Residential exposure to magnetic fields: an empirical examination of alternative measurement strategies

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Abstract

***Objectives*—To investigate the impact of measuring a single home then imputing information from another home among subjects who lived in two homes in a subset of the National Cancer Institute/Children's Cancer Group (NCI/CCG) investigation of residential exposure to magnetic fields and risk of childhood leukaemia.**

***Methods*—Each subject's summary time weighted average (TWA) exposure was derived from measurements of two homes, weighted by the fraction of the reference period lived in the residence. The three cost efficient field work strategies examined were measuring: (*a*) the longer lived in home; (*b*) the currently lived in home; and (*c*) the former lived in home. Two different methods were used for imputing the missing values: (*a*) control mean imputation, (*b*) status specific mean imputation. The subject's summary exposure to magnetic fields estimated with each approach was compared with the subject's TWA calculated from measurements in both homes. The association between estimated exposure to magnetic fields and the risk of leukaemia under different approaches was examined with unconditional logistic regression analysis.**

***Results*—The Pearson correlation coefficient between the two measurements within subjects was 0.31 ($p<10^{-4}$), indicating a lack of independence of measurements. Differences were found between mean exposures in current and former homes of cases, and between longer and shorter lived in homes of controls. All methods with measurements from one of the homes in conjunction with imputation of measurements for the second home led to marked attenuation of risk estimates at the highest exposure category, particularly when measurements from current homes were used and those from former homes were imputed.**

***Conclusion*—Results argue against attempting to estimate lifetime magnetic field exposure from imputed values derived from current residences to fill in gaps caused by unmeasured residences previously lived in.**

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Accurate exposure assessment is a critical challenge in epidemiology. In case-control studies, measurements are often taken long after diagnosis of the cases. In assessment of residential exposures—such as to extremely low frequency magnetic fields or radon—the time required and cost of measuring each home is daunting, so it is important to consider economical strategies to assess exposure and to compare results derived from limited versus more complete measurement protocols. Further, there are inevitably gaps in exposure histories due to failure to locate or gain access to various homes. Weinberg *et al*[1] considered several strategies for imputing exposures when measurements could not be obtained in some homes. They evaluated these strategies with a simulation study that made several assumptions. We evaluated those assumptions with data collected for the National Cancer Institute/Children's Cancer Group (NCI/CCG) Study to investigate residential exposures to magnetic fields and risk of childhood acute lymphoblastic leukaemia (ALL).[2 3] We also assessed the loss of information with non-optimal exposure estimation, and the impact of that loss of information on the risk estimates

Specifically, we investigated the impact of measuring a single home among the subset of cases and controls who lived in two homes that required measurement (for a complete residential exposure assessment) for the NCI/CCG study. We assessed how alternative field strategies (measuring only one home, the home lived in longest, or the home currently lived in) and imputation strategies (measuring only the longer lived in home and imputing a measurement for the other home that was assumed to be missing) compared with risk estimates derived from measurements from both homes. Among strategies for estimating residential exposure for those who lived in two homes, the estimate based on measurements from two homes was called the "gold standard", by contrast with estimates that used only a single direct measurement. As virtually all other published studies have used time weighted average (TWA) as a summary measure, we too used this in the absence of published data that showed the superiority or greater biological plausibility of another measure.[4]

Methods

Details of the methods and results of the main study are given elsewhere[2 3] and are summarised here. Magnetic field measurements were

Table 1 Time (%) within 5 year study period (before diagnosis for cases and reference date for controls) subjects resided in homes

Time subjects resided in homes (%)	Cases (n=149)			Controls (n=127)			Total (n=276)		
	Mean	Min	Max	Mean	Min	Max	Mean	Min	Max
Total time	94.0	70.0	100.0	95.8	70.0	100.0	94.8	70.1	100.00
Duration:									
Longer lived in home	63.8	36.5	88.2	63.5	38.3	89.0	63.7	36.5	89.00
Shorter lived in home	30.2	11.4	50.0	32.3	10.9	50.0	31.1	10.9	50.00
At time of interview:									
Current lived in home	46.6	11.4	88.2	45.3	10.9	85.3	46.0	10.9	88.20
Former lived in home	47.4	11.8	88.0	50.5	14.7	89.0	48.8	11.8	89.00

taken in current and former homes of 638 cases of ALL under the age of 15 at diagnosis and 620 controls selected by random digit dialing and matched on age, race, and first eight digits of the case's telephone number. Other eligibility criteria included: residence at diagnosis or reference date—for example, the date of diagnosis of the corresponding matched case—in one of nine mid-western or mid-Atlantic states; and residential magnetic field measurements covering at least 70% of the 5 year period immediately before diagnosis or reference date. The subset of subjects in the present analysis included all those meeting these eligibility criteria who had lived in two homes. A total of 149 cases and 127 controls were eligible.

The subject's summary TWA exposure was derived from measurements of both of the homes, weighted by the fraction of the reference period lived in each residence.[2 3] We examined the impact of choosing alternative homes for measurement, including strategies similar to those used in earlier studies,[5 6] in which only one home was measured. The three cost efficient fieldwork strategies we examined were to measure: (*a*) the longer lived in home; (*b*) the currently lived in home; and (*c*) the former lived in home.

We evaluated two approaches for analysing data derived from the various field work strategies: (*a*) assigning full weight to the single home measured (ignoring the second measurement); and (*b*) imputing a measurement for the missing home derived from available measurements and calculating the time weighted average based on the measured and imputed values. We used two different methods for imputing the missing values: (*a*) control mean imputation, for which we imputed the mean of all measured control homes to all missing residences—for example, measurements for shorter lived in home were imputed with the mean of the measurements of the longer lived in home for all controls[1]—and (*b*) status-specific mean imputation, for which we imputed the mean of all case or control homes measured to missing case and control residences, respectively.[7]

The subject's summary exposure to magnetic fields estimated with each approach was compared with the subject's TWA calculated from measurements in both homes. The association between estimated exposure to magnetic fields and the risk of leukaemia under different approaches was examined by unconditional logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were computed with the GMBO routine in the EPICURE statistical package.[8 9]

Results

Table 1 shows the percentage of time within the 5 year study period that subjects lived in each of the designated types of homes. The mean percentage of the entire 5 year period covered by two homes (94.8%) was substantially greater than the minimum 70% required. The mean percentages for each type of home were similar for cases and controls.

For the two homes the subject resided in, the Pearson correlation coefficient between the measurements of two homes within subjects was 0.31 ($p<10^{-4}$, fig 1), indicating a lack of independence of measurements. In this subset of data from the NCI/CCG study, measurements from control homes were slightly lower than those of case homes (table 2). The mean magnetic field level for the shorter lived in homes was lower than those for longer lived in homes; this difference was smaller for cases than for controls. The mean magnetic field levels for homes resided in formerly was higher than that of homes lived in currently for both cases and controls; former homes of cases had the highest measurements.

The single home measurement that correlated best with the summary TWA from two homes was that for the longer lived in home (r=0.95, table 3). Estimates from currently lived in homes were not as highly correlated with the summary TWAs from the two homes (r=0.62, table 3). Some of the difference between the correlation coefficients for longer lived in homes plus imputed shorter lived in homes (r=0.95, fig 2) and the currently lived in homes plus imputed former lived in homes (r=0.62, fig 3) is related to the duration of the residency (the subjects resided in longer lived

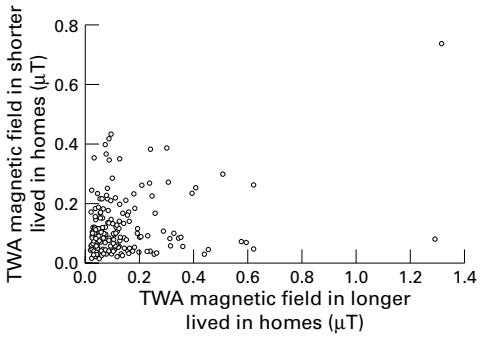

Figure 1 Agreement between measured magnetic field levels (n=276, r=0.31).

Table 2 Mean TWA magnetic field of subjects' homes measured according to temporal characteristics, and case-control status

Temporal characteristics of subject's residences	Cases (n=149)		Controls (n=127)		Total (n=276)	
	Mean (μT)	SD	Mean (μT)	SD	Mean (μT)	SD
Duration:						
Longer lived in homes	0.123	0.126	0.118	0.150	0.120	0.148
Shorter lived in homes	0.119	0.119	0.099	0.095	0.110	0.109
At time of interview:						
Current lived in homes	0.103	0.098	0.102	0.108	0.103	0.103
Former lived in homes	0.138	0.158	0.115	0.142	0.128	0.151

Table 3 Pearson correlation coefficients between subjects' estimated TWA magnetic field from two homes measured, and TWAs based on one home only or one home conjunction with imputed values for the second homes

Subject's TWA calculated from different strategies	Correlation coefficient
TWA, two homes measured	1.00
Longer lived in homes only	0.95
Shorter lived in homes only	0.55
Former lived in homes only	0.90
Current lived in homes only	0.62
Longer lived in home plus shorter lived in homes imputed:	
With control mean*	0.95
With status specific mean†	0.95
Current lived in homes plus former lived in homes imputed:	
With control mean‡	0.62
With status specific mean§	0.62

*Shorter lived in homes were imputed from observed mean of longer lived in control homes.
†Shorter lived in homes were imputed from case mean of longer lived in homes (if case) or from control mean of longer lived in homes (if control).
‡Former lived in homes were imputed from observed mean of current lived in control homes.
§Former lived in homes were imputed from case mean of current lived in homes (if case) or from control mean of current lived in homes (if control).

in homes about twice as long as in shorter lived in homes).

When cases and controls were categorised according to quartiles of exposure to magnetic fields, the risks of childhood ALL associated with measurements from single homes were similar to the risks associated with the TWA

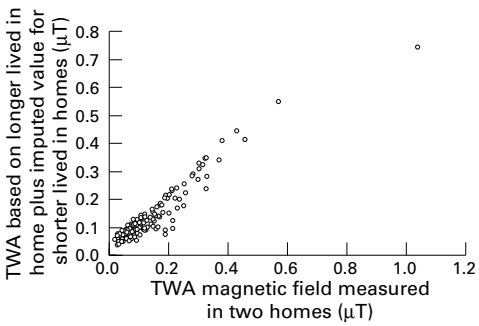

Figure 2 Agreement between measured magnetic fileld levels (n=276, r=0.95).

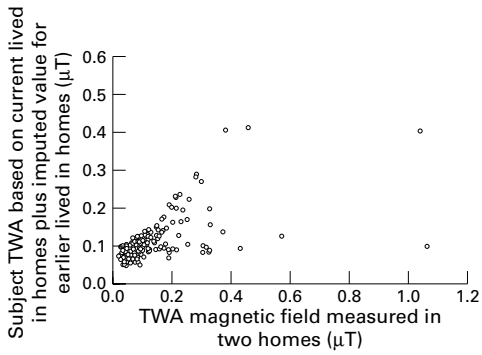

Figure 3 Agreement between measured magnetic field levels (n=276, r=0.62).

summary values derived from both homes (table 4), although, surprisingly, the risks were most dissimilar for longer lived in homes. Risks of ALL associated with the measurement for the longer lived in homes and imputed values for the shorter lived in homes (table 5) were similar to the risks derived from the TWA with both homes, but risks of ALL associated with the measurements for the current lived in homes only were closer to risks associated with TWA measurements derived from both homes than the risks of ALL derived from the measurements of the current lived in homes and imputed values for the former homes (table 4).

With the initial cut off points for exposure to magnetic fields described in our earlier paper,[3] there was greater variability of risks of ALL associated with measurements from a single home (table 6). Risks of ALL among children within the highest exposure category were lowest when the single home evaluated was the home resided in longest. All methods of using measurements from one of the homes in conjunction with imputation of measurements from the second home led to marked attenuation of risk estimates at the highest exposure category, particularly when measurements

Table 4 ORs (95% CI) from different field approaches categorised according to quartiles of magnetic field exposure

Exposure categories according to quartiles*	Relative risk for acute lymphoblastic leukaemia calculated with:															
	TWA from two homes measured				Measurement from longer lived in home only				Measurement from former lived in home only				Measurement from currently lived in home only			
	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI
I	0.041	35	1.00	—	0.033	37	1.00	—	0.035	37	1.00		0.032	35	1.00	—
II	0.067	36	1.06	0.54 to 2.07	0.056	35	0.84	0.43 to 1.64	0.058	36	0.94	0.48 to 1.84	0.054	35	0.97	0.49 to 1.90
III	0.104	39	1.26	0.65 to 2.47	0.100	40	1.16	0.59 to 2.27	0.110	35	0.89	0.46 to 1.74	0.091	41	1.33	0.68 to 2.61
IV	0.258	39	1.26	0.65 to 2.47	0.291	37	0.97	0.50 to 1.90	0.307	41	1.26	0.65 to 2.49	0.231	38	1.16	0.59 to 2.26
			p_{trend}=0.4				p_{trend}=0.8				p_{trend}=0.6				p_{trend}=0.5	

*Categories according to quartiles were calculated for both cases and controls.

Table 5 ORs (95% CI) from different imputation strategies categorised according to quartiles of magnetic field exposure

Exposure categories according to quartiles‡	Relative risk for acute lymphoblastic leukaemia calculated with:															
	Control mean imputation*								Status specific mean imputation†							
	TWA based on longer lived in homes plus imputed value for shorter lived in homes				TWA based on current lived in homes plus imputed value for former lived in homes				TWA based on longer lived in homes plus imputed value for shorter lived in homes				TWA based on current lived in homes plus imputed value for former lived in homes			
	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI
I	0.060	36	1.00	—	0.063	38	1.00	—	0.060	35	1.00	—	0.063	38	1.00	—
II	0.079	35	0.94	0.48 to 1.84	0.082	34	0.79	0.41 to 1.55	0.080	34	0.94	0.48 to 1.84	0.083	32	0.71	0.36 to 1.38
III	0.106	40	1.26	0.65 to 2.48	0.100	38	1.00	0.51 to 1.96	0.107	41	1.42	0.73 to 2.79	0.100	40	1.13	0.58 to 2.21
IV	0.237	38	1.12	0.58 to 2.20	0.164	39	1.06	0.54 to 2.07	0.238	39	1.26	0.65 to 2.47	0.164	39	1.06	0.54 to 2.07
			p_{trend}=0.6				p_{trend}=0.7				p_{trend}=0.3				p_{trend}=0.6	

*Shorter lived in homes were imputed from observed mean of longer lived in control homes; former lived in homes were imputed from observed mean of current lived in control homes.
†Shorter lived in homes were imputed from case mean of longer lived in homes (if case) or from control mean of longer lived in homes (if control); former lived in homes were imputed from case mean of current lived in homes (if case) or from control mean of current lived in homes (if control).
‡Categories according to quartiles were calculated for both cases and controls.

Table 6 ORs (95% CI) from different field approaches categorised according to initial cut off points of magnetic field exposure

Exposure categories (μT)	Relative risk for acute lymphoblastic leukaemia calculated with:															
	TWA from two homes measured				Measurement from longer lived in home only				Measurement from former lived in home only				Measurement from currently lived in home only			
	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI
<0.065	0.047	53	1.00	—	0.042	64	1.00	—	0.042	59	1.00	—	0.042	66	1.00	—
⩾0.065–<0.099	0.082	33	0.97	0.52 to 1.81	0.080	27	1.23	0.62 to 2.39	0.083	22	0.85	0.43 to 1.68	0.079	31	1.28	0.68 to 2.44
>0.100–<0.199	0.137	40	1.14	0.63 to 2.08	0.137	35	1.28	0.69 to 2.38	0.140	39	1.35	0.73 to 2.47	0.133	32	1.09	0.59 to 2.02
⩾0.200	0.350	23	1.81	0.81 to 4.02	0.374	23	1.15	0.57 to 2.33	0.370	29	1.65	0.82 to 3.32	0.322	20	1.47	0.67 to 3.20
			p_{trend}=0.2				p_{trend}=0.3				p_{trend}=0.1				p_{trend}=0.4	

Table 7 ORs (95% CI) from different imputation strategies categorised according to initial cut off points of magnetic field exposure

Exposure categories	Relative risk for acute lymphoblastic leukaemia calculated with:															
	Control mean imputation*								Status specific mean imputation†							
	TWA based on longer lived in homes plus imputed value for shorter lived in homes				TWA based on current lived in homes plus imputed value for former lived in homes				TWA based on longer lived in homes plus imputed value for shorter lived in homes				TWA based on current lived in homes plus imputed value for former lived in homes			
	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI	Mean (μT)	Cases	OR	95% CI
<0.065 μT	0.056	26	1.00	—	0.058	22	1.00	—	0.056	23	1.00	—	0.058	21	1.00	—
⩾0.065–<0.099 μT	0.080	61	0.99	0.51 to 1.95	0.083	74	0.74	0.36 to 1.55	0.081	63	1.17	0.59 to 2.31	0.083	74	0.78	0.37 to 1.63
>0.100–<0.199 μT	0.134	45	1.14	0.56 to 2.32	0.124	46	0.85	0.39 to 1.86	0.134	46	1.31	0.64 to 2.72	0.124	47	0.91	0.41 to 2.00
⩾0.200 μT	0.330	17	1.00	0.41 to 2.45	0.278	7	0.68	0.20 to 2.33	0.331	17	1.13	0.46 to 2.80	0.279	7	0.71	0.21 to 2.47
			p_{trend}=0.8				p_{trend}=0.8				p_{trend}=0.6				p_{trend}=0.6	

*Shorter lived in homes were imputed from observed mean of longer lived in control homes; former lived in homes were imputed from observed mean of current lived in control homes.
†Shorter lived in homes were imputed from case mean of longer lived in homes (if case) or from control mean of longer lived in homes (if control); former lived in homes were imputed from case mean of current lived in homes (if case) or from control mean of current lived in homes (if control).

from current homes were used and those from former lived in homes were imputed (table 7).

Discussion

There is an extensive statistical literature on various methods when there are missing covariates,[10–12] but little has been published on handling gaps in reconstruction of historical exposure. Weinberg *et al*[1] recently considered the problem of gaps in estimating cumulative residential exposure to radon. They concluded that imputation based on the mean of all control residences produced little bias in the risk estimates and no distortion in the coverage of 95% CIs under a linear excess relative risk model; Weinberg *et al*[1] argued that status specific mean imputation (imputing the mean of all case or control homes measured to missing case and control residences, respectively) on the other hand, induces differential misclassification and should therefore be avoided.

We used the standard logistic model that was used in published studies of magnetic fields and cancer. This may not be as robust to Berkson type errors as the linear excess risk model assumed by Weinberg *et al*.[1] Their conclusions may not apply to the measurements of residential magnetic field in our study anyway, because the authors' assumptions about "missingness" were violated. In particular, Weinberg *et al*[1] assumed that the mean measurements were the same for measured and unmeasured homes and that measurements in the two homes of a subject were independent. We found differences between mean exposures in current and former homes within disease categories, and

between longer and shorter lived in homes of controls. We also found a significant lack of independence. These departures from the assumptions of Weinberg *et al*[1] are apparently strong enough to affect the properties of the imputation.

Because it is not unusual for families with young children in the United States to move from a typically urban area with higher levels of residential magnetic field to a lower field suburban setting with lower exposures to residential magnetic field, the higher magnetic field levels we found in former lived in homes might be a general result associated with residential mobility patterns, at least in the United States. In the NCI/CCG population subset that we evaluated, the magnetic field levels in former homes were also somewhat higher for cases than controls; this, in conjunction with the lower field levels in current homes, explains the marked attenuation in estimated RRs when measurements in former homes were imputed with measurement data from current homes, and resulting summary TWA values were categorised with the initial cut off points.

The TWAs based on actual measurements for two homes tend to be less variable than from a single home. This regression to the mean would not cause attenuation of relative risk estimates but would lead to lower statistical power than would be found in a study of people who never moved. Such a study would be difficult in most United States communities, however, as residential mobility characterises most families. If feasible, a study with subjects who lived in only one home offers cost and efficiency advantages. Regression to the mean from averaging measurements from two homes reduces variability, but does not lead to attenuation.[2 13]

There are additional efficiency concerns when imputation is used before categorisation with initial cut off points. The imputation of missing data with average values from measured homes also results in regression of estimated exposures towards the mean, leading to a reduction in the numbers of cases and controls in extreme exposure categories, and hence, less precise risk estimates. In our study, the positive correlation found between measurements leads to less regression to the mean and preserves some of the variability within subjects in TWAs based on actual measurements; the loss of efficiency from imputation is greater in the presence of a positive correlation than when the measurements are independent.

The purpose of our exercise was to investigate how commonly used strategies compared with those suggested by Weinberg *et al*.[1] It is not obvious from our data that the status specific mean imputation performed more poorly than control mean imputation.

Our results suggest the need for caution when imputing missing magnetic field data to reconstruct historical exposures. Our results also suggest that the imputation strategies in Weinberg *et al*[1] may not be robust to violations likely in a study of electromagnetic fields, at least in the United States. Measurements in former homes are more likely to be missing because of the difficulty in gaining access, and are likely to be higher than measurements in current homes. Our results argue against attempting to estimate lifetime exposure to magnetic fields with imputed values derived from current residences to fill in gaps caused by unmeasured residences lived in previously. When possible, imputation in magnetic field studies should be stratified by lived in status—for example, missing data from former homes should be imputed with mean values from measured former homes.

The generalisability of our conclusions depends on housing characteristics and moving patterns which may be different in the other geographical areas of the United States or the world. In studies of other types of residential exposures, measurement data from other populations may be helpful to identify residential characteristics that should be considered when imputing missing residential measurement data. Application of our conclusions to other types of residential exposures depends on the knowledge of distribution of exposure levels or patterns of moving among population subsets. Further research is needed on how best to handle measurements that are missing because of incomplete participation, inability to locate previous homes, or financial and other constraints.

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