Non-Hodgkin's lymphoma among electric utility workers in Ontario: the evaluation of alternate indices of exposure to 60 Hz electric and magnetic fields

Paul J Villeneuve, David A Agnew, Anthony B Miller, Paul N Corey

Abstract

***Objectives*—To examine associations between non-Hodgkin's lymphoma (NHL) and exposures to 60 Hz magnetic and electric fields in electric utility workers with a series of indices that capture a variety of aspects of field strength.**

***Methods*—The study population consisted of 51 cases of NHL and 203 individually matched controls identified from within a cohort of male electric utility workers in Ontario. Odds ratios were calculated for several exposure indices with conditional logistic regression models. Aspects of exposure to electric and magnetic fields that were modelled included: the percentage of time spent above selected threshold field intensities, mean transitions in field strength, SD, and the arithmetic and geometric mean field intensities.**

***Results*—For the most part, there was a lack of an association between exposure indices of magnetic fields and the incidence of NHL. Subjects in the upper tertile of percentage of time spent above electric field intensities of 10 and 40 V/m had odds ratios of 3.05 (95% confidence interval (95% CI) 1.07 to 8.80) and 3.57 (1.30 to 9.80), respectively, when compared with those in the lowest tertile. Moreover, the percentages of time spent above these electric field thresholds were significant predictors of case status over and above the association explained by duration of employment and the arithmetic or geometric mean exposure.**

***Conclusions*—These data suggest that exposures above electric field threshold intensities of 10 and 40 V/m are important predictors of NHL. Consequently, the findings support the hypothesis that electric fields may play a promoting part in the aetiology of this cancer. Further occupational studies that include assessment of exposure to electric fields and measures of field strength above similar threshold cut off points are needed to confirm these findings.**

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In Canada, the age adjusted incidence of non-Hodgkin's lymphoma (NHL) has increased more dramatically than for any other male cancer site between 1970 and 1998.[1] Although certain genetic, infectious, and environmental risk factors have been implicated in the aetiology of NHL, most lymphomas develop in people that have no apparent risk factors.[2] Recent epidemiological investigations suggest that lifestyle factors—such as diet, smoking, and physical activity—are not strongly associated with NHL.[3] For these reasons, it is possible that secular trends in incidence may partly be explained by increased exposure to environmental or occupational agents. Individual exposure to 60 Hz electric and magnetic fields at the level of the general population has increased over the past 30 years due to changes in the generation and use of electricity. The possibility that exposure to electric or magnetic fields increases the risk of NHL has been put forth by several investigators.[4–10] None the less, the hypothesis that such exposures cause any cancer continues to be widely debated.

There are several advantages to studying the relation between cancer and exposure to extremely low frequency electromagnetic fields among electric utility workers. Firstly, as a whole, average field exposures in these workers are typically several orders of magnitude greater than background or residential levels. Also, heterogeneous field exposures between job titles are commonplace. Finally, within our study population, workers were employed for extended periods, which allows for the effects of prolonged exposure to high field values to be evaluated. Occupational studies of cancer have typically focused on evaluating the relation between exposure to magnetic fields and leukaemia and brain cancer. None the less, an increased incidence of NHL has been found in several cohorts of workers with suspected increased exposures to electric and magnetic fields.[4–6] By contrast, recent investigations that have undertaken more elaborate assessment of exposure to magnetic field have yielded inconsistent results.[7–10] The examination of the relation between direct measures of electric fields and NHL has largely been ignored, although a non-significantly increased association with cumulative exposures to electric fields has previously been found within our study population.[8]

Assessment of cancer risk is complicated by the complexities of magnetic and electric fields. Magnetic and electric fields can be measured in several ways as they are characterised by their frequency, waveform, polarisation, and amplitude.[11] Despite numerous independent investigations, in vivo and in vitro work has not firmly established which, if any, is the most biologically relevant aspect of field exposure. The results from several in vitro studies have consistently shown that electric and magnetic fields are not mutagenic.[12–17] On the other hand, experimental studies have provided some support for the hypothesis that electric or magnetic fields act as cancer promoters.[18] Tumour promoting agents are capable of converting a cancer initiated cell to a potentially malignant cell, and are characterised by the reversibility of their effects and the existence of a threshold.[19]

Several biological mechanisms through which electric and magnetic fields may promote cancer have been identified. In particular, in vitro studies have found effects of field exposures on calcium ion homeostasis,[20] protein kinases,[21] ornithine decarboxylase,[22–25] and the immune response of cells.[26] An increased rate of proliferation, which is a direct measure of an agent's promoting ability, has been found in some but not most studies.[27] Evaluating the effects of electric fields in cultured cells is difficult as cell incubators are a known source of exposure to magnetic fields, which may confound the results.[20]

Equivocal results have also been obtained from studies that examined the development of tumours in animals exposed to 50/60 Hz electric and magnetic fields over a range of field intensities.[20] In vivo studies have also shown the ability of extremely low frequency electromagnetic fields to reduce melatonin concentrations.[28 29] Melatonin has been shown to inhibit the growth of a wide range of cancers,[30] and suppress the growth of transplanted tumours under experimental conditions.[31] Further, melatonin is a powerful antioxidant that provides considerable protection for DNA against oxidative damage.[32 33] Therefore, the reduction of melatonin as a result of exposure to either electric or magnetic fields may increase the vulnerability of DNA to cancer initiators or promoters.[34] It should be noted that most animal experiments were not undertaken to measure threshold effects of exposure to 50/60 Hz electric and magnetic fields, and as a result, few have used exposure patterns at levels commonly experienced by humans.[35] Moreover, dosimetric patterns are dependent on body shape and size and therefore, the application of scaling factors between animals and humans is not a straightforward procedure.[21] Another complicating factor in the risk assessment of exposure to electric and magnetic fields in animals is the possibility that dose-response features of field exposure do not follow a linear function, but rather show windows in which the system has enhanced sensitivity.[36] If such a window does exist, then the traditional way of using high doses to identify carcinogenic effects of a specific agent[37] would not be appropriate for studies of extremely low frequency electromagnetic fields.

Previous studies of cancer in workers exposed to electric and magnetic fields have relied on the use of a cumulative time weighted average (TWA) estimate of exposure.[7–10 38–41] These cumulative measures have typically been based on either the arithmetic or geometric mean. The arithmetic mean is more sensitive to skewed data and is better suited for modelling threshold effects whereas the geometric mean, which is closely related to the median of the distribution of exposure, minimises the influence of outliers. The relation between NHL and the cumulative TWA based on the geometric and arithmetic mean exposure in this study population has previously been reported.[8] However, recent analyses to correlate the exposure data indicated that the use of the arithmetic and geometric means, by themselves, does not adequately characterise the variability of exposures to either electric or magnetic fields.[42] The correlation analysis also suggested that alternate indices of exposure—such as the SD of field strength, the percentage of time above a threshold, and fluctuations of field strength over successive time intervals—should be evaluated when examining the relations between field exposure and cancer within this study population. These reasons combined with the findings from experimental studies underscore the need to evaluate exposure indices associated with tumour promoters, in particular, exposures above various threshold cut off points.

Although a detailed examination of the relation between exposure to magnetic fields and NHL was recently performed, the findings are limited by the inability to adjust for concomitant exposures to electric fields.[7] Apart from the study by Sahl *et al*[9] that grouped NHL, multiple myeloma, and Hodgkin's disease together, the relation between alternate indices of exposure to magnetic fields has not been evaluated. Furthermore, to our knowledge, no study has examined the association between alternate indices of electric fields and NHL. Our goal was to explore the relation between NHL and a series of indices of electric and magnetic fields to identify the potentially relevant metric needed to perform risk assessment thereby leading to the development of strategies to reduce potentially harmful workplace exposures.

Methods

STUDY POPULATION

A nested case-control design was used with subjects identified from within a cohort of 31 543 Ontario Hydro male employees. Those employees that had been diagnosed with a cancer were ascertained from record linkage of the total study cohort with records of the Ontario Cancer Registry. Men who were diagnosed with non-Hodgkin's lymphoma during the relevant period and who had at least 1 year of service with Ontario Hydro were retained for analysis. The relevant period for the record linkage was 1970–88 for retired and 1973–88 for active workers. Only the first primary tumour in a person was eligible, except for previous basal or squamous cancer of the skin. Cases of NHL were defined by the international classification of diseases revision nine (ICD-9) codes 200, 202.[43]

Controls were also selected from the files of Ontario Hydro according to an equal probability (random) selection among all employees. For each case, four controls were randomly selected with equal probability from the total population of controls in such a way that they had the same year of birth as the case, were alive in the diagnosis year of the case and had no evidence of earlier diagnosis of any cancer (including ICD-9 225) except basal or squamous cancer of the skin. Our results are based on 51 matched sets. A more detailed description of the study population has already been published.[8]

ASSESSMENT OF EXPOSURE TO ELECTRIC AND MAGNETIC FIELDS

Measurements of electric and magnetic fields were obtained directly from a sample of employees under normal working conditions with the Positron 378100 personal exposure monitors (Positron Industries, Montreal, Canada). These monitors are portable, pocket sized, and battery operated and were designed to monitor immediate personal environmental exposure to 50/60 Hz magnetic and electric fields. The Positron monitor filters the electric and magnetic field devices to limit measurements to fields of 60 Hz. The devices were configured to record electric and magnetic fields every minute and were tested and calibrated before use and at regular intervals during the study. Each reading was assigned according to 16 predefined exposure intervals or bins. The exposure intervals were 0–0.61, 0.61–1.22, 1.22–2.44, . . . 5000–10 000, and >10 000 V/m for electric fields and 0–0.012, 0.012–0.024, 0.024–0.048, . . . 100–200, and >200 μT for magnetic fields. Each reading was assigned the value of the midpoint of the interval. The ability of this monitor to differentiate exposures by occupational group has already been demonstrated.[44]

Measurements were taken over the course of a 5 day working week and were defined according to person, occupational group, work site, and day. Our analyses are based on the measures of 820 workers with valid electric and magnetic field exposures. Data from 75 workers were excluded due to failure of instruments, or strong evidence that the monitor was kept close by (so estimated exposures to magnetic fields were valid) but not worn (so electric field data were not valid). Records from two workers could not be retrieved due to defects in the diskettes containing the raw data. Although estimates of home exposures were made for a sample of workers, these estimates were not included in these analyses as the primary objective was to evaluate the relation between NHL and workplace exposures.

A job exposure matrix (JEM) was constructed for each of the exposure indices identified in previous analyses.[42] Each JEM was defined with 17 job titles and 15 work site locations. Six of the occupational groups, (powerline maintainers, meter readers, foresters, lorry drivers, electrical inspectors, and customer service representatives) received exposures that did vary according to work site. We did not include site data for these groups because these workers spend most of their time away from their assigned work location. For the remaining 11 groups, job title and work site specific means were calculated from the Positron readings obtained from the sampled workers. Although efforts were made to obtain sufficient numbers to estimate exposure by job title, in some instances, the number of subjects in the job title and work site strata were small (<5). In these cases, the overall job title mean and overall work site mean were averaged to produce the estimated exposure for this job title and work site cell of the JEM. The mean exposures for these cells with small sample sizes were weighted by the inverse of the variances of job title and work site exposures.

Where work site information could not be coded from a subject's work history record, exposure was estimated with an overall mean calculated for each occupational group. To calculate this overall mean, we first tabulated the number of person-years spent in each work site, within each occupational grouping, for all cases and controls with site information. The overall mean for each occupational group was then calculated as a mean of the work site means, within the occupational group, weighted by the number of person-years spent in each work site. As before, site data from the six occupational groups that often worked away from their work site were not used in these calculations.

As had been done elsewhere,[7] we decided to evaluate the relation between exposure and risk of cancer for three separate periods: career exposure and exposures 10 and 20 years before the reference date. Within each matched case-control set, the reference date was defined as the date of diagnosis of the case.

The exposure for each subject was calculated by multiplying the duration of employment in each work history record by the corresponding entry of the JEM and summing these products to obtain a cumulative estimate of exposure. Cumulative exposures to electric and magnetic fields were calculated from date of employment until date of cancer diagnosis, or diagnosis date of matched case for controls. It is important to note that for each subject, cumulative exposure estimates were based on sampled measures taken from current workers—no historical correction factors were applied. To compare across the different exposure time windows, an average working exposure for each subject was calculated by dividing the estimate of cumulative exposure by the total duration of employment. Exposures to magnetic and electric fields were grouped into tertiles according to the frequency distribution found in controls for all cancer sites combined.

The JEMs were constructed for several exposure indices (table 1).

Personal identifying information, occupational history, and data related to potential occupational confounders were also collected. Socioeconomic status was categorised with a five level categorisation scheme thought to reflect employee status when first hired. The subjects' exposure to potential occupational confounders

Table 1 Exposure indices

Electric fields	Magnetic fields
Arithmetic mean	Arithmetic mean
Geometric mean	Geometric mean
Field strength (SD)	Field strength (SD)
Autocorrelation at 5 minute lags	Autocorrelation at 5 minute lags
Mean transition in field strength	Mean transition in field strength
Time (%) spent above: 5, 10, 20, 40, 156, 625, and 2500 V/m	Time (%) spent above: 0.2, 0.8, 3.0, 12.5, and 50 µT

was assessed by an industrial hygienist and Ontario Hydro and was made blind to case-control status.[45] Odds ratios (ORs) were generated with a multivariate conditional logistic regression model and were adjusted for socioeconomic status, duration of employment, and

*Table 2 Risk of non-Hodgkin's lymphoma by job title worked ⩾5 y**

Job title	Magnetic field exposure (µT) Arithmetic mean	Magnetic field exposure (µT) Geometric mean	Electric field exposure (V/m) Arithmetic mean	Electric field exposure (V/m) Geometric mean	Work site worked in for ⩾5 y Cases	Control	OR (95% CI)
Clerks, professionals, and managers†	0.20	0.08	7.90	1.69	12	60	1.0 —
Foresters	0.28	0.05	28.14	2.35	2	9	1.71 (0.32 to 9.20)
Technical maintenance and service	0.59	0.13	14.10	2.11	9	28	1.52 (0.56 to 4.14)
Operators	1.61	0.19	12.79	1.75	3	19	0.76 (0.66 to 5.29)
Powerline maintainers	0.57	0.07	75.99	2.60	9	6	1.87 (0.32 to 1.75)
Supervisors (technical and trade)	0.25	0.10	14.31	1.88	9	26	0.94 (0.52 to 12.66)
Truck drivers	0.14	0.05	18.09	2.03	3	6	2.56 (0.53 to 4.74)
Technical other	0.31	0.11	9.85	2.01	6	20	1.58 (0.53 to 4.74)
Trade, general	0.60	0.10	8.54	1.59	6	27	1.06 (0.36 to 3.16)
Other	0.66	0.13	22.75	2.00	10	27	1.98 (0.75 to 5.22)
Total					66	251	

*Subjects who worked ⩾5 y in different jobs were included in each job title.
†Referent category excludes those subjects who worked at a transformer or hydrogenerating station.

*Table 3 Risk of non-Hodgkin's lymphoma by work site worked⩾5 y**

Work site	Magnetic field exposure (µT) Arithmetic mean	Magnetic field exposure (µT) Geometric mean	Electric field exposure (V/m) Arithmetic mean	Electric field exposure (V/m) Geometric mean	Worked in work site ⩾5 y Cases	Control	OR (95% CI)
Administration, nuclear generating station, inspection	0.19	0.07	7.14	1.57	10	40	1.0 —
Transformer station	1.10	0.31	18.36	1.60	4	15	1.69 (0.35 to 8.22)
Service centre	0.26	0.10	16.52	2.22	2	6	1.41 (0.19 to 10.36)
Area office	0.20	0.08	9.85	1.58	5	12	3.02 (0.60 to 15.27)
Construction	0.28	0.06	10.42	1.54	9	50	0.91 (0.29 to 2.82)
Hydroelectric generating station	3.06	0.35	8.45	1.52	8	25	1.85 (0.55 to 6.22)
Thermal generating station	0.38	0.10	9.47	1.75	5	15	2.02 (0.42 to 9.69)
Regional office	0.21	0.08	8.10	1.44	2	4	4.06 (0.53 to 31.06)
District office	1.27	0.21	15.36	2.12	1	6	0.79 (0.07 to 8.57)
Other	0.43	0.17	9.55	1.46	0	2	NE
Total					46	175	

*Subjects who worked ⩾5 y in different work sites were included in each work site.

Table 4 Risk of non-Hodgkin's lymphoma for selected indices of mean exposure to magnetic fields

Mean exposure to magnetic fields (µT)*	Career exposure: Cases	Controls	OR (95% CI)	10 y Before diagnosis: Cases	Controls	OR (95% CI)	20 y Before diagnosis: Cases	Controls	OR (95% CI)
Arithmetic mean:									
0–<0.22	11	74	1.0 —	12	57	1.0	14	46	1.0
0.22–<0.47	25	64	2.82 (0.99 to 8.05)	14	40	1.70 (0.53 to 5.42)	10	38	0.82 (0.25 to 2.67)
>0.47	15	65	1.63 (0.53 to 4.99)	8	27	1.49 (0.42 to 5.21)	10	36	0.65 (0.21 to 2.02)
Geometric mean:									
0–<0.074	19	77	1.0 —	14	49	1.0	15	51	1.0
0.074–<0.100	13	68	0.73 (0.32 to 1.66)	6	37	0.43 (0.11 to 1.61)	5	27	0.68 (0.17 to 2.73)
>0.100	19	58	1.28 (0.56 to 2.91)	14	38	1.19 (0.41 to 3.52)	14	42	1.42 (0.52 to 3.67)
SD:									
0–<0.43	15	75	1.0 —	15	70	1.0	17	62	1.0
0.43–<1.12	20	63	1.22 (0.43 to 3.43)	10	25	3.14 (0.80 to 12.38)	6	17	0.76 (0.16 to 3.76)
>1.12	16	65	0.87 (0.30 to 2.58)	9	29	1.92 (0.55 to 6.76)	11	41	0.72 (0.24 to 2.17)
Autocorrelation at 5 minute lags:									
0–<0.24	13	69	1.0 —	11	44	1.0	9	41	1.0
0.24–<0.26	13	72	1.05 (0.41 to 2.65)	6	37	0.47 (0.11 to 2.05)	9	37	0.97 (0.29 to 3.26)
>0.26	25	62	2.33 (1.01 to 5.40)	17	43	2.26 (0.77 to 6.60)	16	42	1.33 (0.50 to 3.56)
Mean transition in field strength:									
0–<0.53	19	74	1.0 —	15	59	1.0	14	54	1.0
0.53–<0.62	13	60	1.43 (0.56 to 3.67)	9	37	0.84 (0.27 to 2.62)	11	35	0.95 (0.31 to 2.93)
>0.62	19	69	1.13 (0.42 to 3.02)	10	28	0.90 (0.24 to 3.42)	9	31	1.09 (0.30 to 3.94)

*Categorised into tertiles according to the distribution of exposure of all controls; the mean was calculated by dividing the cumulative exposure for the relevant index by the number of years employed.
ORs were adjusted for total duration of employment, socioeconomic status, and exposure to benzene and 2,4,5-T.

Table 5 Risk of non-Hodgkin's lymphoma for selected indices of mean exposure to electric fields

Mean exposure to electric fields (in V/m)*	Exposure time window: Career exposure			10 y Before diagnosis			20 y Before diagnosis		
	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
Arithmetic mean:									
0–<8.58	14	72	1.0 —	12	51	1.0	11	42	1.0
8.58–<13.67	12	65	0.97 (0.36 to 2.58)	7	34	0.96 (0.24 to 3.81)	8	31	0.90 (0.25 to 3.30)
>13.67	25	66	1.97 (0.75 to 5.18)	15	39	1.75 (0.56 to 5.48)	15	47	0.93 (0.29 to 3.05)
Geometric mean:									
0–<1.60	11	81	1.0 —	9	48	1.0	9	38	1.0
1.60–<1.96	21	56	3.24 (1.18 to 8.89)	10	37	2.05 (0.45 to 9.43)	5	42	0.42 (0.09 to 1.95)
>1.96	19	66	2.41 (0.88 to 6.56)	15	39	3.73 (0.80 to 17.33)	20	40	2.26 (0.66 to 7.78)
SD:									
0–<26.22	13	65	1.0 —	10	57	1.0	13	42	1.0
26.22–<52.51	21	76	1.18 (0.49 to 2.81)	13	30	3.00 (0.82 to 10.91)	10	33	1.32 (0.44 to 3.95)
>52.51	17	62	0.94 (0.34 to 2.60)	11	37	1.50 (0.47 to 4.84)	11	45	0.50 (0.16 to 1.60)
Autocorrelation at 5 minute lags:									
0–<0.14	17	67	1.0 —	9	39	1.0	8	27	1.0
0.14–<0.17	12	73	0.76 (0.31 to 1.85)	11	48	0.98 (0.30 to 3.19)	8	50	0.29 (0.08 to 1.12)
>0.17	22	63	1.60 (0.70 to 3.67)	14	37	2.70 (0.70 to 10.36)	18	43	0.96 (0.31 to 2.94)
Mean transition in field strength:									
0–<0.87	16	71	1.0 —	14	52	1.0	12	43	1.0
0.87–<0.96	18	66	0.83 (0.33 to 2.07)	10	34	1.11 (0.33 to 3.80)	8	30	0.80 (0.24 to 3.10)
>0.96	17	66	0.62 (0.22 to 1.74)	10	38	0.63 (0.17 to 2.30)	14	47	0.69 (0.18 to 2.62)

*Categorised into tertiles according to the distribution of exposure of all controls; the mean was calculated by dividing the cumulative exposure for the relevant index by the number of years employed.
ORs were adjusted for total duration of employment, socioeconomic status, and exposure to benzene, and 2,4,5-T.

Table 6 Risk of non-Hodgkin's lymphoma by time (%) spent above selected bin values of magnetic field exposures

Time (%) spent above various magnetic field bin levels*	Exposure time window: Career exposure			10 y Before diagnosis			20 y Before diagnosis		
	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
Bin 6 (0.2 μT)*:									
0–<21.21	16	79	1.0 —	16	56	1.0	12	45	1.0
21.21–<27.00	16	56	1.22 (0.54 to 2.74)	5	25	0.56 (0.17 to 1.89)	10	27	1.20 (0.38 to 3.75)
>27.00	19	68	1.18 (0.52 to 2.68)	13	43	0.82 (0.29 to 2.27)	12	48	1.12 (0.37 to 3.36)
Bin 8 (0.8 μT):									
0–<4.63	14	82	1.0 —	13	60	1.0	13	49	1.0
4.63–<9.38	22	57	1.46 (0.64 to 3.33)	13	31	1.83 (0.62 to 5.35)	11	27	1.72 (0.59 to 5.03)
>9.38	15	64	1.05 (0.42 to 2.64)	8	33	0.84 (0.29 to 2.46)	10	44	0.76 (0.26 to 2.27)
Bin 10 (3.0 μT):									
0–<0.46	13	70	1.0 —	16	65	1.0	14	63	1.0
0.46–<2.21	23	74	1.26 (0.52 to 3.04)	10	32	1.12 (0.41 to 3.09)	10	21	3.20 (0.96 to 10.96)
>2.21	15	59	0.90 (0.34 to 2.44)	8	27	1.12 (0.37 to 3.39)	10	36	1.09 (0.36 to 3.32)
Bin 12 (12 μT):									
0–<0.09	15	67	1.0 —	15	63	1.0	14	57	1.0
0.09–<0.51	19	83	0.83 (0.36 to 1.91)	11	41	1.07 (0.42 to 2.88)	10	29	1.51 (0.50 to 4.54)
>0.51	17	53	1.07 (0.41 to 2.79)	8	20	1.48 (0.47 to 4.68)	10	34	0.97 (0.33 to 2.85)
Bin 14 (50 μT):									
0–<0.02	13	78	1.0 —	16	63	1.0	18	51	1.0
0.02–<0.08	22	71	1.52 (0.66 to 3.48)	9	40	1.10 (0.34 to 0.51)	5	30	0.25 (0.06 to 1.04)
>0.08	16	54	1.22 (0.46 to 3.23)	9	21	1.56 (0.47 to 5.14)	11	39	0.57 (0.20 to 1.61)

*Categorised into tertiles according to the distribution of exposure of all controls.
†( ) represent lower edge of magnetic field for specified bins.
ORs were adjusted for total duration of employment, socioeconomic status, and exposure to 2,4,5-T and benzene.

exposure to benzene and 2,4,5-T. Although information was also collected for exposure to 2,4-D, no cases of NHL or matched controls were deemed to have experienced workplace exposures and therefore, ORs were not adjusted for this variable. All analyses were conducted with the software SAS.[46]

A more in depth analysis of potential threshold effects was examined by estimating the percentage of time spent above specified bin values as defined by the Positron. The lower edges in V/m of the nine bins used were: 2.4, 5, 10, 20, 39, 78, 156, 625, and 2,500. Similarly, cut off points used for magnetic fields (μT) were: 0.2, 0.8, 3.0, 12.5, and 50. As before, the percentage of time spent above a specified threshold was defined by both job title and work site, and was obtained from the appropriate JEM. To assess whether these indices made a substantial improvement in predicting risk above an index conventionally used, these threshold exposure indices were entered into a model that already included the arithmetic mean field strength. This improvement was formally tested with the Wald χ^2 statistic. Further, the relative roles of duration of employment, arithmetic mean exposures to electric and magnetic fields, and percentage of time spent above selected thresholds were assessed by calculating standardised coefficients. As outlined by Selvin,[47] these coefficients represent a suitable means to compare factors that have been measured with different units. Standardised coefficients were calculated by dividing the estimates of regression variable by their SEs.

Results

The mean exposures to magnetic and electric fields by job title are presented in table 2. Foresters and powerline maintainers had the high-

Table 7 Risk of non-Hodgkin's lymphoma by time (%) spent above selected bin values of electric field exposures

Time (%) spent above various electric field bin levels*	Exposure time window: Career exposure			10 y Before diagnosis			20 y Before diagnosis		
	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
Bin 6 (10 V/m)†:									
0–<11.19	11	71	1.0 —	12	52	1.0	11	58	1.0
11.19–<15.27	16	72	1.63 (0.56 to 4.72)	6	35	0.89 (0.23 to 3.47)	4	23	0.94 (0.19 to 4.67)
>15.27	24	60	3.05 (1.07 to 8.80)	16	37	2.31 (0.71 to 7.49)	19	39	2.85 (0.88 to 9.29)
Bin 8 (40 V/m):									
0–<2.80	13	74	1.0 —	10	46	1.0	10	45	1.0
2.80–<4.78	12	77	0.92 (0.34 to 2.46)	10	49	1.18 (0.35 to 3.98)	8	42	0.77 (0.21 to 2.83)
>4.78	26	52	3.57 (1.30 to 9.80)	14	29	2.99 (0.72 to 12.43)	16	33	1.88 (0.59 to 6.01)
Bin 10 (156 V/m):									
0–<0.43	13	72	1.0 —	9	52	1.0	11	43	1.0
0.43–<1.04	14	70	1.08 (0.42 to 2.77)	11	32	2.76 (0.87 to 9.65)	8	31	1.10 (0.33 to 3.70)
>1.04	24	61	2.27 (0.85 to 6.04)	14	40	2.44 (0.72 to 8.27)	15	46	1.09 (0.33 to 3.54)
Bin 12 (625 V/m):									
0–<0.11	15	71	1.0 —	8	49	1.0	14	38	1.0
0.11–<0.27	17	72	1.20 (0.53 to 2.66)	15	38	2.70 (0.85 to 8.56)	9	38	0.63 (0.24 to 2.07)
>0.27	19	60	1.33 (0.53 to 3.33)	11	37	1.53 (0.46 to 5.17)	11	44	0.46 (0.16 to 1.29)
Bin 14 (2500 V/m):									
0–<0.01	16	69	1.0 —	11	52	1.0	13	39	1.0
0.01–<0.05	15	76	0.77 (0.34 to 1.74)	11	39	1.48 (0.48 to 4.56)	10	36	0.90 (0.30 to 2.72)
>0.05	20	58	1.27 (0.49 to 3.28)	12	33	1.73 (0.50 to 5.93)	11	45	0.43 (0.13 to 1.39)

*Categorised into tertiles according to the distribution of exposure of all controls.
†( ) Represent lower edge of magnetic field for specified bins.
‡Odds ratios were adjusted for duration of employment, socioeconomic status, and exposure to 2,4,5-T and benzene.

Table 8 Non-Hodgkin's lymphoma standardised coefficients (SCs) obtained from the conditional logistic model containing terms for duration of employment, time (%) spent above magnetic field threshold and arithmetic mean field exposure*

Exposure index†	Lower bound of magnetic field threshold: 0.2 μT		0.8 μT		3.1 μT		12.5 μT		50 μT	
	SC	p Value‡	SC	p Value	SC	p Value	SC	p Value	SC	p Value
Arithmetic mean (magnetic field)	−0.60	0.55	0.16	0.87	−1.03	0.30	−0.17	0.86	0.50	0.61
Arithmetic mean (electric field)	0.93	0.35	1.11	0.27	0.44	0.66	0.88	0.38	0.96	0.34
Duration of employment	0.32	0.75	0.23	0.82	0.34	0.73	0.32	0.75	0.44	0.66
Time (%) spent above magnetic field threshold	0.12	0.91	−0.74	0.46	0.90	0.37	−0.06	0.95	−0.79	0.43

*SCs were obtained by dividing the regression coefficient by its SE and were adjusted by socioeconomic status and exposure to benzene and 2,4,5-T
†Exposure indices were modelled simultaneously.
‡p Value based on the Wald χ^2 test statistic.

Table 9 Non-Hodgkin's lymphoma standardised coefficients (SCs) obtained from the conditional logistic model containing terms for duration of employment, time (%) spent above electric field threshold and arithmetic mean field exposure*

Exposure index†	Lower bound of electric field threshold: 5 V/m		10 V/m		20 V/m		39 V/m		156 V/m	
	SC	p Value‡	SC	p Value	SC	p Value	SC	p Value	SC	p Value
Arithmetic mean (magnetic field)	−0.62	0.53	−0.65	0.52	−0.48	0.63	−0.53	0.60	−0.43	0.67
Arithmetic mean (electric field)	0.42	0.68	−0.04	0.97	−0.18	0.86	−0.30	0.77	−0.83	0.41
Duration of employment	0.12	0.91	0.33	0.74	0.46	0.64	0.09	0.76	0.211	0.83
Time (%) spent above electric field threshold	1.49	0.14	2.04	0.04	2.28	0.02	1.57	0.12	1.63	0.10

*SCs were obtained by dividing the regression coefficient by its SE and were adjusted by socioeconomic status, and exposure to benzene and 2,4,5-T.
†Exposure indices were modelled simultaneously.
‡p Value based on the Wald χ^2 test statistic.

est exposures to electric fields as indicated by the arithmetic and geometric mean field values. For magnetic fields, those employed as operators had markedly higher field exposures with an arithmetic mean of 1.61 μT (geometric mean 0.19 μT). Although the calculation of ORs within job title categories held for at least 5 years was limited by small sample sizes within each group, ORs >1 were found for seven out of nine job titles relative to clerks, professionals, and managers. This referent group had low exposures to both electric and magnetic fields.

The levels of worksite exposures to electric fields were highest at transformer stations (arithmetic mean 18.36 V/m, table 3). Similarly, magnetic field exposures were increased at hydroelectric generating stations (arithmetic mean 3.06 μT). As with analyses by job title, the precision of the ORs for sites worked in for at least 5 years was poor due to small sample sizes. None the less, ORs >1 were found for six out of eight work sites relative to those in the referent category.

In general, there was a lack of an association between indices of exposure to magnetic fields and incidence of NHL. This was found for career exposures as well as exposures received either 10 or 20 years before diagnosis of the case (table 4). An increased risk of NHL was evident among subjects with higher autocorrelations with magnetic fields based on 5 minute lag intervals received over their entire employment and for exposures received 10 years before the reference date.

With the exception of the geometric mean, most indices of exposure to electric fields were

Table 10 Correlation matrix of selected electric field metrics among sampled Ontario electric utility workers

	GM EF	*AM EF*	*GM MF*	*AM MF*	*ET TH6*	*ET TH8*	*ET TH10*	*ET TH12*	*ET TH14*
GM EF	1.00								
AM EF	0.81	1.00							
GM MF	0.24	0.24	1.00						
AM MF	0.21	0.25	0.86	1.00					
ET TH6	0.39	0.39	0.06	0.06	1.00				
ET TH8	0.55	0.49	0.11	0.11	0.62	1.00			
ET TH10	0.58	0.74	0.18	0.18	0.38	0.68	1.00		
ET TH12	0.64	0.90	0.23	0.23	0.26	0.48	0.80	1.00	
ET TH14	0.78	0.97	0.23	0.23	0.18	0.35	0.61	0.84	1.00

GM EF=geometric mean electric field; AM EF=arithmetic mean electric field; GM MF=geometric mean magnetic field; AM MF=arithmetic mean magnetic field strength; ET TH6–14=time (%) spent above electric field bins 6,8,10,12, and 14 respectively.

Table 11 Correlation matrix of selected magnetic field metrics among sampled Ontario electric utility workers

	GM EF	*AM EF*	*GM MF*	*AM MF*	*MT TH6*	*MT TH8*	*MT TH10*	*MT TH12*	*MT TH14*
GM EF	1.00								
AM EF	0.81	1.00							
GM MF	0.24	0.24	1.00						
AM MF	0.21	0.25	0.86	1.00					
MT TH6	0.10	0.23	0.42	0.36	1.00				
MT TH8	0.14	0.23	0.58	0.51	0.74	1.00			
MT TH10	0.19	0.30	0.68	0.70	0.42	0.64	1.00		
MT TH12	0.24	0.31	0.71	0.85	0.24	0.38	0.69	1.00	
MT TH14	0.07	0.08	0.65	0.84	0.13	0.22	0.40	0.67	1.00

GM EF=geometric mean electric field; AM EF=arithmetic mean electric field; GM MF=geometric mean magnetic field; AM MF=arithmetic mean magnetic field strength; MT TH6–14=Time (%) spent above magnetic field bins 6,8,10,12, and 14 respectively.

not strongly related to case status (table 5). For the geometric mean, those in the highest tertile relative to those in the lowest had ORs of 2.41 (95% CI 0.88 to 6.56), 3.73 (95% CI 0.80 to 17.33) and 2.26 (95% CI 0.66 to 7.78) for career exposures, exposures received 10 years before diagnosis, and 20 years before diagnosis, respectively. The incidence of NHL was associated with increased autocorrelations with electric fields based on 5 minute lag intervals for career exposures and for those received 10 years before the reference date.

The percentage of time spent above a series of magnetic field threshold cut off points was not related to case-control status for the three periods examined (table 6). By contrast, the percentage of time spent above selected thresholds of exposure to electric fields was related to NHL (table 7). These ORs were more pronounced for career exposures and diminished with increased time between case diagnosis and exposure. For career exposures, a convex pattern of risk estimates for the upper tertile categories relative to the lowest was found across increasing thresholds; with the peak in the upper tertile of exposures received above 40 V/m (OR 3.57 95% CI 1.30 to 9.80). Similar convex patterns across increasing thresholds were also found for exposures received 10 and 20 years before diagnosis.

Table 8 presents the results from simultaneously modelling the percentage of time spent above selected threshold values of magnetic fields with duration of employment and the arithmetic mean exposures to electric and magnetic fields. In each of the five models (one for each threshold), the percentage of time spent above the threshold, was not strongly associated with the incidence of NHL.

Standardised coefficients for the percentage of time spent above selected electric field thresholds, with adjustment for arithmetic mean exposures to electric and magnetic fields and duration of employment are provided in table 9. The percentage of time spent above 10 and 40 V/m was positively associated with an increased risk of NHL ($p<0.05$). In all five models, the standardised coefficients were positive and greater in magnitude than duration of employment, and the arithmetic mean electric and magnetic fields. These results did not change appreciably when the geometric rather than arithmetic mean field exposures were entered into the multivariate model.

Correlations between the percentage of time spent above selected electric field thresholds and the geometric and arithmetic mean of both electric and magnetic fields are presented in table 10. The percentage of time spent above 10 and 40 V/m were poorly correlated with the arithmetic mean electric field (r=0.39 and 0.49 respectively). The correlations between the time spent above selected thresholds of magnetic fields and the geometric and arithmetic means are presented in table 11.

Discussion

These analyses extend the previous evaluation between incidence of NHL and exposures to electric and magnetic fields within this cohort[8] by modelling a series of exposure metrics that capture important additional aspects of field strength. Also, we have examined the magnitude of the associations for exposures received at different periods relative to the date of diagnosis. Our results suggest that there is no association between exposure to magnetic fields and NHL. By contrast, we found that exposures above threshold cut off points 10 and 40 V/m were positively related to the incidence of this cancer. Perhaps most importantly, after adjusting for duration of employment and the arithmetic mean exposure to electric fields, the percentage of time spent above 10 and 40 V/m remained an important predictor of case control status.

The arithmetic and geometric mean exposures to electric fields were poorly correlated with metrics representing time spent above 10 and 40 V/m, however, for threshold cut off points above 156 V/m higher correlations were found. Therefore, within this data set, the use of the arithmetic and geometric mean strengths of electric fields are unsuitable for assessing the relation between NHL and exposures above intermediary threshold values (<156 V/m).

Previous analyses of cancer within this population used cumulative time weighted average estimates of exposure based on the geometric and arithmetic means. Our finding of a non-significantly increased risk of NHL in workers with a higher geometric mean exposure to electric fields is consistent with the previously reported increased risk of NHL in the upper tertile of cumulative exposure (OR 2.09, 95% CI 0.87 to 5.01) relative to the lowest.[8] Further, by modelling duration of employment and mean exposure as separate terms in the model we were able to evaluate the separate effects of these two variables. Duration of employment was found not to be an independent predictor of case status.

The JEMs used in this study differ from previous work[8] in that historical changes in exposure were not taken into account. For those analyses, the development of job title and site specific historical adjustment factors was complex and involved interviews with relevant current and retired supervisory personnel, and a combination of data available from Ontario Hydro archives. These data included peak power loads at several specific points in the Ontario Hydro system and overall system data including total energy generated, operating voltages, and total lengths of transmission and distribution circuits. Unfortunately, historical adjustment factors were only available for the arithmetic and geometric mean exposures to electric and magnetic fields. Our inability to take into account historical changes in exposure may result in increased exposure misclassification which limits our ability to detect associations with other metrics. However, no significant differences in ORs were found when the arithmetic and geometric mean career exposures were modelled with historical corrections. None the less, we cannot rule out that the attenuation of ORs for threshold exposures to electric fields received in the distant past may, in part, be the result of an increased misclassification error.

Although misclassification of exposure with job exposure to infer individual exposure matrices is possible, the manner in which exposure to electric and magnetic fields was assessed is a major strength of this study. Few occupational studies have collected information on exposures to electric fields. Also, readings from the Positron monitor were collected from workers each minute over the span of a 5 day working week. This allowed for an extensive set of exposure metrics to be evaluated when assessing risk of cancer. Further, our JEMs were defined according to both job title and worksite location. Worksite location has previously been shown to be an important determinant of risk of leukaemia within this study population.

Our study population was initially assembled as one component of the larger tri-utility study[10] to provide sufficient power to identify an OR of 2.0 for risk of leukaemia had that been the true value. Theoretically therefore, there is limited power to assess significant differences in risk of NHL across indices of exposure to extremely low frequency electromagnetic fields. Analyses of exposure to magnetic fields and risk of NHL in a separate cohort of electric utility workers was performed separately by histological type.[7] It was found that the risk associated with cumulative exposure to magnetic fields was more pronounced for intermediate and high grade NHL relative to low grade. Unfortunately, the small sample size in this population did not permit separate analyses by histological type.

Only a few occupational studies have evaluated the relation between electric fields and cancer.[8 40 48] Assessing exposure to electric fields is much more difficult because, unlike magnetic fields, electric fields are influenced by the body of the worker. As a result, exposures to electric fields are likely to be measured with a greater degree of misclassification than magnetic fields. Therefore, the risks of NHL as they relate to indices of electric fields in this study may be understated.

Our analyses evaluated several exposure indices and therefore several tests of significance were carried out. The effect of this multiple testing is to increase the likelihood of a chance finding. No adjustment was made to the significance levels of these tests because, as pointed out by Rothman,[49] such corrections may cause more problems than they were intended to solve. It is worth noting that we took steps to dramatically reduce the number of possible exposure metrics taken through correlation and principal components analyses[42] and by reviewing the relevant experimental evidence.

In conclusion, this study suggests that electric fields, particularly exposures received above a threshold are associated with an increased risk of NHL. Additional epidemiological studies that incorporate detailed assessment of exposure to electric fields are needed to confirm this result.

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