

RELATIONSHIP BETWEEN RESIDENTIAL AND OCCUPATIONAL EMF AND LEUKEMIA: A META-ANALYSIS

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제 3 회 전자장의 생체영향에 관한 워크숍
July 8-9, 1999

Chungnam National University

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BACKGROUND

- ❑ Increased concern and critical views about possible impact of EMF on public health in Korea.
- ❑ Epidemiologic scientists have showed inconsistent results about the possible association between exposure to electric and magnetic fields and incidence of leukemia.
- ❑ Over the past two decade, results of several epidemiologic studies are still unclear whether there is elevated risk for leukemia among electric and magnetic fields exposure.

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OBJECTIVES

- ❑ To acquire a better understanding of the nature of the reported association between leukemia and exposure of EMF
- ❑ To understand the importance of individual studies in driving overall conclusions about a possible link between electric and magnetic fields exposure and leukemia.
- ❑ To provide sufficient statistical power to influence the present overall conclusion about estimated risk between electric and magnetic fields exposure and leukemia.

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MATERIALS AND METHODS

A Selection of the Statistical Methods

What is Meta-Analysis?

Meta-analysis is a statistical method used to assess combined effects, to identify heterogeneity, and to provide a single summary risk estimate based on a set of similar epidemiologic studies.

1. Vote counting

The simplest method, called vote counting, results in tallies of the number of studies with positive results, the number with negative results, and the number with statistical significant results.

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2. Q test for heterogeneity

To assess constancy of combined results

$$Q = \sum (\theta_i - \theta)^2 \omega_i \sim X^2(k-1)$$

3. Fail-safe n

To determine the number of additional null studies needed to reduce a statistically significant combined effect to nonsignificance.

$$N_{fs} = \kappa (d - d_c) / (d_c - 0) = \kappa (d - d_c) / d_c$$

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4. Fixed-effect model

To assume that the studies have the same true effect size

Within study precision is assessed by weighting individual study results by the inverse of the variance

$$U = \sum (\omega_i \cdot \theta_i)^2 / \sum \omega_i \sim X^2(k-1)$$

5. Random-effects model

To assume that the studies included have different true effect sizes that form a statistical distribution, and it estimates the average effect for the whole population on the basis of observed data, including both inter-study variation and intra-study precision.

$$U = \sum (\psi_i \cdot \theta_i)^2 / \sum \psi_i \sim X^2(k-1)$$

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B. Selection of the Studies

1. Residential Study

Number of used studies in this Meta-Analysis

The 11 studies of residential exposure and leukemia

- Year of publication
- Study type
- Study location and period
- Method used for exposure metrics
- Number of cases and controls
- Results

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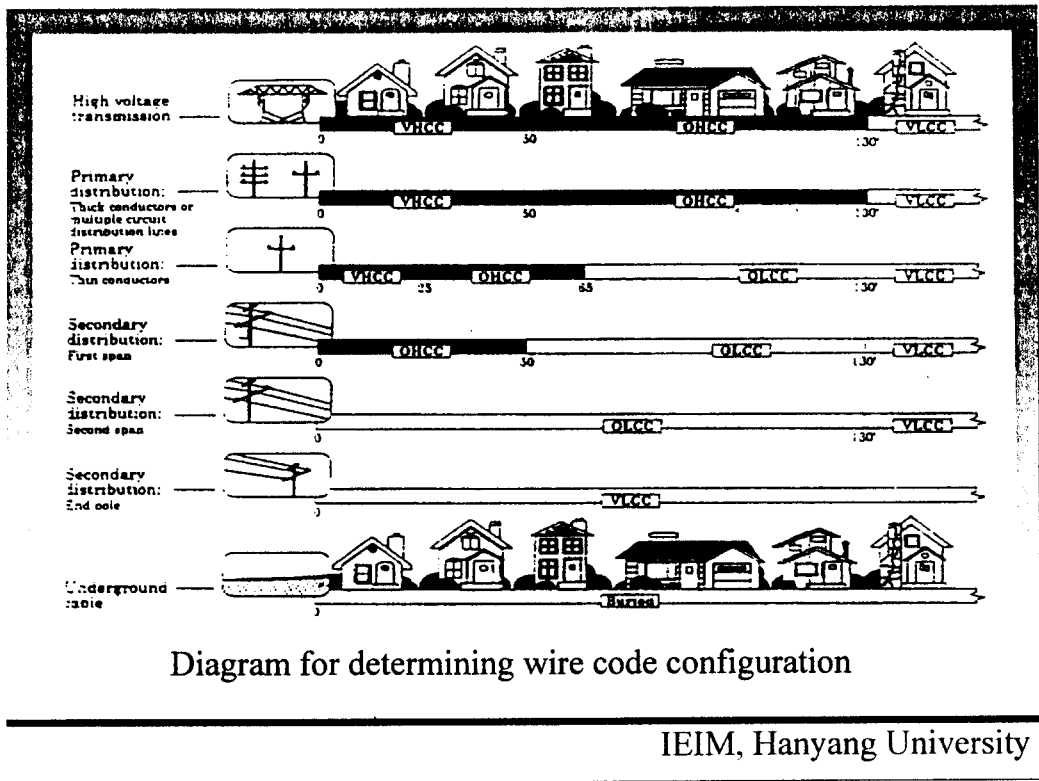
(Classification of exposure metrics in this Meta-Analysis

Studies using wire codes

(High Current Configuration & Low Current Configuration
6 individual studies)

- Studies using distance from electrical source
(50m & 100m : 3 individual studies)
- Studies using wire codes or distance from electrical source
(50m & LCC / HCC, 100m & LCC/HCC : 9 individual studies)
- Studies using calculated magnetic fields (2mG : 4 individual studies)

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Summary of studies on leukemia and residential exposure to MF for a Meta-Analysis.

Study & Study Type	Study Location and Period	Method Used for Exposure Metrics	Number of Cases	Number of Controls	Results
Wertheimer and Leeper, 1979 (Case-control study)	US: persons dying of cancer in Colorado before age 19 in the years 1960-1973, who had a Colorado birth certificate	Wire codes	136 Cases of leukemia (at birth) 155 Cases of leukemia (at death)	136 Controls (at birth) 155 Controls (at death)	OR=2.98(1.72-5.15)
Fulton et al., 1980 (Case-control study)	US: leukemia patients with ages of 0-20 years were obtained from the Rhode Island Hospital, in Denver, Colorado 1964-1978	Wire codes	198 Cases of leukemia patients	225 Controls	RR=1.10(1.0-1.2)
Coleman et al., 1989 (Case-control study)	England: all cases registered with incident leukemia by the Thames Cancer Registry in south-east England after 18 in the years 1965-1980	Distance	771 Cases of leukemias	1432 Cancer controls 231 Population controls	RR=1.45(0.54-3.88) RR=2.0(0.4-9.0) within 100, 50m overhead power-line
Savitz et al., 1988 (Case-control study)	US: all cases were diagnosed Colorado Central Cancer Registry of the Colorado Department of Health among residents of 5 county 1970 Denver, Colorado aged 0-14 aged 1976-1983	Wire codes Spot measurements	97 Cases of leukemia (wire configuration) 36 Cases of leukemia (low power) 37 Cases of leukemia (high power)	259 Controls (wire configuration) 207 Controls (low power) 204 Controls (high power)	OR=1.54(0.90-2.63) OR=1.93(0.67-5.56) OR=1.41(0.57-3.50)
Severson et al., 1988 (Case-control study)	US: all cases with aged 20-79 years were identified Cancer Surveillance System of the Fred Hutchinson Cancer Research Center in western Washington state 1961-1984	Wire codes	89 Cases of leukemia (longest residence 3-10 years before reference date) 97 Cases of leukemia (residence closest to reference dated)	110 Controls (longest residence 3-10 years before reference date) 116 Controls (residence closest to reference date)	OR=0.79(0.22-2.89) OR=0.84(0.24-2.93) at VHCC
Sevitz et al., 1980 (Case-control study)	US: all cases with aged 0-14 years were identified Colorado Cancer Registry in Denver, Colorado 1976-1983	Electric appliances	13 Cases of leukemia (Electric blanket) 3 Cases of leukemia (heated water bed) 48 Cases of leukemia (Bedside electric clock) 7 Cases of leukemia (Heating pad)	57, 67, 21, 60 Controls of leukemia (Electric blanket, Heated water bed, Bedside electric clock, Heating pad)	OR=1.3(0.7-2.6) OR=0.3(0.1-1.2) OR=0.9(0.5-1.6) OR=0.9(0.4-2.2)
London et al., 1991 (Case-control study)	US: all cases from birth to age 10 years were diagnosed Los Angeles County Cancer Surveillance Program in Los Angeles County, California 1960-1987	Wire codes Spot measurements 24hr measurements	206 Cases of leukemia(Wire codes) 140 Cases of leukemia(Spot meas.) 164 Cases of leukemia(24h meas.)	205 Controls (Wire codes) 109 Controls (Spot meas.) 144 Controls (24h meas.)	OR=2.15(1.08-4.26) at VHCC OR=1.22(0.52-2.82) at $\geq 1.24\mu\text{G}$ OR=1.48(0.66-3.29) at $\geq 2.68\text{mG}$
Olsen et al., 1993 (Case-control study)	Denmark: all cases with aged 0-15 years were identified from the files of the Danish Cancer Registry in Denmark 1968-1986	Calculation of Historical MFs	841 Cases of leukemia	1682 Controls	OR=6.0(0.8-44) at $\geq 0.4\mu\text{T}$
Feychting and Ahlbom, 1993 (Case-control study)	Sweden: all cases under age 16 years were identified Swedish Cancer Registry operated by the National Board of Health and Welfare in Sweden 1960-1985	Distance Spot measurements Calculation of Historical MFs	38 Cases of leukemia (Distances) 24 Cases of leukemia (Spot meas.) 49 Cases of leukemia (Cal. MFs)	554 Controls (Distances) 344 Controls (Spot meas.) 633Controls (Cal. MFs)	OR=2.9(1.0-7.3) at 550m OR=0.6(0.2-1.8) at $\geq 0.2\mu\text{T}$ OR=2.7(1.0-6.3) at $\geq 0.2\mu\text{T}$
Linet et al., 1997 (Case-control study)	US: all cases before the age of 15 years who resided in one of nine states(Illinois, Indiana, Iowa, Michigan, Minnesota, New Jersey, Ohio, Pennsylvania, and Wisconsin) 1989-1994	Wire codes Cal. TWA MFs	402 Cases of leukemia (Wire codes) 624 Cases of leukemia (Cal. TWA MFs)	402 Controls (Wire codes) 615 Controls (Cal. TWA MFs)	OR=0.88(0.48-1.63) at VHCC OR=1.53(0.91-2.56) at $\geq 0.2\mu\text{T}$
Tynes and Haldorsen, 1997 (Nested Case-control study)	Norway: all cases with aged 0-14 years were identified Cancer Registry of Norway in Norway 1965-1989	Distances Calculation MFs Cal. TWA MFs	148 Cases of leukemia	579 Controls of leukemia	OR=0.6(0.3-1.3) at 51m OR=0.8(0.3-2.4) at $\geq 0.14\mu\text{T}$ OR=0.3(0.0-2.1) at $\geq 0.14\mu\text{T}$

2. Occupational Study

Number of used studies in this Meta-Analysis

The 25 studies of occupational exposure and leukemia

- Year of publication
- Study type
- Study population, location, and period
- Method used for exposure estimate
- Number of cases or study subjects
- Results

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Classification using this Meta-Analysis

- Job classification (20 individual studies)
 - : Radio repairmen(6) / Electrical engineers(6) / Electricians(6)
 - Electronic technicians(5) / Welders(3) / Power station operators(4)
 - Electric utility workers(6) / linemen(7)

- Leukemia subtypes (13 individual studies)
 - : AML(9) / CML(6) / ALL(4) / CLL(11)

- Country classification (27 individual studies)
 - : U.S.A.(12) / Scandinavia(7) / Others(8)

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Summary of studies on leukemia and occupational exposure to EMF for a Meta-Analysis.

Study	Study Population and Location	Method Used for Exposure Estimate	Study Type	Number of Cases or Study Subjects	Results
Milham, 1982	US: all deaths of Washington State resident men 20 years old or older from 1950 through 1979 were coded to occupation	Occupation code from mortality data	PMR	136 Cases of leukemia: age ≥ 20	PMR=2.58
Wright et al., 1982	US: cases among white males in Los Angeles County 1972-1979	Job titles from census	PIR	35 Cases of leukemia	PIR=1.29(0.90-1.79)
McDowall, 1983	England and Wales: deaths among males 1970-1972 England and Wales: deaths among males 1973	Occupation code from mortality data	PMR RR	85 Cases of leukemia 36 Cases of leukemia	PMR=0.98 RR=2.30(1.40-3.70)
Calle and Savitz, 1985	US: deaths among white men in Wisconsin for 10 electrical occupations 1963-1978	Occupation code from mortality data (used occupational groups based on Milham data)	PMR	81 Cases of leukemia	PMR=1.03(0.80-1.30)
Milham, 1985	US: death among 1691 male licensed amateur radio operators in Washington State and California 1971-1983	Amateur radio operator license according to FCC files	PMR	24 Cases of leukemia	PMR=1.91(1.22-2.83)
Olin et al., 1985	Sweden: deaths among 1,245 male electrical engineers from Royal Institute of Technology in Stockholm 1930-1979	MS in electrical engineering from Royal Institute of Technology, 1930-1950	Cohort	2 Cases of leukemia	SMR=0.9(0.1-3.2)
Pearce et al., 1985	New Zealand: cases among male from New Zealand Cancer Registry 1979-1983	Occupation code from Registry	Case-control	18 Cases of leukemia: age ≥ 20	OR=1.7(0.97-2.97)
Tornqvist et al., 1985	Sweden: cases among 3,358 power linemen and 6,703 power station operators classified in the 1960 population census in Sweden, followed from 1961-1979	Occupation code from census	Cohort	10 Cases of leukemia among power linemen and 16 cases of leukemia among power station operators	SMR=1.30(0.60-2.30) SMR=1.00(0.65-1.57)
Milham, 1988	US: deaths among 67,829 male licensed amateur radio operators in Washington State and California 1979-1984	Amateur radio operator license according to FCC files	Cohort	36 Cases of leukemia	SMR=1.24(0.87-1.72)
Preston-Martin and Peters, 1988	US: cases of CML from the Los Angeles County Cancer Registry April 1, 1979-June 30, 1985	Ever employed in one of 11 specific job titles from questionnaire data	Case-control	137 CML cases: age 20-69	OR=25.40(2.78-232.5)
Guberan et al., 1989	Switzerland: cases among 1,916 male painters and 1,948 male electricians in Geneva 1970-1984	Occupation code from census	Cohort	2 Cases of leukemia	SMR=1.43(0.25-4.50)
Garland et al., 1990	US: cases of cancer among white, male active duty, enlisted naval personnel 1974-1984	Work history	Cohort	102 Cases of leukemia: age 17-64	SIR=0.90(0.8-1.1)
Loomis and Savitz, 1990	US: cases among 410,851 male deaths in 16 US states 1965-1985	Occupation code from death certificates	MOR	3,324 Cases of leukemia: age ≥ 20	OR=1.00(0.8-1.3)
Tornqvist et al., 1991	Sweden: 1,905,660 men employed in 1960, followed from 1961-1979 (133,687 in selected electrical occupations)	Occupation code from census	Cohort	344 Cases of leukemia (in selected electrical occupations): age 20-64	SMR=1.18(1.04-1.34)
Richardson et al., 1992	France: cases in 2 hospitals 1984-1988	Work history and measurements	Case-control	185 Cases of leukemia: age ≥ 30	OR=3.98(1.06-14.69)
Tynes et al., 1992	Norway: cases among cohort of 37,945 male Norwegian electrical workers 1961-1985	Job titles from census (categorized into 5 levels of exposure)	Cohort	107 Cases of leukemia	SIR=1.08(0.89-1.31)
Guendel et al., 1993	Denmark: cases among 2.8 million Danes 1970-1987	Occupation code from Central Population Register and measurements	Cohort	39 Male cases of leukemia: age 20-64	SIR=1.64(1.20-2.24)

Continued.

Study	Study Population and Location	Method Used for Exposure Estimate	Study Type	Number of Cases or Study Subjects	Results
Matanoski et al., 1993	US: cases among white males employed at least 2 yrs identified from mortality records of ATT 1975-1980	Work history and measurements	Case-control	124 Cases of leukemia	OR=2.5(0.7-8.6)
London et al., 1994	US: cases among males with known occupation in Los Angeles County Cancer Registry 1972-1990	Occupation code from Registry and measurements	Case-control	121 Cases of leukemia: age 20-64	OR=1.3(1.1-1.6)
Theriault et al., 1994	France: cases among 170,000 active male utility workers at Electricite de France-Gas de France from 1978-1989 Canada: cases among 31,543 men employed at Ontario Hydro on Jan. 1, 1973 and new employees 1973-1988 Canada: cases among 21,749 men employed at Hydro-Quebec on Jan. 1, 1970 and new employees 1970-1988	Work history and measurements	Case-control	71 Cases of leukemia 45 Cases of leukemia 24 Cases of leukemia	OR=1.4(0.6-3.1) OR=3.1(1.1-9.7) OR=0.3(0.04-1.8)
Tynes et al., 1994	Norway: cases among 13,030 male Norwegian railway workers 1968-1990	Work history and measurements	Case-control	52 Cases of leukemia	OR=0.72(0.37-1.40)
Savitz and Loomis, 1995	US: deaths among 138,905 men employed full-time at least 6 months 1960-1986 at 5 utility companies (all members of the EPRI)	Work history and measurements	Cohort	164 Cases of leukemia	RR=1.01(0.94-1.08)
Baris et al., 1996	Canada: cases among 21,744 male electrical utility workers at Hydro Quebec 1970-1988	Work history and measurements by job exposure matrix	Cohort	20 Cases of leukemia	SMR=1.05(0.64-1.62)
Miller et al., 1996	Canada: cases among 31,543 male Ontario Hydro electric utility workers 1970-1988 and 1973-1988	Occupation code from Registry and measurements	Nested Case-control	26 Cases of leukemia	OR=4.45(1.01-19.70)
Kheifets et al., 1997	US: cases among males with known occupation in Los Angeles County Cancer Registry 1972-1990	Job titles from census and measurements	Case-control	2,355 Cases of leukemia: age 20-64	OR=1.22(0.80-1.86)

RESULTS

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Summary of Meta-Analysis of epidemiologic studies between residential exposure and leukemia.

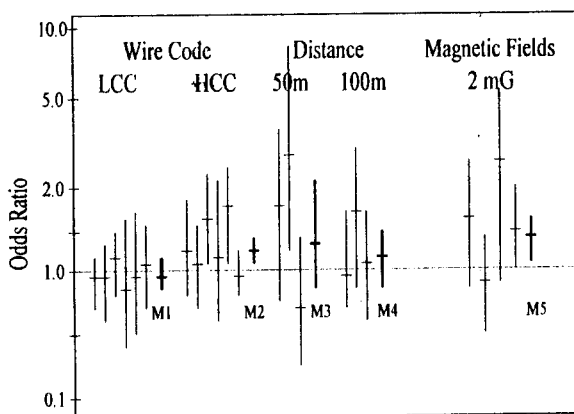
Exposure Metrics	No. of Studies	Vote Counting		Combined OR _{fixed effects}			Combined OR _{random effects}		Fail-Safe n	Plot ID
		No. Positive(%)	No. Statistically Significant(%)	All Studies OR	95% CI	Pr(Q _{het}) ^a	All Studies OR	95% CI		
Wire codes(LCC)	6	3(50)	1(17)	0.98	0.84-1.14	0.93	0.98	0.84-1.15	18	M1
Wire codes(HCC)	6	3(50)	2(33)	1.23*	1.04-1.45	0.27	1.24*	1.02-1.50	130	M2
Distance(< 50m)	3	2(67)	1(33)	1.28	0.80-2.03	0.03	1.38	0.64-2.96	80	M3
Distance(< 100m)	3	2(67)	0(0)	1.08	0.79-1.49	0.45	1.08	0.79-1.49	21	M4
Wire codes(LCC) and Distance(< 50m)	9	5(56)	2(22)	1.01	0.87-1.17	0.30	1.01	0.86-1.20	3	-
Wire codes(LCC) and Distance(< 100m)	9	5(56)	1(11)	1.00	0.87-1.15	0.92	1.00	0.87-1.15	10	-
Wire codes(HCC) and Distance(< 50m)	9	5(56)	3(33)	1.23*	1.05-1.45	0.10	1.26*	1.02-1.55	200	-
Wire codes(HCC) and Distance(< 100m)	9	5(56)	2(22)	1.19*	1.03-1.38	0.40	1.20*	1.03-1.40	165	-
Calculated MP _n (≥ 2mG)	4	3(75)	0(0)	1.31*	1.04-1.66	0.32	1.31*	1.01-1.70	120	M5
All Combined	11	7(64)	3(27)	1.11*	1.04-1.17	0.13	1.11*	1.03-1.20	87	-

Note. OR=odds ratio; CI=confidence interval. * Statistically significant.

^a Probability of homogeneous study results, based on the χ^2 heterogeneity test statistic Q.

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Residential EMF / Leukemia All Exposure Metrics and Cutpoints



Results of meta-analyses of data from individual studies of the association between residential exposure to electric fields and magnetic fields and leukemia by wire code, distance, and magnetic fields.

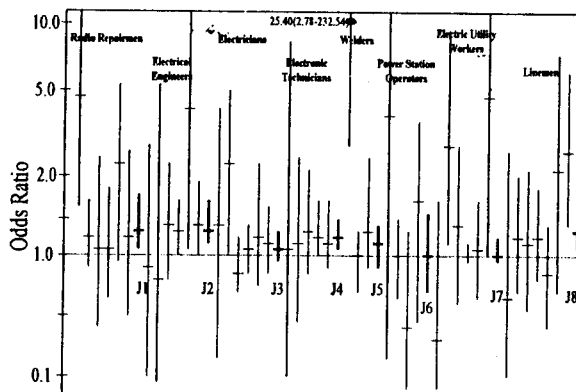
Summary of Meta-Analysis of occupational epidemiologic studies by job classification.

Exposure Metrics	No. of Studies	Vote Counting		Combined OR _{fixed effects}			Combined OR _{random effects}		Fail-Safe n	Plot ID
		No. Positive(%)	No. Statistically Significant(%)	All Studies OR	95% CI	Pr(Q _{het}) ^a	All Studies OR	95% CI		
Radio Repairmen	6	6 (100)	0 (0)	1.36*	1.06-1.75	0.16	1.44*	1.03-2.02	212	J1
Electrical Engineers	6	4 (67)	1 (17)	1.37*	1.13-1.65	0.67	1.37*	1.13-1.65	213	J2
Electricians	6	5 (83)	0 (0)	1.09	0.91-1.29	0.19	1.11	0.90-1.37	49	J3
Electronic Technicians	5	5 (100)	0 (0)	1.27*	1.05-1.52	0.98	1.27*	1.05-1.52	128	J4
Welders	3	2 (67)	1 (33)	1.16	0.89-1.49	0.01	1.37	0.80-2.35	43	J5
Power Station Operators	4	2 (50)	0 (0)	1.01	0.67-1.54	0.45	1.01	0.67-1.54	2	J6
Electric Utility Workers	6	3 (60)	1 (20)	1.02	0.95-1.09	0.07	1.06	0.91-1.23	5	J7
Lineamen	7	5 (71)	0 (0)	1.35*	1.04-1.75	0.19	1.37	0.99-1.89	239	J8
All Combined	20	14 (70)	3 (15)	1.10*	1.05-1.16	0.01	1.18*	1.07-1.29	73	-

Note. OR=odds ratio; CI=confidence interval. * Statistically significant.

^a Probability of homogeneous study results, based on the χ^2 heterogeneity test statistic Q.

Occupational EMF / Leukemia Job Classification



Results of meta-analyses of data from individual studies of the association between occupational exposure to electric and magnetic fields and leukemia by job classification.

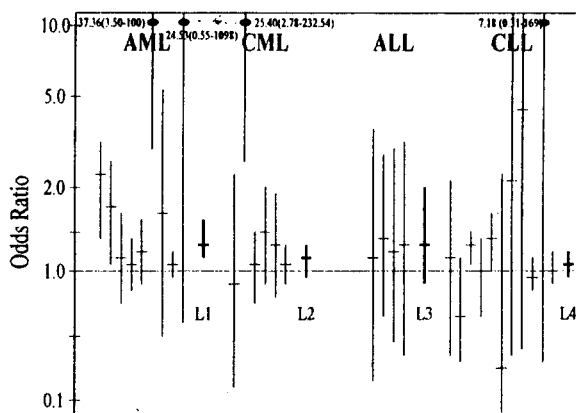
Summary of Meta-Analysis of occupational epidemiologic studies by leukemia subtypes.

Exposure Metrics	No. of Studies	Vote Counting		Combined OR ^{total effects}			Combined OR ^{random effects}		Fail-Safe n	Plot ID
		No. Positive(%)	No. Statistically Significant(%)	All Studies OR	95% CI	Pr(Q _{test}) ^a	All Studies OR	95% CI		
Acute Myeloid Leukemia	9	6 (67)	1 (11)	1.17*	1.07-1.27	0.00	1.36*	1.10-1.69	142	L1
Chronic Myeloid Leukemia	6	3 (50)	1 (17)	1.14	0.98-1.33	0.08	1.21	0.95-1.53	80	L2
Acute Lymphoid Leukemia	4	4 (100)	0 (0)	1.40	0.85-2.30	0.99	1.40	0.85-2.30	153	L3
Chronic Lymphoid Leukemia	11	5 (45)	1 (9)	1.07	0.98-1.18	0.16	1.08	0.95-1.23	71	L4
All Combined	13	7 (54)	3 (23)	1.13*	1.07-1.20	0.44	1.13*	1.07-1.20	47	-

Note. OR=odds ratio; CI=confidence interval. * Statistically significant.

^a Probability of homogeneous study results, based on the χ^2 heterogeneity test statistic Q.

Occupational EMF / Leukemia Leukemia Subtypes



Results of meta-analyses of data from individual studies of the association between occupational exposure to electric and magnetic fields and leukemia by leukemia subtypes.

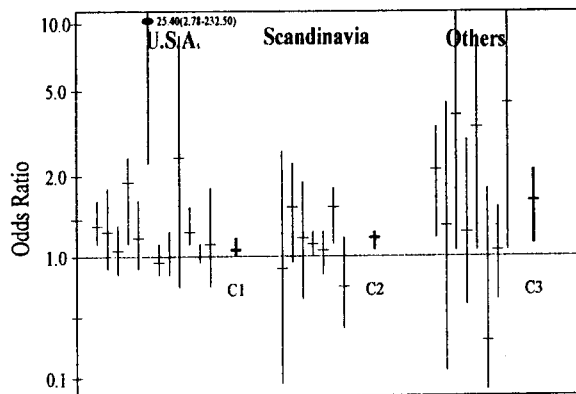
Summary of Meta-Analysis of occupational epidemiologic studies by country classification.

Exposure Metrics	No. of Studies	Vote Counting		Combined OR _{fixed effects}			Combined OR _{random effects}		Fail-Safe n	Plot ID
		No. Positive(%)	No. Statistically Significant(%)	All Studies OR	95% CI	I ² (Q _{het}) ^a	All Studies OR	95% CI		
U.S.A.	12	9 (75)	3 (25)	1.07*	1.02-1.13	0.01	1.17*	1.04-1.31	76	C1
Scandinavia	7	5 (71)	2 (29)	1.19*	1.08-1.31	0.18	1.21*	1.06-1.39	128	C2
Other	8	6 (25)	2 (25)	1.65*	1.25-2.18	0.06	1.75*	1.15-2.67	514	C3
All Combined	27	20 (74)	7 (26)	1.11*	1.06-1.16	0.01	1.17*	1.05-1.30	29	

Note. OR=odds ratio; CI=confidence interval. * Statistically significant.

^a Probability of homogeneous study results, based on the χ^2 heterogeneity test statistic Q.

Occupational EMF / Leukemia Country Classification



Results of meta-analyses of data from individual studies of the association between occupational exposure to electric and magnetic fields and leukemia by country classification.

CONCLUSIONS

1. Residential Study

- ☑ Pooled results of 6 studies of wire code using LCC and HCC as the dichotomous cutpoint showed slightly stronger evidence for an association in the HCC analysis.
- ☑ Pooled results of 3 studies of distance from electrical source using 50m and 100m as the dichotomous cutpoint were fairly similar although the results showed slightly stronger evidence for an association in the 50m analysis.
- ☑ The results of the meta-analysis suggested that magnetic field exposure from electrical sources and high current might be associated with an increased incidence of leukemia.

2. Occupational Study

- ❑ Pooled results of 20 studies using job classification showed stronger association between occupational electric and magnetic fields exposure and leukemia in the electric engineers and radio repairmen than any other occupational groups.
- ❑ Pooled results of 13 studies using leukemia subtypes showed stronger association in the acute lymphoid leukemia than any other leukemia subtypes.
- ❑ Pooled results of 27 studies using country classification showed 7% increase in leukemia risk of occupational exposure to EMF in the U.S.A, 19% in the Scandinavian countries, and 65% increase in other countries .

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- ❑ The vote-counting results had elevated odds ratios at least a half of percentage in the most combined results exception only 2 categories, ie, "CLL" by leukemia subtypes and "Other" by country classification on occupational study.
- ❑ Publication bias was assessed by the 'fail-safe n' that may be not influence for all combined results exception a few categories, ie, "50m & LCC" by exposure metrics on residential study, and "power station operators" and "electric utility workers" by job classification on occupational study.
- ❑ All combined odds ratio results were similar for fixed-effects models and random-effects models, with slightly higher risk estimates for the random-effects model in situations where there was significant heterogeneity, ie, Q-statistic significant ($P < 0.05$).

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LIMITATIONS AND SUGGESTIONS

- Small number of epidemiologic studies included this meta-analysis
- Necessity of combined P values probability test
- Necessity of influence analysis
- Necessity of meta-analysis to provide association between electric and magnetic fields exposure and brain cancer, breast cancer, and CNS tumors.

Further study should provide basic information for epidemiologic studies on the association between electric and magnetic fields and incidence of each cancer in Korea.

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