# Chapter 4 — Non-Hodgkin's Lymphoma

In contrast to leukemia, which is declining, the incidence of non-Hodgkin's lymphoma (NHL) continues to rise in Canada at the rate of 1–1.5% per year. The disease has an age-standardized incidence of 19.3/100,000 per year, and for Canadians the lifelong probability of getting any form of lymphoma is 2.5% for women and 2.9% for men.

Thirty-two papers on NHL were included in the assessment process and 27 met the quality criteria for inclusion. The study designs were as follows:

• Cohort studies: 11 (9 positive association, 3 with statistical significance, 2 negative)

• Case-control studies: 14 (12 positive association, 8 with statistical significance, 2 negative)

• Ecological: 2 (2 positive association).

Five studies were excluded on quality criteria (4 positive association, 1 with statistical significance, 1 negative). The remaining 27 studies were given 4 or 5 out of 7 by both readers, with only 2 studies receiving 6, both positive studies (24, 32).

## Cohort Studies

There were 12 cohort studies. Asp et al. (10) did not find an increase in NHL incidence in a group of Finnish chlorphenoxy herbicide applicators, however the low number of deaths (384 in total) did not allow any conclusions to be drawn. Becher et al. (11) found an SMR of 326 (CI 119–710) for NHL in a group of workers in phenoxy herbicide plants in Germany, the excess occurring in the groups with higher exposure to dioxins and other contaminants of phenoxy acids (including pesticides now banned in Canada, such as 2,4,5-T). Hansen et al. (12) found an SMR of 200 (CI 86–393), though not statistically significant, in a cohort of Danish gardeners. Hooiveld et al. (13) found an RR of 1.7 (CI 0.2–16.5) with RR increasing parallel to serum levels of TCDD (a dioxin contaminant of phenoxy herbicides) indicating an exposure-related risk. However the main product of the factory was 2,4,5-T, which is banned in Canada, though the dioxin contaminant, TCDD, occurred previously in 2,4-D production. Kross et al. (14) looked at golf course superintendents, a group who experiences increased exposure to a number of environmental hazards such as pesticides, fertilizers, and diesel fumes. The PMR for NHL was 237 (CI 137–410) though the total number of NHL deaths was only 12.

Lynge et al. (15) did not find an elevated risk of NHL among a group of Danish phenoxy herbicide factory workers exposed to the herbicide MCPA. MacLennan et al. (16) found an SMR of 372 (101–952) for NHL among workers at a triazine herbicide factory. The authors, however, conclude that the almost fourfold increase was likely not due to triazine exposure, because the increase was not concentrated in the subgroup who had been long-term employees of the factory. Morrison et al. (17) conducted a large study of 155,000 farmers in Canada and found a statistically significant increase in NHL (RR 2.11, CI 1.1–3.9), the risk increasing with the number of acres sprayed. Sathiakumar et al. (18) found an SMR of 385 (CI 79–1134) for NHL and triazine exposure though the numbers were small (only 3 NHL deaths with 1.78 expected). The study group was young (only 13% were over 45 years old) and had been employed a relatively short time. Sperati et al. (19) looked at the mortality of pesticide users and their wives and found a not statistically significant increase in NHL among the female (SMR 2.29, CI 0.62–5.86) but not among the male pesticide users. The small numbers and poor exposure history, however, make it difficult to interpret this result. Thorn et al. (20) did not find elevated rates of NHL among Swedish lumberjacks exposed to phenoxy herbicides. Zahm (21) found a slight excess of NHL (SMR 1.14, CI 0.31–2.91) among employees of a lawn-care company. However, the cohort was young, with short-duration employment (with more than half having been employed less than 6 months) and a short follow-up period (averaging 7.8 years), making conclusions difficult to draw, as lag time between exposure and illness can be decades.

## Case-Control studies

There were 14 case-control studies. The pooled data study of Blair et al. (22) found an OR of 1.5 (CI 1.1–2.0) for farmers who had ever used lindane, though this was reduced by adjusting for exposure to other pesticides and was greater among proxy respondents. Buckley et al. (23) found elevated ORs in children from homes where pesticides were used a majority of days (OR 7.3, $p < 0.05$), for professional home exterminations (OR 3.0, $p = 0.002$), and for postnatal exposure (OR 2.4, $p = 0.001$). There was an elevated but not significant OR (1.74) for parental occupational exposure. Cantor et al. (24), one of the studies that received a rating of 6, showed a slightly increased OR (1.2, CI 1.0–1.5) of NHL in farmers in Iowa and Minnesota. The study by Costantini et al. (26) did show excess small-cell lymphoma (a subtype of NHL) in male agricultural workers, OR 1.4 (1.0–1.9). However such a study which groups occupations in categories may be less reliable, as the "agricultural worker" category may be too crude to enable assessment of pesticide exposure.

Hardell et al. (27, 28) reported on two case-control studies. The first (27) found elevated risks in males over 25 years old for exposure to herbicides (OR 1.6, CI 1.0–25), fungicides (OR 3.7, CI 1.1–132.0), and, specifically, phenoxy acids (OR 1.5, CI 0.9–2.4). The more recent study (28) described two case-control studies, one on NHL alone and one specifically on hairy-cell leukemia, a rare form of NHL, with respect to pesticide exposure (with many different pesticides and exposure levels tested). A pooled analysis (done in order to increase numbers) revealed elevated ORs with statistical significance for herbicides in general, phenoxyacetic acids, glyphosate, and MCPA. Also there were dose–response effects in these pesticide groups, most with statistical significance.

The study by Clavel et al. (25) showed an OR of 7.5 (CI 0.9–61.5) for hairy-cell leukemia in farmers exposed to organophosphate insecticides. Lack of quantitative data for 50% of the farmers prevented testing for a dose–response relationship.

Hoar et al. (29) pooled data from three case-control studies and concluded that there is little evidence to suggest a causal role of atrazine in the development of NHL. Kogevinas et al. (30) did not reveal an elevated NHL risk in connection with several phenoxy herbicides, though small excesses were found with some herbicides not used in Canada and with TCDD, a contaminant. MacDuffie et al. (31) showed elevated ORs (adjusting for many variables) for NHL with exposure to fungicides, organophosphate and carbamate insecticides, and dicamba herbicides, but without statistical significance. Specifics of pesticide exposure history were not discussed. MacDuffie et al. (32) found increased ORs for NHL with exposure to decamba, mecoprop, and aldrin (1.96, 2.22, and 3.42, respectively). This was a well-designed study that received a rating of 6, which began by assessing risks of exposure first to major classes of pesticides and then by individual compounds within those classes; the study stratified by days per year of exposure, and included many potential confounders.

Persson et al. (33) found an OR of 2.3 (CI 0.7–7.2) for NHL with occupational exposure to phenoxy herbicides, though the exposure was not quantified. Waddell et al. (34) was a pooled data study that showed a statistically significant 50% increase in NHL with exposure to organophosphate insecticides; however, proxy respondents indicated a much higher risk (OR 3.0) than did direct interviews (OR 1.2), making interpretation difficult.

Zheng et al. (35) found elevated ORs for NHL with carbaryl exposure, which persisted after adjusting for other major classes of pesticide, some with statistical significance.

## Ecological Studies

The two ecological studies were both positive. Fontana et al. (36) found higher rates of NHL in rice-growing areas of Italy where concentrations of 2,4-D (common in Canada) and 2,4,5-T (banned in Canada) were high in soil and water. In men, NHL rates were increased 50–60% in the most polluted areas. A nested case-control study showed elevated risk of NHL for women in rice-growing jobs (OR 1.9, CI 0.6–6.0). The other ecological study by Schreinemachers et al. (37) found higher rates of NHL for women (SRR 1.35, CI 1.09–1.66) in agricultural regions of Minnesota.

## Excluded Studies

Five studies were excluded. The study by Zahm et al. (42) was one of the few studies on women and pesticides and it found a statistically significant 4–5-fold increase in NHL with the handling of organophosphates. However, it sampled only a very small number of women who handled pesticides, so the study was excluded.

Two studies (39, 41) were excluded on the basis of poor methodology (small sample size, few confounders measured, and poor exposure histories), and though their findings were positive, they were not statistically significant. Burns et al. (40) and Bloeman et al. (38) showed a not statistically significant increase in NHL. Both were excluded for methodological reasons; moreover, Dow Chemical funded both studies.

## Summary

The etiology of NHL is considered to combine immunological and environmental factors. Predisposing immunodefective conditions, such as immunosuppressive medication after organ transplantation and HIV infection, are known risk factors, and viral infections such as EBV have also been implicated. Previous studies have pointed to certain pesticides, such as 2,4-D, as possible precipitants of NHL, and the findings of this review are clearly consistent with this. Out of 27 studies, 23 show associations between pesticide exposure and NHL, many with statistical significance. Exposure misclassification, a perpetual problem with cohort studies, tends to skew results towards the null, so in fact the associations in these studies may be underestimated. This review uncovered compelling evidence of the link between pesticide exposure and the development of NHL. This warrants further investigation, particularly in the area of cytogenetics, and also political action to address this public health issue. In addition, the public should try to minimize occupational and environmental exposure to pesticides. Ways to do this would include: avoiding use at home, on pets, and in the garden; avoiding—if possible—exposure via purchased food; and wearing protective gear if pesticide use is deemed necessary.

## Chapter 4 — Non-Hodgkin's Lymphoma

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# Chapter 4 — Non-Hodgkin's Lymphoma

## Table

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
|---|---|---|---|---|---|---|
| ***Cohort Studies*** | | | | | | |
| Asp 1994 | Cohort study; employers from 4 chemical brushwood control companies in Finland; selected by convenience sampling; n=1909 | Chlorophenoxy herbicides; exposure measured by self-report /questionnaire | Smoking habits | SMR, SIR, Poisson; follow-up complete | The overall cancer mortality was slightly less than the general population (SMR 0.83, 95% CI 0.75–0.94); no deaths due to NHL, although one case of NHL found. | 4,4 |
| Becher 1996 | Cohort study; 2479 workers at one of four herbicide factories in Germany; selected by convenience sampling. | Phenoxy herbicides; exposure measured by records (a registry of workers exposed to phenoxy herbicides). | Smoking history (for some cohorts) | SMR, Cox regression; follow-up was not complete | There was an increase in risk of NHL associated with exposure to phenoxy herbicides (SMR 326, 95% CI 119–710) overall, SMR 0 for 0–10 yrs after exposure, SMR 364 (CI 44–1314) for 10–20 years after exposure, SMR 425 (CI 115–1088) or exposure over 20 years prior. | 5,5 |
| Hansen 1992 | Cohort study; members of a trade union of gardeners in Denmark; selected by convenience sampling; n=4015 followed from 1975–1984 with regards to cancer incidence. | Combination; exposure measured by records. | None | SMR, Poisson; follow-up was complete | There was a small increase in NHL in gardeners (SMR 200, 95% CI 86–393); for male gardeners the SMR was 173 (CI 63–376 and females 364 (CI 44–1314). | 4,4 |
| Hooiveld 1998 | Retrospective cohort, all people employed in a chemical factory in the Netherlands b/t 1955–1985 (many were exposed to an accident there in 1963); followed them to look for causes of death; 562 exposed, 567 non-exposed, 27 unknown. | Phenoxy herbicides; occupational exposure assessed by questionnaire (unclear if subject completed or company). | Age, calendar period, time since first employment (exposure) | SMR, Poisson | Increased risk of NHL (RR 1.7, CI 0.2–16.5); SMR 3.8 (CI 0.8–11.0); SMR for those exposed as a result of the accident 3.9 (CI 0.1–21.8) | 4,4 |
| Kross 1996 | Retrospective cohort of white male golf course superintendents, members of a professional association, died between 1970 and | No exposure histories, no comment on specific pesticides, but high use of insecticides, fungicides and | No covariates | PMR, compared to white males in the U.S. population, CI | PMR 237 (CI 137–410) | 4,4 |

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
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| | 1992, total of 203 cancer deaths. | herbicides with large differences in volume depending on region | | calculated by method of Jensen et al (1991) | | |
| Lynge 1998 | Retrospective cohort; workers from 2 factories in Denmark; followed 2119 individuals. | Phenoxy herbicides; exposure measurements based on pesticide production; workers assessed according to their work area noted in personnel files. | None mentioned | SIR, Poisson | No risk indicated of NHL (SIR 1.1, CI 0.4–2.6). | 4,4 |
| MacLennan 2003 | Retrospective cohort, followed workers from a pesticide plant (worked there for at least 6 most); 2213 followed for cause of mortality. | Triazine herbicides; proxy exposure according to area of the plant employed and work history, job description. | Age | SMR, Poisson | There were elevated levels of NHL (SMR 372, CI 101–952); for white men the SMR was 257 (CI 31–927) and non-white men 832 (CI 101–3007). | 4,4 |
| Morrison 1994 | Retrospective cohort of male farm operators in Saskatchewan, Alberta, Manitoba in 1971; 155,547 farmers followed for cause of death. | Herbicides; exposure assessed by number of acres sprayed with herb from Census of Agriculture; farmers for farms of less than 1000 acres included. | Age, calendar yr period, number of acres sprayed | RR, Poisson | Increased risk of NHL with increased spraying (RR 2.11, CI 1.1–3.91); OR's ranged between 0.9–2.96 according to level of spraying for different western provinces. | 4,5 |
| Sathiakumar 1996 | Retrospective cohort of workers from herbicide manufacturing plants in Alabama, followed 4917 men – worked at least 1 month b/t 1951–1986 in jobs related to chemical production and formulation. | Triazine herbicides; proxy exposure from work records – are worked, job description, classified as definite, probable, or possible contact with triazines; person-yrs accumulation. | None really – race? | SMR, Poisson | Exposed group had increased deaths from definite or probable NHL (SMR 385, CI 79–1124); for possible NHL SMR 1.0, total NHL SMR 279 (CI 91–652). | 4,4 |
| Sperati 1999 | Retrospective cohort of male farmers and their wives in Italy; these farmers were licensed for buying and handling pesticides b/t | Mixed pesticides; exposure assessment method unclear; appears to be from some record of pesticide | Age, gender, calendar period | SMR, Poisson | NHL increased among women (SMR 2.29, CI 0.62–5.86), but not male farmers (SMR 0.90, CI 0.24–2.30). | 4,4 |

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
|---|---|---|---|---|---|---|
| | 1971–1973; followed for causes of mortality; 2978 men and 2586 wives. | license only – traced from this point until death. | | | | |
| Thorn 2000 | Retrospective cohort of Swedish lumberjacks; employees of forestry company b/t 1954–1967; excluded if exposed to pest other than phenoxy acids and DDT; 261 exposed and 250 unexposed. | Phenoxy acids; considered exposed if worked for 5 or more days (payslips, work records); notes about work types – 'pocketing' vs. 'spraying'; workers. | Age, calendar time, sex, county | SMR, SIR, Poisson | Three cases of NHL found – 2 were among the exposed workers (SIR 235, CI 29–850); SIR for male lumberjacks 192 (CI 3–1070), female lumberjacks 303 (CI 4–1686), and unexposed lumberjacks 81 (CI 1–452). | 4,4 |
| Zahm 1997 | Retrospective cohort of employees of a lawn care company (n=32, 600); looked at mortality cause. | Herbicide, 2,4-D; exposure determined from work records; number of year worked and type of work done. | Gender, age, race, calendar time | SMR, Liddell method | There were four deaths due to NHL (SMR 1.14, CI 0.31–2.91) for all employees; SMR for men only 1.46, CI 0.29–4.27). | 5,5 |
| ***Case-Control Studies*** | | | | | | |
| Blair 1998 | Case-control; men in Iowa, Kansas, Nebraska, and Minnesota; selected by convenience sampling; 986 cases and 2895 population controls. | Lindane (insecticide); exposure measured by self-reports and questionnaires. | Age, marital status, smoking history, state of residence, use of private wells, hair dye use | Logistic regression, OR | The use of lindane is associated with an increase in NHL (OR 1.5, 95% CI 1.1–2.0) overall; OR's for lindane use ranged between 1.2–2.4 when controlled for different pesticides (Table ii); OR's ranged between 1–6.1 for a variety of other factors (Table i). | 5,5 |
| Buckley 2000 | Case-control; children under 20 yrs of age with NHL newly dx b/t 1986–1990; 268 cases, 254 controls. | Mixed exposure; questionnaires re: occ and home exposures around time of index pregnancy and exposure of the child; ad hoc score of exposure created from this info. | Maternal ed, maternal race | OR, conditional logistic regression | Signif assoc with pest use in home (OR 7.3, extermination within home OR 3, postnatal ex OR 2.4); OR's ranged between 0.98–7.33 for different exposures and different family members exposed (Table 3). | 4,5 |
| Cantor 1992 | Case-control study; men in Iowa and Minnesota; selected by convenience sampling; 622 cases and 1245 | Combination; exposure measured by self-reports and questionnaires | Age, hair dye use, family history, smoking | Logistic regression, OR | There was a small increase in NHL in farmers (OR 1.2, 95% CI 1.0–1.5); OR's ranged between 0.9–1.4 | 6,5 |

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
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| | population based controls. | | history, method of application, use of protective equipment | | according to ever having been a farmer, timing of farming occupation, and average size of farm (Table 2); OR's ranged between 0.6–3.1 for different pesticide groups (Table 3). | |
| Costantini 2001 | Case-control; all incident cases b/t 20–74 yrs age from 12 areas in Italy b/t 1991–1993; 2737 cases and 1779 controls. | All pesticides and solvents; occ exposure assessed by questionnaire; ever/never exposed; exposure also determined by job type. | Smoking habits, age, hair dye use, x-rays, meds, education, occ history | OR, Mantel-hanzel | The only positive finding was an increase in small cell lymphoma in male agricultural workers OR 1.4 (CI 1.0–1.9). | 5,5 |
| Hardell 1999 | Case-control study; all cases reported to the regional cancer registry in northern and middle Sweden greater than 25 yrs of age; all men; 442 cases and 741 controls. | Mainly phenoxyacetic acids, but also other pesticides; exposure determined through questionnaire about all exposure (home, occupational); cumulative exposure was assessed in yrs and days. | Smoking habits, diet, previous diseases, other exposures | OR, logistic regression | There was increased NHL with exposure to fungicides (OR 3.7, CI 1.1–13) and herbicides (OR 1.6, CI 1.0–2.5); OR's ranged between 1.1–3.7 for different pesticides; dose-response OR's for herbicides ranged between 1.0–6.8 (Table 2). | 5,5 |
| Hardell 2002 | Case-control; cases age 25 and over, male, and living, with NHL and hairy cell leukemia; 515 cases and 1141 controls (also includes people dx with NHL); Sweden | Questionnaire; all pesticides – names of different ones collected in interview; exposure calculated as years exposed and number of days of exposure. | Area of residence | OR; conditional logistic regression | Increased risk for NHL found for herbicides (OR 1.75, CI 1.26–2.42), insecticides (OR 1.43, CI 1.08–1.87), fungicide (OR 3.11, CI 1.56–6.27) and impregnating agents (OR 1.48, CI 1.11–1.96); dose-response effect present for herbicides in general, and each of phenoxy acids, MCPA and "other." | 4,5 |
| Hoar 1993 | Case-control study; pooled data from smaller studies; all newly dx white men with NHL, over the age of 20 yrs; 993 cases and 2918 controls. | Atrazine; also adjusted for 2,4-D use; exposure assessed by questionnaire; years of use, way handled, use of protective equip, used to determine | Age; use of 2,4-D | OR, maximum likelihoods | Unlikely that exposure to atrazine causes increased risk of NHL; slight increase which was eliminated after adjusting for 2,4-D use; OR's ranged between 0.9–3.2 according to atrazine use (Table 2) | 5,4 |

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
|---|---|---|---|---|---|---|
| | | exposure. | | | when not adjusted for atrazine. | |
| Kogevinas 1995 | Case-control study; cases from international agency for research in cancer, cancer registries, and death cert; 11 sarcoma, 55 controls; 32 NHL and 158 controls, 2 nested case-control studies. | Occ exposure assessed by industrial hygienists from job/company records – categorized into low, medium, high. | Year of first exposure, year from first exposure to disease | OR, logistic regression | Generally weak associations b/t NHL and pesticides except to 1,4,5-T (OR 1.9, CI 0.7–4.8); OR's ranged between 0.62–4.19 for varying chemicals at varying levels of exposure (Table 3). | 4,5 |
| McDuffie 2002 | Case-control study of farmers in 6 Canadian provinces; all men (aged 19 and over) with NHL who lived or worked on a farm were cases; 235 cases and 673 controls. | Mixed exposure; assessed through mail-out questionnaire; questions about exposure, handling of pesticides, use of protective equip, accidents, animal handling; % who replied yes to these questions. | Age, province of residence, measles, personal history of cancer, length of farm residence | OR, conditional logistic regression | Cases and controls not that different with regards to pesticide exposure, but there was increased OR's for other variables (exposure to diesel fuel and exhaust, certain animals, previous history of measles); OR's ranged between 0.76–1.45 for pesticide safety handling practices (Table 1), none with statistical significance; in multivariate analysis for fungicide, carbamate insecticides, organophosphate insecticides and dicamba herbicides exposures, OR's were 1.04–1.86, none with statistical significance. | 4,4 |
| McDuffie 2001 | Case-control; men in six Canadian provinces; cases dx with STS, HD, NHL, or MM b/t 1991–1994, and over the age of 19 yrs; from a variety of occupations; 517 cases and 1506 controls. | Mail-out questionnaire followed by telephone interview for those with pesticide exposure of 10h/yr or more; mixed pesticide exposure (included herbicides, insect, fungi, and fumigants); exposure classified by the number of pesticides reported by cases and controls as well as the number of days/yr of | Age, province of residence, history of measles, positive history of cancer in first degree relatives, other medical history | OR, conditional logistic regression | Risk of NHL increased by exposure to phenoxyherbicides, organophosph insecticides, dicamba (OR's 1.38–1.92, with stat. signif.) after adjustments for some covariates, still OR's 1.32–2.33 with stat. signif., for 2,4-D, mecoprop, dicamba, some insecticides; when adjusted for more covariates, OR's of 1.96–3.42, with stat. signif. for dicamba, mecoprop and aldrin. | 5,6 |

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
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| | | exposure to individual compounds. | | | | |
| Persson 1993 | Case-control study; cases dx with NHL, HD b/t 1975–1984 in Sweden (at least 20 yrs old, and living in catchment area); 31 HD, 93 NHL, 204 controls. | Phenoxy herb and 'other pesticides;' mail-out questionnaire; to be included had to have min exposure of 1 yr; questions about occ exposure to herb. | Smoking habits, x-ray, age, time at dx, some meds | OR, logistic regression | Increased risk of NHL with increased exposure to phenoxy herb (OR 2.3, CI 0.7–7.2). | 4,4 |
| Waddell 2001 | Pooled case-control studies; random sample of NHL cases in Kansas, Nebraska, Iowa, and Minnesota, all men, farmers; 748 cases and 2236 controls. | Organophosphate pesticides; questionnaire with detailed questions on agricultural practices, types of pesticides, adys per/yr, type of crops. | Age, state, respondent type, smoking history, diet, alcohol | OR, logistic regression | Increased risk in farmers with organophosph use (50%); OR's ranged between 0.9–3.2 by type and class of OPP used (Table 4). | 5,5 |
| Zheng 2001 | Case-control pooled analysis (seems to be the same group as the other studies from these researchers); Iowa, Minnesota, Nebraska, Kansas; male farmers over the age of 21 yrs; 985 cases, 2895 controls. | Carbamate insecticides; questionnaire regarding pest use, personal handling, year of first and last use, crop, animals. | Age at dx, type of respondent, state of res, first degree family history of cancer, use of hair dye, use of private wells, smoking history | OR, unconditional logistic regression | Farmers who had ever used carbamate insect had a 30% to 50% increased risk of NHL; ORs' ranged between 1.0–1.6 for carbamate use; 0.6–3.7 for carbaryl use, 1.0–3.7 for carbofuran use. | 5,4 |
| ***Ecological Studies*** | | | | | | |
| Fontana 1998 | Ecological study; to see if increased NHL in polluted areas of Italy; whole pop (900,000) b/t 1985–1988 and 1991–1993 – all cases of NHL and HD b/t people ages b/t 20–74. | 2,4-D and 2,4,5-trichlorophenoxyacetic acid; exposure assessed through soil and water samples in area to determine level of pollution. | Age | OR, direct standardization | Areas with more phenoxy pollution had signif more NHL (60–100%); OR's in areas ranged between 0.8–1.9; women in rice growing job (from case-control study) increased NHL (OR 1.9, CI 0.6–6.0). | 4,4 |
| Schreinermachers 1999 | Ecological study; compared cancer mortality in 4 agricultural regions of Minnesota. | Mixed pesticides; survey and questionnaires about most frequently used pest, | Gender, race, age | SRR, Poisson | Excess NHL for women in agricultural regions (SRR 1.35, CI 1.09–1.66). | 5,4 |

| Reference | Population Description | Pesticides Type and Exposure Assessment | Covariates | Statistical Analysis | Measures of Association and Values | Global Rating |
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| | | crop type, to get a proxy level of exposure. | | | | |