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Residential mobility and childhood leukemia

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ABSTRACT

Aims: Studies of environmental exposures and childhood leukemia studies do not usually account for residential mobility. Yet, in addition to being a potential risk factor, mobility can induce selection bias, confounding, or measurement error in such studies. Using data collected for California Powerline Study (CAPS), we attempt to disentangle the effect of mobility.

Methods: We analyzed data from a population-based case-control study of childhood leukemia using cases who were born in California and diagnosed between 1988 and 2008 and birth certificate controls. We used stratified logistic regression, case-only analysis, and propensity-score adjustments to assess predictors of residential mobility between birth and diagnosis, and account for potential confounding due to residential mobility.

Results: Children who moved tended to be older, lived in housing other than single-family homes, had younger mothers and fewer siblings, and were of lower socioeconomic status. Odds ratios for leukemia among non-movers living < 50 meters (m) from a 200 + kilovolt line (OR: 1.62; 95% CI: 0.72–3.65) and for calculated fields ≥ 0.4 microTesla (OR: 1.71; 95% CI: 0.65–4.52) were slightly higher than previously reported overall results. Adjustments for propensity scores based on all variables predictive of mobility, including dwelling type, increased odds ratios for leukemia to 2.61 (95% CI: 1.76–3.86) for living < 50 m from a 200 + kilovolt line and to 1.98 (1.11–3.52) for calculated fields. Individual or propensity-score adjustments for all variables, except dwelling type, did not materially change the estimates of power line exposures on childhood leukemia.

Conclusion: The residential mobility of childhood leukemia cases varied by several sociodemographic characteristics, but not by the distance to the nearest power line or calculated magnetic fields. Mobility appears to be an unlikely explanation for the associations observed between power lines exposure and childhood leukemia.

1. Introduction

The majority of studies that have evaluated the role that environmental exposures play in the development of childhood leukemia have considered exposure at only a single residential address for each child (e.g., home at birth, home at time of diagnosis, longest lived home) and not the mobility of subjects. Residential mobility, or moving between time of birth and diagnosis, can involve short distances, such as moving within the same neighborhood, or longer distance moves; the likelihood of experiencing similar environmental exposures before and after a move may depend on distance. Subjects can also move out of the study area and be lost to follow-up. As only one residential address is available in most studies, few studies can directly assess residential mobility.

Mobility has been considered a source of potential bias in childhood leukemia studies as it can affect study participation and selection, result

in exposure misclassification, or confound the results (Kheifets et al., 2017b). We explore each of the possible connections in subsequent paragraphs. Fig. 1 provides a simplified directed acyclic graph illustrating how mobility could affect studies of childhood leukemia and electro-magnetic fields (EMF) in particular, but is relevant as well for many other environmental exposures.

Exposure misclassification can occur if the period of assessment is not the etiologically relevant critical time period in a child's development. This misclassification will affect sensitivity thereby reducing the power to detect associations. The problem can further be compounded by mobility, as the relevant exposure may occur at a different home than the one captured (Urayama et al., 2009), leading to biased results when estimating risk of childhood leukemia, especially if mobility is differential between cases and controls. Several studies have reported higher residential mobility among cases compared to age-matched

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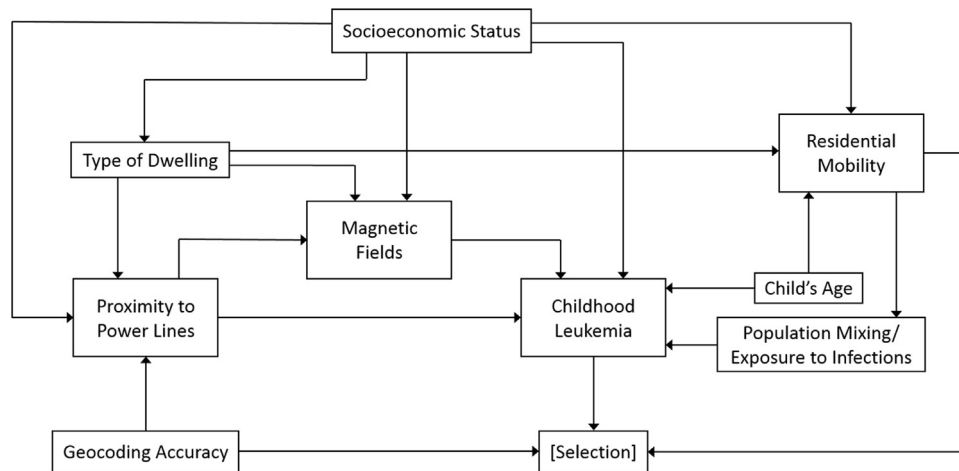


Fig. 1. Simplified directed acyclic graph (DAG) depicting possible connections of residential mobility in the study of EMF exposures on childhood leukemia.

controls (Green et al., 1999; Kleinerman et al., 1997; McBride et al., 1999).

Mobility can affect selection through the availability of data. Often, cases are by design residentially more stable as they must both reside and be diagnosed in the same geographic area (region, state or country) while the same requirement does not apply to controls. There is, also, the possibility that subjects move outside the study area and are not captured as cases.

Further, mobility may differ by exposure, either directly or through differential socioeconomic status (SES). In a California study, moving between time of birth and diagnosis was associated with lower community-based SES, as well as lower individual measures of SES, such as parental education and household income (Urayama et al., 2009). SES is also associated with exposure to magnetic fields as it could be related to the number, type, and quality of appliances within the home, the dwelling type (apartment vs. single-family home), and the location of the home in relation to overhead power lines (Hatch et al., 2000; Wartenberg et al., 2010). SES has also been shown to be associated with participation in studies when direct subject involvement is required (Mezei and Kheifets, 2006).

Type of dwelling, such as apartment or single-family home, can affect not only a subject's exposure but also exposure assessment. For example, when geographic information system (GIS) methods are utilized to assess proximity to power lines and to calculate magnetic fields, mobile homes are more likely to result in poor GIS matching of the residential address. Similarly, apartments, particularly in complexes, may lead to greater misclassification of exposure (Feychting and Ahlbom, 1993; Vergara et al., 2015). Home ownership, and subsequently dwelling type, is also associated with SES and mobility (McCarthy et al., 2001).

Residential mobility can also function as a marker for other risk factors for childhood leukemia such as older age of the child at diagnosis, younger maternal age at birth, and maternal place of birth (Urayama et al., 2009). Additionally, mobility might be related to increased exposure to viruses or other infections possibly associated with higher leukemia risk (Kinlen, 2012; Sahl, 1994). The distance moved (e.g. within vs. outside of a neighborhood) could be an indicator for exposure to new infections. A study of childhood leukemia in the United Kingdom (UK) found that increased migration from greater distances was associated with higher incidence of childhood leukemia (Stiller and Boyle, 1996). Another recent UK study (Kendall et al., 2015) found that 44% of childhood leukemia cases had not moved at all between birth and diagnosis, and about two-thirds of those who did move were living within 2 kilometers (km) of their birth residence.

It has been hypothesized that mobility can explain an association between EMF and childhood leukemia (Sahl, 1994). A previous study

(Jones et al., 1993) found that people who moved had a higher proportion of “high” wire codes (an imperfect exposure surrogate) than those who were residentially stable. Another study evaluated residential mobility of adults and proximity to power lines in the UK (Swanson, 2013), but found that proximity did not appear to clearly affect the likelihood of moving. Direct data on mobility of children is lacking.

We conducted a large epidemiologic case-control study in California to examine the associations of childhood leukemia with calculated magnetic fields and with distance from the birth address to the nearest high-voltage overhead transmission line. In common with other case-control studies of childhood cancers, cases, but not controls, had to reside in California at time of diagnosis. The aims of this analysis are to: (i) describe factors that affect or predict mobility among childhood leukemia cases; (ii) use such factors as proxies to adjust for mobility; and (iii) evaluate potential confounding due to residential mobility in the study of the potential effect of EMF exposure from nearby power lines on childhood leukemia.

2. Methods

The California Power Lines Study (CAPS) included childhood leukemia cases younger than 16 years diagnosed in California between 1988 and 2008 who were also born in California. Cases were identified from the California Cancer Registry (CCR; www.ccrca.org), which requires mandatory reporting of incident cancers and is 99% complete (Schoendorf and Branum, 2006). Information on child's age, sex, residence at the time of diagnosis, as well as information on cancer types and characteristics was extracted from the CCR. Cancer registry data were linked to the California Birth Registry (CBR; California Department of Public Health, Vital Statistics Branch) which is also over 99% complete (Schoendorf and Branum, 2006). Controls were randomly selected from the CBR and matched to cases (1:1). Controls were excluded if they were diagnosed with any type of cancer in California before the matched case's date of diagnosis. Detailed descriptions of the study design and methods have been previously published (Kheifets et al., 2015), as have the results of the calculated magnetic fields and distance analyses (Crespi et al., 2016; Kheifets et al., 2017a).

Although cases had to be both born in and diagnosed in California, because controls were selected from birth records, they were born in California, but were not required to be residing in the state at time of diagnosis of the corresponding case. Thus, we had birth addresses for both cases and controls, but address at diagnosis for cases only.

The CBR provided information on socio-demographic and perinatal factors of study subjects, including mother's residential address at time of birth, child's date of birth, sex, race and ethnicity, birth weight, birth

order, number of live births living, parental ages, parental education, parental race and ethnicity, and source of payment for delivery. We examine race and ethnicity separately and combined. Combined child race/ethnicity was defined as White if both parents were White, Black if either parent was Black, Asian if either parent was Asian, Hispanic if either parent was Hispanic and neither parent was Black or Asian, and Other otherwise. We also examined both individual SES and a census-based SES derived using principal component analysis based on seven indicator variables at the census block level (Yost et al., 2001) (high if ≥ 60 th percentile of the principal components score, low otherwise). In addition, because variables indicative of SES collected on birth records varied from year to year, we developed a composite SES indicator (high or low) based hierarchically as available for each subject: the father's years of education (high if ≥ 12 years, low otherwise), mother's years of education (high if ≥ 12 years, low otherwise), payment method for hospital delivery (low if government programs or no coverage, high otherwise), and, finally, census-based SES. More information on race/ethnicity and SES indicators in CAPS is available in previous publications (Oksuzyan et al., 2012, 2015a, 2015b).

We determined geocoded latitudes and longitudes for cases' residential addresses using the University of Southern California (USC) GIS Laboratory's open-source geocoder, which uses parcel level data for Los Angeles County and street level data for the whole of California (Goldberg and Cockburn, 2010). Only addresses with parcel or street segment matching, which corresponds to more precise geocoding, were included in this analysis.

We created three categories of residential mobility for cases: 1) not moved, 2) moved within a neighborhood, defined as distance between birth and diagnosis addresses 50–2000 meters (m), and 3) moved outside of a neighborhood, defined as distance between birth and diagnosis addresses of 2000 m or further. For the primary analysis, the latter two were collapsed and cases were classified as either residentially stable (did not move) or residentially mobile (moved). To allow for minor geocoding differences over the years, if the distance between birth and diagnosis addresses was 0–50 m, we assumed the subject lived in the same property and did not move. This assumption was verified by examining Google satellite images for a larger set of residences (with distances < 100 m between birth and diagnosis addresses). 50 m was chosen to increase specificity and make estimates more conservative.

Proximity to power lines was defined as distance from the child's address to any power line or to the nearest power line of 200 kilovolts (kV) and above (Kheifets et al., 2015) and was classified into 8 categories: < 50 m, $50- < 100$ m, $100- < 200$ m, $200- < 300$ m, $300- < 400$ m, $400- < 500$ m, $500- < 600$ m, and no lines within 600 m. Due to small numbers in one of the categories, a sensitivity analyses was run in which the closest two categories were combined (< 100 m). Birth homes located close to lines were site-visited to verify distance, collect additional information needed for magnetic fields calculations, and ascertain dwelling type (single-family homes vs other). Site visits, only available for a subset of subjects ($n = 178$), were conducted blind to case-control status to reduce bias. Calculated fields estimating fields at time of birth were classified into three categories: ≥ 0.4 microTesla (μT), $0.1- < 0.4 \mu\text{T}$, and $< 0.1 \mu\text{T}$ (Vergara et al., 2015).

We considered the following variables as covariates: child's age at diagnosis, number of siblings living, census-based SES, race/ethnicity, mother's age, mother's years of education, father's years of education, mother's place of birth, the payment source for delivery, type of dwelling, proximity to high voltage power lines, and calculated fields. All covariates were modeled as categorical variables. For more details, see a previous study (Oksuzyan et al., 2015b).

2.1. Statistical analysis

2.1.1. Stratified analyses

The primary analysis assessed the impact of mobility on the associations between proximity to overhead power lines 200 kV or greater

and calculated fields and childhood leukemia. For this analysis, we stratified on mobility (not moved, moved within same neighborhood, moved outside neighborhood) and used logistic regression with case/control status as the dependent variable and exposure as the independent variable. To increase power and avoid sparse data, all controls were used in each stratum. Models were adjusted for age, sex, race/ethnicity, and composite SES.

2.1.2. Case-only analyses predicting mobility

We conducted case-only analysis using mobility as the outcome variable to determine covariates associated with moving. We fit logistic regression models with the binary outcome of moved versus did not move and with the 3-category multinomial outcome (did not move (reference), moved within neighborhood and moved outside of neighborhood).

2.1.3. Comparison of birth and diagnosis home characteristics in movers

In residentially mobile cases, birth and diagnosis homes were compared to assess changes in census-based SES, distance to nearest power lines, and calculated magnetic fields. Changes in exposure categories were analyzed by chi-square tests; mean calculated fields and proximity to power lines at birth and diagnosis were compared using Wilcoxon signed-rank tests.

2.1.4. Adjusted analyses of exposure-leukemia associations indirectly accounting for mobility

Mobility was not available for controls and thus direct adjustment for mobility as a potential confounder in the relation between exposure and childhood leukemia was not possible. We therefore conducted analyses adjusting for variables associated with mobility as proxies We examined models adjusting for each proxy singly, with additional adjustment for age and sex, and we also used propensity score methods to simultaneously control for all the proxies (Rosenbaum and Rubin, 1983; Guo and Fraser, 2014)], to avoid over adjustment. The propensity scores were created using multinomial logistic regression with the variables associated with mobility as predictors. We estimated propensity scores for each subject as the predicted probability from the model based on their covariate values. We then fit logistic regression models for the outcome of childhood leukemia that included the exposure variable (proximity or calculated field) with and without adjusting for the propensity score, to assess whether the adjustment changed the childhood leukemia risk estimate. This approach assumes that including propensity scores in the model provides a reasonable proxy for adjusting for residential mobility.

Analyses were conducted using SAS software version 9.3. Copyright © 2017 SAS Institute Inc. CAPS was approved by University of California, Los Angeles Office for the Protection of Research Subjects.

3. Results

Out of 6645 eligible childhood leukemia cases identified from the CCR, 87.1% (5788) were born in California and were successfully linked to birth records. Of these, 4879 were matched at either parcel or street segment levels for both birth and diagnosis addresses and included in the analysis. A majority of cases were male (55.3%), Hispanic (52.1%), and had acute lymphoblastic leukemia (ALL) (81.5%). The median age at time of diagnosis was 3.8 years. Most cases (2982, 61.1%) moved between birth and diagnosis. Among those who moved, 618 stayed within 2 km of their birth home, while 1992 moved outside of their birth neighborhood. Additional characteristics are presented in Table 1. There were no differences in characteristics between cases and controls. However, among cases who moved, children tended to be older, live in housing other than single-family homes, and have younger mothers. Fewer siblings and lower SES were also more common among children who moved.

Table 1
Characteristics of cases by mobility status in California Power Lines Study, 1986–2008.

Characteristic	Controls		Cases		Did Not Move		Moved	
	n	%	n	%	n	%	n	%
Gender								
Male	2718	56.2	2700	55.3	1038	54.7	1662	55.7
Female	2117	43.8	2179	44.7	859	45.3	1320	44.3
Age (years)								
< 1	349	7.2	323	6.6	240	12.7	83	2.8
1–5	3095	64.0	3145	64.5	1363	71.9	1782	59.8
6–9	821	17.0	828	17.0	205	10.8	623	20.9
10–15	570	11.8	583	12.0	89	4.7	494	16.6
Race/Ethnicity								
White	1513	32.1	1425	29.8	633	33.9	792	27.1
Black	423	9.0	248	5.2	65	3.5	183	6.3
Asian	467	9.9	535	11.2	245	13.1	290	9.9
Other	87	1.9	86	1.8	35	1.9	51	1.8
Hispanic	2220	47.1	2493	52.1	890	47.6	1603	54.9
Leukemia Type								
ALL	–	–	3974	81.5	1505	79.3	2469	82.8
AML	–	–	722	14.8	303	16.0	419	14.1
Other	–	–	183	3.8	89	4.7	94	3.2
Downs Syndrome								
Yes	4	0.1	36	1.0	16	1.1	20	0.9
No	3567	99.9	3541	99.0	1437	98.9	2104	99.1
Dwelling Type at Birth								
Single-Family Home	66	72.5	59	67.8	19	73.1	40	65.6
Other	25	27.5	28	32.2	7	26.9	21	34.4
Maternal Age (years)								
< 25	1704	35.3	1562	32.0	429	22.6	1133	38.0
25–34	2497	51.7	2577	52.8	1055	55.6	1522	51.1
> =35	633	13.1	739	15.2	413	21.8	326	10.9
Siblings								
0	1974	40.8	1886	38.9	660	34.8	1226	41.1
1	1545	32.0	1549	31.8	636	33.5	913	30.6
2	753	15.6	805	16.5	335	17.7	470	15.8
3	327	6.8	368	7.5	166	8.8	202	6.8
4 +	236	4.9	271	5.6	100	5.3	171	5.7
Maternal Place of Birth								
US	2737	56.6	2633	54.0	1057	55.7	1576	52.9
Non-US	2098	43.4	2246	46.0	840	44.3	1406	47.2
Socioeconomic Status								
Low	3294	70.0	3296	69.4	1187	63.4	2109	73.3
High	1413	30.0	1453	30.6	684	36.6	769	26.7

ALL = acute lymphoblastic leukemia. AML = acute myeloid leukemia.

3.1. Stratified analyses

As reported previously, using all leukemia cases and controls, we found an OR for childhood leukemia of 1.44 (95% CI 0.74–2.77) for those whose birth residence was within 50 m of a 200 + kV line, (Crespi et al., 2016) and an OR (95% CI) of 1.50 (0.70–3.21) for the highest exposure of calculated fields ($\geq 0.4 \mu\text{T}$) (Kheifets et al., 2017a). The results of analyses stratified by the mobility status of the cases are presented in Table 2.

Among non-movers, moderate associations for childhood leukemia and both living within 50 m of voltage 200 + kV power line (OR: 1.62, 95% CI: 0.72–3.65) and living in higher calculated fields (OR: 1.71, 95% CI: 0.65–4.52) at birth home were observed. Among those who moved, the OR was slightly lower for the proximity analysis (OR: 1.28, 95% CI: 0.60–2.75) than the overall proximity OR (1.44) reported previously, but did not change for calculated fields. These analyses used all controls in each stratum because while similar point estimates were found when stratifying controls, the results were less stable (data not shown).

We also conducted analyses stratifying cases by distance of move,

with the strata of “moved within birth neighborhood” and “moved outside birth neighborhood.” A slightly stronger association was noted for those who moved out of the neighborhood for both those living < 50 m from a 200 + kV line and those with $\geq 0.4 \mu\text{T}$ calculated fields at the birth home (Table 2). All results from stratified analyses were imprecise.

3.2. Case-only analyses predicting mobility

Results of the case-only analyses with mobility status as the outcome are presented in Table 3. In unadjusted analyses with a binary mobility outcome (moved vs. not moved), greater likelihood of mobility was associated with older age at diagnosis (p-value for trend < 0.001), leukemia subtype, Black and Hispanic race/ethnicities, younger maternal age at birth, being an only child or having many siblings, non-US maternal place of birth, and lower SES. Not living in a single-family home was also associated with likelihood of moving (OR:1.43; 95% CI: 0.52–3.93), but results were imprecise as type of dwelling was recorded only for site-visited homes. No association was detected for sex or Down syndrome (data not shown). Similar results were obtained when race and ethnicity were assessed separately (data not shown), thus for the remaining analyses, the combined race/ethnicity variable was used. Crude and adjusted ORs were similar for all variables associated with mobility (Table 3).

Similar results were found in the multinomial logistic analysis using the three-level mobility as an outcome. Older child's age at diagnosis was more strongly associated with moving outside the birth neighborhood than the association within the same neighborhood. In contrast, Hispanic race/ethnicity was associated with moving within a neighborhood but not with moving more than 2 km away (Table 3). Neither calculated fields, nor proximity to 200 + kV power lines appeared to be associated with moving, although numbers were too small to assess movement with regards to the birth neighborhood (Table 3).

3.3. Comparison of birth and diagnosis home characteristics in movers

Among cases who moved, there were few differences in characteristics between birth and diagnosis homes. Calculated fields changed in only 51 cases, unsurprising, since the overwhelming majority of subjects had calculated fields of < 0.1 μT . Only two children changed exposure categories, possibly since only three exposure categories were used and few cases were classified at the highest exposure level ($\geq 0.4 \mu\text{T}$). Among those who moved, 6% of subjects moved into closer distance categories to overhead 200 + kV power lines while another 6% moved farther away. When considering all voltages, equal numbers of cases moved into the closer or farther categories (16%). Due to censoring of distance data beyond 2000 m, these percentages do not account for subjects who moved closer or farther but remained beyond 2000 m. No differences were noted in the average distances from the closest power lines, 200 + kV or any voltage, nor in average calculated fields for children who moved between birth and diagnosis (data not shown).

About 17% of all subjects changed the status of their census-based SES from low to high or the reverse. Among both non-movers and movers, relative census-based SES appeared to increase from birth to diagnosis (7.6% and 13.6%, respectively), but this difference was not significant. These changes were not absolute changes, but change in quintile. Fig. 2 shows the distribution of changes in census-based SES using quintiles.

3.4. Adjusted analyses of exposure-leukemia associations indirectly accounting for mobility

Both unadjusted and adjusted results in subsets of observations using variables associated with mobility are presented for comparison (Table 4). Adjustment for most variables had no impact on the results.

Table 2
Odds ratios of leukemia by calculated fields and proximity to power lines, stratified by mobility of cases.

		Total AOR (95% CI)	Cases Who Did Not Move AOR (95% CI)	Cases Who Moved AOR (95% CI)	Cases Who Moved < 2 km AOR (95% CI)	Cases Who Moved ≥ 2 km AOR (95% CI)
Calculated fields	< 0.1	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	0.1–0.4	0.90 (0.57–1.41)	0.58 (0.29–1.18)	1.09 (0.66–1.78)	1.24 (0.55–2.80)	1.03 (0.54–2.00)
	> =0.4	1.49 (0.69–3.19)	1.71 (0.65–4.52)	1.50 (0.63–3.58)	N < 5	1.64 (0.63–4.26)
Distance to 200 + kV Power Line	600 +	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	500- < 600	1.18 (0.82–1.71)	1.34 (0.83–2.16)	1.08 (0.70–1.65)	0.94 (0.42–2.10)	1.12 (0.71–1.76)
	400- < 500	0.87 (0.60–1.28)	0.74 (0.43–1.29)	0.95 (0.62–1.46)	0.78 (0.35–1.74)	1.01 (0.64–1.60)
	300- < 400	1.11 (0.78–1.59)	1.17 (0.73–1.87)	1.07 (0.71–1.61)	1.28 (0.66–2.47)	1.03 (0.66–1.61)
	200- < 300	0.85 (0.59–1.22)	0.96 (0.59–1.55)	0.78 (0.51–1.21)	N < 5	0.89 (0.56–1.39)
	100- < 200	0.77 (0.53–1.11)	0.72 (0.42–1.23)	0.79 (0.52–1.21)	1.17 (0.61–2.25)	0.68 (0.41–1.11)
	50- < 100	0.96 (0.56–1.64)	0.42 (0.16–1.10)	1.31 (0.74–2.33)	N < 5	1.42 (0.78–2.61)
	< 50	1.38 (0.71–2.67)	1.62 (0.72–3.65)	1.28 (0.60–2.75)	N < 5	1.54 (0.70–3.36)

All controls were used in each stratum to increase stability of estimates and avoid small cell counts. Analyses were adjusted for age, sex, race/ethnicity, and composite SES.

Table 3
Odds ratios for associations of residential mobility with selected characteristics in childhood leukemia cases in the California Power Lines Study, 1986–2008 – Case-Only.

Characteristic	Moved vs. Not Moved (reference)		Moved Within Neighborhood vs. Not Moved (reference)	Moved Outside Neighborhood vs. Not Moved (reference)
	Crude OR (95% CI)	Adjusted ^a OR (95% CI)	AOR ^b (95% CI)	AOR ^b (95% CI)
Age (years)				
< 1	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1–5	3.78 (2.92–4.90)	3.84 (2.90–5.09)	2.76 (1.78–4.27)	4.39 (3.18–6.06)
6–9	8.79 (6.54–11.81)	8.26 (6.03–11.33)	6.04 (3.75–9.72)	9.37 (6.57–13.37)
10–15	16.05 (11.46–22.47)	14.98 (10.51–21.35)	8.11 (4.83–13.62)	18.40 (12.47–27.17)
Race/Ethnicity				
White	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Black	2.25 (1.66–3.04)	1.69 (1.22–2.35)	1.41 (0.83–2.40)	1.75 (1.25–2.45)
Asian	0.95 (0.78–1.16)	0.92 (0.72–1.16)	0.92 (0.63–1.36)	0.94 (0.73–1.20)
Other	1.17 (0.75–1.81)	0.97 (0.60–1.57)	1.59 (0.81–3.12)	0.84 (0.50–1.40)
Hispanic	1.44 (1.26–1.64)	1.13 (0.95–1.33)	1.54 (1.18–2.02)	1.03 (0.86–1.23)
Leukemia Type				
ALL	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
AML	0.84 (0.72–0.99)	0.93 (0.77–1.12)	0.90 (0.68–1.19)	0.94 (0.77–1.15)
Other	0.64 (0.48–0.87)	0.79 (0.57–1.11)	0.74 (0.44–1.26)	0.81 (0.57–1.16)
Maternal Age (years)				
< 25	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
25–34	0.55 (0.48–0.63)	0.59 (0.50–0.69)	0.59 (0.47–0.74)	0.59 (0.50–0.69)
> =35	0.30 (0.25–0.36)	0.34 (0.27–0.42)	0.44 (0.32–0.61)	0.31 (0.24–0.39)
Siblings				
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	0.77 (0.67–0.89)	0.86 (0.74–1.00)	0.92 (0.73–1.16)	0.84 (0.72–0.99)
2	0.76 (0.64–0.89)	0.95 (0.79–1.15)	1.12 (0.85–1.48)	0.90 (0.74–1.10)
3	0.66 (0.52–0.82)	0.85 (0.66–1.10)	0.80 (0.54–1.19)	0.87 (0.66–1.14)
4+	0.92 (0.71–1.20)	1.30 (0.96–1.77)	1.40 (0.91–2.14)	1.26 (0.91–1.75)
Maternal Place of Birth				
US	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Non-US	1.12 (1.00–1.26)	1.13 (0.97–1.32)	1.58 (1.27–1.98)	1.01 (0.86–1.19)
SES				
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	0.63 (0.56–0.72)	0.85 (0.74–0.98)	0.75 (0.60–0.94)	0.88 (0.76–1.03)
Calculated Field (μT)				
< 0.1	1.00 (reference)	1.00 (reference) ^b	NA	NA
0.1- < 0.4	1.77 (0.86–3.67)	1.81 (0.83–3.93) ^b	NA	NA
≥ 0.4	0.94 (0.36–2.47)	1.07 (0.39–2.93) ^b	NA	NA
Distance to Closest 200 + kV Power Line (m)				
≥ 600	1.00 (reference)	1.00 (reference) ^b	NA	NA
500- < 600	0.90 (0.55–1.49)	0.74 (0.43–1.26) ^b	NA	NA
400- < 500	1.36 (0.76–2.43)	1.31 (0.71–2.40) ^b	NA	NA
300- < 400	1.00 (0.61–1.63)	0.79 (0.47–1.33) ^b	NA	NA
200- < 300	0.88 (0.52–1.50)	0.85 (0.48–1.51) ^b	NA	NA
100- < 200	1.21 (0.68–2.15)	1.22 (0.66–2.28) ^b	NA	NA
50- < 100	2.90 (1.10–7.66)	2.23 (0.82–6.06) ^b	NA	NA
< 50	0.79 (0.34–1.83)	0.97 (0.40–2.33) ^b	NA	NA

^a Adjusted for all other non-exposure-of-interest covariates in model.

^b Adjusted for age of child, leukemia type, maternal age at birth, race/ethnicity, number of siblings, mother's place of birth and SES. Numbers too small to analyze with regards to neighborhood.

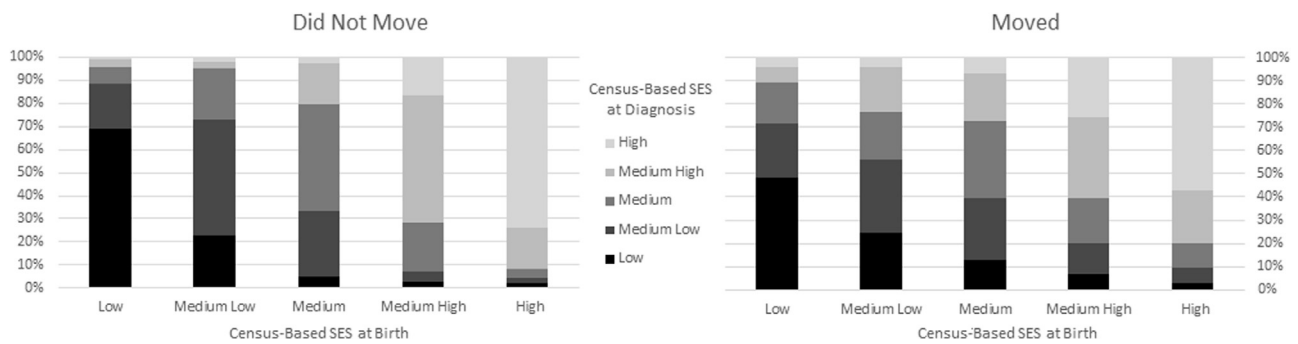


Fig. 2. Changes in census-based socioeconomic status from time of birth to diagnosis in cases, stratified by mobility.

Analyses focusing on dwelling type of site-visited residences, showed a higher association between power lines and childhood leukemia in this subset across all strata, although estimates were imprecise due to smaller numbers. However, adjustment for dwelling type did not change the estimates in comparison to unadjusted analyses in the same subset. For distance, adjustment for maternal age at birth and number of siblings showed a minimal increase in associations with childhood leukemia among those who did not move. Adjustment for race/ethnicity showed a similar slight increase in associations in the analysis of calculated fields. All results were imprecise (Table 4).

When all variables related to mobility except for dwelling type were included in the models via propensity scores, the OR for living < 50 m from a 200 + kV line and for high calculated fields largely remained similar to unadjusted results in previous findings (Table 5). Dwelling type, assessed for a small subset of residences within specific distances from overhead power lines and with likely higher exposure to MF, was not available beyond 200 m for most subjects. With dwelling included in the propensity score in the smaller subset of data, the OR for living < 50 m from a 200 + kV line and for calculated fields ≥ 0.4 μT increased to 2.61 (95% CI: 1.76–3.86) and 1.98 (95% CI: 1.11–3.52), respectively.

4. Discussion

In our study of residential mobility in CAPS, many childhood leukemia cases were mobile, with 61% having changed residence between birth and diagnosis. This excludes about 13% of leukemia cases identified in the CCR born outside of California and an unknown, but likely smaller, number of children born in California who moved out of state before developing leukemia.

Similar to previous findings (Urayama et al., 2009), cases diagnosed at older ages had higher odds of moving between birth and diagnosis, while older maternal age at birth was associated with decreased odds of moving. In our study, we also noted increased likelihood of moving with Black and Hispanic race/ethnicity, being an only child, and a non-US maternal place of birth when analyzed alone, although some associations disappeared when adjusting for other covariates. Racial and ethnic differences in moving preferences have been examined in previous studies, including specific factors such as neighborhood racial/ethnic compositions in California. Most respondents generally preferred neighborhoods comprised of their own race/ethnicity and were likely to move within such neighborhoods or into similar ones. Suburbanization also differed by race/ethnicity (Alba and Logan, 1991; Charles et al., 2003; Clark, 1992). Dwelling type was also associated with mobility,

Table 4

Odds ratios for childhood leukemia by levels of calculated fields and proximity to 200 + kV power lines adjusted for various characteristics associated with mobility, stratified by mobility status of cases.

	Characteristic	Adjustment	Total	Did Not Move	Moved
Distance to 200+ kV Line < 50 m (vs. ≥ 600 m)	Race/Ethnicity	Not adjusted ^a	1.43 (0.74–2.77)	1.61 (0.71–3.62)	1.31 (0.61–2.82)
		Adjusted ^b	1.37 (0.71–2.66)	1.59 (0.70–3.57)	1.28 (0.60–2.76)
	SES	Not adjusted ^a	1.52 (0.79–2.91)	1.62 (0.72–3.64)	1.43 (0.68–3.02)
		Adjusted ^b	1.52 (0.79–2.92)	1.69 (0.75–3.81)	1.42 (0.67–3.00)
	Maternal Age at Birth	Not adjusted ^a	1.51 (0.79–1.61)	1.63 (0.72–3.67)	1.42 (0.67–3.00)
		Adjusted ^b	1.51 (0.79–2.90)	1.75 (0.77–3.96)	1.43 (0.68–3.02)
	Mother's Place of Birth	Not adjusted ^a	1.51 (0.79–2.91)	1.63 (0.73–3.67)	1.42 (0.67–3.00)
		Adjusted ^b	1.51 (0.79–2.91)	1.63 (0.72–3.67)	1.42 (0.68–3.01)
	Number of Siblings	Not adjusted ^a	1.51 (0.79–2.91)	1.63 (0.73–3.67)	1.42 (0.67–3.00)
		Adjusted ^b	1.51 (0.79–2.91)	1.74 (0.77–3.93)	1.41 (0.67–2.98)
Dwelling Type ^c	Not adjusted ^a	2.82 (1.08–7.35)	3.99 (1.09–14.57)	2.31 (0.79–6.74)	
	Adjusted ^b	2.94 (1.12–7.72)	4.18 (1.11–15.81)	2.49 (0.84–7.36)	
Calculated Fields ≥ 0.4 μT (vs. < 0.1 μT)	Race/Ethnicity	Not adjusted ^a	1.51 (0.70–3.22)	1.65 (0.63–4.35)	1.51 (0.64–3.58)
		Adjusted ^b	1.48 (0.69–3.18)	1.72 (0.65–4.55)	1.50 (0.63–3.59)
	SES	Not adjusted ^a	1.52 (0.71–3.25)	1.66 (0.63–4.36)	1.53 (0.64–3.62)
		Adjusted ^b	1.52 (0.71–3.26)	1.68 (0.64–4.42)	1.51 (0.64–3.57)
	Maternal Age at Birth	Not adjusted ^a	1.52 (0.71–3.25)	1.67 (0.63–4.41)	1.52 (0.64–3.60)
		Adjusted ^b	1.51 (0.71–3.23)	1.62 (0.61–4.33)	1.52 (0.64–3.61)
	Mother's Place of Birth	Not adjusted ^a	1.52 (0.71–3.25)	1.67 (0.63–4.41)	1.52 (0.64–3.60)
		Adjusted ^b	1.51 (0.71–3.23)	1.67 (0.63–4.40)	1.52 (0.64–3.61)
	Number of Siblings	Not adjusted ^a	1.52 (0.71–3.25)	1.67 (0.63–4.41)	1.52 (0.64–3.60)
		Adjusted ^b	1.50 (0.70–3.21)	1.66 (0.63–4.41)	1.53 (0.64–3.62)
	Dwelling Type ^c	Not adjusted ^a	2.20 (0.80–6.08)	4.45 (1.07–18.54)	1.78 (0.54–5.81)
		Adjusted ^b	2.17 (0.79–6.01)	4.63 (1.11–19.29)	1.74 (0.53–5.69)

^a Adjusted for age and sex.

^b Adjusted for age, sex, and the variable in question.

^c Only available for small subset of site-visited residences.

Table 5

Odds ratios for childhood leukemia by levels calculated fields exposure and proximity to 200 + kV power lines, adjusted for variables associated with mobility using propensity scores.

Variable	Without Dwelling		With Dwelling	
	Case/Control	AOR (95% CI) ^a	Case/Control	AOR (95% CI) ^b
Distance (m)				
≥ 600	4,318/4,244	1.00 (reference)	33/43	1.00 (reference)
100- < 200	51/66	0.76 (0.67–0.87)	17/15	1.48 (1.05–2.07)
50- < 100	27/27	0.98 (0.81–1.19)	17/18	1.23 (0.89–1.71)
< 50	22/15	1.44 (1.14–1.82)	16/8	2.61 (1.76–3.86)
Calculated Fields (μT)				
< 0.1	4,604/4,533	1.00 (reference)	47/50	1.00 (reference)
0.1- < 0.4	37/40	0.91 (0.70–1.18)	24/29	0.88 (0.60–1.30)
≥ 0.4	17/11	1.52 (0.98–2.36)	13/7	1.98 (1.11–3.52)

^a Adjusted for age of child, sex, race/ethnicity, SES, maternal age at birth, mother's place of birth, and number of siblings.

^b Adjusted for age of child, sex, race/ethnicity, SES, maternal age at birth, mother's place of birth, number of siblings, and dwelling type.

but the numbers were small, leading to imprecise estimates. Similar results were found when considering moving within and outside neighborhoods, with some variables showing slightly more pronounced results for those moving outside the birth neighborhood while Hispanic race/ethnicity and non-US maternal place of birth were more strongly associated with moving within the same neighborhood. Interestingly, neither high calculated fields nor close proximity to 200 + kV power lines were associated with greater likelihood of moving.

It seems obvious for age at diagnosis to be positively correlated with likelihood of residential mobility as more time means more opportunity to change residence. However, several studies indicated greater likelihood of moving around the time of birth, as families prepare or adjust to their new addition, particularly true for the birth of the first child (Clark and Huang, 2003; Kulu, 2005; Rabe and Taylor, 2009). A Texas study on residential mobility, environmental exposures, and birth defects found ~30% each of case and control mothers moved between the time of conception and delivery (Canfield et al., 2006). In a UK study, approximately 20% of mothers of infants moved (Champion, 2005). Further exploration of how mobility intersects with age of the child, parental age, birth order, and dwelling type is warranted.

Using the composite SES, we found that lower SES was associated with greater likelihood of moving, as in previous studies (Urayama et al., 2009). Although for most participants, individual measures of SES were used, the composite SES variable also included census-based SES, which could differ between time of birth and diagnosis, even for residentially stable subjects, because census-based SES may change over time. The census-based SES measure was based on seven different factors, any number of which could have shifted for each census tract. Similarly, definitions of the factors may have also changed (e.g. federal poverty level, calculation of education index, etc.). However, there did not appear to be any material trend in changes in SES from birth to diagnosis or for distance to power lines or calculated fields among those who moved.

To assess how mobility may affect the relationship of exposure to MF and childhood leukemia, we stratified by the mobility of the cases. In the strata of cases who did not move, a slightly stronger association was found for both proximity to power lines and MF, suggesting that birth home may be a better indicator of exposure in these children. When looking at cases who moved greater than 2 km away from their birth home, we also saw an increase in effect. Children moving outside

their birth neighborhoods may have more opportunity to encounter new infections, consistent with the infectious disease etiology. Another possibility is that these cases moved due to pre-diagnostic conditions or perhaps other environmental characteristics associated with their proximity to power lines, but not captured in our dataset. This subgroup of movers might have unmeasured susceptibility to leukemia also associated with their moving farther away. However, all results were imprecise, so larger datasets would be needed to explore any of these hypotheses.

While the mobility of controls was unknown, the variables associated with mobility were known for both cases and controls. Thus, we used them as a surrogate of mobility to evaluate if they modified the relationship between proximity to power lines and MF on childhood leukemia. We observed an increase in the ORs for both MF and distance. Dwelling type, in particular, seems to be a major predictor of mobility, however, this information was available only for site-visited homes within certain distances of overhead power lines (n = 178). Dwelling type can indicate quality of exposure assessment, in particular for MF, where calculation of MF in non-single-family homes more likely to lead to misclassification (Feychting and Ahlbom, 1993; Vergara et al., 2015). Further exploration is needed in datasets with more complete residential information.

Strengths of this study include the use of population registries to obtain data, thus avoiding participation bias and exposure assessment blind to case-control status to reduce information bias. To increase accuracy of exposure and outcome assessment, we excluded from analyses all cases and controls with imprecise geocode matching for birth or diagnosis address. Another strength was the large sample size, which increased the power to detect associations, should they exist. Despite the large sample size, in some analyses, especially those involving dwelling type, the analytic sample was reduced because the variable was only available for site-visited residences. Since site visits were conducted blind to case-control status, the potential for biases was probably small, and the impact was mainly on the precision of the estimates.

A potential limitation of our study was misclassification of residential mobility. We defined residential mobility by distance between the geocoded points of birth and diagnosis addresses of cases. Although some misclassification was inevitable, we minimized it by manually investigating, mapping, and visually inspecting all distances between birth and diagnosis residences that were less than 100 m. Based on our visual inspection and geocoding accuracy considerations, we developed the 50 m cut point to decide whether a case moved or not to maintain high specificity. *A priori* sensitivity analysis performed using differing cut points showed similar results (Oksuzyan, 2013). The propensity scores allowed us to adjust for the propensity to move for both cases and controls and thus partially overcome lack of mobility information for controls.

Although CAPS focused on power lines and EMF exposure, we believe the findings on mobility are relevant to other environmental exposures and other childhood outcome studies. Exposure misclassification due to mobility in particular has been expressed as a concern in birth outcome studies (Chen et al., 2010; Lupo et al., 2010; Madsen et al., 2010; Schulman et al., 1993). It may also be pertinent to consider maternal mobility during pregnancy as prenatal exposures are associated with a variety of birth and childhood outcomes.

In conclusion, because our controls were potentially less residentially stable than our cases, we examined whether the observed association of childhood leukemia with exposure to MF or distance to power lines could be due to this potential difference. We found that the effects of distance to power lines and MF exposure on childhood leukemia were similar for a residentially stable subset of cases and overall results were unchanged when we controlled for proxies of mobility, except for dwelling. These results suggest that confounding by mobility is an unlikely explanation for the associations observed.

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