A Nested Case-Control Study of Residential and Personal Magnetic Field Measures and Miscarriages

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Abstract: We conducted a nested case-control study (177 cases, 550 controls) to assess the relation between retrospective magnetic field measures and clinical miscarriage among members of the northern California Kaiser Permanente medical care system. We also conducted a prospective substudy of 219 participants of the same parent cohort to determine whether 12-week and 30-week exposure assessments were similar. We evaluated wire codes, area measures, and three personal meter metrics: (1) the average difference between consecutive levels (a rate-of-change metric), (2) the maximum level, and (3) the time-weighted average. For wire codes and area measures we found little association. For the personal metrics (30 weeks after last menstrual period), we found positive associations. Each exposure was divided into quartiles, with the lowest quartile as referent. Starting with the highest quartile, adjusted odds ratios and 95% confidence intervals were 3.1 (95% CI = 1.6–6.0), 2.3 (95% CI = 1.2–4.4), and 1.5 (95% CI = 0.8–3.1) for the rate-of-change metric; 2.3 (95% CI = 1.2–4.4), 1.9 (95% CI = 1.0–3.5), and 1.4 (95% CI = 0.7–2.8) for the maximum value; and 1.7 (95% CI = 0.9–3.3), 1.7 (95% CI = 0.9–3.3), and 1.7 (95% CI = 0.9–3.3) for the time-weighted average. The odds ratio conveyed by being above a 24-hour time-weighted average of 2 milligauss was 1.0 (95% CI = 0.5–2.1). Exposure assessment measurements at 12 weeks were poorly correlated with those taken at 30 weeks. Nonetheless, the prospective substudy results regarding miscarriage risk were consistent with the nested study results. (EPIDEMIOLOGY 2002;13:21–31)

Key words: miscarriage, spontaneous abortion, magnetic fields, electromagnetic fields, maternal exposure, wire codes.

Reports of miscarriages among women who used video display terminals (VDT) prompted the initial concern about electric and magnetic fields (EMFs) and miscarriage. Most epidemiologic studies of VDTs showed relative risks slightly above 1.0,[1,2] but most of these studies did not assess EMF exposures directly. Two VDT studies[3,4] with adequate exposure assessment were inconsistent. Only one (Lindbohm *et al*[4]) had a sufficient range of exposure (based on laboratory measures of the VDT); this study found a clear dose response.

Results from studies of electric bed heaters, assumed to be a source of strong magnetic fields, have also been inconsistent.[5–7] The studies of both VDTs and electric bed heaters used surrogate rather than personal measures to assess magnetic field exposures possibly resulting in lower risk estimates due to nondifferential misclassification (see Wilson *et al*[8]).

One nested case-control study[9] measured magnetic fields at the front door and found a fivefold (95% CI = 1.0–25) increased risk of preclinical miscarriage, but this was based on a small number of exposed women.

We conducted a case-control study nested in a prospective miscarriage study. We defined cases as women who had a clinical miscarriage before 20 weeks of gestation and controls as women who had a livebirth.

We hypothesized that cases were more likely than controls to: (1) live near high-current power lines (a potential source for high magnetic field levels), (2) have higher residential magnetic field area (spot) measures, and (3) have higher personal magnetic field exposures.

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Subjects and Methods

Subject Recruitment

We recruited subjects from a cohort of 3,403 pregnant women who participated in a large prospective reproductive health study. The parent prospective study by Swan and coworkers is described elsewhere.[10] Eligible participants of the parent study were at least 18 years of age, enrolled at 13 weeks' gestation or less, spoke English or Spanish, and were members of a California Kaiser Permanente Medical Care Program. We recruited the study participants from the Northern California Kaiser Permanente Medical Care Program facilities.

We assumed that magnetic fields measured at 30 weeks' gestation would be similar to those experienced during the first trimester of pregnancy measured before a miscarriage, if any, had occurred. To validate this assumption, we also conducted a substudy to correlate early and later measures and to determine whether substudy (12-week gestation) results regarding the relation between magnetic fields and miscarriage were similar to the full nested case-control study results, based on 30-week measurements.

For the substudy, we selected a random sample of subjects from the parent cohort each week from March 1990 through April 1991. Pregnancies were medically confirmed. We obtained magnetic field measurements twice, first around 12 weeks' gestation and then again around 30 weeks' gestation. A total of 219 of the 531 initially sampled women permitted a first measurement; 201 became controls and 18 became cases (Figure 1). Of these, 80% (166 controls and 10 cases) participated in the second measurement period.

For the nested study, we first assessed pregnancy status around 25–30 weeks' gestation by medical chart review. We then attempted to recruit, on a weekly basis between July 1990 and November 1991, the 328 women with a reported miscarriage (cases) and a random sample of 806 women who were still pregnant at the time (noncases, potential controls) (Figure 1). Miscarriage was defined as the loss of a conceptus before 20 weeks of gestation. Virtually all pregnancy outcomes were confirmed within a year of the participant's last menstrual period (see Swan *et al*[10]) About 51 per cent (N = 167) of the cases and 48 per cent (N = 384) of the noncases participated in this component of the study, which involved 30-week magnetic field measurements.

Combining women from the prospective substudy and the nested study resulted in a total of 177 cases [51%, 177/(18+328)] and 550 controls [55%, 550/(201+806)] (Figure 1). Unless otherwise indicated, we included in the analyses only those who, at the time of the 30-week measurement, still lived in the same home as during their first trimester (155 cases and 509 controls).

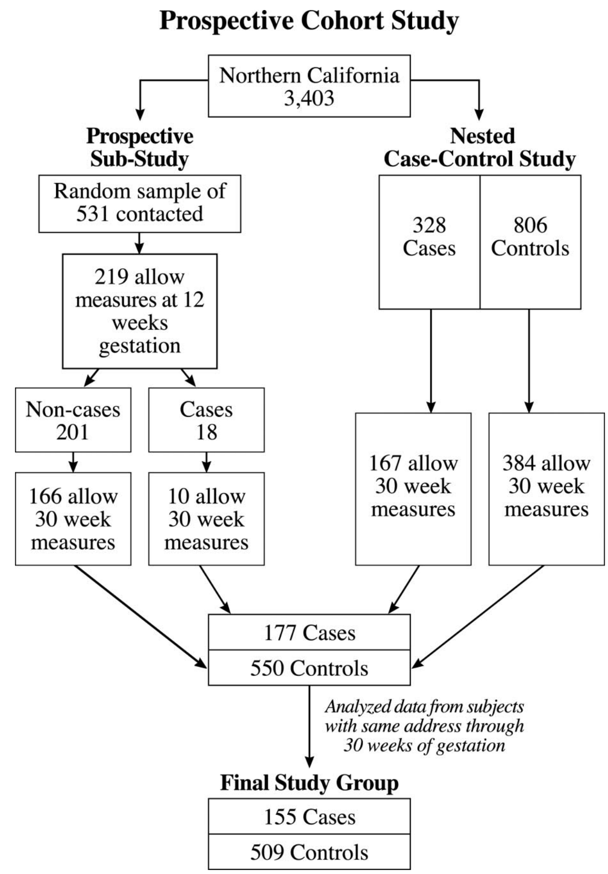

FIGURE 1. Flow chart to illustrate recruitment and participation in the study.

Interviews for the Entire Prospective Cohort

We had collected information in the original cohort about demographics, reproductive and medical history, and potential confounders for miscarriage during the women's first trimester of pregnancy (on average, 8 weeks' gestation), using a standardized computer-assisted telephone interview.

Residential Power Line Assessment

We classified the participants' home into the Wertheimer and Leeper wire code categories[11] on the basis of the types of nearby power lines and their distance from the home. This classification system assumes that homes close to lines with high current-carrying potential (such as transmission lines and major overhead primary distribution lines) have higher magnetic fields than those homes far from such lines or those homes close to lines with low current-carrying potential (such as overhead secondary distribution lines). We evaluated up to three overhead power lines within 150 feet from each participant's residence. We measured the shortest distance from the power line to the property line closest to the home. For apartments, we measured the distance to the nearest boundary wall of the woman's unit. The participant's home wire code was based on the power line and distance associated with the highest wire code. We classified the homes as having very high current configuration (VHCC), ordinary high current configuration (OHCC), ordinary low current configuration (OLCC), and only nearby lines buried underground (used as a reference group). This classification system also has a very low configuration category (VLCC), but we found no homes that fit this category.

Magnetic Field Measures

For both the personal and residential area (spot) magnetic field measurements, we used the EMDEX-C meter (calibrated to measure a frequency range of 40–800 Hz), set on a 10-second sampling rate. We defined the magnetic field as the resultant field of the three orthogonal axes' root mean square levels. We obtained all measurements at waist level and without the participant or the field worker knowing the levels.

For the personal measurements, participants used the meter for a 24-hour period and recorded on an activity card the time, displayed by the meter, when they entered a new environment; thus, their 24-hour exposure could be partitioned into magnetic fields received at home, at work, outside home and work, and at night while sleeping. For both cases and controls, we took these measurements at about 30 weeks after their last menstrual period. The participants followed their usual activity routine and wore the meter as much as possible during the measurement period. For the overnight measurement, the participant placed the meter in a pouch located on the edge of the mattress midway on her side of the bed. We excluded measurements that occurred when the meter was set aside during such activities as bathing.

Three personal magnetic field metrics were chosen *a priori*: (1) the time-weighted average (TWA), (2) a rate-of-change metric (RCM) assessing the absolute change in field levels between successive samples (Wilson *et al*[9]), and (3) the maximum level (MAX) assessing the highest value encountered during a 24-hour period.

Immediately after the 24-hour personal measurement period, field workers used the same meter worn by the participant to obtain the area or spot measurements. For this, they took 1-minute readings outside the front door (for both measurement periods) and inside the home (for the 30th week of gestation measurement period) in the center of the kitchen, living room, and participant's bedroom.

Statistical Analyses

We compared cases with controls (for the nested study) and miscarriage rates of women with high exposures with miscarriage rates of those with low exposures (for the prospective substudy). We did this with respect to: (1) residential wire codes, (2) residential area measures, and (3) personal 24-hour magnetic field measures. We partitioned exposure into the environments described above by assessing odds ratios or relative risks associated with high magnetic field levels. We defined high magnetic fields as VHCC homes for wire codes, area measures, or personal TWA levels at or above 2.0 milligauss (mG), as well as personal TWA, RCM, and maximum levels at or above the 50th and the 75th percentile cutpoint values. The 2.0 mG value was the cutpoint used for previously published childhood cancer studies.[12] For the prospective substudy, the denominator for the miscarriage rates included all livebirths, miscarriages, and stillbirths.

We used multiple logistic regression to assess the independent association of magnetic field measurements and wire codes with miscarriages. We initially considered the following variables as potential confounders by Mantel-Haenszel stratified analysis[13]: maternal age, gestational age at the time of the prospective study phone interview (gestation at interview), prior fetal loss, nausea, race, income, education, body mass index, physical activity, perception of health, cigarette use at conception, alcohol consumption at conception, coffee and caffeine consumption at conception, season of magnetic field measurement, and Kaiser Permanente Medical Care Program facility. The variables we included in the final logistic regression models were those with homogenous odds ratios across strata and those that produced a 10% change in the odds ratio after the Mantel-Haenszel adjustment. For the final models, miscarriage was the dependent variable; the magnetic field exposures (wire codes, area measures, and personal measures) were the independent variables; and the covariates were maternal age, coffee consumption at conception, income, race, gestation at interview, and each of the other personal 24-hour exposures not defined as the independent variable for the personal exposure models.

We also evaluated effect modification between high magnetic field exposures (including high wire code) and gestation at interview, income, race, and house type. No effect modification was found.

We assessed dose response for the personal magnetic field metrics by comparing each of the three upper-exposure quartiles with the lowest-exposure quartile (the reference group).

Results

Nested Study Participants Compared with Nonparticipants

Among the cases in the nested study, participants were less likely than nonparticipants to be white, to use cigarettes at conception, and to have a lower income after adjusting for each of the other variables (Table 1). Among the controls, participants were also less likely to

TABLE 1. Comparison of Nested Study Nonparticipants with Participants by Case-Control Status

	Cases		Control	
	Nonparticipant	Participant	Nonparticipant	Participant
Variable*	%	%	%	%
Wire codes and housing variables (at 30 weeks' gestation)	(N = 124)*	(N = 155)*	(N = 420)*	(N = 509)*
Wire code				
VHCC	7.3	16.1	11.7	13.2
OHCC	18.5	21.9	20.9	23.5
OLCC	25.8	25.2	28.6	26.4
Buried	48.4	36.8	38.8	36.9
House type				
Single-family home	48.0	74.8	28.9	12.8
Apartment	32.0	12.9	11.6	21.4
Other	20.0	12.3	59.5	65.8
Other variables	(N = 151)*	(N = 155)*	(N = 2,525)*	(N = 509)*
Maternal age (years)				
<35	82.8	78.1	89.4	86.1
35+	17.2	21.9	10.6	13.9
Interview gestation (weeks)				
Up to 6	26.5	31.6	20.9	27.7
6–<10	59.6	59.4	55.6	55.0
10+	13.9	9.0	23.5	17.3
Prior fetal death				
No	77.5	75.5	80.4	73.9
Yes	22.5	24.5	19.6	26.1
Race				
White	58.3	73.4	68.8	79.0
Hispanic	13.2	8.4	13.7	13.2
Other	28.5	18.1	17..5	7.8
Cigarette consumption around conception				
No	76.2	88.4	81.8	81.3
Yes	23.8	11.6	18.2	18.7
Alcohol consumption around conception				
No	62.9	58.1	62.1	55.8
Yes	37.1	41.9	37.9	44.2
Coffee consumption around conception				
<2 cups	75.8	67.7	76.0	69.5
2+ cups	24.2	32.3	24.0	30.5
Income				
<$50,000	46.3	22.9	41.0	29.2
$50,000+	53.7	77.1	59.0	70.8
Body mass index (kg/m^2)				
Thin	33.1	27.1	30.7	24.4
Average	50.3	56.1	48.9	53.0
Heavy	16.6	16.8	20.4	22.6

VHCC = very high current configuration; OHCC = ordinary high current configuration; OLCC = ordinary low current configuration.
* Numbers of some, but not all, variables have missing data; these are the approximate totals. Sixty-three participants who moved during pregnancy are excluded.

be white and to have a lower income than nonparticipants. In addition, control participants were more likely to have had a prior fetal loss.

Nested Study Compared with Full Cohort

To evaluate potential selection bias, we compared the nested study participants and the parent cohort with regard to odds ratios of the relation between various important risk factors and miscarriages (Table 2). The odds ratios are similar, suggesting that the nested study participants are representative of the larger parent cohort.

Nested Study Cases and Controls

Compared with controls, cases were more likely to be older, to be interviewed earlier in gestation, to be categorized racially as other than white and Hispanic, not to use cigarettes around conception, to have a household income less than $50,000, and to reside in a single-family home (Tables 1 and 2). In addition, cases were less likely to experience nausea during their first trimester of pregnancy. The distributions of education, perception of health, physical activity, season of measurement, and the other possible risk factors were similar between cases and controls.

Nested Study Correlation among Magnetic Field Exposure Estimates

We used four different estimates of magnetic field exposure (wire code, personal time-weighted average, personal average rate-of-change metric, and personal maximum value) on the assumption that they captured

TABLE 2. Odds Ratios* for Miscarriage Risk among Nested Case-Control Study Participants and among the Parent Northern California Prospective Cohort

		Nested Study (N = 664)		Parent Cohort (N = 3,403)	
Variable*	Categories	OR	95% CI	OR	95% CI
Maternal Age (years)	<35, 35+	1.9	1.1–3.1	2.3	1.6–3.1
Gestation week	<8, 8+	1.0	0.7–1.5	1.4	1.1–1.8
Prior fetal loss	No/Yes	0.9	0.5–1.4	1.1	0.8–1.4
Race 1	Other *vs* white	2.1	1.1–3.9	1.4	1.0–2.0
Race 2	Hispanic *vs* white	0.9	0.5–1.9	1.0	0.7–1.5
Cigarette consumption at LMP	No/Yes	0.7	0.4–1.3	1.1	0.8–1.6
Alcohol consumption at LMP	No/Yes	0.7	0.5–1.1	0.9	0.7–1.1
Coffee consumption at LMP	No/Yes	1.2	0.7–1.9	1.2	0.9–1.6
Body mass index 1	Thin *vs* average	1.1	0.7–1.8	1.0	0.8–1.4
Body mass index 2	Heavy *vs* average	0.8	0.5–1.4	0.8	0.6–1.2
Income	<$50,000, $50,000+	0.8	0.5–1.8	1.0	0.7–1.2
House type†	Single *vs* other	0.9	0.5–1.8	0.7	0.5–1.1
Wire code†	VHCC *vs* other	1.2	0.7–2.2	1.0	0.7–1.6

LMP = last menstrual period.
* Adjusted for all other variables excluding house type and wire code.
† Information about house type and wire code was obtained for all of the nested study participants but for only a 15% random sample of the parent cohort; adjusted for all other variables including house type and wire code.

different aspects of a person's magnetic field exposure. Table 3 shows that wire code is weakly associated with the 90th percentile TWA value and is not associated with the other personal exposure estimates. Table 4 shows a moderate to high correlation between each of the pairs of personal metrics. The highest correlation was between the maximum value and the RCM measure.

Wire Codes and Miscarriage Risk

As shown in Table 5, participant cases were 1.2 (95% CI = 0.7–2.1) times more likely than participant controls to live in VHCC homes during their first trimester. Cases and controls were equally likely to live in OHCC and OLCC homes. The results were similar even after adjusting for maternal age, gestation at interview, coffee consumption at conception, income, and race. It may not be appropriate to use the buried wire code category as a reference group because of possibilities of socioeconomic differences for residential settings with and without overhead distribution lines. When we used the lowest overhead wire code category (OLCC) as the reference group, however, the results were similar.

To evaluate whether recruitment was associated with wire code category, we assessed the wire codes for the first-trimester homes. This was available for 97% of participant cases, for 77% of the nonparticipant cases, and for a 13% random sample of the nonparticipant controls (Table 5). Nonparticipant cases were less likely than nonparticipant controls to live in any of the overhead wire code homes, with the observation being strongest for VHCC homes (OR = 0.5; 95% CI = 0.2–1.1).

Nested Study TWA and Area Measures and Miscarriage Risk

Cases and controls were similar with respect to the time spent in each of the environments (Table 6). For both the magnetic field personal and residential measures, a cutpoint of 2.0 mG was used to distinguish between high and low exposures. Cases were slightly less likely than controls to have personal TWA exposures at or above 2.0 mG for the overnight bed, total home, other, and work environments. Cases were slightly more likely than controls to have residential front door measures and personal home TWA exposures at or above 2.0 mG. Cases and controls were similar with respect to

TABLE 3. Median and 90th Percentile Cutpoint Values of Personal Total Home Magnetic Field Measures by Wire Code for Time-Weighted Average (TWA), Rate-of-Change Metric (RCM), and Maximum Level (MAX)*

		Personal Total Home Magnetic Field Measures					
		TWA		RCM		MAX	
Wire Code Category	N	Median	90th Percentile	Median	90th Percentile	Median	90th Percentile
VHCC	84	0.50	2.52	0.43	1.05	13.22	37.48
OHCC	142	0.85	1.67	0.39	1.06	12.92	38.64
OLCC	164	0.74	1.58	0.43	1.21	14.29	37.02
Buried	221	0.80	1.45	0.72	1.25	13.40	36.41

VHCC = very high current configuration; OHCC = ordinary high current configuration; OLCC = ordinary low current configuration.
* Associations between 30-week gestation residence wire codes and concurrent personal exposure measurements in 611 subjects who at 30 weeks of gestation still lived in the same house as at 12 weeks of gestation.

TABLE 4. Pearson's Correlation Coefficients (*r*) Assessing the Relatedness of the Three Personal Magnetic Field Total 24-Hour Exposure Metrics for Nested Study Participants (N = 614)

Metric Comparison	*r*
LogTWA *vs* LogMAX	0.44
LogTWA *vs* RCM	0.49
LogMAX *vs* RCM	0.62
TWA *vs* MAX	0.86
TWA *vs* RCM	0.78
MAX *vs* RCM	0.96

TWA = time-weighted average; MAX = maximum value; RCM = rate-of-change metric; LogTWA = log of the time-weighted average; LogMAX = log of the maximum field value.

their residential, inside spot measurements, and personal total 24-hour exposures.

Table 7 compares the odds ratios among the personal 24-hour exposure quartiles. For the TWA metric, we did not find a trend of progressively higher odds ratios with higher TWA quartiles. However, we found a modest step function; cases were about 1.7 (95% CI = 0.9–3.3) times more likely than controls to have a personal total 24-hour TWA exposure above 0.72 mG (the 25th percentile value).

Having TWAs above the median in two or more environments during the day conveyed an odds ratio of 2.2 (95% CI = 1.2–4.1) as compared with individuals

TABLE 5. Odds Ratios for the Association of Miscarriage with Wire Code Category*

	Participants			Nonparticipants		
Wire Code	N	Crude OR	95% CI	N	Crude OR	95% CI
VHCC						
Cases	26	1.2	0.7–2.1	9	0.5	0.2–1.1
Controls	68			48		
OHCC						
Cases	35	0.9	0.6–1.4	23	0.7	0.4–1.2
Controls	127			82		
OLCC						
Cases	46	1.0	0.7–1.6	32	0.7	0.4–1.2
Controls	144			113		
Buried						
Cases†	64	1.0		60	1.0	
Controls	203			153		

* Based on the first trimester-address wire code. Computed separately for the 713 participants (including those who moved) and a random sample of 520 nonparticipants.
† Reference category.

TABLE 6. Odds Ratios for the Association of Miscarriage with Magnetic Field Personal Time-Weighted Average and Average Home Spot Measures by Area Location*

	N	Median Time (hours)	% Above 2.0 mG	Crude OR	95% CI	Adjusted† OR	95% CI
Total 24-hour							
Cases	131	23.3	9.9	1.0	0.5–2.0	1.0	0.5–2.1
Controls	483	23.2	9.7				
Total Home							
Cases	131	14.7	5.3	0.6	0.3–1.3	0.8	0.2–3.5
Controls	482	16.6	8.9				
Bed							
Cases	136	8.8	5.9	0.7	0.3–1.6	0.6	0.2–2.0
Controls	494	9.0	8.1				
Home							
Cases	131	6.0	7.6	1.0	0.6–1.8	1.4	0.5–4.0
Controls	481	7.0	7.7				
Other							
Cases	127	2.7	7.9	0.9	0.4–1.8	0.9	0.3–2.6
Controls	440	2.5	8.9				
Work							
Cases	82	7.6	17.1	0.8	0.4–1.5	0.7	0.3–1.5
Controls	239	7.6	20.5				
Front door spot							
Cases	155	1 minute	9.1	1.3	0.7–2.5	1.2	0.6–2.5
Controls	501	1 minute	7.2				
Inside spots							
Cases	155	4 minutes	7.7	1.3	0.7–2.7	1.1	0.5–2.2
Controls	506	4 minutes	5.9				

* Cutpoint for exposure comparison is 2.0 mG. This includes nested study participants who resided in their first trimester house at the time of 30-week gestation measurements.
† Adjusted for maternal age, gestation at interview, coffee consumption around conception, income, race, and each of the other personal 24-hour exposures (excluding total 24-hour).

TABLE 7. Odds Ratios for the Association of Miscarriage with Total 24-hour Personal Magnetic Field Time-Weighted Average, Rate-of-Change Metric, and Maximum Value by Quartiles

	Number	Crude OR	95% CI	Adjusted OR*	95% CI
Time-weighted average (mG)					
1.28+					
Case	35	1.6	0.9–2.8	1.7	0.9–3.2
Control	123				
0.93–<1.28					
Case	37	1.8	1.0–3.1	1.7	0.9–3.3
Control	114				
0.72–<0.93					
Case	36	1.5	0.9–2.8	1.7	0.9–3.3
Control	122				
<0.72					
Case†	23	1.0		1.0	
Control	124		χ^2 Trend $P = 0.17$		
Rate-of-change metric (mG)					
0.94+					
Case	46	3.3	1.8–6.0	3.1	1.6–6.0
Control	109				
0.62–<0.94					
Case	37	2.4	1.3–4.5	2.3	1.2–4.4
Control	118				
0.43–<0.62					
Case	31	1.9	1.0–3.6	1.5	0.8–3.1
Control	126				
<0.43					
Case†	17	1.0		1.0	
Control	131		χ^2 Trend $P = 0.00$		
Maximum value (mG)					
35.05+					
Case	39	2.1	1.2–3.8	2.3	1.2–4.4
Control	115				
23.42–<35.05					
Case	38	2.1	1.2–3.4	1.9	1.0–3.5
Control	115				
14.31–<23.43					
Case	33	1.7	0.9–3.1	1.4	0.7–2.8
Control	121				
<14.31					
Case†	21	1.0		1.0	
Control	132		χ^2 Trend $P = 0.00$		

* Adjusted for: maternal age, interview at gestation, coffee consumption at conception, income, and race.
† Reference category.

whose TWA in all environments was below the overall median (data not shown).

Nested Study RCM Levels and Miscarriage Risk

We observed a trend for progressively higher odds ratios with higher RCM quartiles (Table 7). Adjusted odds ratios and 95% confidence intervals for the higher quartiles in comparison with the lowest quartile, respectively, were 3.1 (95% CI = 1.6–6.0), 2.3 (95% CI = 1.2–4.4), and 1.5 (95% CI = 0.8–3.1).

We also observed a gradient in miscarriage risk as the number of environments with exposures at or above the 50th percentile level increased. The adjusted odds ratio for RCM "exposure" in two environments was 2.4 (95% CI = 1.2–4.1).

Nested Study Maximum Value Levels and Miscarriage Risk

There was also a trend of progressively higher odds ratios for higher-maximum value quartiles (Table 7). Adjusted odds ratios and 95% confidence intervals for the higher quartiles compared with the lowest quartile were 2.3 (95% CI = 1.2–4.4), 1.9 (95% CI = 1.0–3.5), and 1.4 (95% CI = 0.7–2.8).

As with both the TWA and RCM results, we observed a gradient in miscarriage risk as the number of environments with exposures at or above the 50th percentile level increased. The adjusted odds ratio for maximum "exposure" in at least two environments was 3.1 (95% CI = 1.6–5.9).

Prospective Substudy Results

We conducted the prospective substudy to evaluate the stability of the measurements over time (12-week measures *vs* 30-week measures) and to determine whether the miscarriage risk results based on 12-week measures are similar to the nested study results based on measurement at 30 weeks. We found that measurements obtained around 30 weeks' gestation were not well cor-

TABLE 8. Thirty-Week Gestation Measures *vs* 12-week Gestation Measures for Subjects Who Participated in Both Measurement Periods*

Category	N	Sensitivity	Specificity	Predictive Value of a: Positive Test	Predictive Value of a: Negative Test
Front door spot	168	54.6	93.0	35.3	96.7
Personal TWA total 24-hour	155	76.9	95.8	62.5	97.8
Personal RCM total 24-hour	155	55.7	51.2	48.2	58.7
Personal maximum total 24-hour	155	60.0	50.6	49.4	60.0

TWA = time-weighted average; RCM = rate-of-change metric.
* The median value of the 30-week measurement is the dichotomy used: Front door = 0.68 mG; TWA = 0.93 mG; RCM = 0.62 mG; maximum value = 23.43 mG.

related with measurements obtained around 12 weeks' gestation, especially for the RCM and maximum levels (Table 8). The correlations between measurements at 12 weeks and 30 weeks were respectively 0.64, 0.09, and 0.19 for 24-hour TWA, maximum level, and RCM. Despite these poor correlations, we found that miscarriage risk results for women with 12-week personal total 24-hour magnetic field exposure at or above the 50th percentile for the RCM and the maximum value were consistent with the results found in the nested study results (Table 9 and Figure 2). Women with these measures were about two times more likely to have a miscarriage than those women with personal exposures below these values. Also, consistent with the nested study results, there was no clear association found between wire code and miscarriage.

Unlike the nested study results, the personal TWA magnetic field exposures above 2.0 mG for the total home and for the other environments were positively associated with miscarriage risk (Table 9).

Discussion

The maximum personal magnetic field exposures and the exposures with large average differences between consecutive levels (the RCM) are associated with the risk of clinical miscarriages. These metrics show a dose response with an increase in exposure and with the number of environments that have exposures above the 50th percentile level. The TWA personal metric, the more traditional metric, demonstrated a small risk in the form of a step function. This discrepancy is not unex-

TABLE 9. Relative Risk for the Association of Miscarriage with Wire Code, Front Door Magnetic Field Spot, and 12-Week Personal Magnetic Field Time-Weighted Average (TWA), Rate-of-Change Metric (RCM), and Maximum Value (MAX), among Prospective Substudy Participants

	N	% Miscarriage	RR	95% CI
Wire code				
VHCC	18	0.0	0	
OHCC	59	8.5	1.3	0.39–4.20
OLCC	61	9.8	1.5	0.48–4.67
Buried*	76	6.6	1.0	
Front door spot (mG)				
2.0+	14	21.4	3.1	1.0–9.7
<2.0*	188	8.0	1.0	
TWA (mG)				
Total home				
2.0+	20	20.0	3.0	1.1–8.4
<2.0*	197	6.6	1.0	
Other				
2.0+	15	26.7	4.2	1.5–11.4
<2.0*	189	6.4	1.0	
Work				
2.0+	26	0.0	0	
<2.0*	122	10.7	1.0	
Total 24-hour				
2.0+	22	13.6	1.9	0.6–6.1
<2.0*	195	7.2	1.0	
RCM, total 24-hour (mG)				
50th percentile cutpoint				
0.69+	108	11.1	2.4	0.9–6.6
<0.69*	109	4.6	1.0	
MAX, total 24-hour (mG)				
50th percentile cutpoint				
26.85+	109	11.0	2.6	0.9–7.6
<26.85*	108	4.6	1.0	

* Reference category.

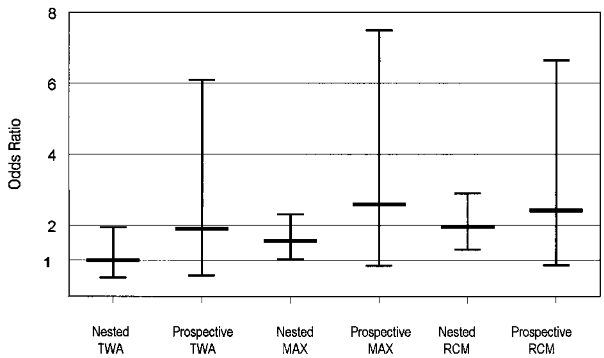

FIGURE 2. Odds ratios conveyed by being above the median of several magnetic field exposure metrics in the nested case-control study and the small prospective substudy. TWA = time-weighted average; MAX = maximum level; RCM = rate-of-change metric.

pected given that the TWA was not completely correlated with the other two metrics.

The association of TWA with miscarriage risk was not strengthened in the nested study when cuts were made at 2, 3, or 4 mG, as has been seen in studies of childhood leukemia.[12] There was such an association in our small prospective subset, although this was not confirmed in the larger prospective study by Li *et al.*[14]

The parent cohort and the nested study participants were quite healthy and had a low prevalence of known miscarriage risk factors. This is also the case with the complete parent cohort.[10] This should not have affected the internal validity of the study results.

There are two main strengths of this study. First, among studies of the relation of miscarriage with exposures to electric and magnetic fields, this study is the first to evaluate personal magnetic field exposures for three different *a priori* summary metrics and for different types of daily environments (at home, at work, and outside the work and home environment). Previous studies have assessed only indirect or surrogate exposure estimates such as residential wire codes and self-reported use of electrical devices.[1,2,5–7] These surrogate measures may not fully characterize a person's exposure to magnetic fields.

Secondly, the study was large enough to assess all of the known risk factors for miscarriage for possible confounding and effect modification, including physical activity, a variable thought to be associated with changing or maximum field levels (D. Bracken, January 2000, personal communication). We found little or no confounding and effect modification by physical activity or the other variables considered. Eskenazi and coworkers[15] also found that physical activity was not associated with any of the personal magnetic field metrics or miscarriages.

There are two main limitations to the study. First, we obtained personal magnetic field measures for only 50% of those recruited for the study. This could result in selection bias if participation were differential with respect to exposure status. The nested design allowed us to evaluate selection bias. Overall, selection bias appeared to be minimal for important, known miscarriage risk factors. However, bias cannot be entirely dismissed. We found that participating cases were less likely to live in VHCC homes than were nonparticipating cases. A selection bias may have led to the slightly increased odds ratio for participants residing in the VHCC wire code homes. Differential participation as a function of wire code status would not have produced the increased risks observed for the personal magnetic field maximum values and RCM levels, because these metrics were not associated with wire code, and wire code was not strongly associated with miscarriages. However, we cannot rule out bias from differential loss for reasons we are unable to assess. For this to occur subjects would need to have been aware of sources of brief high fields, and the cases and controls would have had to differentially enter the study on the basis of this exposure. The coherent results of the prospective study argue somewhat against this.

Secondly, we obtained the magnetic field measurements months after the occurrence of the miscarriage. Perhaps exposures measured later in pregnancy do not reflect earlier exposures. This could be true differentially for the still-pregnant women, whose activities at 30 weeks' gestation might be different from what they were earlier in pregnancy. For a subset of prospective substudy participants, their later measurements were not completely consistent with their earlier measurements, especially for the RCM and maximum values. This inconsistency should be evaluated in future studies. Nonetheless, the associations between miscarriage and maximum field or RCM were similar in the prospective and nested studies (see Figure 2).

The nested study results are inconsistent with the results of our electric blanket and miscarriage study, in which we found a decreased risk of miscarriages for electric blanket use at low settings during the first trimester of pregnancy and an increased risk for those few who used the blankets at a high setting for a short time period.[7] The participants of both studies were from the same parent cohort. In the previous study we found RCM levels higher than background for electric blankets regardless of blanket setting for locations directly under (*ie*, body surface position) to 10 cm under the blanket (*ie*, uterus position). RCM levels were similar to background levels for areas 10 cm away for the edge of the blanket (*ie*, retina position relevant to the melatonin hypothesis[16]). Given this, and the findings of the nested study, one would expect that reported use of electric blankets during the first trimester of pregnancy would be positively associated with miscarriages, especially if the uterus were the target organ. If the mechanism were related to melatonin from the pineal gland by the same retinal pathway used by visible light,[16] we would expect no association of miscarriage with electric blanket use. Perhaps the inconsistency is due to the fact that the majority of electric blanket users kept their blankets on low settings for most of the night, and at this setting blankets may not have cycled (or may have stopped cycling) and thereby emitted no or little magnetic field. Hence, reported use of electric blankets may not reflect high nighttime exposure to magnetic field.

The association found for the magnetic field front door spot measures in the nested study is smaller (OR = 1.2 95% CI = 0.6–2.5) than the fivefold increase in preclinical miscarriages reported by Juutilainen and coworkers[9] among women who had front door measures above 3.0 mG. Perhaps risk of magnetic field spot measures are easier to detect for preclinical miscarriages than for clinical miscarriages; our study only assessed clinical miscarriages. Front door measures taken closer to the critical exposure period reflect a woman's first-trimester personal magnetic field exposure more than measures obtained some time after this. This is a possibility, as the prospective substudy's front door spot measurement results were more consistent with the findings of Juutilainen and coworkers.[9]

The personal magnetic field RCM and maximum values were lowest for overnight periods and highest for work environments. High RCM values and maximum levels were not associated with proximity to power lines, which we assessed through the wire code. To date, there are no published studies that have quantified the sources for these types of brief high exposure.

About three-fourths of our participants experienced a personal maximum field exposure above 14 mG or an average change in fields (RCM) above 0.42 mG during the 24-hour measurement period. An odds ratio of about 2.0 or higher was found for these metric values. Hence, if these exposures were actually causal, they could account for a nontrivial proportion of the background rate of miscarriages. If these metric values were lowered to below the 25th percentile levels and if the associations were causal, the rate of miscarriage in our study would theoretically be reduced by a few percentage points. A gradual increase in the rate of clinically recognized miscarriages with an increase in electricity use through the last century might not necessarily have been noticed because miscarriages are not routinely monitored; an increase in exposure would have occurred only gradually in any one location over time, and there has been a concomitant improvement in prenatal care over time.

These findings are not consistent with the results of mechanistic and mammalian studies.[17] However, a number of laboratory studies have reported alterations in the development of chick embryos exposed to EMF.[18–21]

A preliminary analysis of this study led our program (The California EMF Program) to fund a prospective study by Li *et al*,[14] which is also published in this issue. Analyses in that study led in turn to the analytic strategy in our study demonstrating the associations with the RCM and maximum levels.

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References

1. Shaw GM. Human adverse reproductive outcomes and electromagnetic fields: a brief summary of the epidemiologic literature. *Bioelectromagnetics* 2001;5(suppl):S5–S18.
2. Delpizzo V. Epidemiological studies of work with video display terminals and adverse pregnancy outcomes (1984–1992). *Am J Ind Med* 1994:26:456–480.
3. Schnorr TM, Grajewski BA, Hornung RW, *et al.* Video display terminals and the risk of spontaneous abortion. *New Engl J Med* 1991;324:727–733.
4. Lindbohm M-L, Hietanen M, Kyyronen P, *et al.* Magnetic fields of video display terminals and spontaneous abortion. *Am J Epidemiol* 1992;136:1041–1051.
5. Wertheimer N, Leeper E. Possible effects of electric blankets and heated waterbeds on fetal development. *Bioelectromagnetics* 1986; 7:13–22.
6. Belanger K, Leaderer B, Hellenbrand K, *et al.* Spontaneous abortion and exposure to electric blankets and heated water beds. *Epidemiology* 1998;9:36–42.
7. Lee GM, Neutra RR, Hristova L, *et al.* The use of electric bed heaters and the risk of clinically recognized spontaneous abortions. *Epidemiology* 2000;11:406–415.
8. Wilson BW, Lee GM, Yost MG, *et al.* Magnetic field characteristics of electric bed-heating devices. *Bioelectromagnetics* 1996;17: 174–179.
9. Juutilainen J, Matilainen P, Saarikoski S, *et al.* Early pregnancy loss and exposure to 50-Hz magnetic fields. *Bioelectromagnetics* 1993;14:229–236.
10. Swan SH, Waller K, Hopkins B, *et al.* A prospective study of spontaneous abortion: relation to amount and source of drinking water consumed in early pregnancy. *Epidemiology* 1998;9:126–133.
11. Wertheimer N, Leeper E. Adult cancer related to electrical wires near the home. *Int J Epidemiol* 1982;11:345–355.
12. Savitz DA, Wachtel H, Barnes FA, *et al.* Case-control study of childhood cancer and exposure to 60-Hz magnetic fields. *Am J Epidemiol* 1988;128:21–38.
13. Breslow NE, Day NE. Statistical Methods in Cancer Research. vol. 1. The Analysis of Case-Control Studies. IARC Scientific Pub. No. 32. Lyon: International Agency for Research on Cancer, 1980.
14. Li KD, Oudouli R, Wi S, *et al.* A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of spontaneous abortion. *Epidemiology* 2002;13: 9–20.
15. Eskenazi B, Fenster L, Wight S, *et al.* Physical exertion as a risk factor for spontaneous abortion. *Epidemiology* 1994;5:6–13.
16. Stevens RG. Electric power use and breast cancer: a hypothesis. *Am J Epidemiol* 1987;125:556–561.

17. Portier C, Wolfe MS, eds. Assessment of Health Effects from Exposure to Power-Line Frequency Electric and Magnetic Fields. National Institute of Environmental Health Sciences Working Group Report. Research Triangle Park, NC: National Institute of Environmental Health Sciences, 1998.
18. Delgado JMR, Leal J, Monteagudo JL, *et al*. Embryological changes induced by weak, extremely low frequency electromagnetic fields. *J Anat* 1982;134:533–551.
19. Juutilaiinen J, Saaili K. Development of chick embryos in 1 Hz to 100 kHz magnetic fields. *Radiat Environ Biophys* 1986;25:135–140.
20. Pafkova H, Jerabek J. Interaction of MF 50 Hz, 20 mT with high dose of X-rays: evaluation of embryotoxicity in chick embryos. *Rev Environ Health* 1994;10:235–241.
21. Farrell JM, Litovitz TL, Penafiel M, *et al*. The effect of pulsed and sinusoidal magnetic fields on the morphology of developing chick embryos. *Bioelectromagnetics* 1997;18:431–438.