Appendix Six

A Population-Based Prospective Study of Personal Exposure to Magnetic Fields During Pregnancy and the Risk of Spontaneous Abortion

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A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of spontaneous abortion

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Running head: Prenatal MF exposure and spontaneous abortion

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ABSTRACT

Background. The effect of magnetic fields (MF) on the risk of spontaneous abortion (SAB) is largely unknown. Most reported studies were based on insensitive MF measurements that were often misclassified and measured retrospectively.

Methods. We conducted a population-based prospective cohort study among pregnant women within a large HMO. All women with a positive pregnancy test at less than 10 weeks of gestation and residing in the San Francisco area were contacted for participation in the study. We conducted in-person interviews to obtain information on risk factors for SAB and other potential confounders. All participants were also asked to wear a MF measuring meter for 24 hours and to keep a dairy of their activities. Pregnancy outcomes were obtained for all participants by searching the HMO's databases, reviewing medical charts, and telephone follow-up. The Cox proportional hazard model was employed for examining the MF-SAB association.

Results. Among 969 subjects included in the final analyses, SAB risk increased with an increasing level of maximum MF exposure (MMF) with a threshold around 16 milligauss (mG): Rate ratio (RR) associated with MMF ≥ 16 mG (versus < 16 mG) was 1.8 (95% confidence interval: 1.2-2.7). The risk remained elevated for all levels of MMF ≥16 mG. The association was stronger for early SABs (< 10 weeks of gestation) (RR=2.2, 1.2-4.0) and among "susceptible" women with multiple prior fetal losses or subfertility (RR=3.1, 1.3-7.7). After excluding women who indicated that their daily activity pattern during the measurements did not represent their typical daily activity during pregnancy, the association was strengthened: RR=2.9 (1.6-5.3) for MMF ≥ 16 mG, RR=5.7 (2.1-15.7) for early SAB, and RR=4.0 (1.4-11.5) among the susceptible women.

Conclusions. Our findings provide for the first time strong prospective evidence that prenatal MMF exposure above a certain level (possibly around 16 mG) may be associated with SAB risk. This observed association is unlikely to be due to uncontrolled biases or unmeasured confounders.

Key words EMF, spontaneous abortion, epidemiology, cohort study.

The health effect of magnetic fields (MF) of extremely low frequency has remained controversial despite efforts to reach consensus [1,2]. The main challenges in studying MF are (1) accurately measuring MF exposure level during the relevant time period, and (2) identifying susceptible populations.

Although the correct measurement of MF exposure should be *personal* exposure during the etiologically relevant time period, MF exposure in most studies was measured by surrogate including wire code classification of the residence or residential spot measurement, frequently measured retrospectively [3-5]. Residential spot measurement does not capture all personal MF exposure at home, and ignores exposure outside the residence. Wire code classification correlates poorly with actual residential MF level [6]. Imprecise measurement of MF exposure coupled with mis-specification of the relevant exposure period could lead to significant misclassification of MF exposure level, which, if non-differential, would dilute any true effect. Consequently, it was not surprising that many studies failed to detect an effect of MF exposure, if one exists. However, more recent studies with more accurate measurement of MF exposure in the relevant time period have tended to report an association with exposure.[5,7-11].

With rare exceptions [12], no attempt has been made to identify a population susceptible to MF. It is conceivable that the biological effects of MF will most likely be felt among the population most vulnerable to environmental insults such as MF. If a true MF effect is difficult to detect due to exposure misclassification, then a failure to identify susceptible populations further reduces the ability to detect a MF effect, especially if the susceptible population consists of only a small part of the study population.

The association between MF exposure and the risk of spontaneous abortion (SAB) has been examined mostly for exposure to video display terminals (VDTs). However, because of the limited effect of MF from VDTs on overall exposure[13], VDTs are unlikely a major source of MF in a woman's daily life. Therefore, it would be difficult to detect an association of SAB with VDT use, if one exists[14,15]. However, one study with actual measurement of VDT magnetic fields (MF) indicated that when a woman was exposed to a VDT with a high MF level [a peak level > 9 milligauss (mG)] during pregnancy, she had a more than 3-fold increased SAB risk.[16]. Another case-control study reported a significant association between an increased residential spot MF level obtained retrospectively and SAB risk including sub-clinic abortion determined by measuring serum hCG level [17]. Use of electric blankets has also been associated with SAB risk [18].

We carried out a prospective cohort study to examine the association between 24-hour personal MF exposure and spontaneous abortion. A previous, as yet unpublished, small prospective study had suggested that a time-weighted-average (TWA) MF exposure above 2 mG conveyed an excess risk [19]. The current study was funded by the California EMF Program to test this hypothesis. The funding authorities agreed that the authors were free to evaluate the association of other exposure metrics with spontaneous abortion. Accordingly, in addition to TWA, we also examined one metric of interest to us, the maximum magnetic field (MMF) encountered during the day.

METHODS

All female members of the Kaiser Permanente Medical Care Program (KPMCP) in Northern California who resided in San Francisco county and adjacent parts of San Mateo county and who had a positive pregnancy test at either KPMCP's San Francisco or South San Francisco Facility from October of 1996 through October of 1998 were identified through the computerized laboratory database as potential eligible subjects. An invitational flyer describing the purposes and procedures of the study was distributed to every woman who submitted a urine sample for a pregnancy test. The flyer included a postage-paid and self-addressed return refusal postcard. Those women with positive tests from whom we did not receive the refusal postcard were contacted by a well-trained female interviewer to determine their eligibility for the study. All English-speaking women who indicated their intention to carry their pregnancy to term at this contact and whose gestational age at the pregnancy test was 10 complete weeks or less were eligible for the study.

We identified a total of 2729 eligible pregnant women. Among them, 1380 (50.6 %) women initially agreed to participate in the study, of whom 1063 (39.0 %) completed an in-person interview and MF exposure measurement. The remaining subjects (11.6%) were never able to schedule the interview despite their initial agreement. In addition, 164 women were not interviewed because they were too far along in their pregnancy (> 15 weeks of gestation) when they were finally reached by our interviewers.

In-person interview

All participating women were interviewed in-person by a well-trained interviewer to obtain detailed information on known risk factors for SAB and other adverse pregnancy outcomes, as well as potential confounders. The women were also asked about their residential and occupational exposures to MF including the use of appliances, as well as their daily activities during pregnancy.

MF measurements

Measurement of personal MF exposure

To measure her MF exposure during pregnancy, each participating woman was asked to wear an EMDEX-II meter for 24 hours starting immediately after the in-person interview. The EMDEX-II was initiated in advance with a custom program to collect MF measurements every ten seconds and store both broadband (40-800 Hertz) and harmonic (100-800 Hertz) resultant magnetic field levels. The meter was specifically programmed only to show the time of day on the display without revealing any MF exposure level so that the woman would remain blinded to the MF exposure level. The woman was also asked to keep a diary recording her activities during this period.

At the end of the measurement period, a technician from Enertech Consultants Inc. (ETC), the contracting firm for conducting MF measurements, examined the data both alone and in combination with the subject's diary. The technician resolved any concerns about the data or diary with the subject at this time. The diary and a copy of the data then were forwarded to T. Dan Bracken Inc., the contracting firm for performing data management on MF exposure, for further review and incorporation into the final MF database to create summary exposure measurements for analyses. Following these examinations, women whose EMDEX II data did not match the activity diary or suggested that they failed to wear the meter (no MF recording) were excluded from the analysis (a total of 73 subjects).

Residential spot MF measurements

Spot measurements were taken in the subject's bedroom, the kitchen, and the most frequently occupied room that was neither a bedroom nor a kitchen. Measurements were made at the abdominal level in the center of each room as well as the location that the subject typically occupied. In addition, measurements were taken at the front entrance of the residence and at approximately fifteen-foot intervals proceeding clockwise around the residence. A measurement was also made at the outside location nearest the subject's bedroom.

Wire code and external wiring information

The ETC technicians performed wire coding and collected information on external wiring by producing an aerial sketch of the residence and all overhead electric system lines within 150 feet of the residence. This information was used to determine the Wertheimer-Leeper wire-code categories, which were classified as underground, very-low-current configuration, ordinary low-current configuration, ordinary high-current configuration, and very-high-current configuration.

Pregnancy outcomes

The pregnancy outcomes for all participants were ascertained through one of the following methods: linking various automated KPMCP databases, reviewing medical charts, and telephoning those whose outcomes could not be identified through the previous two methods. Among 1063 women who participated in the study, pregnancy outcomes for 1058 (99.5%) participants were identified. Although the final outcomes were unknown for the remaining five subjects due to their moving out of the area, they were included in the final analysis and their pregnancy was censored at the gestational age at which they were known to have remained pregnant (all beyond 20 weeks of gestation). After excluding 21 additional women with missing data on personal exposure information or with incomplete interviews, 969 subjects were left in the final analysis.

Statistical analysis

The Cox Proportional Hazard model was employed to examine the SAB risk associated with MF exposure during pregnancy while controlling for potential confounders and taking into account different gestational ages at entry. A woman was considered at risk of SAB as soon as she had a positive pregnancy test (entry time). Gestational age in days was used as the time variable. The woman continued to be considered at risk until either she had a spontaneous abortion or was censored. Women who had other pregnancy outcomes including ectopic pregnancy or induced abortion (3.6%) were censored at the time when those outcomes occurred. Women who remained pregnant beyond 20 weeks of gestational age (80%) were censored at 20 weeks of gestation because by definition, no spontaneous abortion occurs after 20 weeks of gestation.

To take into account the entry at various gestational ages, the time variable (gestational age) with left-truncation was used in the proportional hazard model [20,21]. The association between MF exposure during pregnancy and SAB risk was evaluated at any specific gestational age only among those women who were pregnant and had entered into the study at that time. Using the left-truncation of the time variable to reflect participants' actual contribution of their person-time to the risk assessment in the Cox Proportional Hazard model allowed control of any potential biases due to the association of gestational age at entry with MF exposure and SAB risk. The potential confounders included in the Cox Proportional Hazard model were based on the known or potential risk factors for spontaneous abortion as well as sociodemographic variables.

Since the mechanism of the potential effect of MF during pregnancy and the SAB risk was not clear, we decided to examine the effect of the maximum MF (MMF) level exposed for a potential threshold effect, in addition to the effect of average dose (TWA) as required by the California EMF Program contract. It seemed more plausible to us that MF exposure has a threshold below which any exposure is biologically irrelevant. Thus, we postulated that MMF is a better measure for detecting the MF biological effect than TWA which, combining MF doses at all levels, is a diluted and insensitive measure.

RESULTS

At the request of the California EMF program, we first evaluated the SAB risk associated with 24-hour TWA MF exposure ≥ 3 mG. The cut point of 3 mG had been chosen by the California EMF program to maximize power by assuming a shallow linear dose-response and by examining the exposure distribution of the cohort without knowing the case status. The rate ratio (RR) associated with TWA ≥ 3 mG was 1.2 with 95% confidence interval (CI) of 0.7-2.2. Thus, using the TWA metric failed to confirm the original findings that prompted this study.

To evaluate a potential threshold effect of MF exposure, we first examined the relationship between MMF level in deciles and the SAB risk. Figure 1 shows that a woman's MMF level during the 24-hour measurement period appeared to be associated with an increased SAB risk, starting around 12-18 mG. The risk remained elevated with increasing MMF exposure level. Therefore, we chose 16 mG as the cutoff for all subsequent analyses. In addition, the subsequent evaluations of dose-response relationship for MMF ≥16 mG were based on tertiles of the exposure level. Although 12 mG would have been a better cutoff from the view of the threshold effect, 16 mG was the only available cutoff point between 10 and 20 mG, chosen before the data collection, upon which many parameters for exposure dose (e.g., total sum of MF, duration, and number of times above the cutoff point) were constructed.

Overall, there was little difference between the two cohorts (MMF< 16 mG and MMF ≥ 16 mG) in demographic characteristics, potential risk factors for SAB, reproductive history, and gestational age at entry to the study. The exposed women (MMF≥ 16 mG) were more likely to have been employed before conception, to have had fever during pregnancy, and to have drunk tap water; but they were less likely to have had a history of subfertility defined as failure in conceiving after having had regular intercourse without contraception for more than 12 months.

Prenatal exposure to MF ≥ 16 mG was associated with an 80 percent increased SAB risk. This observed association was quite robust against potential confounders, for the estimate barely changed after adjustment for about 30 known risk factors for SAB or potential confounders: crude RR=1.81 vs. adjusted RR=1.80. In addition, the association persisted irrespective of the sources/locations of MMF exposure (at home, at work, during travel, and other). Using total sum of MF amount ≥16 mG as a measure of dose above the threshold (taking into account both MMF level and duration above the threshold), SAB risk remained elevated for higher doses of MMF exposure, although the trend was not statistically significant (table 1). Using other dose parameters including MMF in quartiles, and duration or number of times above the threshold (≥ 16 mG) showed a similar relationship.

To evaluate whether fetuses at an early gestational age are more susceptible to MMF exposure, we examined the effect of MMF separately for fetal loss before and after 10 weeks of gestation. Table 2 shows that the SAB risk associated with MMF was higher for fetal loss before 10 weeks of gestation (aRR=2.2, 95% CI: 1.2-4.0). If a fetus had survived to 10 weeks or more, the effect of MMF exposure was noticeably reduced (aRR=1.4, 95% CI: 0.8-2.5). The test of whether the rate ratio associated with MMF exposure was constant over gestational age showed a statistically significant interaction ($p<0.05$) between the effect of MMF exposure and gestational age in days. However, when the gestational period was grouped into two groups (before or after 10 weeks of gestation), the difference of the two rate ratios did not reach statistical significance ($p >0.05$).

To examine whether the effect of prenatal MMF exposure was greater for women who might be more susceptible to environmental insults, we restricted analyses to women who had a history of either multiple spontaneous abortions (2 or more) or subfertility. Table 3 shows that overall, the MMF effect on spontaneous abortion was stronger in this group of women than in the overall population: aRR=3.1 (95% CI 1.3-7.7) for the exposure MMF ≥ 16 mG and aRR=4.7 (1.4-15.9) for the exposure before 10 weeks of gestation.

Spot measurements did not show a consistent pattern of an association between increased exposure level (in quartiles) and the risk of spontaneous abortion. In our study, the residential wire-code category was not associated with either MMF or the risk of spontaneous abortion (the results can be obtained upon request).

DISCUSSION

Several potential limitations need to be kept in mind when one interprets the results of this study. First, our information on personal MF exposure was based on 24-hour measurement during the index pregnancy. When compared to many other studies that measured current MF exposure to reflect past MF exposure, one of the strengths of this study was that we measured MF exposure during the relevant period and used personal measurement to capture MF exposure from all sources encountered by a woman. However, the single 24-hour measurement may not be representative of the MF exposure level during the entire relevant gestational period, resulting in misclassification of the MF exposure level. Since any misclassification of the MF exposure was unlikely to be associated with the risk of spontaneous abortion and therefore non-differential, it would probably have resulted in attenuation of the observed association. Nonetheless, we decided to further examine the factors that may influence this exposure misclassification.

The potential misclassification of MF exposure was likely to be influenced by two factors: temporal variation in MF level and activity pattern. Few studies have evaluated the temporal variation of MF exposure level. One such study used repeated measurements over 12-26 months and concluded that MF level is relatively stable over time and that MF measurement on a single visit is a good indicator of average personal exposure levels over time, although the temporal stability of the MMF metric was not specifically examined [6].

To determine whether the daily activity pattern at the 24-hour measurement represented her typical day during pregnancy, we asked the participant at the end of the 24-hour measurement if the patterns of the following activities were “fairly similar” or “quite different”: home in bed, home not in bed, at work, during travel, and other activities. If a participant answered that the daily activity pattern was “quite different” for any of these five activity categories, her measurement day was considered non-typical; thus, her MF measurements on that day may not reflect her true exposure level during her pregnancy.

To examine the potential influence of a change of activity patterns on the effect of MMF found in our study, we stratified the analysis of the effect on women depending on whether the measurement day was a typical day during this pregnancy. If MMF exposure is truly associated with the SAB risk, one would expect the association to be stronger among women whose measurement day reflected their typical day during pregnancy. Table 4 shows that the association was indeed strengthened among women whose MMF measurement likely reflected their true exposure during pregnancy (aRR=2.9; 95% C.I. 1.6-5.3), while the association disappeared among women whose MMF measurements were not likely to have reflected their true exposure during pregnancy (aRR=0.9; 95% C.I. 0.5-1.8). Compared to tables 2 and 3, table 5 also shows that after excluding the subjects with any aspect of their day characterized as non-typical, a greater MMF effect on SAB risk was consistently observed under various examinations. This observation provides further evidence that prenatal MMF exposure may be genuinely related to SAB risk.

Although the overall participation rate (39%) was low, this was a prospective cohort study and MMF exposure level was largely unknown to the general public. Thus, the low participation rate was unlikely to be associated with MMF exposure. In addition, the SAB rate among non-participants was 17.2 percent, indicating comparability between participants and non-participants with regard to their SAB risk. Because we recruited women at an early gestational age (median gestational age of 40 days), 78 subjects had already had a SAB (49% of all SAB cases) at the time of initial contact for their participation. They were included in the study because measurements taken soon after SAB (median interval of 22 days) were considered still representative of their MMF exposure level before SAB. Separate analyses stratifying SAB cases depending on whether their measurements were taken before or after their SAB showed essentially the same results for both types of cases: for SAB < 10 weeks of gestation, aRR=5.6 and 6.1 for cases measured before and after SAB, respectively; for SAB ≥10 weeks, aRR=1.7 and 1.6, respectively.

Our study did not have information on the exact sources of measured MMF ≥ 16 mG. Fields of such magnitude can be found near electric appliances (e.g., microwave ovens and fluorescent desk lamps), very close to devices with electrical motors (e.g., hair dryers, can openers, and fans), electric equipment in the work place, electrically powered transit systems, and under or above certain types of power lines. Studies identifying actual sources of MF exposure ≥ 16 mG encountered by pregnant women in their daily life will be needed.

This population-based cohort study with prospectively measured MF exposure level revealed for the first time (based on our search of Medline) an increased SAB risk associated with a MMF exposure level ≥ 16 mG. The adverse MMF effect appeared to have a threshold around 16 mG and persisted regardless of the sources/locations of MMF exposure. Prenatal

MMF exposure had a greater effect on early spontaneous abortion (< 10 weeks of gestation) when embryos or fetuses are much more sensitive to environmental insults, and among women who may be more susceptible to environmental exposures. The association was much stronger when women whose 24-hour MF measurements may not reflect their true prenatal MF exposure were excluded. These biologically coherent observations, all based on *a priori* hypotheses, provide strong evidence that prenatal MF exposure above a certain level (possibly around 16 mG) may increase SAB risk. It is also unlikely that the observed association was due to biases or unmeasured confounders because any such biases or confounders would have to explain the above observations simultaneously. The robustness of the association against potential confounders was further supported by the evidence that despite adjusting for more than 30 variables of known or suspected risk factors for SAB, the estimates were barely altered. Moreover, prompted by the findings in this study, Lee et al reanalyzed the data from the study in which the findings related to TWA exposure led to funding the current study, and confirmed our observed association between MMF and SAB risk [19]. These findings raise the question of the effect of MMF on reproductive outcomes and other health endpoints. The MMF exposure level in our study population was quite comparable to that found in a nation-wide survey [22] and our study population was racially/ethnically and socio-economically diverse. Thus, the findings from our study should have wide implications.

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Figure 1. Spontaneous Abortion (SAB) Rate by Maximum Magnetic Field (MF) Exposure

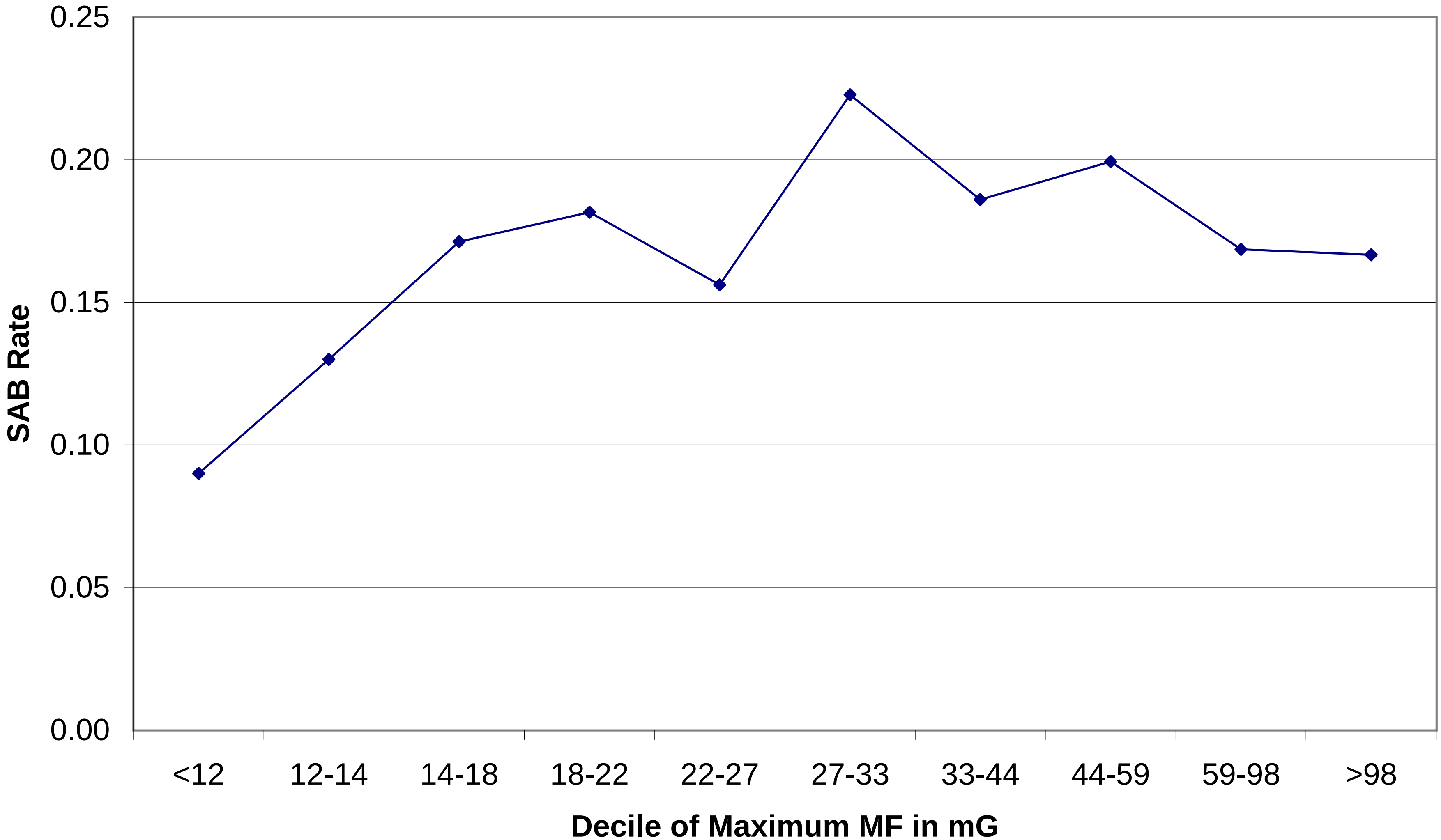

Table 1. Daily maximum magnetic field exposure during pregnancy and the risk of spontaneous abortion, California, 1999.

Daily exposure	Spontaneous abortion Yes n=159 (16.4%)	No n=810 (83.6%)	RR*	95% C.I.
Maximum magnetic field				
<16 mG	27 (10.7)	225 (89.3)	1.0	referent
≥16 mG	132 (18.4)	585 (81.6)	1.8	[1.2, 2.7]
Total sum of exposure over 16 mG in tertiles				
160-1079 mG-sec	41 (17.5)	194 (82.6)	1.7	[1.1, 2.8]
1080-4759 mG-sec	43 (18.1)	195 (81.9)	1.8	[1.1, 2.9]
≥4760 mG-sec	48 (19.7)	196 (80.3)	2.0	[1.2, 3.1]

*Adjusted for previous spontaneous abortion, education, maternal age, gravidity, race, and smoked since last menstrual period.

Table 2. Daily maximum magnetic field exposure during pregnancy and the risk of spontaneous abortion by gestational age, California, 1999.

Gestational age at spontaneous abortion	Spontaneous abortion n(%)	Person-days#	RR*	95% C.I.
0-9 weeks				
<16mG	13(0.21)	6,347		
≥16mG	81(0.48)	16,963	2.2	[1.2, 4.0]
≥10 weeks				
<16mG	14(0.09)	15,109		
≥16mG	51(0.13)	39,644	1.4	[0.8, 2.5]

*Adjusted for previous spontaneous abortion, education, maternal age, gravidity, race, and smoked since last menstrual period.
#Cumulative days at risk of spontaneous abortion.

Table 3. Daily maximum magnetic field exposure during pregnancy and the risk of spontaneous abortion among susceptible populations – women with a history of sub-fertility and/or multiple spontaneous abortions, California, 1999.

	Spontaneous abortion			
	Yes	No		
Daily exposure	**n=41 (17.2%)**	**n=198 (82.9%)**	**RR***	**95% C.I.**
Maximum magnetic field				
<16 mG	6 (8.0)	69 (92.0)	1.0	referent
≥16 mG	35 (21.3)	129 (78.7)	3.1	[1.3, 7.7]
Total sum of exposure over 16 mG				
160-1079 mG-sec	7 (14.0)	43 (86.0)	2.3	[0.7, 7.2]
1080-4759 mG-sec	15 (26.8)	41 (73.2)	3.7	[1.4, 10.2]
≥4760 mG-sec	13 (22.4)	45 (77.6)	3.3	[1.2, 9.2]
Gestational age at spontaneous abortion	**n(%)**	**Person-days#**		
0-9 weeks				
<16mG	3(0.17)	1772		
≥16mG	27(0.77)	3503	4.7	[1.4, 16.0]
≥10 weeks				
<16mG	3(0.07)	4461		
≥16mG	8(0.09)	8476	1.6	[0.4, 5.9]

*Adjusted for previous spontaneous abortion, education, maternal age, gravidity, race, and smoked since last menstrual period.
#Cumulative days at risk of spontaneous abortion.

Table 4. Daily maximum magnetic field exposure during pregnancy and the risk of spontaneous abortion by women whose daily activities at measurement were and were not their typical daily activities during pregnancy, California, 1999.

Daily activity pattern at measurement	Spontaneous abortion Yes n=159 (16.4%)	No n=810 (83.6%)	RR*	95% C.I.
Typical				
<16 mG	13 (8.2)	146 (91.8)	1.0	referent
≥16 mG	95 (20.5)	368 (79.5)	2.9	[1.6, 5.3]
Not typical				
<16mG	14 (15.1)	79 (84.9)	1.0	referent
≥16mG	37 (14.6)	217 (85.4)	0.9	[0.5, 1.8]

*Adjusted for previous spontaneous abortion, education, maternal age, gravidity, race, and smoked since last menstrual period.

Table 5. Various measures of the amount of daily magnetic field exposure during pregnancy and the risk of spontaneous abortion among women whose daily activities at measurement were their typical daily activities during pregnancy, California, 1999.

	Spontaneous abortion			
	Yes	No		
Exposure on typical day	n=108 (17.4%)	n=514 (82.6%)	RR*	95% C.I.
Dose-response relationship				
Maximum magnetic field				
<16mG	13 (8.2)	146 (91.8)	1.0	referent
Total sum of exposure over 16 mG in tertiles				
160-1079 mG-sec	32 (21.2)	119 (78.8)	2.9	[1.5, 5.6]
1080-4759 mG-sec	32 (20.3)	126 (79.7)	2.9	[1.5, 5.7]
≥4760 mG-sec	31 (20.1)	123 (79.9)	3.0	[1.5, 5.7]
Effect on early or late spontaneous abortion				
Gestational age at spontaneous abortion	**n(%)**	**Person-days#**		
0-9 weeks				
<16mG	4 (.10)	4,030	1.0	referent
≥16mG	59 (.54)	11,016	5.7	[2.1, 15.7]
≥10 weeks				
<16mG	9 (.09)	9,892	1.0	referent
≥16mG	36 (.14)	25,265	1.7	[.8, 3.6]

Among susceptible population

Maximum magnetic field	Spontaneous abortion Yes n=29 (18.1%)	Spontaneous abortion No n=131 (81.9%)		
<16 mG	5 (9.1)	50 (90.9)	1.0	referent
≥16 mG	24 (22.9)	81 (77.1)	4.0	[1.4, 11.5]

*Adjusted for previous spontaneous abortion, education, maternal age, gravidity, race, and smoked since last menstrual period.
#Cumulative days at risk of spontaneous abortion.

Appendix. Characteristics of Study Population by highest level of daily MF exposure less than or greater than 16 mG

Characteristic	Chapter A otal n=969	Maximum <16 mG n=252(%)	Maximum ≥16 mG n=717(%)	p-value
Maternal age (years)				
<20	28	7 (2.8)	21 (2.9)	
20-24	107	29 (11.5)	78(10.9)	
25-29	266	69 (27.4)	197 (27.5)	
30-34	327	85 (33.7)	242 (33.8)	
≥35	241	62 (24.6)	179 (25.0)	0.99
Race				
White	372	89 (35.3)	283 (39.8)	
Black	70	22 (8.7)	48 (6.7)	
Hispanic	204	54 (21.4)	150 (20.1)	
Asian or Pacific Islander	265	73 (29.0)	192 (27.0)	
Other	53	14 (5.6)	39 (5.5)	0.69
Education				
< High school diploma	44	12 (4.8)	32 (4.5)	
H.S. diploma or G.E.D.	181	51 (20.2)	130 (18.2)	
Trade school/some college	311	78 (31.0)	233 (32.5)	
College degree	278	72 (28.6)	206 (28.8)	
Graduate school	154	39 (15.5)	115 (16.1)	0.96
Household income				
<$20,000	86	15 (6.4)	72 (10.5)	
$20,000-$29,000	99	25 (10.6)	75 (11.0)	
$30,000-$39,000	140	40 (17.0)	100 (14.6)	

$40,000-$49,000	240	67 (28.5)	175 (25.6)	
≥$50,000	348	88 (37.5)	263 (38.4)	0.35
Marital status				
Single	86	17 (6.8)	69 (9.6)	
Partner	102	22 (8.8)	80 (11.2)	
Married	779	212 (84.5)	567 (79.2)	0.19
Born in United States				
Yes	541	136 (54.0)	405 (56.5)	
No	428	116 (46.0)	312 (43.5)	0.49
Worked in last year				
Yes	839	207 (82.1)	632 (88.3)	
No	129	45 (17.9)	84 (11.7)	0.01
Smoked since last menstrual period (LMP)				
Yes	96	20 (7.9)	76 (10.6)	
No	873	232 (92.1)	641 (89.4)	0.22
People smoke in house				
Yes	82	20 (7.9)	62 (8.7)	
No	887	232 (92.1)	655 (91.4)	0.73
Coffee intake since LMP				
0 cups/day	662	180 (71.4)	482 (67.2)	
0-1	251	58 (23.0)	193 (26.9)	
>1	56	14 (5.6)	42 (5.9)	0.45
Alcohol use since LMP				
Yes	408	97 (38.5)	311 (43.4)	
No	561	155 (61.5)	406 (56.6)	0.18

Drug use since LMP				
Yes	51	11 (4.4)	40 (5.6)	
No	918	241 (95.6)	677 (94.4)	0.46
No. of previous pregnancies				
0	262	62 (24.6)	200 (27.9)	
1	284	82 (32.5)	202 (28.2)	
2	175	44 (17.5)	131 (18.3)	
≥3	248	64 (25.4)	183 (25.7)	0.57
Previous spontaneous abortion				
0	771	201 (79.8)	570 (79.5)	
1	147	37 (14.7)	110 (15.3)	
≥2	51	14 (5.6)	37 (5.2)	0.95
Previous induced abortion				
0	627	165 (65.5)	462 (64.5)	
1	201	55 (21.8)	147 (20.5)	
2	97	22(8.7)	75 (10.5)	
≥3	41	10 (4.0)	32 (4.5)	0.84
History of sub-infertility*				
Yes	203	64 (25.6)	139 (19.6)	
No	755	186 (74.4)	569 (80.4)	0.05
Vaginal bleeding since LMP				
Yes	192	51 (20.4)	141 (19.7)	
No	777	201 (79.8)	576 (80.3)	0.84
Urinary tract infection since LMP				
Yes	44	13 (5.2)	31 (4.3)	
No	923	238 (94.8)	685 (95.7)	0.58

Fever since LMP				
Yes	55	9 (3.6)	46 (6.5)	
No	906	242 (96.4)	664 (93.5)	0.09
Flu or cold since LMP				
Yes	199	43 (17.1)	156 (21.8)	
No	770	209 (82.9)	561 (78.2)	0.11
Strenuous exercise				
Yes	132	32 (12.7)	100 (14.0)	
No	837	220 (87.3)	617 (86.1)	0.62
Carry loads > 10lbs				
Yes	474	115 (47.3)	359 (52.6)	
No	452	128 (52.7)	324 (47.4)	0.16
Used Jacuzzi since LMP				
Yes	95	19 (7.5)	76 (10.6)	
No	872	233 (92.5)	639 (89.4)	0.16
X-ray since LMP				
Yes	79	20 (8.0)	59 (8.3)	
No	886	231 (92.0)	655 (91.7)	0.88
Drinks tap water				
Yes	719	166 (65.9)	553 (77.1)	
No	250	86 (34.1)	164 (22.9)	<0.01
Solvent use				
Yes	602	152 (61.0)	450 (63.1)	
No	360	97 (39.0)	263 (36.9)	0.56
Vitamin use				
Yes	708	177 (70.2)	531 (74.1)	
No	261	75 (29.8)	186 (25.9)	0.24

Diabetes				
Yes	24	7 (2.8)	17 (2.4)	
No	944	245 (97.2)	699 (97.6)	0.72
Gestational age at study entry				
0-48 days	696	189 (75.0)	507 (70.7)	
49-69 days	218	50 (19.8)	168 (23.4)	
70-140 days	55	13 (5.2)	42 (5.9)	0.43

* No pregnancy after one year or more of regular intercourse without contraception