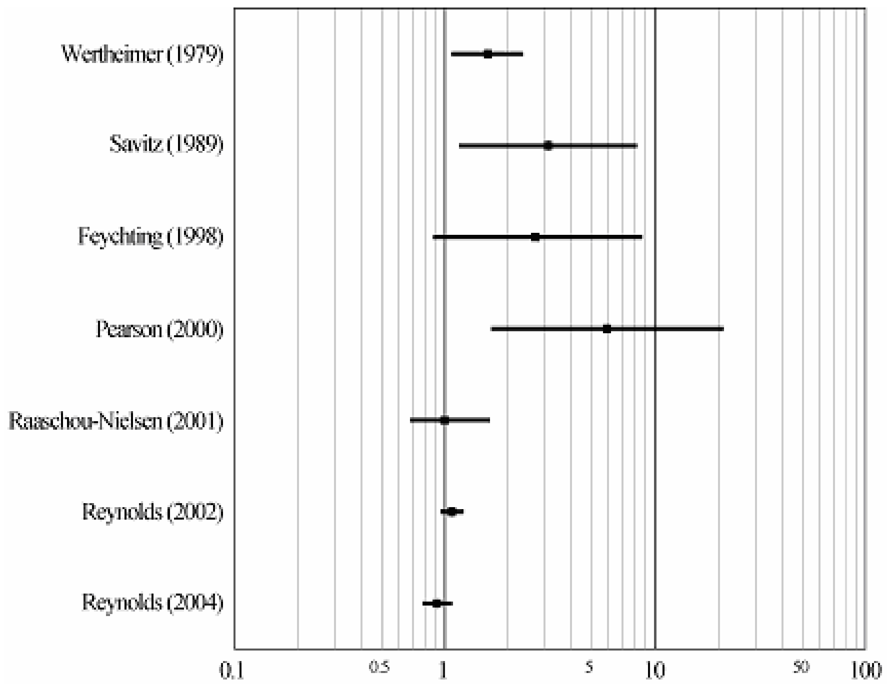

Figure 1: Odds ratios and 95% confidence intervals for childhood cancer in proximity to highest vs. lowest levels of traffic-associated exposures for seven published studies.

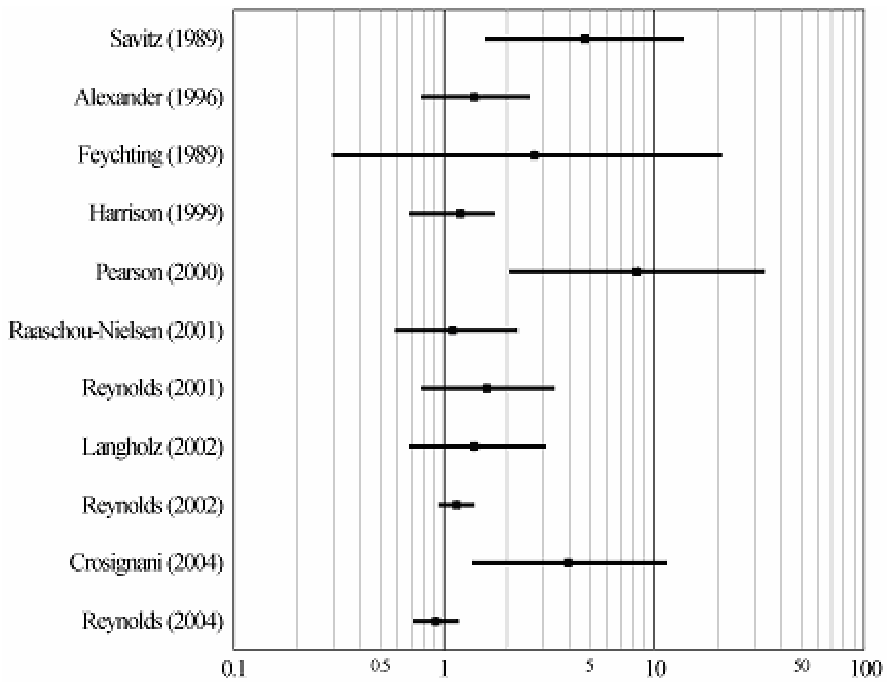

Figure 2. Odds ratios and 95% confidence intervals for childhood leukaemia in proximity to highest vs. lowest levels of traffic-associated exposures for eleven published studies.

Considerations for evaluating the weight of the evidence from this mixed literature to date include issues of study design, sample size, disease heterogeneity, exposure assessment and analytic strategies. Figure 1 presents a summary of risk estimates (and 95% confidence intervals) for all sites of childhood cancer combined in reviewed studies. Figure 2 summarizes the same information for studies reporting results only for the childhood leukemias. These summaries emphasize the observation that positive evidence comes largely from earlier and smaller studies. More recent and larger studies tend to find null associations. Along with qualitative features of the studies to date, it appears from the evidence that it is unlikely that residential proximity to traffic density (and associated emissions) poses a risk for childhood cancer in general or the leukaemias in particular. It is conceivable, nonetheless, that future approaches that can more precisely assess exposure potential as well as account more thoroughly for disease heterogeneity and host vulnerability may further elucidate this biologically plausible risk association.

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