Childhood Cancer in Relation to a Modified Residential Wire Code

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Several studies have found associations between wire configuration codes, a proxy for historical residential magnetic field exposure, and childhood cancer. The Wertheimer-Leeper coding method was modified by eliminating the distinction between thick and thin primaries, distinguishing only between open and spun secondaries, and reducing the number of categories from five to three. The association between the modified code and measured magnetic fields was similar to the association with the original wire code. The modified code was used to reanalyze data from a case–control study of childhood cancer in the Denver metropolitan area. In the original study, cases were diagnosed from 1976 to 1983 among children under age 15 and compared to controls selected through random digit dialing. Wire codes for the residence at diagnosis yielded imprecise elevations of two and above for very high current configuration homes or modest 1.5-fold elevations for a dichotomous wire code. In contrast, the modified Wertheimer-Leeper code generated risk estimates that were both precise and markedly elevated for the high wire code (HWC) compared to low wire code (LWC) classifications, with medium wire code (MWC) showing little or no increase in risk. High wire code yielded odds ratios of 1.9 for total cancers (95% CI: 1.1–3.2), 2.9 for leukemias (95% CI: 1.5–5.5), and 2.5 for brain cancer (95% CI: 1.1–5.5) that were not confounded by measured potential risk factors for childhood cancer. These risk estimates are larger than the dichotomized results and more precise than those from the original five-level wire code, though limitations in the original study remain, particularly potential control selection bias. This refined and greatly simplified approach to wire configuration coding may be useful in other studies. **Key words:** brain neoplasms, electromagnetic fields, leukemia, wire configuration codes. *Environ Health Perspect 101(1):76–80*

Wertheimer and Leeper (*1*) first reported an association between wire configuration codes, a surrogate measure of residential magnetic field exposure, and childhood cancer. A persistent concern has been the validity of classifying exposure based on attributes of the power lines in the vicinity of the home (*2*). Subsequent studies in both the USA (*3,4*) and Europe (*5,6*) considered both characteristics of nearby distribution and transmission lines and exposure indicators based on measured fields. In general, although not as strong as Wertheimer and Leeper's (*1*) original results, subsequent studies have reported relative risks of about 1.5–2.0 based on Wertheimer-Leeper wire codes (*3,4*). One of the most surprising aspects of studies that included both measured magnetic fields and wire codes was that associations with cancer were generally weaker for measured fields than for wire codes (*3,4*).

Measured fields have consistently been correlated, albeit weakly, with wire codes (*1,3,7*), providing empirical evidence that wire codes are a proxy for contemporaneous magnetic field exposure in the home. If the only goal was to determine present-day exposure to the home occupants, measured fields would have to be considered superior to wire codes. However, the goal of all epidemiologic studies conducted to date has been to characterize long-term historical exposure. Given an interest in residential exposures over a period as long as 15 or 20 years, the question of whether the present measured field is a better surrogate than a wire code is not easily answered. Distribution wiring is believed to change infrequently, so that the wire code of the present is probably identical to the wire code that would have been assigned in the past. In contrast, measured fields are influenced by both stable attributes, such as the components produced by nearby power lines, and transient sources, such as in-home wiring and electrical load on the powerline grid at the time of measurement. Recent unpublished results from Sweden addressing transmission line exposures (*8*) support the contention that present-day measured fields may not be as useful a surrogate for historical exposure as wiring characteristics, particularly when combined with information on historical electric loads.

Wire codes not only may have the theoretical advantage of historical stability, but they provide many logistical advantages in conducting epidemiologic studies. Foremost is the opportunity to collect wire coding information without disrupting the occupants of the home. Because entry into the home or yard is seldom required to obtain information on wiring attributes, nonresponse proportions may be markedly lower and data collection can be scheduled much more efficiently than when respondent cooperation is needed, as is required for obtaining in-home measurements. For example, in the study on which this paper is based (*3*), measurements were obtained for 36% of case homes and 75% of control homes, in contrast to wire codes, which were obtained for 90% of cases and 93% of controls. Compared to measurements, which integrate across all sources, wire codes have the advantage of more explicitly defining the source of the magnetic field exposure. Finally, it is principally wire codes that have been associated with cancer and, regardless of whether this is reflective of an influence of magnetic fields or some other attribute of the residence, wire codes are worthy of further study simply because of the reported associations.

Because of the clear logistical advantages of wire codes, the possible theoretical advantages, and their rather consistent association with risk of childhood cancer, we have proposed refinements to the original Wertheimer-Leeper code (Kaune and Savitz, submitted) using data from the previously reported study of magnetic fields and childhood cancer (*3*). These refinements make no sacrifice in the ability to predict measured fields, yet avoid the most subjective elements of the coding method and create fewer categories. By avoiding the major sources of inaccuracy in assessing wire thickness and distinguishing among first-span, short first-span, and second-span secondary lines, we may well reduce random error in classification. Wire thickness, for example, is a subjective distinction based on a comparison among wires, lacking any gold standard of validity. The resulting error, almost certain to be nondifferential with respect to case or control status because the data were collected blindly, would dilute measures of association. By creating a smaller number of categories, the precision of the risk estimates is enhanced relative to the previously reported five-level code. Therefore, we analyzed

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the association between the modified Wertheimer-Leeper code and childhood cancer in the Denver, Colorado, area and contrasted the results to those from the original analysis.

Methods

The data used here were collected between 1984 and 1986 as part of a case–control study of childhood cancer and residential magnetic field exposure, details of which are reported elsewhere (*3*). Briefly, all cases of cancer in children under age 15 were identified among residents of the 1970 Denver Standard Metropolitan Statistical Area (Adams, Arapahoe, Boulder, Denver, and Jefferson counties), from 1January 1976 through 31 December 1983. The Colorado Central Cancer Registry provided most of the cases, with complete registration for the period 1979–1982, supplemented by data from area hospitals before and after that time. Diagnostic accuracy was assured through microscopic confirmation (over 95%) and review by a pediatric oncologist. Incidence rates in the study area were similar to those reported in the Surveillance, Epidemiology and End Results (SEER) registries (*9*), suggesting essentially complete ascertainment.

We chose controls through random-digit dialing by starting with each case's telephone number at the time of diagnosis and randomly replacing the last two digits. A child of similar age (±3 years) and sex was sought (*3*). An undesirable aspect of identifying controls some years after the cases had been diagnosed is that only eligible controls who remained in the home occupied at the time of the case's diagnosis were identifiable. Therefore, controls were more residentially stable than cases. In the analysis, we examined a marker of residential stability as a potential confounder or effect modifier.

We conducted a structured interview addressing a wide range of potential childhood cancer risk factors with the mother or alternate respondent for those cases whose physicians permitted us to contact them and who agreed to participate in the study, along with identified, cooperative controls. We assigned wire configuration codes based on residence at the time of diagnosis for cases or the assigned "diagnosis" date for controls, regardless of duration of occupancy. Lists of the addresses of interest were provided to a coder who was unaware of the case or control status of the occupant of each residence. The coder sketched a map of the distribution and transmission lines in the vicinity of the homes and used a coding sheet to record detailed information on wiring.

As reported in the original analysis (*3*), we analyzed the Wertheimer-Leeper code using the four levels plus buried wire category (*10*), as well as by dichotomizing the wire codes as low (ordinary low current configuration, very low current configuration, buried wire) or high (very high current configuration, ordinary high current configuration). The modified wire codes analyzed in this paper, whose levels are low wire code (LWC), medium wire code (MWC), and high wire code (HWC), were derived based on their relations with measured fields. This new coding system assigns HWC to homes within 20 m of a transmission or three-phase primary line and MWC to homes that are not HWC but have a transmission line or three-phase primary line within 46 m or an open secondary line within 26 m (Kaune and Savitz, submitted). Both the original Wertheimer-Leeper code and modified code were able to account for approximately 20% of the variance in measured fields, but there is a clear separation in the means across the wire code categories in both instances (Kaune and Savitz, submitted).

We calculated crude odds ratios and 95% confidence intervals for total cases and subgroups of acute lymphocytic leukemia (ALL), brain tumors, lymphomas, soft tissue tumors, and other cancers. With the five-level code, we contrasted each of the four upper levels with buried wire as the referent. For the dichotomous codes, we contrasted high with low, and for the modified Wertheimer-Leeper code, both HWC and MWC were contrasted with LWC.

Potential confounding was examined for age at diagnosis (0–4, 5–9, 10–14 years), gender (male, female), race (white, black/other), mother's age (<20 versus ≥21 years), mother's smoking (yes, no), father's education (<16 versus ≥16), per capita income (<$7,000 versus ≥$7,000 per year), year of diagnosis (before 1979, 1980 or later), residential stability (stable residence from birth to diagnosis, moved between birth and diagnosis), and residence type (single family dwelling, other). We computed adjusted odds ratios and confidence intervals using the Mantel-Haenszel technique (*11*). Logistic regression models were constructed that simultaneously adjusted for age at diagnosis, race, mother's smoking, per capita income, year of diagnosis, and residential stability. Age at diagnosis, gender, father's education, per capita income, year of diagnosis, residential stability, and residence type were also examined as potential effect modifiers.

Results

As noted in the earlier report (*3*), 356 cases were identified, among whom wire codes at diagnosis were obtained for 320 (90%), and interviews were obtained for 252 (71%). For controls, 378 were identified, with an estimated 79% response in the random-digit dialing phase, among whom wire codes were obtained for 259 (93%) and interviews for 222 (80%). In conducting the subject-by-subject review for this reanalysis, we identified two additional wire codes, one for a case and one for a control, increasing the totals to 321 cases and 260 controls. Among the cases, there were 103 leukemias (98 with wire codes), 83 acute lymphocytic leukemias (78 with wire codes), 67 brain tumors (59 with wire codes), 35 lymphomas (30 with wire codes), 32 soft tissue sarcomas (all with wire codes), and 119 other cancer types (102 with wire codes). The results are presented initially for all eligible subjects with wire codes, but for analyses examining confounding or effect modification, only the subset of subjects with both wire codes and completed interviews could be included.

Table 1 summarizes the results of the original analysis by five-level wire code. An increase in risk with higher wire codes was found, restricted largely to the very high-current configuration residences [odds ratios (ORs) of 1.6–3.3]. These measures are rather imprecise, particularly for the specific cancer types. Suggestions of increased risk among ordinary high-current configuration homes were found for total cancers, leukemias, brain tumors, and other cancer, with ORs of 1.4–2.0. The dichotomous wire code (Table 2) yielded much more precise evidence of elevated risks for all cancers except lymphomas (OR = 0.8, 95% CI: 0.3–2.2). Total cancers, leukemias, and other cancers yielded ORs around 1.5, with brain tumors showing a stronger association (OR = 2.1, 95% CI: 1.1–3.8). The impact of restricting the data to interviewed subjects is presented in Table 2 as well, indicating that in the absence of any adjustments for confounding, interviewed subjects had slightly higher ORs for leukemia and lower ORs for brain tumors.

The mapping of the original five-level Wertheimer-Leeper code to the modified three-level Wertheimer-Leeper code is described in Table 3. Because the modified wire codes are hypothesized to be the more accurate, we examined the potential misclassification introduced in reassigning homes from the modified to the Wertheimer-Leeper codes. Overall, the pattern of movement was as expected, with LWC homes predominantly migrating to the lowest three levels of Wertheimer-Leeper wire code, MWC homes going to the middle groups, and HWC homes moving to the two higher current-configuration categories. Examination of the pattern of movement of cases versus controls yields rather consistent results for the two groups.

Table 1. Summary of results using original Wertheimer-Leeper five-level wire configuration codes: Denver, Colorado,1976–1983, all eligible subjects

Wire configuration	Total Controls	Total Cases	Leukemia	ALL	Brain	Lymphoma	Soft tissue sarcoma	Other
Very high current								
No. of subjects	8	19	7	6	3	3	2	4
Odds ratio		2.2	2.8	2.8	1.9	3.3	1.7	1.6
95% CI		0.9–5.3	0.9–8.3	0.9–8.7	0.5–8.1	0.8–14.5	0.3–8.9	0.5–5.8
Ordinary high current								
No. of subjects	44	70	20	13	17	2	7	24
Odds ratio		1.5	1.4	1.1	2.0	0.4	1.1	1.8
95% CI		0.9–2.4	0.7–2.8	0.5–2.3	0.9–4.3	0.1–1.9	0.4–2.9	0.9–3.4
Ordinary low current								
No. of subjects	102	108	70	33	17	11	8	34
Odds ratio		1.0	2.2	1.2	0.9	0.9	0.5	1.1
95% CI		0.7–1.5	0.7–2.1	0.7–2.2	0.4–1.8	0.4–2.3	0.2–1.3	0.6–1.9
Very low current								
No. of subjects	18	29	5	2	5	4	2	13
Odds ratio		1.5	0.9	0.4	1.4	2.0	0.8	2.4
95% CI		0.8–2.9	0.3–2.6	0.1–1.9	0.5–4.4	0.6–6.9	0.2–3.6	1.0–5.4
Buried wire (referent)								
No. of subjects	88	95	28	24	17	10	13	27

ALL, acute lymphocytic leukemia.

Table 2. Summary of results using original dichotomous Wertheimer-Leeper wire configuration codes: Denver, Colorado, 1976–1983, eligible and interviewed subjects

Wire configuration	Total Controls	Total Cases	Leukemia	ALL	Brain	Lymphoma	Soft tissue sarcoma	Other
All eligible subjects								
High								
No. of subjects	52	89	27	19	20	5	9	28
Odds ratio		1.5	1.5	1.3	2.1	0.8	1.6	1.5
95% CI		1.0–2.3	0.9–2.6	0.7–2.3	1.1–3.8	0.3–2.2	0.7–3.6	0.9–2.6
Low (referent)								
No. of subjects	208	232	71	59	39	25	23	74
All interviewed subjects								
High								
No. of subjects	40	65	21	15	13	5	7	19
Odds ratio		1.6	1.8	1.5	1.8	1.0	1.5	1.6
95% CI		1.0–2.5	1.0–3.3	0.8–3.0	0.8–3.7	0.4–2.8	0.6–3.7	0.9–3.1
Low (referent)								
No. of subjects	158	161	47	39	29	20	19	46

High, very high current configuration or ordinary high current configuration; low, ordinary low current configuration, very low current configuration, or buried wires; ALL, acute lymphocytic leukemia.

Table 3. Reassignment from original to modified Wertheimer-Leeper wire configuration codes for cases and controls: Denver, Colorado, 1976–1983, eligible subjects

Original wire code	Modified wire code: LWC No.	LWC %	MWC No.	MWC %	HWC No.	HWC %
Cancer cases						
Buried wire	95	58	0	0	0	0
Very low current	24	15	5	5	0	0
Ordinary low current	36	22	71	69	1	2
Ordinary high current	8	5	27	26	35	64
Very high current	0	0	0	0	19	35
Controls						
Buried wire	88	61	0	0	0	0
Very low current	14	10	4	4	0	0
Ordinary low current	31	21	71	80	0	0
Ordinary high current	12	8	14	16	18	69
Very high current	0	0	0	0	8	31

LWC, low wire code; MWC, medium wire code; HWC, high wire code.

Focusing on the dichotomy of the lowest three to the upper two categories, 35 of 266 LWC and MWC cases combined (13%) were in the upper group versus 26 of 234 LWC and MWC controls (11%). The likelihood of an HWC subject being assigned to the very high current configuration category was also similar, with 35% of cases and only 31% of controls moving in that direction. The misclassification thus appears to be basically nondifferential.

Analysis of cancer risk in relation to the modified Wertheimer-Leeper code yields ORs that are more precise than the results based on the five-level wire code analysis and more markedly elevated than the results based on the dichotomous codes (Table 4). In the HWC versus LWC contrast, total cancers showed nearly a 2-fold increased risk, with leukemias (OR = 2.9, 95% CI: 1.5–5.5) and brain tumors (OR = 2.5, 95% CI: 1.1–5.5) particularly strongly associated. In contrast to the 7 leukemias and 3 brain tumor cases in the very high current configuration group, there were 22 leukemias and 12 brain tumor cases in the HWC category, markedly improving the precision of the estimates. Lymphoma and soft tissue sarcoma showed more modest and imprecise ORs of 1.6 and 1.7, respectively, and the aggregation of other cancers showed no association (OR = 1.0, 95% CI: 0.5–2.2). The contrast of MWC with LWC yielded no association for total cancers, but leukemias and brain tumor cases showed a modest association (ORs of 1.3 and 1.2, respectively). The risk elevations were basically restricted to the HWC group.

Potential confounding was examined (Table 5) and generally found to be absent. Only results for the HWC versus LWC are presented, with the contrast of MWC versus LWC remaining near the null value with or without adjustment. As in the original analysis, the baseline risk estimates were different after restriction to interviewed subjects, with the overall ORs rising from 1.9 to 2.1 for all cases, 2.9 to 3.5 for leukemias, and falling from 2.5 to 1.9 for brain tumor cases. Thus, confounding was evaluated relative to that benchmark.

Adjusted ORs for total cancers, leukemias, and acute lymphocytic leukemia showed no evidence of substantial confounding, defined as adjusted estimates more than 10% larger or smaller than the unadjusted estimates. For brain tumors, a modest decrease in the OR was found after adjustment by race and a modest increase with adjustment for year of diagnosis. Logistic regression models were constructed for total cancers, leukemias, and brain cancer, with age at diagnosis, race, maternal smoking, per capita income, year of diagnosis, and residential stability

Table 4. Results using modified Wertheimer-Leeper three-level wire configuration code: Denver, Colorado, 1976–1983, eligible subjects

Wire configuration	Total Controls	Total Cases	Leukemia	ALL	Brain	Lymphoma	Soft tissue sarcoma	Other
HWC								
No. of subjects	26	55	22	16	12	5	6	10
Odds ratio		1.9	2.9	2.6	2.5	1.6	1.7	1.0
95% CI		1.1–3.2	1.5–5.5	1.3–5.4	1.1–5.5	0.6–4.8	0.6–4.6	0.5–2.2
MWC								
No. of subjects	89	103	33	28	20	8	6	36
Odds ratio		1.0	1.3	1.3	1.2	0.8	0.5	1.0
95% CI		0.7–1.5	0.7–2.1	0.8–2.4	0.6–2.3	0.3–1.9	0.2–1.3	0.6–1.7
LWC (referent)								
No. of subjects	145	163	43	34	27	17	20	56

HWC, high wire code; MWC, medium wire code; LWC, low wire code; ALL, acute lymphocytic leukemia.

Table 5. Crude and adjusted results (odds ratios) for high versus low modified Wertheimer-Leeper wire code: Denver, Colorado,1976–1983, interviewed subjects

Adjusted for	Total cancers	Leukemia	Brain cancer
Crude	2.1	3.5	1.9
Age at diagnosis	2.1	3.7	2.3
Gender	2.0	3.4	2.0
Race	2.0	3.6	1.6
Mother's age	2.0	3.5	2.0
Mother's smoking	1.7	3.1	2.0
Father's education	2.0	3.5	1.9
Per capita income	2.0	3.3	1.7
Year of diagnosis	2.2	3.8	2.2
Residence stability	2.1	3.8	1.9
Age at diagnosis, race, mother's smoking, per capita income, year of diagnosis, residential stability	2.0	3.8	2.4
95% CI	1.0-4.0	1.6-9.0	0.8-7.6

Table 6. Stratum-specific results (odds ratios and 95% confidence intervals) for high wire code versus low wire code: Denver, Colorado, 1976–1983, interviewed subjects

Parameter	Total cancers OR	Total cancers CI	Leukemia OR	Leukemia CI	Brain cancer OR	Brain cancer CI
Age at diagnosis						
0–4 years	1.9	0.9–4.2	3.9	1.4–10.6	1.0	0.2–5.3
5–9 years	1.8	0.3–10.2	2.3	0.3–19.0	2.3	0.3–19.0
10–14 years	2.9	1.0–8.5	4.1	0.9–19.0	6.2	1.0–38.2
Gender						
Male	1.6	0.8–3.3	2.4	1.0-6.0	1.7	0.5–6.2
Female	3.3	1.2–9.1	7.0	1.9–26.3	2.4	0.5–11.2
Father's education						
<16 years	1.8	0.9–3.8	4.2	1.6–11.1	2.3	0.8–7.0
≥16 years	2.3	0.8–6.2	2.5	0.7–8.9	—	
Per capita income						
<$7000/year	2.1	1.0–4.4	3.6	1.5–8.9	1.7	0.6–5.2
≥$7000/year	1.8	1.1–3.1	2.8	0.7–11.4	1.8	0.2–18.5
Year of diagnosis						
Before 1980	1.3	0.5–3.5	1.8	0.5–6.3	0.9	0.2–5.0
1980 or later	3.7	1.4–9.7	7.1	2.3–22.1	3.8	1.5–9.9
Residential stablility						
Unstable	2.9	1.3–6.6	4.7	1.8–12.5	1.7	0.4–7.1
Stable	1.5	0.6–3.6	2.7	0.8–9.4	2.1	0.5–8.5
Residence type						
Single family	2.1	1.1–4.1	3.9	1.7–8.9	2.0	0.6–6.2
Other	2.0	0.4–11.2	2.8	0.3–28.3	1.4	0.1–13.6

included as potential confounders. In those models, the adjusted ORs contrasting HWC and LWC were 2.0 for total cancers (95% CI: 1.0–4.0) , 3.8 for leukemias (95% CI: 1.6–9.0), and 2.4 for brain tumors (95% CI: 0.8–7.6). With adjustment, the modest elevations for medium versus low modified wire code were eliminated, with ORs of 0.8 for total cancers (95% CI: 0.5–1.2) , 0.9 for leukemias (95% CI: 0.4–1.8), and 0.8 for brain tumors (95% CI: 0.4–1.9).

Indications of effect modification were examined for the cancers with the most adequate numbers, namely, total cancers, leukemias, and brain tumors (Table 6). For total cancers, and especially for brain tumor cases, the increased risk for HWC was concentrated among the older cases. Females had higher ORs than males, especially for leukemias. Social class indicators have received considerable attention because of possible selection bias in the manner in which controls were chosen and recruited (*12*). Risk estimates were somewhat greater in the lower paternal education and lower income strata but were still present in the higher education and higher income strata. Residential stability is also of particular concern given the restrictions that were imposed on the controls but not on the cases. For total cancers and leukemia cases, ORs were less markedly elevated for stable cases (same residence from birth to diagnosis), with a tendency in the opposite direction for brain tumor cases. Finally, the strongest indication of effect modification was found for year of diagnosis, in which much of the elevation in risk was found for cases and controls with diagnosis dates of 1980 or later.

Discussion

The principal result of this reanalysis of data on wire configuration codes and childhood cancer is the stronger relations found for the modified HWC as compared to the analysis based on the original dichotomized Wertheimer and Leeper wire configuration coding system. In fact, the ORs based on the modified HWC were similar in magnitude but markedly more precise than the ORs previously noted for very high current configuration alone. The original dichotomous Wertheimer-Leeper code yielded ORs of 1.5 and 2.1 for leukemias and brain cancers, respectively, and the HWC produced ORs of 2.9 and 2.5, respectively. A modestly elevated risk was associated with MWC compared to LWC, but that elevation was eliminated by adjusting for potential confounding factors.

Additional contrasts from the earlier analysis concern the magnitude of risk associated with different cancer types. The

analysis of the dichotomous Wertheimer-Leeper codes produced rather consistent 1.5-fold increased risks for all cancer types, with a slightly larger risk for brain cancer, and no increased risk for lymphomas. The modified high wire code was notably more strongly linked to leukemia (OR = 2.9) and brain cancer (OR = 2.5) than to lymphoma (OR = 1.6), soft tissue sarcoma (OR = 1.7), or to the heterogeneous other cancer group (OR = 1.0). Small numbers of lymphoma and soft tissue sarcoma cases limit the certainty of this pattern, however.

In addition to the hypothesized sources of spurious elevations in risk associated with wire configuration code, a principal source of dilution in risk measures has been assumed to be nondifferential misclassification of exposure (*12,13*). Under the assumption that an association is truly present, reducing the extent of that misclassification would yield stronger indices of association. The modified wire code is believed to be more valid as an exposure marker than the original code because the most subjective elements in the data collection process are eliminated, and the relation between the wire code and field measurements is similar. In fact, the pattern of results relative to the Wertheimer-Leeper wire code is consistent with the hypothesis that nondifferential misclassification has been reduced. Inherent uncertainties resulting from lack of information on exposures outside the home and lack of detailed information about the use of appliances remain. However, regardless of the absolute level of accuracy in wire codes as a proxy of exposure, which is currently unknown, the improvement in wire codes yielded a corresponding increase in the measures of association for leukemia and brain cancer. Such a pattern is consistent with an underlying causal association not only between wire codes and cancer but, because the modified code was derived from spot measurements of magnetic fields, it is consistent with the possibility of an effect of average magnetic field on childhood cancer.

A number of aspects of the data call into question the presence of an etiologic relation between wire code and childhood cancer. The design of the study yielded controls who were more residentially stable than cases (*3*), with residential stability potentially related to wire configuration code. Instead of stable subjects (those who lived in the same home from birth to diagnosis) yielding stronger associations, as might be expected if longer duration of occupancy improved discrimination of relevant exposure levels, the risk estimates for residentially stable subjects were actually somewhat lower than for unstable subjects in relation to leukemia (ORs of 2.7 and 4.7) and modestly higher for brain cancer (ORs of 2.1 and 1.7, respectively). However, residential stability is closely associated with age at diagnosis, so that the lower risk for stable subjects reflects in large part a lower risk for younger subjects.

Another aspect of control selection that raises questions about the validity of our results is the loss of potential controls in the random-digit dialing process, either because potential candidates lacked telephones, refused at the screening stage, or refused to be interviewed. Wire code information was available for most subjects who made it past the screening stage, but the others are not included in the control group. It might be postulated that such persons would be most prevalent in the lower socioeconomic status stratum. Measured by either father's education or per capita income, ORs for leukemia were greater among lower socioeconomic status subjects, but not markedly so. In the higher education and income strata, ORs were still 2.5 or greater, and for brain cancer, there was no difference in the risk estimates across education and income strata.

One unexplained source of effect modification was related to year of diagnosis. Virtually all of the increase in risk for HWC homes was among subjects diagnosed in 1980 or later, for whom the ORs were strikingly large and imprecise. The ORs were 3.7 (95% CI: 1.4–9.7) for total cancers, 7.1 (95% CI: 2.3–22.1) for leukemias, and 3.8 (95% CI: 1.5–9.9) for brain cancer. It might be speculated that wire codes are somehow more valid exposure markers for more recent cases and controls, e.g., if modifications to the distribution system were unexpectedly frequent over time, but the reason for enhanced risks in more recently diagnosed subjects remains unknown.

At a minimum, this reanalysis should serve to encourage other investigators to consider the modified wire code as an addition to, and perhaps even an alternative to, the original Wertheimer-Leeper coding system. The pursuit of this research avenue is largely driven by epidemiologic findings, and the empirical basis for further study of the modified code is more compelling than for the original wire configuration code based on the Denver study analyzed here. The logistical advantages of the method (Kaune and Savitz, submitted) add to the incentive to restrict studies to the modified code alone.

The generalizability of these results to the other studies that have used the Wertheimer-Leeper method (*1,4,10*) would be of great interest. In a single study, the potential for inexplicable and perhaps random processes to yield a pattern must be acknowledged. If the modified coding method enhanced associations with cancer risk across study settings, its validity would markedly increased.

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