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Parental occupational exposure to benzene and the risk of childhood cancer: A census-based cohort study

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ABSTRACT

Background: Previous studies on occupational exposures in parents and cancer risks in their children support a link between solvents and paints with childhood leukaemia. Few studies have focused specifically on benzene.
Objectives: To examine whether parental occupational exposure to benzene is associated with an increased cancer risk in a census-based cohort of children.
Methods: From a census-based cohort study in Switzerland, we included children aged < 16 years at national censuses (1990, 2000). We retrieved parental occupations reported at census and assessed exposure to benzene using a job exposure matrix. We identified incident cancer cases through record linkage with the Swiss Childhood Cancer Registry. We fitted Cox proportional-hazards models to assess associations between exposures and the following outcomes: any cancer, leukaemia, acute lymphoid leukaemia (ALL), acute myeloid leukaemia (AML), lymphoma, non-Hodgkin lymphoma, central nervous system (CNS) tumours, and glioma. We adjusted models for a range of socio-economic, perinatal and environmental factors.
Results: Analyses of maternal (paternal) exposure were based on 9.0 (13.2) million person years at risk and included 1004 (1520) cases of cancer, of which 285 (438) had leukaemia, 186 (281) lymphoma, 227 (339) a CNS tumour. Maternal exposure was associated with an increased risk of childhood leukaemia (hazard ratio 1.73, 95% CI 1.12–2.67) and ALL (1.88, 1.16–3.04). We found little evidence of an association for other outcomes or for paternal exposure. Adjusting for potential confounders did not materially affect the results.
Conclusions: This nationwide cohort study suggests an increased risk of leukaemia among children whose mothers were exposed to benzene at work.

1. Introduction

Cancer is rare in childhood and the extent to which risks are determined by environmental risk factors is uncertain. It has been suggested that parents' occupational exposure to mutagenic substances, such as benzene, may increase the risk of cancer in their offspring (Colt and Blair, 1998; Pyatt and Hays, 2010). Proposed causal pathways include genetic alterations in parental germ cells, particularly of the father's sperm (Anderson et al., 2000), trans-placental exposure of the fetus during pregnancy (Anderson et al., 2000; Badham et al., 2010), or postnatal exposure of the child to substances brought home from the workplace (Colt and Blair, 1998). Benzene has been widely used as a solvent in paints and adhesives in the past. In occupationally exposed adults, it causes acute myeloid leukaemia (AML) and possibly other blood cancers including acute lymphoid leukaemia (ALL), chronic lymphoid leukaemia, multiple myeloma and non-Hodgkin lymphoma (Chiu and Hou, 2015; IARC, 2012; Vlaanderen et al., 2011, 2012). The major source of benzene exposure in children is ambient air pollution

Abbreviations: ALL, acute lymphoid leukaemia; AML, acute myeloid leukaemia; BEN-JEM, benzene job exposure matrix; CNS, central nervous system; HR, hazard ratio; CI, confidence interval; ICCC-3, International Classification of Childhood Cancer 3rd edition; ISCO, International Classification of Occupations; JEM, job exposure matrix; SCCR, Swiss Childhood Cancer Registry; SEP, socioeconomic position; SNC, Swiss National Cohort study

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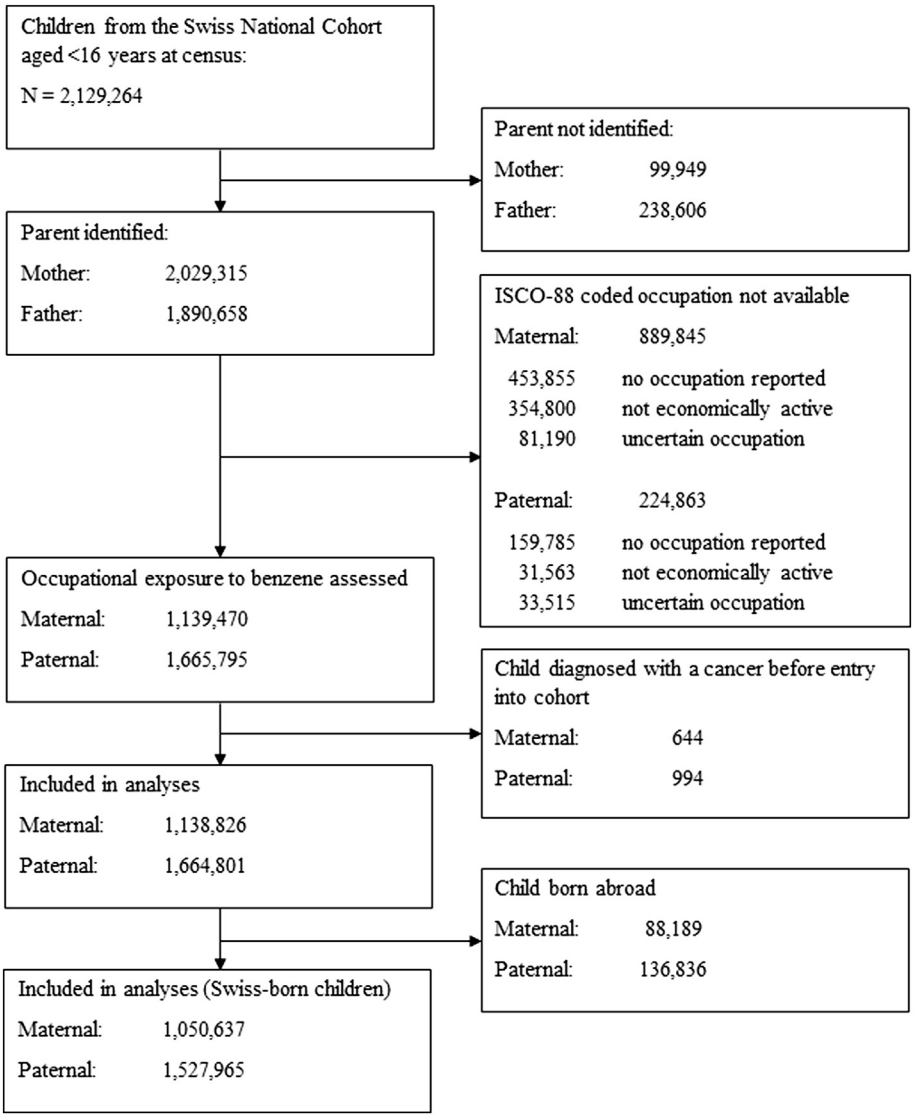

Fig. 1. Flow-chart of included parent-child pairs.

(Duarte-Davidson et al., 2001). Benzene concentrations tend to be higher indoors where children spend most of their time, particularly if a family member smokes (Duarte-Davidson et al., 2001; Wallace, 1996). Maternal intake of benzene, for instance from occupational exposure, can be transmitted to children prenatally through transplacental migration or in infancy through breastfeeding. Cord blood has been found to contain benzene in similar quantities as maternal blood (Dowty et al., 1976) and benzene has been found in breastmilk (Fabietti et al., 2004).

Numerous studies have investigated associations between parental occupational exposures and childhood cancers including leukaemia, ALL, and central nervous system (CNS) tumours. A review of studies up to 1997 supports increased risks associated with benzene-related occupational exposures such as exposure to paints, solvents or exhaust fumes both for childhood leukaemia and CNS tumours (Colt and Blair, 1998). For childhood leukaemia, the majority of more recent studies have also reported increased risks associated with benzene-related occupational exposures, either for paternal (Feychting et al., 2001; Metayer et al., 2016; Miligi et al., 2013; Reid et al., 2011) or maternal exposure (Infante-Rivard et al., 2005; McKinney et al., 2008; Miligi et al., 2013; Reid et al., 2011; Schuz et al., 2000; Shu et al., 1999). However, two large recent studies (Bailey et al., 2014; Keegan et al., 2012), including a study of the Childhood Leukaemia International Consortium (CLIC) focusing on parental occupational exposure to paint (Bailey et al., 2014), found no evidence of an association. Most previous studies looked at broad occupational or substance groups while only a minority considered exposure to benzene specifically. Results from studies that have specifically investigated occupational exposure to benzene also tend to support a link with childhood leukaemia, particularly for maternal exposure (Carlos-Wallace et al., 2016). Since the review by Colt and Blair, increased risks in children of parents with benzene related occupational exposures have also been reported for CNS tumours (Ali et al., 2004; Cordier et al., 1997; Cordier et al., 2001; Keegan et al., 2013; McKean-Cowdin et al., 1998; Peters et al., 2014; Peters et al., 2013), lymphoma (Mutanen and Hemminki, 2001), and non-Hodgkin lymphoma (McKinney et al., 2008; Miligi et al., 2013).

Various methodological issues make it difficult to draw firm conclusions from this research. Most previous studies were case-control studies susceptible to selection bias. For example, if controls with low socioeconomic status - and thus higher risk of exposure - are less likely to participate while cases are likely to participate regardless of socioeconomic status, the estimated association between exposure and outcome will be biased upward (Mezei et al., 2006). To our knowledge, only two previous studies were cohort studies (Feychting et al., 2001; Mutanen and Hemminki, 2001) and none of these specifically investigated maternal occupational exposure to benzene. Studies relying on self-reported exposure to specific substances are susceptible to recall bias (Schuz et al., 2003). Furthermore, most previous studies investigated a wide range of broad occupational or exposure groups in an