[129] von Kries R, Gobel U, Hachmeister A, Kaletsch U, Michaelis J. Vitamin K and childhood cancer: a population based case–control study in Lower Saxony, Germany. *BMJ* 1996;**313:**199–203.

[130] Yeazel MW, Buckley JD, Woods WG, Ruccione K, Robison LL. History of maternal fetal loss and increased risk of childhood acute leukemia at an early age. A report from the Childrens Cancer Group. *Cancer* 1995;**75:**1718–27.

[131] Chow W-H, Linet MS, Liff JM, Greenberg RS. Cancers in children. In: Schottenfeld D, Fraumeni JF (eds). *Cancer Epidemiology and Prevention. 2nd edn*. New York: Oxford, 1996.

[132] Borugian MJ, Spinelli JJ, Mezei G, Wilkins R, Abanto Z, McBride ML. Childhood leukemia and socioeconomic status in Canada. *Epidemiology* 2005;**16:**526–31.

[133] Savitz DA, Wachtel H, Barnes FA, John EM, Tvrdik JG. Case–control study of childhood cancer and exposure to 60-Hz magnetic fields. *Am J Epidemiol* 1988;**128:**21–38.

[134] Savitz DA. *Supplement to contractor's final report: case–control study of childhood cancer and residential exposure to electric and magnetic fields. Report to the New York State Department of Health, Power Lines Project 218217*, 1988.

[135] Hartge P, Brinton LA, Rosenthal JF *et al*. Random digit dialing in selecting a population-based control group. *Am J Epidemiol* 1984;**120:**825–33.

[136] Poole C, Trichopoulos D. Extremely low-frequency electric and magnetic fields and cancer. *Cancer Causes Control* 1991;**2:**267–76.

[137] Olson SH, Kelsey JL, Pearson TA *et al*. Evaluation of random digit dialing as a method of control selection in case–control studies. *Am J Epidemiol* 1992;**135:**210–22.

[138] Gurney JG, Severson RK, Davis S, Robison LL. Incidence of cancer in children in the United States. *Cancer* 1995;**75:**2186–95.

[139] Brogan DJ, Denniston MM, Liff JM, Flagg EW, Coates RJ, Brinton LA. Comparison of telephone sampling and area sampling: response rates and within-household coverage. *Am J Epidemiol* 2001;**153:** 1119–27.

[140] Hatch EE, Kleinerman RA, Linet MS *et al*. Do confounding or selection factors of residential wire codes and magnetic fields distort findings of electromagnetic fields studies? *Epidemiology* 2000;**11:** 189–98.

[141] Voight LF, Koepsell TD, Daling JR. Characteristics of telephone survey respondents according to willingness to participate. *Am J Epidemiol* 2003;**157:**66–73.

[142] Ross JA, Severson RK, Pollock BH *et al*. Childhood cancer in the United States. A geographical analysis of cases from the Pediatric Cooperative Clinical Trials groups. *Cancer* 1996;**77:** 201–07.

Published by Oxford University Press on behalf of the International Epidemiological Association *International Journal of Epidemiology* 2006;**35:**384–385

doi:10.1093/ije/dyl034

Commentary: Numerous, heterogeneous, and often poor—the studies on childhood leukaemia and socioeconomic status

Claudia E Kuehni* and Marcel Zwahlen

Accepted 9 Feburary 2006

Inequalities in health between socioeconomic groups are a major public health concern. Numerous epidemiological studies have found higher rates of mortality and morbidity among infants, children, and adults of lower socioeconomic status (SES), defined at an individual or area-level.[1–3] Together with allergic diseases, childhood leukaemia seemed to be one of the rare exceptions, being reportedly more common among children of high SES.[4] Although the evidence is far from conclusive, such an association has led to speculation about a range of potential aetiological factors linked with affluence and modern lifestyle, which could act via altered host susceptibility or environmental exposures.

In this issue, Poole *et al*.[5] present an extensive review of the literature on the association between SES and childhood leukaemia, summarizing the 47 distinct studies identified according to direction of the association (positive or negative) with SES. They included all papers comparing incidence or mortality for children or young adults and providing enough data on an SES measure to determine at least the direction of the association and a *P*-value. Owing to the vast differences in SES measures used, and in the social implications of measures over time and place, they wisely abstained from a quantitative meta-analysis. Of the 47 studies included in this review, about half found a positive, and the other half a negative association between leukaemia and SES. The direction of the association depended on the study design and the measure used for SES: if the mother's or father's level of education was considered, the studies showed predominantly negative associations (i.e. higher rates associated with lower SES), while occupational class was usually positively associated with SES (i.e. higher rates associated

Swiss Childhood Cancer Registry, Department of Social and Preventive Medicine, University of Berne, Switzerland.

* Corresponding author. Department of Social and Preventive Medicine, University of Berne, Finkenhubelweg 11, CH-3012 Berne, Switzerland. E-mail: kuehni@ispm.unibe.ch

with higher SES). Registry-based and record-based studies generally produced positive associations, whereas interview-based case–control studies showed negative associations. There was also some temporal heterogeneity, with more positive associations in older studies and negative associations in newer studies.

Selection bias related to SES might be a major cause underlying the heterogeneous results, with case–control studies including most cases, but only a selected subset of all relevant controls, resulting in an overrepresentation of high-SES controls owing to a lower response rate in families of lower SES not affected by leukaemia. In contrast, registry-based studies might suffer from a tendency to underrepresent cases from lower social class owing to differentials in the willingness to take part in such studies. The authors conclude that future studies need to measure and report SES in more detail, including several 'versions' of individual and ecological SES measures, and investigate the sensitivity of results in function of different SES measures. This would allow an assessment of the robustness of the association between SES and leukaemia.

The main strength of this review is the very broad and sensitive search strategy, including all papers that have reported on SES measures up to August 2002. Several important studies have been published since, including studies on large populations with low probabilities of selection bias. For instance, a study based on 5240 leukaemia cases from the Canadian cancer registries (which cover at least 95% of all Canadian cancer cases), using a neighbourhood-based SES measure (income quintiles from census data), found a lower risk of childhood leukaemia in the poorest compared with the highest income quintile, with no clear time trends.[6] A recent publication from the Danish Cancer Registry calls attention to the fact that SES is an exposure that evolves over time and that SES measured at birth might not mean the same as SES assessed at the time of diagnosis or death.[7] Their study found an association between leukaemia and low community income at birth but no association with community characteristics or individual SES measures at the time of diagnosis, thus emphasizing the need to consider the timing of repeated and correlated exposures within the framework of a life course approach.[8–10] The associations between the development of chronic disease and SES measures assessed at different points in life has recently been studied by performing stepwise adjustments for these factors in multivariable analyses.[11–13]

The review by Poole *et al*. reminds us that the published information on important public health questions is often of poor quality, especially if the exposure of interest is difficult to measure, depends on social context, and cannot be studied in controlled trials. This is all the more sobering considering that the association between SES and childhood leukaemia should be easy to tackle, compared with other associations between SES and childhood diseases. In many countries there are cancer registries with near-complete coverage and socioeconomic measures at different time points (at least birth and diagnosis) available from population registries. In addition, the case definition 'leukaemia' is reasonably clear, and case detection in industrialized countries is unlikely to depend on SES of the families. The situation is much more difficult for other conditions such as childhood asthma or musculoskeletal disorders, where there are no registries, and, even worse, there is no diagnostic standard. Case definitions then often depend on parental interpretation and reporting of symptoms, and on the interpretation of these symptoms by physicians, all of which are likely to be strongly associated with SES.[14,15] By highlighting these methodological difficulties we do not want to imply that the question of SES and its association with important childhood diseases should not be studied. On the contrary, the review by Poole *et al*. provides useful information on how future studies need to be designed to provide better answers to this important question.

References

1 Saxena S, Majeed A, Jones M. Socioeconomic differences in childhood consultation rates in general practice in England and Wales: prospective cohort study. *BMJ* 1999;**318:**642–46.

2 Huisman M, Kunst AE, Bopp M, Borgan JK, Borrell C, Costa G *et al*. Educational inequalities in cause-specific mortality in middle-aged and older men and women in eight western European populations. *Lancet* 2005;**365:**493–500.

3 Arntzen A, Samuelsen SO, Bakketeig LS, Stoltenberg C. Socio-economic status and risk of infant death. A population-based study of trends in Norway, 1967–1998. *Int J Epidemiol* 2004;**33:**279–88.

4 Greenberg RS, Shuster JL Jr. Epidemiology of cancer in children. *Epidemiol Rev* 1985;**7:**22–48.

5 Poole C, Greenland S, Luetters C, Kelsey J, Mezei G. Childhood leukemia and socioeconomic status: a review. *Int J Epidemiol* 2006;**35**:370–84.

6 Borugian MJ, Spinelli JJ, Mezei G, Wilkins R, Abanto Z, McBride ML. Childhood leukemia and socioeconomic status in Canada. *Epidemiology* 2005;**16:**526–31.

7 Raaschou-Nielsen O, Obel J, Dalton S, TjOnneland A, Hansen J. Socioeconomic status and risk of childhood leukaemia in Denmark. *Scand J Public Health* 2004;**32:**279–86.

8 Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. *J Epidemiol Community Health* 2003;**57:**778–83.

9 Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and inter-disciplinary perspectives. *Int J Epidemiol* 2002;**31:**285–93.

10 De Stavola BL, Nitsch D, dos Santos Silva I, McCormack V, Hardy R, Mann V *et al*. Statistical issues in life course epidemiology. *Am J Epidemiol* 2006;**163:**84–96.

11 Power C, Hertzman C, Matthews S, Manor O. Social differences in health: life-cycle effects between ages 23 and 33 in the 1958 British birth cohort. *Am J Public Health* 1997;**87:**1499–503.

12 Khatun M, Ahlgren C, Hammarstrom A. The influence of factors identified in adolescence and early adulthood on social class inequities of musculoskeletal disorders at age 30: a prospective population-based cohort study. *Int J Epidemiol* 2004;**33:** 1353–60.

13 Cooper R, Lawlor DA, Hardy R, Ebrahim S, Leon DA, Wadsworth ME *et al*. Socio-economic position across the life course and hysterectomy in three British cohorts: a cross-cohort comparative study. *BJOG* 2005;**112:**1126–33.

14 Gehring U, Pattenden S, Slachtova H, Antova T, Braun-Fahrlander C, Fabianova E *et al*. Parental education and children's respiratory and allergic symptoms in the Pollution and the Young (PATY) study. *Eur Respir J* 2006;**27**:95–107.

15 Braun-Fahrlander C, Gassner M, Grize L, Minder C, Varonier HS, Vuille JC *et al*. Comparison of responses to an asthma symptom questionnaire (ISAAC core questions) completed by adolescents and their parents. *Pediatric Pulmonology* 1998;**25**:159–166.