DRAFT-
Risk of total and cell specific non-Hodgkin Lymphoma and pesticide use in the Agricultural Health Study

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Comment [AEB1]: How is this going to be determined?

February 6, 2013

Saved as: AlavanjaNHL Feb 2013(1)

ABBREVIATIONS

Agricultural Health Study (AHS)

Rate ratios (RR)

95% confidence intervals (CI)

Organochlorine insecticides (OC)

Organophosphate insecticides (OP)

United States Environmental Protection Agency (U.S. EPA)

International Agency for Research on Cancer (IARC)

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Running Title: Pesticides and Non-Hodgkin Lymphoma

<u>**List of Tables:**</u>

Table 1: Baseline characteristics of AHS study participants in the NHL incidence analysis from 1993 through 2008

Table2: Occupational exposures of AHS participants in the NHL incidence analysis from 1993 through 2008

Table 3: Pesticide exposure (Lifetime Days [LD] & intensity weighted Lifetime Days [IWLD]) and the age-adjusted risk of NHL incidence (1993 through 2008)

Table 4: Pesticides exposure (Lifetime days [LD]) and the age-adjusted risk of NHL by cell type (1993-2008).

Table 5: Number of different pesticides used by pesticide type (in the NHL incidence analysis from 1993 through 2008) for B cell sub-types

Questions: *1. Should we make supplemental table 5 → table 6 in the report?*
2. We need to reduce the number of supplemental tables which ones are expendable?
3. Justify not including multiple myeloma as an NHL since it is now classified as NHL.
4.Word limit for EHP: 250 Abstract, 7000 for manuscript, tables and references we have>8150 words

Comment [AEB2]: Can stay as a Supplemental table.

Comment [AEB3]: Is there a limit on supplemental tables? What is it?

Comment [AEB4]: Almost all of the previous work on pesticides and NHL has kept myeloma separate. If you do not, it will be unclear whether differences are real or due to disease classification differences.

Supplemental Table 1: Other pesticide exposures (lifetime days [LD} and intensity weighted total days) and age-adjusted risk of NHL incidence (1993 through 2008).

Supplemental Table 2: Pesticide exposures (total days and intensity weight total days) fully adjusted risks of NHL incidence (1993 through 2008).

Supplemental Table 1A: Chlorinated Insecticide exposure (in total days and intensity weighted days) and NHL age-adjusted relative risk(1993 through 2008).

Supplemental Table 2A: Chlorinated Insecticide exposure (in total days and intensity weighted days) and NHL fully adjusted relative risk (1993 through 2008).

Supplemental Table 3: Herbicide exposures (Life-time days) and age-adjusted NHL risk by cell type (1993 through 2008).

Supplemental Table 4: Insecticides, fungicide and fumigant exposure (life-time days) and age-adjusted risk of NHL by cell type (1993 through 2008).

Supplemental Table 5: Estimated individual and joint effects of pesticide combinations and age-adjusted risk of NHL

ABSTRACT

Background: Farming and eExposure to pesticides haves been linked to non-Hodgkin lymphoma (NHL) in a number of previous studies. **Objective**: To evaluate specific pesticides for associations with NHL and NHL subtypes in a prospective cohort of registered pesticide applicators. **Methods**: We examined NHL incidence in a prospective cohort of 57,310 licensed pesticide applicators in Iowa and North Carolina from 1993- 2008. Exposure information and health histories were obtained from a self-administered questionnaire administered at enrollment (1993-1997) and in a telephone follow-up questionnaire administered approximately five years later (1998-2004). Poisson regression modeling was used to evaluate the association between use of specific pesticides and the rate ratios of NHL and NHL subtypes while adjusting for age and other potential confounding variables. (Mention lagging?)**Results**: Statistically significant increases in the risk of overall NHL were observed with increasing life-time exposure days for two pesticide, lindane (organochlorine insecticide) and butylate (thiocarbamate herbicide), among 43 pesticides evaluated. Significantly increasing risk of specific NHL subtypes with increasing life-time exposure days of individual pesticides use were observed for lindane, butylate, dicamba, terbufos, alachlor, EPTC, imazethapry and trifluralin. The total number of different pesticides used was not associated with NHL risk overall, but the number of different chlorinated and organophosphate insecticide and triazine herbicides used was related to risk in specific NHL subtypes. **Conclusions**: A wide variety of chemically-distinct herbicides and insecticides were significantly associated with different NHL subtypes. Most pesticides are associated with only one NHL subtype. The risk of the CLL/SLL NHL subtype is associated with the number of different chlorinated and organophophorous insecticides used. While the risk

Comment [AEB5]: Need to be clearer here. What subtypes with which pesticides?

Comment [a6]: Supplemental table: we did not find evidence that the use of different combinations of pesticides potentiated risk. However, since the timing of pesticides could not be ascertain in the AHS, this evaluation may well have limited value.

of other B-cell lymphomas is significantly associated with the number of triazine herbicides used.

(abstract-273 → 250 word limit for EHP; >8150 words in manuscript, references and 5 tables→EHP word limit 7,000 words)

Keywords: Cohort Study, Farming, Pesticide Exposure, Non-Hodgkin Lymphoma.

INTRODUCTION

Non-Hodgkin lymphomas (NHLs) are a heterogeneous group of over 20 different B and T-cell neoplasms affecting the immune system/ lymphatic system arising primarily in the lymph nodes (Swerlow et al. 2008; Shankland et al., 2012). The established risk factors for NHL include genetic susceptibility and a previous history of malignant disease (Wang et al. 2007) and different immunosuppressive states including human immunodeficiency virus (HIV), autoimmune diseases as Sjogren's syndrome, systemic lupus erythematosis rheumatoid arthritis, and psoriasis and celiac disease (Simard JF, et al 2012). Exposure to pesticides, particularly phenoxy acid herbicides (Dich et al 1997; Hardell L et al., 1981; Hoar SK et al., 1986; Zahm et al, 1990, (Eriksson M et al.,2008) and chlorinated pesticides ((Spinelli JJ et al 2007;Brauner EV, et al., 2012, Mark Purdue looked a chlorinated in AHS), have been suggested as causes of NHL, but the evidence has been inconsistent. Little evidence of an association between phenoxy acid herbicides and NHL was observed in New Zealand (Pearce NE et al 1987;;), Washington state (USA) (Woods JS, et al 1987), or Minnesota and Iowa (USA) (Cantor KP et al, 1992) and little evidence for chlorinated pesticides was observed in a European study that measure pesticide metabolites in plasma samples (Cocco P et al, 2008). A meta-analysis of 13 case-control studies published between1993-2005 observed an overall significant meta-odds ratio between occupational exposure to pesticides and NHL (OR=1.35; 95% CI: 1.2-1.5). When observations were limited to those that had more than 10 years of exposure the risk increased (OR=1.65; 95% CI: 1.08-1.95) (Merhi M, et al., 2007). While the meta-analysis supports the hypothesis that pesticides are associated with NHL, they lack sufficient detail about pesticide exposure and other information on risk factors for hematopoietic cancers to identify specific causes (Merhi M, et al., 2007).

In another study from the six Canadian provinces case-control study, the risk of NHL increased with the number of different pesticides used (Hohenadel K et al., 2011). These results are somewhat similar to those reported by De Roos and colleagues who observed a super-additive effect in which atrazine amplified risk of NHL when used in combination with several other pesticides including alachlor, diazinon and carbofuran (De Roos et al., 2003)

In two other epidemiological studies the association of specific pesticides with NHL was largely limited to NHL cases with chromosomal translocations t(14;18) (Schroeder JV et al, 2001; Chiu BCH et al., 2006).

Comment [AEB7]: I would change the structure of the introduction.
-The AHS is a study of farmers, so I would start with what is known about NHL and farmers.
- Then describe what is known about pesticides.
- Put comments about immunodeficiency next.
-Finish with what AHS can contribute

Comment [AEB8]: Probably need to reference these other papers on 2,4-D (Morrison (1994), McDuffie et al. (2001), Miligi et al (2006),Burns et al (2011), Cocco, 2013).

Comment [AEB9]: Might check to see what McDuffie(2010) and Milgi (2006)say about chlorinated pesticides.

Comment [AEB10]: Might want to mention the effect from use of multiple pesticdes that DeRoos and Hohenadel both saw.

Comment [AEB11]: These were not limited to cases with t(14;18) translocations. They compared RR for pesticides and other things among those with and without these translocations.

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In the Agricultural Health Study we had the opportunity to evaluate risk factors for NHL incidence overall and by cell type in a prospective cohort study of licensed pesticide applicators.

MATTERIALS & METHODS

Study Population

The AHS is a prospective cohort study of 52,394 licensed private pesticide applicators in Iowa and North Carolina and 4,916 licensed commercial applicators from Iowa. The cohort has been described in detail (Alavanja et al., 1996). Briefly, the cohort included individuals seeking licenses for restricted use pesticides from December 1993 through December 1997 (82% of the target population enrolled). The protocol was approved by relevant institutional review boards. We obtained cancer incidence information by regular linkage to cancer registry files in Iowa (Surveillance Epidemiology and End Results Program) and North Carolina (National Program of Cancer Registries*)*. In addition, we matched cohort members to state residential mortality registries and the National Death Index to identify vital status, and to address records of the Internal Revenue Service, motor vehicle registration files, and pesticide license registries of state agricultural departments to determine residence in Iowa or North Carolina. The current analysis included all incident non-Hodgkin lymphomas (n=333) diagnosed from enrollment (1993-1997) through December 31, 2008. We censored follow-up at diagnosis of NHL, date of death, movement out of state, or December 31, 2008, whichever was earlier. Person-years of follow-up summed to 714,770.

Tumor Characteristics

Information on tumor characteristics was obtained from state cancer registries. Cases were characterized by five~~5~~ grouping of cell types and are listed in appendix 1 (reference). The first group includes 117 cases including chronic B-cell lymphocytic lymphomas, small B-cell lymphomas and mantle-cell lymphomas. The second group includes 94 diffuse large B-cell lymphomas, the third group includes 53 follicular lymphomas. There were 34 other B-cell lymphomas including precursor non-Hodgkin lymphoma, lymphoplasmacytic lymphoma, Waldenstrom macro glubulinemia, Burkitt lymphoma/leukemia, extra-nodal Marginal Zone Lymphomas (MZL), MALT type, Nodal MZL, hairy-cell leukemia and B-cell non-Hodgkin lymphoma not otherwise specified. The fifth grouping included 35 cases consisting of T-cell lymphomas and non-Hodgkin lymphoma of unknown lineage. The fifth grouping was excluded from cell type-specific analyses because of small numbers of cases with identified cell types.

Comment [a12]: MA will fill in Reference.

Exposure Assessment

Information on lifetime use of 50 pesticides was captured in two self-administered questionnaires (http://aghealth.org/questionnaires.html) completed during cohort enrollment (Phase 1). All 57,310 applicators completed the first enrollment questionnaire, which inquired about ever/never use of the 50 pesticides, as well as duration (years) and frequency (average days/year) of use for a subset of 22 pesticides. In addition, 25,291/57,310 (44.1%) of the applicators returned the second (take-home) questionnaire, which inquired about duration and frequency of use for the

Comment [AEB13]: I would move the sentences that indicate information from Phase I and Phase II is used to characterize exposure to the beginning of this section. Then describe what Phase I and II each entailed, follow this with the imputation action, and finally how the exposure metrics were created.

remaining 28 pesticides. We used 2 exposure metrics to assess cumulative exposure to each pesticide: (i) lifetime days of pesticide use, i.e. the product of years of use of a specific pesticide and the number of days used per year; and (ii) intensity-weighted lifetime days of use, i.e. the product of lifetime days of use and a measure of exposure intensity. Intensity was derived from an algorithm using questionnaire data on mixing status, application method, equipment repair and use of personal protective equipment (Coble et al. 2011 and Dosemeci et al. 2002).

A follow-up questionnaire, which ascertained pesticide use since enrollment, was administered 5 years after enrollment (Phase 2) and completed by 36,342 (63%) of the original participants. For participants who did not complete a Phase 2 questionnaire (20,968 applicators, 37%), a data-driven multiple imputation procedure was employed to impute use of specific pesticides in Phase 2 (Heltshe et al.,2012). Briefly, logistic regression and stratified sampling were used to impute use of specific pesticides in Phase 2. All variables from Phase 1 that had the potential to be associated with either missingness or pesticide use were considered. ~~The variables most strongly predictive of use of any pesticide on the Phase 2 questionnaire were gender, marital status, farm ownership, farm size, days/year mixing pesticides, percent time personally mixing pesticides, percent time personally applying pesticides, and application of any pesticide in the prior year. Covariates associated with non-response to Phase 2 were age, education, state, applicator type, and years mixing chemicals.~~ Covariates from participants with complete data from both phases were modeled, and then applied to the model for participants missing Phase 2 data to obtain estimates of the missing data. To assess the imputation procedure, a 20% random sample of participants was withheld for comparison. The observed and imputed prevalence of any

Comment [AEB14]: I think I would just reference Coble here. With both it gives the impression that the earlier score by Dosemeci was used somehow. At least make it clear that it was exposure scores from Coble that were used here.

Comment [a15]: Suggestions for reducing the this description of imputation procedures are needed.

pesticide use in the holdout dataset were 85.7% and 85.3%, respectively, indicating that the logistic regression model for the multiple imputation performed well.

We combined Phase 1 and Phase 2 information to generate cumulative intensity-weighted and un-weighted days of use and assessed the risk of total NHL incidence and major cell subtypes. Data were obtained from AHS data release versions P1REL201005.00 (for Phase 1) and P2REL201007.00 (for Phase 2).

In additional to analyzing pesticides individually, we also examined the NHL risk associated with the number of different pesticide reported in two ways. First we examined total NHL risk by the total number of different pesticides reported in a working lifetime, next we examined the number of different pesticides used within a chemical class by NHL and NHL cell type.

Comment [a16]: Results will be available shortly

Comment [AEB17]: In case-control studies in the US (DeRoos) and Canada (Hohenadel) there was a pretty strong association with the number of pesticides used that were classified as probable or possible carcinogens. Should look at this also.

Statistical Analyses

Comment [AEB18]: I think we should start doing some stratified analyses by type of use of protective equipment. I know we include this in the intensity estimates, but it may not be the same for every pesticide and individuals who answer positively to our questions may take other protective action. Stratified analyses on this factor have found associations in other studies.

In primary analyses, we used unlagged exposures, but also explored lagged analyses for both lifetime and intensity-weighted days. For each chemical, we categorized exposure into non-exposed and tertiles of exposure based on the distribution of exposed cases. We used Poisson regression to calculate rate ratios (RR) and 95% confidence intervals (95% CI) and used the MIANALYZE procedure in SAS, version 9.2 (SAS Institute, Cary, North Carolina), to obtain the appropriate variance when using Phase 2 imputed data in the 95% CI calculation. We evaluated only pesticides with 15 or more exposed cases of NHL, thereby excluding trichlorofon, ziram, aluminum phosphide, parathion, ethylene dibromide, captan, and carbon tetrachloride/carbon disulfide. A first set of rate ratios were adjusted for age and a second set of rate ratios were adjusted for age and other statistically significant (α=0.05) predictors of NHL in the AHS. We evaluated several lifestyle and demographic measures and identified the following as potential confounding variables: age at enrollment (<40, 40-49, 50-59, 60-70, ≥70), race (White, Black, other, missing), state (Iowa, North Carolina), family history of lymphoma in first-degree relatives (yes, no, missing), cigarette smoking history (never, former, current, missing), alcohol consumption per week (none, < once per week, ≥ once per week) and several occupational exposures (i.e., number of livestock, poultry, acres planted, welding, diesel use, number of different pesticides used). We further adjusted models for other pesticides shown to be associated with NHL in the current analysis. Separate analyses were conducted by cell type. Likelihood ratio tests were used to assess differences between strata (p-interaction). We also analyzed Phase 1 data only to assess the impact of the additional information collected or imputed from Phase 2. All tests were two-sided and conducted at the α=0.05 level. Tests for trend used the midpoint value of each exposure category treated as grouped linear in regression models.

Comment [AEB19]: Certainly reasonable to have a cutpoint. You might consider lowering the cutpoint just to make sure that is not something interesting occurs with a pesticide that is just under the cutpoint, e.g., 14.

Comment [AEB20]: Did all of these factors show an association with NHL?

RESULTS

The risk of NHL increased significantly and in a near monotonic fashion with age in the AHS cohort (Table 1). The age-adjusted risk of NHL is significantly lower in NC compared to IA and among current smokers compared to nonsmokers. Other demographic factors including gender, license type, educational level, alcohol consumption and a family history of lymphomas were not significant risk factors of NHL in this cohort.

Age-adjusted NHL risk increased with a number of occupational factors (Table 2). Cohort members with 100 to 999 livestock had a non-significantly elevated risk of NHL (RR=1.3 [0.98-1.8]), while cohort members with over 1,000 livestock had a significant risk of NHL (RR=1.6 [1.1-2.4]) compared to farms with no livestock. Cohort members who drove diesel power vehicles once or more per week were also at a significantly elevated NHL risk compared to those who drove diesel powered vehicles less frequently (RR=1.6 [1.0-2.7]). The number of poultry on a farm, the number of acres planted, welding more than once per month, the total number of pesticide exposure days and the number of different pesticides used in a working-life time were not associated with a significantly elevated NHL risk.

Comment [a21]: How do we deal with saying we controlled for confounders without including table 2? Little confounding was observed.

Comment [AEB22]: Do not need to list all in a table. Common to say you evaluated a factors as a possible confounder without presenting the actual ORs. Presenting the ORs here is particular problem for the non-pesticide agricultural exposures because they will be the focus of another paper. Can delete them from the table and the ORs from the text. Just say you evaluated them for confounding and indicate which ones you included in the model. You have a plenty of tables anyhow.

The age-adjusted risk of NHL associated with tertiles of two exposure metrics (i.e., total days of use, and intensity weighted days of use) compared to those with no exposure to these chemicals are shown for 22 insecticides, herbicides, fungicides and fumigants in Table 3 (age-adjusted risk of NHL for additional pesticides may be found in supplemental table 1 and fully-adjusted risk of NHL in supplemental table 2). Lindane (a chlorinated insecticide no longer on the market in the US) is the only pesticide showing a monotonic rise in overall NHL risk with increasing life-time days of use (RR= 1.0 (ref), 1.0 [0.5-2.0], 1.2[0.6-2.3], 2.7[1.4-5.1]; p trend=0.003) and intensity-weighted lifetime days of use (RR= 1.0 (ref), 1.1[0.6-2.0], 1.4 [0.7-2.6], 1.9 [0.95-3.7]; p trend=0.05). Butylate , a thiocarbamate herbicide, showed a significant increasing trend in life-time days of use (RR=1.0 (ref), 1.0 [0.6-1.5], 2.8 [1.7-4.7], 1.1 [0.5-2.4]; p trend=0.004) and intensity-weighted lifetime days of use (RR=1.0 (ref), 0.9 [0.5-1.5], 2.1[1.2-3.5], 1.5[0.9-2.6]; p trend=0.04) but the associations were not monotonic. Other pesticides (i.e., the insecticides

Comment [AEB23]: I think you might include a row for "ever" exposed in this table. There are a few pesticides with excesses, but no monotonic trend with either of the metrics that might be of interest in an ever/never comparison. Another approach would be to present an ever/never table and then only include pesticides in an exposure-response table that show some evidence of an excess among ever exposed.

Comment [AEB24]: What determines whether pesticides are shown in the regular or supplemental tables? Wasn't obvious to me.

phorate and terbufos, the herbicides chlorimuron-ethyl, dicamba, metribuzin and 2,4,5-T the fungicide benomyl, and the fumigant methyl bromide) showed individual point estimates of NHL risk that were significant but did not show a consistent pattern of increasing risk with increasing exposure. There was no association between the use of the other pesticides evaluated in the AHS cohort (supplemental table listed OC insecticides, triazine herbicides, phenoxy-acid herbicides and overall NHL cancer risk).

Results were comparable (not shown) for both metrics (lifetime and intensity-weighted lifetime days) for 5 year and 15 year lagged and unlagged exposures, therefore we present RRs for unlagged total days of exposure only. Similarly the results from fully adjusted risk of NHL (i.e., Age [<45,45-49,50-54,55-59,60-64,65-69,≥70], smoking status(current, former, never), number of livestock (0,,<100,100-999,>999),drove diesel tractor(<weekly,≥weekly, state (NC, IA) [shown in supplemental table 2] were comparable to the age-adjusted risk.

We also evaluated risk by the four major categories of B cell type lymphomas by number of days of use of individual pesticide (Table 4), and by the number of different pesticides used in a chemical class and results are presented in Table ~~5~~4.~~.~~

Comment [a25]: Update runs to include potential confounders.

For the CLL/SLL/PLL/MCL group of lymphomas, dicamba , a carbamate herbicide, (RR= 1[ref], 1.5 [0.9-2.6], 1.5 [0.9-3.4], 2.0 [1.1-3.4]; p trend=0.03), lindane, a chlorinated insecticide,(1[ref], 1.6 [0.7-3.6], 1.1 [0.5-4.8], 3.8 [1.5-9.6]; p trend=0.005) and butylate, a thiocarbamate herbicide, (1.0[ref],0.8 [0.4-1.9], 3.5[1.6-7.6], 1.3 [0.4-4.3]; p trend=0.04) were observed to have a significant increased trend of risk with increasing lifetime-days of use.

Comment [AEB26]: Trends not monotonic. List pesticides here in the order they occur in Table 4

Metribuzin, a triazine herbicide, (RR=1[Ref]. 1.5[0.7-2.0], 2.1[1.1-4.0], 1.8 [0.6-5.2]; p trend=0.06) had a near significant relationship with this group of lymphomas. Carbaryl, a carbamate insecticide, was observed to have a significant inverse relationship (RR=1[ref], 1.1[0.5-2.2], 1.0 [0.2-4.2], 0.4[0.2-0.8].

Other B-cell lymphomas are a group of 8 different cell types previously defined. A significant increase in the risk of this group was associated with the number of life-time days of use of five (or six) herbicides: alachlor, an acetanilide herbicide, (RR=1.0[ref], 1.6 [0.6-4.4], 2.1[0.8-5.3], 4.0 [1.2-13.0]; p trend=0.02); butylate, a thiocarbamate herbicide, (RR=1.0 [ref], 3.0 [0.8-11.3], 4.0 [1.2-13.7], 2.4 [0.3-19.7]p trend=0.499); dicamba, a benzoic acid herbicide (1.0[ref],3.2 [1.0-9.9], 5.2 [1.6-16.6], 5.1 [1.6-16.1]; p trend=0.02); EPTC use, a thio-carbamate herbicide (RR=1.0[ref], 2.1 [0.7-6.0], 2.1 [0.6-7.1], 4.9 [1.4-16.7]; p trend=0.01) : imazethapry, imadazoline herbicide (RR=1.0 [ref], 1.6 [0.6-3.8], 5.2 [1.6-16.6], 3.2 [1.0-10.0]; p trend=0.03; trifluralin use, a dinitro-aniline herbicide (RR=1.0 [ref], 1.2 [0.4-3.2], 2.7 [1.0-7.0], 3.3 [1.2-9.1]; p trend=0.01); and the organophosphate insecticide terbufos (RR= 1.0[ref], 2.3[0.8-6.6], 3.1 [1.1-9.2], 4.1[1.4-11.9]; p trend=0.01) (Table 4). Risk of other B-cell lymphomas was also associated with a non-significant elevated risk for the low and medium exposure categories and was significantly associated with the highest category of exposure for atrazine use (RR=3.6 [1.2-10.8]. Several other pesticides including butylate, cyanazine, and metolachlor showed one or more individual point estimates of other B-cell lymphoma risk that were significant but did not show a general pattern of increasing risk with increasing exposure.

Comment [AEB27]: List these in order that they occur in Table 4

Comment [a28]: Exclude EPTC –too few cases?

Comment [AEB29]: Maybe should mention atrazine also.

No pesticide had a significant exposure response pattern with either diffuse large B-cell lymphomas or follicular B-cell lymphomas, although significant point estimates of risk were identified for butylate (a carbamate herbicide), terbufos (a organophosphate insecticide), and methyl bromide (an organic halide).

Comment [AEB30]: I wonder in relation to follicular NHL we should comment about lindane

The association between the age-adjusted risk of the four NHL B-cell sub-types and the total number of different pesticides by chemical class is presented in Table 5. For the CLL/SLL/PLL/MCL group of lymphomas, the number of different chlorinated insecticides (RR= 1.0 (ref), 1.6 (0.7-3.8), 2.2 (0.95-5.0), 2.4 (1.2-5.2); p trend=0.02) and the number of different organophosphate insecticides (1.0 (ref), 0.93(0.4-2.7), 1.4 (0.6-2.5), 1.3 (0.6-2.5), 1.7 (0.92-3.2); p trend= 0.03) showed a significant trend of increase risk with increasing lifetime days of use. Similar trends were observed for the number of different triazine herbicides (RR= 1.0 (ref), 0.8 (0.5-1.4), 1.0 (0.6-1.7), 1.5 (0.91-2.5); p trend=0.07), other herbicides (RR=1.0 (ref), 1.2 (0.5-2.8), 0.9 (0.4-2.2), 1.2 (0.5-2.8), 1.7(0.7-4.1); p trend=0.06) and fungicides (RR=1.0 (ref), 1.3 (0.4-3.6), 1.7 (0.6-4.6); p trend=0.11) but the trends were not statistically significant.

Comment [AEB31]: Maybe mention fungicides for this group.

For the other B-cell lymphoma group, the number of different triazine herbicides (RR=1.0 (ref), 2.0 (0.6-6.6), 2.5 (0.8-8.3), 4.2 (1.4-13.1); p trend=0.006) and the number of different acetamide herbicides (RR=1.0 (ref), 1.4 (0.5-4.0), 3.9 (1.2-8.2); p trend= 0.009) both were observed to have a significant trend of increasing risk with increasing days of use. Similar trends were observed for the number of different carbamate herbicides (RR=1.0 (ref), 1.5 (0.7-3.4), 2.2 (0.9-5.7); p trend=0.11) and 'other herbicides' (RR=1.0 (ref), 0.6 (0.1-3.1), 0.94 (0.2-4.6), 1.2 (0.3-5.7), 1.7 (0.4-7.6); p trend=0.06) but these trends were not statistically significant.

Comment [a32]: These will be adjusted for total number of exposure days to chemicals in this class.

For either diffuse large B-cell lymphomas or follicular B-cell lymphomas, no pesticide class had a significant pattern of increasing risk with number of pesticides used , although a significant decreased risk with increasing number of pesticides used was observed for chlorinated pesticides (p trend=0.05) and other insecticides (p trend= 0.04) with the diffuse large B-cell lymphoma group.

DISCUSSION

In this analysis, we observed a significant increase in the risk of overall NHL with only two pesticides, lindane an organochlorine insecticide no longer registered for use in the U.S and butylate a thio-carbamate herbicide widely used in the United States and other countries. Our findings for total NHL are inconsistent with a number of other studies which found increased risks with a variety of chlorinated and organophosphate insecticides and triazine and phenoxy acid herbicides (Dich et al 1997; Hardell L et al., 1981; Hoar SK et al., 1986; Zahm et al, 1990). However, we did find significantly increasing risk of specific NHL subtypes with increasing life-time exposure days of individual pesticides use. Butylate and dicamba (a carbamate herbicide) and lindane were observed to have a significant increasing risk of the CLL/SLL/PLL/ MCL lymphomas sub-types with increasing lifetime-days of use.

Comment [AEB33]: I would do an ever/never analysis for all the pesticides with a sufficient number of cases, then start the discussion with a description of the ever/never analysis.

Comment [AEB34]: This paragraph is a little hard to follow. Mentions an association with lindane, an organochlorine, then says the findings are inconsistent with other studies showing excesses for organochlorine. I think it would be easier to deal first with individual pesticides by comparing findings here with those in the literature. Then move to a higher level of discussing chemical classes. Finally discuss the findings by subtype. Think the Discussion needs a expansion of the issue of histologic type and pesticides. Gigi Coco (2013) recently had a paper on this in OEM.

Other B-cell lymphomas are a varied group including 8 different cell types of lymphomas. Excess risks of other B-cell lymphomas were observed for several widely-used pesticides including: the organophosphorous insecticide terbufos, for alachlor, an acetanilide-herbicide, imazethapry which is an imidazoline-herbicides and trifluralin a dinitroaniline-herbicide and for butylate, dicamba, and, EPTC which all belong to the family of carbamate herbicides, but to different sub-groups within the family. The triazine herbicides atrazine and cyanazine had specific point estimates that were elevated but the trends of risk were neither significant nor monotonic. Metribuzin, a third triazine herbicide in our analysis, had too few other B-cell lymphomas to evaluate. The wide array of functional groups and chemical classes that are associated with an increased risk of Other B-cell lymphomas does not suggest a single known mechanism of action. Multiple pathways may be involved.

Comment [AEB35]: Should probe a little regarding the various lymphomas in this complex group. See if there is any indication of a specific subtype driving the association with several pesticides. Even a lead without statistical significance would interesting and could be explored elsewhere, i.e., the U.S./Canada NHL case-control pooling project, or Epilymph.

In a Swedish case-control study a significant excess risk of NHL was associated with the phenoxy herbicide MCPA and glyphosate (Ericksson et al., 2008). 2,4-D and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) have been banned from Sweden and could not be evaluated (Eriksson M et al.,2008). In our study we could not evaluate MCPA but found no excess risk of NHL or its subtypes with the use of glyphospate, 2,4-D or 2,4,5-T.

Comment [AEB36]: Should mention the results from other studies on NHL and these pesticides (Canada cohort and case-control, NCI and Italy case-control studies on these pesticides and NHL.

In a population-based case-control study conducted in six Canadian provinces increased risk to NHL was associated with a positive family history of cancer both with and without pesticide exposure [OR=1.72 (95% CI 1.21-2.45) and OR=1.43 (95% CI: 1.12-1.83), respectively] (McDuffie HH, et.al, 2009). In this same case-control study six pesticides/pesticide analytes also showed a significant association with NHL [beta-hexachlorocyclohexane, *p, p'*- dichloro-diphenyl-dichloroethylene (DDE), hexachlorobenzene, mirex, oxychlordane and trans-nonachlor] (Spinelli et al., 2007). The strongest association was found for oxychlordane, a metabolite of the pesticide chlordane (highest vs. lowest quartile OR=2.68, 95% CI 1.69-4.2).

These finding were not confirmed in a recent analysis of plasma samples from 174 NHL cases and 203 controls from France, Germany and Spain. The risk of NHL did not increase with plasma levels of hexachlorobenzene, beta-hexachlorobenzene or DDE (Cocco et al., 2008). In our study NHL was associated with lindane but no excess risk was observed for chlordane and no excess risk was observed among those with a family history of lymphoma. The other chemicals evaluated in the Canadian six province study were not evaluated in the AHS cohort.

A few studiesPreliminary evidence suggests that asthma, allergies or asthma and allergies and hay fever combined with the use of specific pesticides (e.g., MCPA) may enhance the risk to NHL. *This observation was not confirmed among the pesticides evaluated in the Agricultural Health Cohort (data note shown). {add more or defer discussion?}.*

New evidence linking NHL with specific chlorinated pesticide use and two studies linking the number of different pesticides used with NHL give further support to earlier findings suggesting specific pesticides are etiological linked to NHL (reference, Hohenadel K et al., 2011). While the number of different pesticides used overall was not associated with NHL risk in the AHS, a significant increase in the CLL/SLL/PLL/MCL sub-group of NHL was observed with the number of different chlorinated pesticides used and the number of different organophosphate chemicals used. A similar pattern of increase risk was observed in the other B-cell lymphoma subgroup of NHL with an increasing number of triazine pesticides use. {a bit more detail here? Suggestions?}.

Discussion of interaction of pairs of pesticides here? (supplemental table 5).

Comment [a37]: Defer discussion of this topic?

Comment [AEB38]: I think it is worth discussing if you have data from any analyses on this point? Might be worthwhile to look. No need to discuss it if you do not have any findings on this point.

Comment [AEB39]: In regards to the number of pesticides used, the findings from DeRoos and Hohenadel were mainly for pesticides classified as probable or possible carcinogens. You could use the classifications from those papers to do the same analysis in AHS.

Comment [a40]: Do we need this table in the manuscript? No exciting data. It is inconsistent with some previous literature, but timing of the exposure to the pesticides was uncertain here. In the other studies as well?

Comment [AEB41]: I think it is a good thing to put in supplemental tables. There are only a few studies of NHL that have done this. They provide some hints but nothing too strong. It is entirely negative here, so that is worth pointing out in the Results and Discussion.

A strength of this investigation is that a relatively large population of licensed pesticide applicators provided reliable information regarding their pesticide application history (Blair et al.; Coble et al. 2011) prior to diagnosis of disease. In the AHS, a priori derived algorithm scores that incorporated several exposure determinants were used to predict urinary pesticide levels (Thomas et al., Coble 2011). Few studies of pesticide use with a prospective design have been large enough or had sufficiently detailed exposure information, to evaluate the potential link between NHL, NHL subtypes and specific pesticide exposures. Also, because occupational pesticide users are seldom exposed to a single agent, we controlled for the total pesticide exposure days, and found no meaningful change in the associations. Additionally, potential confounding was reported to be minimal in the AHS and not likely to be associated with pesticide exposure (Coble et al., 2002).

Comment [AEB42]: Are there any other prospective studies with data on specific pesticides?

Comment [AEB43]: I am not sure this type of analysis controls for possible other pesticide confounding. There are associations with some pesticides, yet there is no association with the number of pesticides used. I think this means that using an overall indicator of pesticide is so watered down that it does not control for any individual links (which do occur). I think the only way to do this is to adjust a NHL – specific pesticide association for other pesticides that are associated with NHL in the AHS study.

Cell-type information in the AHS was obtained from the cancer registry database and did not involve pathologic re-review of diagnostic slides.

Comment [AEB44]: Need to add limitations associated with pesticide exposure assessment and the effects this would have on RR.

Although it is possible that t (14;18) translocations are an initiating event of a causative cascade leading to an NHL subtype, follicular lymphoma (FL), much more work needs to be done to establish this. Nevertheless, it has been shown that NHL subtypes with t (14;18) translocations are associated with the chlorinated insecticides dieldrin, lindane, and toxaphene and the triazine herbicide atrazine. We were unable to evaluate translocations in this analysis. In our study no pesticide had a significant exposure response pattern with either diffuse large B-cell lymphomas or follicular B-cell lymphomas, although significant point estimates of risk were identified for butylate (a carbamate herbicide), terbufos (a organophosphate insecticide), and methyl bromide (an organic halide) were observed, but not for dieldrin, lindane, toxaphene, or atrazine.

Comment [AEB45]: Not sure of the relevance of this discussion since this analysis has no information on t (14;18) translocations. Would be relevant if this information is used to explain study findings and/or to propose new work.

Conclusion:

In summary, our results suggest that there is subtype specificity in associations between NHL and specific pesticides. The varying etiology of NHL sub-types may have masked real associations between specific pesticides and NHL previously. Although information fromthe epidemiologic studies on al evidence for associations between specific pesticides and specific cell types is growing, there are no clear patterns as of yet. Differences by cell type does suggest this could be a fruitful are of research.the observation that pesticides of different chemical and functional classes and different known toxicological properties are associated with the same cell type indicates that relatively little is known about the biological/toxicological mechanisms by which these compounds may be contributing to this disease. Cautious interpretation of these results is advised since the number of exposed cases for each subgroup of NHL in the AHS is still relatively small.

Comment [AEB46]: I think you study start with a summary of link between NHL overall and pesticides. Then go to histologic types.

Acknowledgements
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This work was supported by the Intramural Research Program of the National Institutes of Health, NCI, Division of Cancer Epidemiology and Genetics (Z01CPxxxxxx) and the National Institutes of Environmental Health Science (Z01 xxxxxxx). Collection of cancer incidence data was supported in Iowa by contract numbers HHSN261201000032C, N)1-PC-35143 and N01-PC-67008 and in North Carolina by agreement (XXXX).

Comment [a47]: Get correct contract numbers here.

The authors have no conflicts of interest in connection with this manuscript.

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Table 1. Baseline characteristics of AHS study participants in the NHL incidence analysis from 1993 through 2008				
	All NHL cases	Cohort Person-years.	RR[1]	95% CI
Age at Enrollment				
<45	51	368,766.80	1.0 (ref)	
45-49	34	88,648.48	2.8	1.8-4.3
50-54	51	75,781.37	4.9	3.3-7.2
55-59	59	67,981.37	6.3	4.3-9.1
60-64	46	53,346.73	6.2	4.2-9.3
65-69	46	34,532.71	9.6	6.5-14.4
≥70	46	25,713.12	12.9	8.7-19.3
Gender				
Male	328 (ref)	695,190.90	1.0 (ref)	
Female	5	19,579.34	0.5	0.2-1.3
State				
IA	213 (ref)	461,697.24	1.0 (ref)	
NC	120	253,072.27	0.8	0.6-0.97
License type				
Private	318	652,562.25	1.0 (ref)	
Commercial	15	62,207.89	0.9	0.5-1.5
Education				
<12 yrs.	57	61,656.39	1.0 (ref)	
HS/GED	143	326,344.92	0.8	0.6-1.1
>12 yrs.	121	297,437.85	1.0	0.7-1.4
Smoking Status				

Never	165	371,929.66	1.0 (ref)	
Former	127	203,445.28	0.93	0.7-1.2
Current	29	116,254.87	0.6	0.4-0.9
Alcohol consumption per week				
None	128	212,928.70	1.0 (ref)	
<once a week	89	217,015.35	1.0	0.8-1.4
≥once a week	89	240,745.51	1.0	0.8-1.4
Relative with lymphoma				
No	291	639,748.82	1 (ref)	
Yes	7	12,606.85	1.1	0.5-2.4

[1] All variables except age are age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

[2] Numbers do not sum to totals (333 cases, 714,770 person-years) due to missing data.

Table 2. Occupational exposures of AHS participants in the NHL incidence analysis from 1993 through 2008				
	All NHL cases	Cohort Person-years.	RR [1]	95% CI
Livestock				
None	99	203,211.17	1.0 (ref)	
<100	53	130,786.46	0.9	1.0
100-999	89	185,041.99	1.3	0.98-1.8
≥1000	42	83,968.59	1.6	1.1-2.4
Poultry				
None	252	536,832.57	1.0 (ref)	
<100	16	35,332.57	1.1	0.7-1.8
100-999	4	8,279.30	1.3	0.5-3.4
≥1000	7	14,437.82	1.2	0.6-2.6
Number of Acres planted				
None	19	32,456.03	1.0 (ref)	
<50	41	79,472.84	0.95	0.6-1.5
50-499	139	274151.16	1.1	0.6-1.8
≥500	93	225,668.35	0.7	0.4-1.3
Welding				
< Once/month	55	100,838.68	1.0	1
≥Once /month	95	177,869.05	1.4	0.95-2.0
Diesel				
<use once/week	20	41,552.80	1.0 (ref)	
≥once week	131	237,013.38	1.6	1.0-2.7
Number different pesticides used				

Comment [AEB48]: I would not provide the information on other agricultural exposures in a table. I takes away from later papers on NHL. Since the issue here is confounding, just say in the text you looked at these factors and either adjusted for them or did not.

<5	37	50,085.09	1.0 (ref)	
5-8	59	46,562.60	1.3	0.9-2.0
9-11	54	26,470.50	1.4	0.9-2.2
12-16	60	91,721.69	1.0	0.7-1.5
17-20	49	67,968.72	1.3	0.9-2.0
>20	70	423,710.03	1.3	0.9-2.0

[1] Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

[2] Numbers do not sum to totals (333 cases, 714,770 person-years) due to missing data.

Table 3. Pesticide exposure (Lifetime Days [LD] & intensity weighted Lifetime Days [IWLD]) and the age-adjusted risk of NHL incidence (1993 through 2008)

Insecticides and Fungicides

	NHL Cases	RR[1] (95%) by Total Days of Exposure	NHL Cases	RR[1] (95% CI) Intensity-weighted days of exposure
Benomyl				
(carbamate-fungicide)				
None	134	1.0 (ref)	134	1.0 (ref)
low	6	5.6 (2.4-12.6)	6	4.1(1.8-9.3)
medium	5	1.0 (0.4-2.6)	5	1.0 (0.4-2.6)
high	5	0.8 (0.3-1.9)	5	0.8 (0.3-1.9)
		P for trend=0.50		P for trend=0.57
Carbaryl				
(carbamate-insecticide)				
None	81	1.0 (ref)	81	1.0 (ref)
Low	31	0.9 (0.5-1.5)	27	0.9 (0.5-1.5)
Medium	23	0.7 (0.4-1.1)	26	0.8 (0.5-1.4)
High	25	0.9 (0.6-1.5)	26	0.8 (0.5-1.3)
		P trend=0.86		P trend=0.47
Carbofuran				
(carbamate-insecticide)				
None	199	1.0 (ref)	199	1.0 (ref)
Low	35	1.1 (0.8-1.6)	29	1.2 (0.8-1.8)
Medium	25	1.0 (0.7-1.6)	29	0.9 (0.6-1.3)
High	28	1.0 (0.7-1.5)	28	1.1 (0.8-1.7)
		P trend=0.81		P trend=0.74
Chlorpyrifos				

(organophosphate-insecticide)				
None	189	1.0 (ref)	189	1.0 (ref)
Low	44	1.1 (0.7-1.5)	40	1.1 (0.8-1.5)
Medium	45	1.3(0.9-1.8)	41	1.0 (0.7-1.5)
High	43	0.9 (0.7-1.3)	39	1.1 (0.8-1.5)
		P trend=0.57		P trend=0.67
Diazinon				
(organophosphosphorous-insecticide)				
None	113	1.0 (ref)	113	1.0 (ref)
Low	19	1.2 (0.7-2.0)	14	1.3 (0.7-2.2)
Medium	10	0.7 (0.3-1.7)	15	0.9 (0.5-1.7)
High	13	1.1 (0.6-2.1)	13	1.1 (0.6-1.9)
		P trend=0.73		P trend=0.92
Malathion				
(organophosphorous-insecticide)				
None	55	1.0 (ref)	55	1.0 (ref)
Low	46	1.0 (0.7-1.5)	37	1.0 (0.7-1.6)
Medium	28	0.7 (0.4-1.2)	38	0.8 (0.5-1.3)
High	36	1.0 (0.7-1.6)	35	0.91 (0.6-1.4)
		P trend=0.74		P trend=0.71
Permethrin Animals				
(pyrethroid-insecticide)				
None	263	1.0 (ref)	263	1.0 (ref)
Low	15	1.3 (0.8-2.3)	10	1.3 (0.7-2.5)
Medium	5	0.8 (0.3-2.5)	10	0.8 (0.4-1.7)
High	9	0.6 (0.3-1.2)	9	0.8 (0.4-1.5)
		P trend= 0.18		P trend=0.43

Phorate				
(organophosphate-insecticide)				
None	102	1.0 (ref)	102	1.0 (ref)
low	20	1. (0.6-1.6)	17	0.9(0.5-1.5)
medium	20	2.2 (1.4-3.5)	17	1.9 (1.1-3.1)
high	10	0.7 (0.4-1.3)	16	1.0(0.6-1.7)
		P for trend=0.80		P for trend=0.67
Terbufos				
(organophosphorous-insecticide)				
None	157	1.0 (ref)	157	1.0 (ref)
Low	58	1.4 (1.1-1.9)	43	1.3 (0.92-1.8)
Medium	38	2.0 (1.4-2.8)	43	2.0 (1.4-2.8)
High	34	1.2 (0.8-1.7)	42	1.2 (0.9-1.8)
		P trend=0.23		P trend=0.19
		Chlorinated Insecticide		
Chlordane				
None	113	1.0 (ref)	113	1.0 (ref)
Low	23	0.9 (0.6-1.4)	13	1.1 (0.7-2.0)
Medium	6	1.7 (0.7-3.8)	13	0.9 (0.5-1.6)
High	9	0.8 (0.4-1.6)	12	0.9 (0.5-1.6)
		P trend=0.66		P trend=0.76
DDT				
None	97	1.0 (ref)	97	1.0 (ref)
Low	20	0.8 (0.5-1.3)	19	0.9 (0.6-1.5)
Medium	18	0.9 (0.6-1.5)	18	0.8 (0.5-1.4)
High	17	1.5 (0.9-2.5)	18	1.4 (0.8-2.2)
		P trend=0.14		P trend=0.28

Lindane				
None	122	1.0 (ref)	122	1.0 (ref)
Low	11	1.0(0.5-2.0)	10	1.1(0.6-2.0)
Medium	10	1.2(0.6-2.3)	11	1.4(0.7-2.6)
High	10	2.7(1.4-5.1)	9	1.9(0.95-3.7)
		P trend=0.003		P trend=0.05
		Herbicides		
Alachlor				
(acetamide-herbicide)				
None	138	1.0 (ref)	138	1.0 (ref)
Low	65	1.0 (0.7-1.3)	53	1.0 (0.7-1.3)
Medium	49	0.9(0.6-1.2)	50	0.9 (0.6-1.2)
High	43	1.3(0.9-1.9)	51	1.2 (0.9-1.7)
		P trend=0.12		P trend=0.19
Atrazine				
(triazine-herbicide)				
None	85	1.0 (ref)	85	1.0 (ref)
Low	88	1.2(0.8-1.7)	79	1.1(0.8-1.6)
Medium	72	1.3(0.96-1.9)	78	1.4(1.0-2.0)
High	77	1.2(0.9-1.6)	78	1.2(0.8-1.6)
		P trend=0.56		P trend=0.68
Butylate				
(thiocarbamate-herbicide)				
None	107	1.0 (ref)	107	1.0 (ref)
Low	22	1.0(0.6-1.5)	16	0.9(0.5-1.5)
Medium	18	2.8(1.7-4.7)	16	2.1(1.2-3.5)
High	7	1.1(0.5-2.4)	15	1.5(0.9-2.6)

		P trend=0.004		P trend=0.04
Chlorimuron-ethyl				
(benzoic acid ester-herbicide)				
None	105	1.0 (ref)	105	1.0 (ref)
low	28	1.2(0.9-1.8)	18	1.1(0.6-1.9)
medium	18	1.9(1.2-3.2)	18	1.5(0.9-2.5)
high	7	0.7(0.3-1.5)	17	1.1(0.7-1.9)
		P for trend=0.83		P for trend=0.60
Cyanazine				
(triazine-herbicide)				
None	162	1.0 (ref)	162	1.0 (ref)
Low	58	1.4(0.9-1.9)	45	1.3(0.8-1.7)
Medium	43	1.2(0.8-1.7)	45	1.4(1.0-1.9)
High	35	1.1(0.8-1.6)	44	1.1(0.8-1.5)
		P for trend=0.81		P for trend=0.67
Dicamba				
(benzoic-herbicide)				
None	121	1.0 (ref)	121	1.0 (ref)
Low	66	1.3(0.94-1.8)	24	1.2(0.9-1.8)
Medium	52	1.5(1.1-2.1)	54	1.5(1.1-2.1)
High	47	1.2(0.9-1.7)	55	1.3(0.9-1.8)
		P trend=0.38	P trend=0.23	
2,4-D				
(phenoxy-herbicide)				
None	71	1.0 (ref)	71	1.0 (ref)
Low	83	1.0(0.7-1.4)	82	1.0(0.7-1.4)
Medium	83	1.2(0.8-1.6)	83	1.1(0.8-1.6)

High	82	1.0(0.7-1.4)	81	1.0(0.7-1.4)
		P trend=0.96		P trend=0.94
EPTC				
(thiocarbamate-herbicide)				
None	229	1.0 (ref)	229	1.0 (ref)
Low	28	1.3(0.9-2.0)	20	1.3(0.8-2.1)
Medium	14	1.0(0.6-1.7)	20	1.2(0.7-1.8)
High	18	1.3(0.8-2.0)	19	1.1(0.7-1.8)
		P trend=0.35		P trend=0.54
Glyphosate				
(phosphinic acid-herbicide)				
None	70	1.0 (ref)	70	1.0 (ref)
Low	89	0.8(0.6-1.2)	83	0.9(0.6-1.3)
Medium	78	0.8(0.6-1.2)	84	0.8(0.5-1.1)
High	83	1.0(0.7-1.4)	82	1.0(0.7-1.3)
		P trend=0.58		P trend=0.81
Imazethapry				
(imidazolinone-herbicide)				
None	181	1.0 (ref)	181	1.0 (ref)
Low	39	0.9(0.6-1.3)	36	1.0(0.7-1.4)
Medium	34	0.9(0.6-1.4)	37	0.9(0.6-1.3)
High	35	1.2(0.8-1.7)	35	1.2(0.8-1.7)
		P trend=0.54		P trend=0.55
Metribuzin				
(triazine-herbicide)				
None	94	1.0 (ref)	94	1.0 (ref)
Low	28	1.0 (0.7-1.7)	21	1.2(0.7-2.0)

Medium	15	0.9(0.5-1.6)	23	1.1(0.7-1.7)
High	20	1.7(1.0-2.7)	19	1.3(0.8-2.2)
		P trend=0.06		P trend=0.28
Trifluralin				
(dinitroaniline-herbicide)				
None	140	1.0 (ref)	140	1.0 (ref)
Low	51	1.0 (0.7-1.4)	50	1.0(0.7-1.4)
Medium	58	1.1(0.8-1.5)	52	1.1(0.8-1.5)
High	43	1.0(0.7-1.3)	48	0.9(0.7-1.3)
		P trend=0.81		P trend=0.65
2,4,5 T				
(phenoxyacetic acid)				
None	71	1.0 (ref)	71	1.0 (ref)
low	30	1.7(1.1-2.5)	17	1.6(0.9-2.8)
medium	4	1.2(0.4-3.3)	16	1.9(1.1-3.2)
high	15	1.2(0.7-2.2)	16	1.0(0.6-1.7)
		P for trend=0.52		P for trend=0.51

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

[2] Numbers do not sum to NHL subtype total in methods due to missing data.

Table 4. Pesticides exposure (Lifetime-days and the age-adjusted risk of NHL by cell type (1993-2008).								
Insecticides, fungicide and fumigant								
	CLL, SLL, PLL, MCL		Diffuse Large B-cell		Follicular B-cell		Other B-cell types	
	RR[1] (95% CI)	n	RR[1] (95% CI)	n	RR[1] (95% CI)	n	RR[1] (95% CI)	n
Carbaryl								
None	1.0 (ref)	32	1.0 (ref)	23	1.0 (ref)	9	1.0 (ref)	9
Low	1.1(0.5-2.2)	15	0.7(0.3-1.5)	10	1.1(0.3-4.0)	5	xxx	6
Medium	1.0(0.2-4.2)	2	1.3(0.6-3.0)	8	1.8(0.6-5.9)	4	xxx	0
High	0.4(0.2-0.8)	8	1.5(0.7-3.5)	8	1.3(0.4-4.1)	4	xxx-	1
	P trend=0.007		P trend=0.19		P trend=0.66		P trend=xxx	
Carbofuran								
None	1.0(ref)	67	1.0(ref)	58	1.0(ref)	9	1.0(ref)	19
Low	1.4 (0.8-2.5)	15	0.9 (0.4-1.9)	8	0.96(0.4-2.5)	5	1.0(04-2.7)	5
Medium	1.2 (0.6-2.4)	10	0.9 (0.4-1.8)	9	1.6(0.7-3.9)	4	1.4(0.2-10.7)	1
High	1.3 (0.7-2.4)	12	1.1 (0.5-2.9)	5	0.6(0.2-2.0)	4	0.94(0.2-4.1)	2
	P trend=0.36		P trend=0.81		P trend=0.79		P trend=0.99	
Chlorpyrifos								
None	1.0 (ref)	69	1.0 (ref)	55	1.0 (ref)	26	1.0 (ref)	18
Low	0.9(0.5-1.7)	15	1.2(0.6-2.1)	13	1.4(0.7-3.1)	10	0.9(0.3-2.6)	5
Medium	1.1(0.7-2.0)	16	1.0(0.5-1.7)	15	1.2(0.5-2.9)	7	4.2(1.7-10.6)	6
High	1.0(0.5-1.7)	14	0.9(0.6-4.0)	7	1.4(0.6-3.4)	6	0.8(0.3-2.3)	4
	P trend=0.99		P trend=0.66		P trend=0.56		P trend=0.97	
Diazinon								
None	1.0 (ref)	40	1.0 (ref)	33	1.0 (ref)	13	1.0 (ref)	12

Low	1.5(0.7-3.1)	9	1.2(0.4-3.1)	5	1.6(0.4-5.5)	3	xxx	2
Medium	1.2(0.4-3.6)	5	0.9(0.3-2.8)	4	1.6(0.4-7.4)	3	xxx-	1
High	1.2(0.5-3.0)	5	1.2(0.4-3.8)	3	2.0(0.4-10.0)	2	xxx	0
	P trend=0.72		P trend=0.84		P trend=0.35		P trend=xxx	
Malathion								
None	1.0 (ref)	21	1.0 (ref)	16	1.0 (ref)	5	1.0 (ref)	6
Low	0.94(0.5-1.8)	17	0.8(0.4-1.7)	16	1.0(0.3-3.6)	6	xxx-	8
Medium	0.8(0.4-1.7)	11	0.9(0.4-2.1)	8	1.2(0.3-4.3)	5	-xxx	0
High	0.8(0.4-1.7)	11	1.7(0.8-3.8)	11	1.5(0.4-4.9)	5	-xxx	3
	P trend=0.52		P trend=0.07		P trend=0.48		P trend=xxx	
Permethrin animals								
None	1.0 (ref)	95	1.0 (ref)	78	1.0 (ref)	38	1.0 (ref)	25
Low	1.3(0.5-3.3)	5	Xxx	1	2.8(1.1-7.0)	5	xxx-	1
Medium	0.9(0.2-3.7)	3	xxx	1	2.9(0.7-12.0)	2	-xxx	2
High	0.8(0.3-2.5)	3	-xxx	0	0.8(0.2-3.5)	2	-xxx	0
	P trend=0.75		P trend=xxx		P trend=0.93		P trend=xxx	
Terbufos								
None	1.0 (ref)	53	1.0 (ref)	47	1.0 (ref)	26	1.0 (ref)	10
Low	1.8(1.0-3.1)	17	0.9(0.4-1.7)	12	2.5(1.1-5.4)	8	2.3 (0.8-6.6)	6
Medium	2.2(1.3-3.6)	21	2.2(1.2-4.2)	12	1.8(0.7-4.3)	7	3.1(1.1-9.2)	5
High	1.4(0.8-2.6)	13	1.1(0.5-2.3)	10	0.7(0.3-1.8)	6	4.1(1.4-11.9)	5
	P trend=0.16		P trend=0.34		P trend=0.54		P trend=0.01	
Chlorinated pesticides								
Chlordane								
None	1.0 (ref)	74	1.0 (ref)	68	1.0 (ref)	35	1.0 (ref)	21
Low	1.4 (0.7-2.7)	10	0.8 (0.4-2.0)	6	1.6 (0.4-6.9)	2	xxx	1

Medium	2.8 (0.9-9.0)	3	1.8 (0.6-5.1)	4	0.8 (0.2-3.4)	2	xxx	2
High	0.8 (0.3-2.7)	3	1.0 (0.2-4.1)	2	0.7 (0.1-5.1)	1	xxx	0
	P trend=0.56		P trend=0.09		P trend=0.92		P trend=xxx	
DDT								
None	1.0 (ref)	62	1.0 (ref)	53	1.0 (ref)	36	1.0 (ref)	22
Low	0.91 (0.4-2.0)	8	1.1 (0.5-2.6)	7	1.1 (0.4-3.4)	4	0.4 (0.1-1.9)	2
Medium	1.1 (0.5-2.4)	8	2.3 (1.0-5.4)	7	0.3 (0.1-2.6)	1	1.4 (0.3-6.2)	2
High	2.3 (1.0-5.3)	7	1.2 (0.5-2.9)	6	0.7 (0.1-5.0)	1	0.9 (0.1-6.7)	1
	P trend=0.45		P trend=0.31		P trend=0.72		P trend=0.77	
Lindane								
None	1.0 (ref)	41	1.0 (ref)	39	1.0 (ref)	14	1.0 (ref)	14
Low	1.6(0.7-3.6)	8	0.7(0.2-3.0)	9	2.7(0.8-9.4)	3	xxx	1
Medium	1.1(0.3-4.8)	3	1.1(0.3-3.7)	6	3.6(0.8-15.9)	2	xxx	0
High	3.8(1.5-9.6)	5	1.3(0.2-9.7)	5	2.4(0.5-10.4)	2	xxx	0
	P trend=0.005		P trend=0.25		P trend=0.25		P trend=xxx	
Herbicides								
Alachlor (acetanilide)								
None	1.0 (ref)	53	1.0 (ref)	42	1.0 (ref)	22	1.0 (ref)	9
Low	0.9(0.6-1.5)	23	0.9(0.5-1.6)	13	1.3(0.6-2.6)	10	1.6 (0.6-4.4)	7
Medium	0.8(0.5-1.4)	18	0.7(0.4-1.3)	14	0.8(0.3-1.6)	9	2.1 (0.8-5.3)	10
High	1.1(0.6-2.1)	14	0.8(0.4-1.6)	10	1.1(0.4-2.7)	6	4.0 (1.2-13.0)	4
	P =0.67		P trend=0.52		P trend=0.99		P trend=0.02	
Atrazine (triazine)								
None	1.0 (ref)	34	1.0 (ref)	26	1.0 (ref)	12	1.0 (ref)	5
Low	1.0 (0.6-1.7)	29	1.1(0.6-2.0)	21	1.7(0.7-3.9)	17	2.4 (0.9-6.8)	13

Medium	1.2 (0.7-2.0)	25	1.1(0.6-2.2)	23	1.3(0.5-3.4)	10	1.7(0.5-5.9)	6
High	1.0 (0.6-1.7)	26	0.9(0.5-1.7)	19	1.4(0.6-3.4)	13	3.6 (1.2-10.8)	9
	P trend=0.90		P trend=0.62		P trend=0.83		P trend=0.06	
Butylate (thio-carbamate-)								
None	1.0 (ref)	40	1.0 (ref)	33	1.0 (ref)	14	1.0 (ref)	8
Low	0.8(0.4-1.9)	7	1.1(0.4-3.0)	4	0.8(0.2-2.9)	3	3.0 (0.8-11.3)	3
Medium	3.5(1.6-7.6)	8	1.2(0.4-3.5)	4	6.3(2.1-19.3)	4	4.0(1.2-13.7)	4
High	1.3(0.4-4.3)	3	0.8(0.2-2.5)	3	1.0(0.1-7.9)	1	2.4 (0.3-19.7)	1
	P trend=0.04		P trend=0.69		P trend=0.07		P trend=0.0499	
Cyanazine (triazine)								
None	1.0 (ref)	65	1.0 (ref)	46	1.0 (ref)	24	1.0 (ref)	10
Low	1.2 (0.7-2.2)	15	1.4 (0.8-2.4)	16	1.9(0.9-3.8)	12	3.7(1.4-9.7)	7
Medium	0.9 (0.5-1.6)	16	0.8 (0.4-1.8)	8	1.7(0.8-3.6)	9	2.9 (1.5-7.5)	8
High	1.1(0.6-2.0)	14	1.0 (0.5-2.1)	8	0.8(0.3-2.2)	4	2.6(0.9-7.5)	5
	P trend=0.93		P trend=0.93		P trend=0.87		P trend=0.17	
2,4-D (Chlorinated Phenoxy)								
None	1.0 (ref)	25	1.0 (ref)	23	1.0 (ref)	9	1.0 (ref)	5
Low	0.90(0.5-1.5)	31	0.9(0.5-1.7)	23	1.8(0.8-4.4)	14	1.9 (0.6-6.2)	10
Medium	1.2(0.7-2.0)	29	1.0(0.6-1.9)	21	1.0(0.4-2.4)	14	1.7 (0.5-5.6)	9
High	1.3(0.7-2.2)	29	0.7(0.4-1.3)	21	1.4(0.6-3.4)	12	2.2 (0.7-7.2)	9
	P trend=0.20		P trend=0.23		P trend=0.84		P trend=0.35	
Dicamba (benzoic								

acid)								
None	1.0 (ref)	39	1.0 (ref)	40	1.0 (ref)	22	1.0 (ref)	6
Low	1.5 (0.9-2.6)	23	1.1 (0.6-2.1)	12	1.5(0.7-3.4)	9	3.2 (1.0-9.9)	8
Medium	1.5 (0.9-3.4)	20	1.1 (0.6-2.1)	13	1.8(0.90-4.0)	10	5.2(1.6-16.6)	7
High	2.0 (1.1-3.4)	20	0.7 (0.4-1.4)	11	0.7(0.3-1.5)	8	5.1(1.6-16.1)	7
	P trend=0.03		P trend=0.26		P trend=0.32		P trend=0.02	
EPTC (thio-carbamate)								
None	1.0 (ref)	86	1.0 (ref)	62	1.0 (ref)	40	1.0 (ref)	19
Low	1,2(0.6-2.3)	9	1.2(0.6-2.7)	7	xxx	3	2.1 (0.7-6.0)	4
Medium	1.2(0.6-2.5)	8	1.7(0.7-4.2)	5	xxx	0	2.1 (0.6-7.1)	3
High	1.4(0.6-3.4)	5	0.8(0.3-2.3)	4	xxx	1	4.9 (1.4-16.7)	3
	P trend= 0.41		P trend=0.98		P trend=0.10		P trend=0.01	
Glyphosate (isopropyl-amine)								
None	1.0 (ref)	25	1.0 (ref)	19	1.0 (ref)	13	1.0 (ref)	10
Low	0.6(0.4-1.1)	32	1.3(0.7-2.6)	23	0.7(0.3-1.7)	15	0.4 (0.1-1.2)	9
Medium	1.1(0.6-1.9)	29	1.1(0.5-2.1)	23	0.6(0.2-1.4)	11	0.6 (0.2-1.6)	7
High	1.1(0.6-1.8)	29	0.7(0.4-1.3)	22	0.7(0.3-1.8)	12	0.6 (0.2-1.8)	7
	P trend=0.21		P trend=0.05		P trend=0.66		P trend=0.98	
Imazethapry (imid-azolinone)								
None	1.0 (ref)	68	1.0 (ref)	57	1.0 (ref)	29	1.0 (ref)	12
Low	1.0(0.6-1.8)	16	0.7(0.3-1.4)	10	0.7(0.3-1.7)	6	1.6 (0.6-3.8)	8
Medium	0.8(0.4-1.6)	11	0.6(0.3-1.4)	6	1.1(0.3-3.5)	6	5.2 (1.6-16.6)	4

High	1.2(0.6-2.2)	12	0.5(0.2-1.2)	5	1.0(0.4-2.8)	5	3.2 (1.0-10.0)	4
	P trend=0.71		P trend=0.16		P trend=0.90		P trend=0.03	
Metolachlor (chlor-acetanilide)								
None	1.0 (ref)	52	1.0 (ref)	48	1.0 (ref)	20	1.0 (ref)	10
Low	1.2(0.7-2.0)	23	0.9(0.4-2.1)	11	1.4(0.6-3.2)	9	2.7 (1.0-7.0)	9
Medium	1.7(0.95-3.2)	17	1.3(0.7-2.4)	12	1.4(0.6-3.7)	9	2.1 (0.6-7.7)	4
igh	1.3(0.8-2.3)	18	0.4(0.2-0.9)	9	1.5(0.7-3.6)	8	2.6 (0.9-7.2)	6
	P trend=0.19		P trend=0.02		P trend=0.43		P trend=0.19	
Metribuzin (Triazinone)								
None	1.0 (ref)	30	1.0 (ref)	35	1.0 (ref)	13	1.0 (ref)	9
Low	1.5(0.7-2.9)	11	0.5(0.2-1.4)	5	1.4(0.5-3.9)	5	1.0 (0.2-4.9)	3
Medium	2.1(1.1-4.0)	13	0.5(0.1-2.0)	3	0.8(0.2-2.9)	3	2.8 (0.9-8.9)	5
High	1.8(0.6-5.2)	4	0.4(0.1-1.6)	2	1.3(0.2-9.8)	1	-	0
	P trend=0.06		P trend=0.13		P trend=0.88		P trend=0.60	
Trifluralin (dinitro-aniline)								
None	1.0 (ref)	45	1.0 (ref)	43	1.0 (ref)	25	1.0 (ref)	10
Low	1.1(0.7-1.9)	23	0.9(0.5-1.7)	14	0.9(0.4-1.9)	8	1.2 (0.4-3.2)	7
Medium	1.6(0.9-2.6)	21	0.8(0.4-1.7)	11	0.8(0.4-1.8)	8	2.7 (1.0-7.0)	7
High	1.1(0.6-1.9)	15	0.6(0.3-1.2)	11	0.8(0.3-1.9)	7	3.3 (1.2-9.1)	6
	P trend= 0.81		P trend=0.13		P trend=0.62		P trend=0.01	

[1] Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)
[2] Numbers do not sum to NHL subtype totals due to missing data.

Table 5. Number of different pesticides used by pesticide type (in the NHL incidence analysis from 1993 through 2008) for B cell sub-types.								
	CLL, SLL, PLL, MCL		Diffuse Large B-cell		Follicular B-cell		Other B-cell types	
	RR[1] (95% CI)	n	RR[1] (95% CI)	n	RR[1] (95% CI)	n	RR[1] (95% CI)	n
Insecticides								
Carbamate insecticides								
0	1.0 (ref)	34	1.0(ref)	33	1.0(ref)	12	1.0 (ref)	13
1	0.8 (0.5-1.3)	45	0.7(0.4-1.2)	36	1.5(0.8-3.0)	26	0.3 (0.1-0.8)	7
2-3	1.1 (0.7-1.7)	32	0.7(0.4-1.2)	20	1.2(0.5-2.7)	12	1.2 (0.5-2.5)	13
	P trend= 0.82		P trend=0.21		P trend=0.63		P trend= 0.75	
Chlorinated insecticides								
None	1.0 (ref)	8	1.0(ref)	16	1.0(ref)	3	1.0 (ref0	6
1	1.6 (0.7-3.8)	17	0.9 (04-1.7)	18	4.1(1.2-14.1)	15	0.9 (0.3-2.7)	7
2	2.2 (0.95-5.0)	19	0.6(0.3-1.3)	10	2.5(0.6-9.6)	7	0.5 (0.1-1.9)	3
≥3	2.4 (1.2-5.2)	41	0.5(0.3-1.0)	17	1.7(0.5-6.5)	9	0.8 (0.3-2.3)	10
	P trend=0.02		P trend=0.05		P trend=0.73		P trend= 0.48	
Organophosphate Insecticides								
0	1.0 (ref)	13	1.0 (ref)	14	1.0(ref)	5	1.0	5
1	0.93(0.4-2.0)	15	1.2(0.6-2.4)	21	1.3(0.4-3.9)	8	0.8 (0.2-2.8)	5
2	1.4 (0.7-2.7)	25	1.0(0.5-2.0)	20	1.7(0.6-4.7)	12	1.3 (0.4-4.0)	9
3	1.3 (0.6-2.5)	20	0.8(0.4-1.7)	14	1.4(0.5-4.1)	9	0.5 (0.1-2.1)	3
≥4	1.7 (0.92-3.2)	42	0.8(0.4-1.6)	23	1.6(0.6-4.4)	17	1.3 (0.5-3.7)	12

	P trend =0.03		P trend= 0.28		P trend=0.38		P trend=0.67	
Other Insecticides								
0	1.0 (ref)	86	1.0 (ref)	71	1.0(ref)	35	1.0 (ref)	22
1	0.94 (0.6-1.6)	19	0.5(0.2-1.0)	9	1.3(0.6-2.4)	12	1.1 (0.5-2.8)	6
	P trend=0.78		P trend= .04		P trend=0.49	6	P trend=0.82	
Herbicides								
Acetamide Herbicide								
0	1.0 (ref)	37	1.0(ref)	32	1.0(ref)	14	1.0	6
1	0.97 (0.6-1.5)	35	1.0(0.6-1.6)	32	1.3(0.7-2.6)	19	1.4 (0.5-4.0)	8
2	1.2 (0.8-2.0)	39	0.6(0.4-1.1)	18	1.2(0.6-2.4)	15	3.9 (1.2-8.2)	16
	P trend=0.35		P trend=0.16		P trend=0.72		P trend= 0.009	
Carbamate Herbicide								
0	1.0 (ref)	67	1.0(ref)	58	1.0(ref)	27	1.0	16
1	0.98 (0.6-1.5)	27	0.7(0.4-1.2)	17	1.3(0.7-2.5)	16	1.5 (0.7-3.4)	10
2	1.5 (0.9-2.5)	17	0.9(0.4-1.7)	9	0.6(0.2-1.8)	3	2.2 (0.9-5.7)	6
	P trend=0.29		P trend=0.33		P trend=0.71		P trend=0.11	
Other herbicides								
0	1.0 (ref)	6	1.0(ref)	6	1.0(ref)	1	1.0	2
1-2	1.2(0.5-2.8)	25	1.0(0.4-2.5)	22	3.2(0.5-27.0)	13	0.6 (0.1-3.1)	4
2-4	0.9 (0.4-2.2)	20	1.4(0.6-3.4)	33	2.5(0.3-19.2)	10	0.94(0.2-4.6)	7
5-6	1.2 (0.5-2.8)	26	0.7(0.3-1.7)	16	4.0(0.5-29.8)	17	1.2(0.3-5.7)	9
≥7	1.7 (0.7-4.1)	38	0.7(0.3-1.7)	16	2.5(0.3-19.3)	11	1.7(0.4-7.6)	12
	P trend=0.06		P trend=0.08		P trend=0.84		P trend= 0.06	
Triazine herbicides								
0	1.0	29	1.0 (ref)	22	1.0(ref)	6	1.0 (ref)	4
1	0.8 (0.5-1.4)	24	1.5(0.9-2.6)	34	3.2(1.3-8.0)	20	2.0 (0.6-6.6)	8
2	1.0(0.6-1.7)	27	0.8(0.4-1.5)	17	2.1(0.8-6.7)	13	2.5 (0.8-8.3)	9

3	1.5 (0.91-2.5)	35	1.1(0.6-2.0)	20	2.3(0.9-6.1)	13	4.2 (1.4-13.1)	13
	P trend=0.07		P trend=0.64		P trend=0.30		P trend=.006	
Fungicides and Fumigants								
Fungicides								
0	1.0 (ref)	4	1.0 (ref)	6	1.0(ref)	3	1.0	2
1	1.3 (0.4-3.6)	29	0.7(0.3-1.8)	28	1.1(0.3-3.6)	23	1.2 (0.3-5.6)	14
2	1.7 (0.6-4.6)	81	0.8(0.3-1.8)	58	0.6(0.2-2.1)	26	0.8 (0.2-3.4)	18
	P trend=0.11		P trend=0.75		P trend=0.10		P trend=0.29	
Fumigants								
0	1.0 (ref)	43	1.0 (ref)	30	1.0(ref)	25	1.0	9
1	1.0 (0.6-1.9)	13	2.0(1.1-3.7)	17	0.6(0.2-1.7)	4	2.8 (1.0-7.4)	7
≥2	0.95(0.6-1.4)	58	1.1(0.7-1.8)	45	0.7(0.4-1.2)	22	1.5(0.7-3.3)	18
	P trend=0.81		P trend=0.75		Ptrend=0.20		P trend=0.43	

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

[2] Numbers do not sum to NHL subtype totals due to missing data

Supplemental Table 1 Other pesticide exposures (lifetime days [LD} and intensity weighted total days) and age-adjusted risk of NHL incidence (1993 through 2008).				
	NHL Cases	RR (95%) by Lifetime- Days of Exposure	NHL Cases	RR (95% CI) Intensity weighted Lifetime-Days of exposure
Aldicarb (carbamate-insecticide)				
None	145	1.0 (ref)	145	1.0 (ref)
low	5	1.2 (0.5-2.9)	4	1.3 (0.4-4.0)
medium	4	2.1 (0.7-6.7)	5	1.2 (0.5-3.0)
high	3	0.3 (0.1-1.3)	3	0.4 (0.1-1.5)
		P for trend =0.25		P for trend=0.26
Captan (dicarboximide-fungicide)				
None	258	1.0 (ref)	258	1.0 (ref)
low	8	0.6 (0.3-1.3)	8	0.7 (0.4-1.5)
medium	8	1.6 (0.6-4.1)	7	1.2 (0.5-2.9)
high	7	0.6 (0.3-1.5)	7	0.5 (0.2-1.3)
		P for trend=0.33		P for trend=0.20
Chlorthalonil (thalonitrile-fungicide)				
None	301	1.0 (ref)	301	1.0 (ref)
low	7	1.3 (0.6-2.7)	7	1.1 (0.5-2.4)
medium	6	0.6 (0.2-1.6)	6	0.6 (0.2-1.5)
high	6	0.6 (0.2-1.2)	6	0.7 (0.3-1.5)
		P for trend=0.12		P for trend=0.23
Coumaphos (0rganophosphate-				

insecticide)				
None	258	1.0(ref)	258	1.0 (ref)
Low	12	1.2 (0.7-2.2)	10	1.6 (0.8-2.9)
medium	10	1.4 (0.8-2.7)	11	1.2 (0.6-2.1)
High	8	1.2 (0.6-2.4)	9	1.2 (0.6-2.3)
		P for trend=0.41		P for trend=0.55
DDVP **(dimethyl phosphate-insecticide)**				
None	261	1.0 (ref)	261	1.0 (ref)
low	10	1.2 (0.6-2.2)	10	1.2 (0.7-2.3)
medium	11	1.1 (0.6-2.0)	9	0.8 (0.4-1.6)
high	7	0.7 (0.3-1.5)	9	1.0 (0.5-1.9)
		P for trend=0.42		P for trend=0.95
Fonofos **(phosphonothioate-insecticide)**				
None	220	1.0 (ref)	220	1.0 (ref)
low	28	1.3 (0.9-1.9)	23	1.2 (0.8-1.9)
medium	19	1.2 (0.8-2.0)	23	1.4 (0.93-2.2)
high	22	1.1 (0.7-1.7)	22	1.0 (0.6-1.5)
		P for trend=0.67		P for trend=0.98
Maneb/macozeb **(thiocarbamate-fungicide)**				
None	139	1.0 (ref)	139	1.0 (ref)
Low	5	1.7 (0.7-4.2)	5	1.8(0.7-4.4)
Medium	5	0.9 (0.3-2.3)	5	1.0 (0.4-2.4)
High	4	0.8 (0.3-2.3)	4	0.7 (0.3-1.9)

		P for trend=0.71		P for trend=0.50
Matalaxyl **(analine methyl ester-fungicide)**				
None	126	1.0 (ref)	126	1.0 (ref)
Low	10	1.2 (0.6-2.2)	10	1.8 (0.95-3.4)
medium	11	0.9 (0.5-1.7)	11	0.7 (0.4-1.4)
high	9	0.8 (0.4-1.5)	9	0.8 (0.4-1.5)
		P for trend=0.43		P for trend=028
Methyl bromide **(methyl halide-fumigant)**				
None	268	1.0 (ref)	268	1.0 (ref)
Low	25	1.9 (1.2-2.8)	17	1.9 (1.2-3.1)
medium	9	0.9 (0.4-1.7)	16	1.3 (0.8-2.1)
high	16	0.6 (0.3-0.9)	16	0.5 (0.3-0.9)
		P for trend=0.03		P for trend=0.02
Permethrin Crops **(pyrethroid-insecticide)**				
None	249	1.0 (ref)	249	1.0 (ref)
low	17	1.0 (0.6-1.7)	12	1.1 (0.5-2.2)
medium	9	1.1 (0.5-2.3)	12	1.2 (0.7-2.2)
high	10	0.7 (0.4-1.4)	11	0.6 (0.3-1.1)
		P for trend=0.36		P for trend=0.15
Herbicide exposures				
	Life-time days of Exposure		Intensity weighted days of exposure*	
	NHL Cases	RR (95%)	NHL Cases	RR (95% CI)

Herbicide Oil				
None	120	1.0 (ref)	120	1.0 (ref)
low	14	1.0(0.6-1.9)	13	1.3(0.7-2.3)
medium	13	1.8(1.0-1.1)	12	1.1(0.6-1.9)
high	10	1.0(0.5-2.0)	12	1.3(0.7-2.4)
		P for trend=0.84		P for trend=0.36
Metolachlor				
None	145	1.0 (ref)	145	1.0 (ref)
low	50	1.2(0.9-1.7)	49	1.2(0.8-1.6)
medium	54	1.3(0.94-1.5)	49	1.4(1.0-2.0)
high	44	1.1(0.8-1.5)	48	1.1(0.8-1.5)
		P for trend=0.67		P for trend=0.28
Paraquat				
None	127	1.0 (ref)	127	1.0 (ref)
low	10	1.5(0.8-2.8)	10	1.9(1.0-3.7)
medium	10	0.8(0.4-1.5)	9	0.5(0.3-1.1)
high	8	1.0(0.5-2.0)	9	1.5(0.8-3.0)
		P for trend= 0.88		P for trend=0.26
Pendimethalin				
None	96	1.0 (ref)	96	1.0 (ref)
low	32	1.1(0.7-1.6)	25	1.1(0.6-1.8)
medium	23	1.2(0.7-2.0)	26	1.0(0.7-1.6)
high	20	1.0(0.6-1.6)	24	1.2(0.7-1.8)
		P for trend=0.87		P for trend=0.52

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

Supplemental Table 2. Pesticide exposures (total days and intensity weight total days) fully adjusted risks of NHL incidence (1993 through 2008).				
	NHL Cases	RR (95%) by Total Days of Exposure	NHL Cases	RR (95% CI) Intensity weighted days of exposure
Aldicarb				
none	145	1.0 (ref)	145	1.0 (ref)
low	5	1.5 (0.6-3.7)	4	1.4 (0.4-4.7)
medium	4	2.5 (0.8-8.4)	5	1.5 (0.6-3.9)
high	3	0.5 (0.1-1.8)	3	0.5 (0.1-2.1)
		P trend (full)=0.53		P trend (full)=0.56
Benomyl				
none	134	1.0 (ref)	134	1.0 (ref)
low	6	6.1(2.7-13.8)	6	4.6 (2.0-10.6)
medium	5	1.0(0.4-2.6)	5	1.4 (0.6-3.5)
high	5	1.0(0.4-2.6)	5	1.1 (0.4-2.8)
		P trend (full)=0.98		P trend (full)=0.94
Captan				
none	258	1.0 (ref)	258	1.0 (ref)
low	8	0.6(0.3-1.2)	8	0.7 (0.3-1.4)
medium	8	1.7(0.7-4.3)	7	1.2 (0.5-2.0)
high	7	0.7(0.3-1.6)	7	0.6 (0.2-1.4)
		P trend (full)=0.45		P trend (full)=0.28
Carbaryl				
none	81	1.0(ref)	81	1.0 (ref)
low	31	0.96(0.6-1.6)	27	0.91 (0.6-1.5)
medium	23	0.8(0.5-1.4)	26	0.99 (0.6-1.6)
high	25	1.3(0.8-2.2)	26	1.1 (0.7-1.9)

		P trend (full)=0.26		P trend (full)=0.54
Carbofuran				
none	199	1.0 (ref)	199	1.0 (ref)
low	35	1.0(0.7-1.5)	29	1.1(0.8-1.6)
medium	25	0.97(0.6-1.5)	29	0.8(0.5-1.2)
high	28	0.96(0.6-1.4)	28	1.1(0.7-1.6)
		P trend (full)=0.83		P trend (full)=0.95
Chlorthalonil				
none	301	1.0 (ref)	301	1.0 (ref)
low	7	1.4(0.7-3.0)	7	1.2 (0.6-2.6)
Medium	6	0.7(0.3-1.8)	6	0.6 (0.2-1.9)
High	6	0.6 (0.3-1.4)	6	0.7 (0.3-1.6)
		P trend (full)=0.21		P trend (full)=0.37
Chlorpyrifos				
None	189	1.0 (ref)	189	1.0 (ref)
Low	44	1.0(0.7-1.5)	40	1.0 (0.7-1.5)
Medium	45	1.2(0.9-1.7)	41	0.94 (0.7-1.3)
High	43	0.8(0.6-1.2)	39	1.0 (0.7-1.4)
		P trend (full)=0.31		P trend (full)=0.99
Coumaphos				
none	258	1.0 (ref)	258	1.0 (ref)
low	12	1.1(0.6-2.0)	10	1.4 (0.8-2.7)
medium	10	1.3 (0.7-2.5)	11	1.1 (0.6-2.0)
high	8	1.1(0.5-2.2)	9	1.1 (0.6-2.1)
		P trend (full)=0.62		P trend (full)=0.75

Diazinon				
None	113	1.0 (ref)	113	1.0 (ref)
low	19	1.3(0.8-2.1)	14	1.3 (0.7-2.2)
medium	10	0.8(0.3-1.8)	15	0.9 (0.5-1.7)
high	13	1.3(0.7-2.5)	13	1.3 (0.7-2.3)
		P trend (full)=0.41		P trend (full)=0.50
DDVP				
none	261	1.0 (ref)	261	1.0 (ref)
low	10	1.0 (0.5-1.9)	10	1.1 (0.6-2.1)
medium	11	0.92 (0.5-1.7)	9	0.7 (0.4-1.4)
high	7	0.6 (0.3-1.3)	9	0.9 (0.4-1.7)
		P trend (full)=0.22		P trend (full)=0.61
Fonofos				
None	220	1.0 (ref)	220	1.0 (ref)
low	28	1.2(0.8-1.7)	23	1.1(0.7-1.7)
medium	19	1.1(0.7-1.7)	23	1.2(0.8-1.9)
high	22	0.9 (0.6-1.5)	22	0.9(0.5-1.3)
		P trend (full)=0.76		P trend (full)=0.51
Lindane				
None	122	1.0 (ref)	122	1.0 (ref)
low	11	0.9(0.5-1.8)	10	1.0(0.5-1.8)
medium	10	1.0(0.5-2.0)	11	1.2(0.6-2.3)
high	10	2.3(1.2-4.5)	9	1.7(0.9-3.3)
		P trend (full)=0.01		P trend (full)=0.12
Malathion				
none	55	1.0 (ref)	55	1.0 (ref)
low	46	0.9(0.6-1.3)	37	0.9 (0.6-1.4)

medium	28	0.7(0.4-1.1)	38	0.8 (0.5-1.1)
high	36	1.0(0.7-1.5)	35	0.9 (0.6-1.4)
		P trend (full)=0.68		P trend (full)=0.91
Maneb				
none	139	1.0 (ref)	139	1.0 (ref)
low	5	2.3(0.9-5.7)	5	2.4 (0.94-5.9)
medium	5	1.2(0.5-3.3)	5	1.4 (0.6-3.5)
high	4	1.2(0.4-3.4)	4	1.0 (0.4-2.9)
		P trend (full)=0.76		P trend (full)=0.95
Metalaxyl				
none	126	1.0 (ref)	126	1.0 (ref)
low	10	1.2(0.6-2.4)	10	1.7 (0.9-3.4)
medium	11	1.1(0.6-2.2)	11	0.9 (0.4-1.7)
high	9	1.1(0.5-2.3)	9	1.0 (0.5-2.2)
		P trend (full)=0.89		P trend (full)=0.93
Methyl bromide				
none	268	1.0 (ref)	268	1.0 (ref)
low	25	2.2 (1.4-3.4)	17	2.3 (1.4-3.8)
medium	9	1.1 (0.5-2.1)	16	1.5 (0.9-2.6)
high	16	0.7 (0.4-1.2)	16	0.7 (0.4-1.1)
		P trend (full)=0.13		P trend (full)=0.07
Permethrin Animals				
None	263	1.0 (ref)	263	1.0 (ref)
low	15	1.1(0.7-1.9)	10	1.1(0.6-2.1)
medium	5	0.7(0.2-2.1)	10	0.7(0.3-1.4)
high	9	0.5(0.3-1.0)	9	0.6(0.3-1.2)
		P trend (full)=0.055		P trend (full)=0.15

Permethrin Crops				
None	249	1.0 (ref)	249	1.0 (ref)
low	17	0.9(0.5-1.6)	12	1.0(0.5-2.0)
medium	9	1.1(0.5-2.2)	12	1.2(0.7-2.2)
high	10	0.8(0.4-1.5)	11	0.6(0.3-1.2)
		P trend (full)=0.44		P trend (full)=0.18
Phorate				
none	102	1.0 (ref)	102	1.0 (ref)
low	20	0.8(0.5-1.3)	17	0.7 (0.4-1.2)
medium	20	1.7(1.0-2.8)	17	1.5 (0.9-2.5)
high	10	0.6(0.3-1.0)	16	0.8 (0.5-1.4)
		P trend (full)=0.26		P trend (full)=0.70
Terbufos				
None	157	1.0 (ref)	157	1.0 (ref)
low	58	1.3(0.9-1.8)	43	1.2(0.8-1.7)
medium	38	1.7(1.2-2.5)	43	1.7(1.2-2.4)
high	34	1.0(0.7-1.5)	42	1.1(0.8-1.6)
		P trend (full)=0.78		P trend (full)=0.65
Herbicide exposures				
	Life-time days of Exposure		Intensity weighted days of exposure*	
	NHL Cases	RR (95%)	NHL Cases	RR (95% CI)
Alachlor				
None	138	1.0 (ref)	138	1.0 (ref)
low	65	0.9 (0.7-1.2)	53	0.9(0.7-1.2)
medium	49	0.8((0.6-1.1)	50	0.8 (0.6-1.1)
high	43	1.2((0.9-1.8)	51	1.2 (0.8-1.6)

		P trend (full)=0.20		P trend (full)=0.27
Atrazine				
None	85	1.0 (ref)	85	1.0 (ref)
low	88	1.1(0.8-1.5)	79	1.0(0.7-1.4)
medium	72	1.2 (0.8-1.6)	78	1.2(0.9-1.7)
high	77	1.0 (0.7-1.4)	78	0.98(0.7-1.4)
		P trend (full)= 0.72		P trend (full)=0.73
Butylate				
None	107	1.0 (ref)	107	1.0 (ref)
low	22	0.9(0.5-1.4)	16	0.8 (0.5-1.3)
medium	18	2.4(1.4-4.0)	16	1.8 (1.0-3.0)
high	7	1.0(0.4-2.1)	15	1.3 (0.8-2.3)
		P trend (full)=0.0.3		P trend (full)=0.14
Chlorimuron-ethyl				
None	105	1.0 (ref)	105	1.0 (ref)
low	28	1.1 (0.7-1.7)	18	1.0 (0.6-1.7)
medium	18	1.7 (1.0-2.9)	18	1.3(0.8-2.2)
high	7	0.7 (0.3-1.5)	17	1.1(0.6-1.8)
		P trend (full)=0.69		P trend (full)=0.68
Cyanazine				
None	162	1.0 (ref)	162	1.0 (ref)
low	58	1.3(0.94-1.8)	45	1.2(0.8-1.7)
medium	43	1.1(0.8-1.6)	45	1.3(0.9-1.8)
high	35	1.0(0.7-1.4)	44	1.0(0.7-1.4)
		P trend (full)=0.65		P trend (full)=0.76
Dicamba				
None	121	1.0 (ref)	121	1.0 (ref)

low	66	1.2 (0.8-1.7)	24	1.1(0.7-1.6)
medium	52	1.3 (0.9-1.9)	54	1.3(0.9-1.9)
high	47	1.1 (0.7-1.6)	55	1.1(0.8-1.6)
		P trend (full)=0.99		P trend (full)=0.76
2,4-D				
None	71	1.0 (ref)	71	1.0 (ref)
low	83	0.9(0.6-1.3)	82	0.9 (0.6-1.2)
medium	83	1.0(0.7-1.4)	83	0.97 (0.7-1.4)
high	82	0.8(0.6-1.2)	81	0.9 (0.6-1.2)
		P trend (full)=0.35		P trend (full)=0.46
EPTC				
None	229	1.0 (ref)	229	1.0 (ref)
low	28	1.2(0.8-1.8)	20	1.2 (0.8-2.0)
medium	14	0.9(0.7-1.9)	20	1.1 (0.7-1.7)
high	18	1.2(0.7-1.9)	19	1.0 (0.6-1.7)
		P trend (full)=0.56		P trend (full)=0.85
Glyphosate				
None	70	1.0 (ref)	70	1.0 (ref)
low	89	0.8(0.6-1.2)	83	0.91 (0.6-1.3)
medium	78	0.8(0.6-1.2)	84	0.8 (0.5-1.1)
high	83	1.0(0.7-1.4)	82	0.97 (0.7-1.4)
		P trend (full)=0.63		P trend (full)=0.69
Herbicide Oil				
None	120	1.0 (ref)	120	1.0 (ref)
low	14	1.0(0.6-1.7)	13	1.2 (0.6-2.1)
medium	13	1.7(0.93-2.9)	12	1.0 (0.5-1.8)
high	10	0.9((0.5-1.8)	12	1.2 (0.7-2.2)

		P for trend (full)=0.88		P for trend (full)=0.56
Imazethapry				
None	181	1.0 (ref)	181	1.0 (ref)
low	39	0.8(0.5-1.2)	36	0.8 (0.6-1.2)
medium	34	0.8(0.5-1.2)	37	0.7 (0.5-1.1)
high	35	1.0(0.7-1.5)	35	0.99 (0.7-1.5)
		P trend (full)=0.90		P trend (full)=0.92
Metolachlor				
None	145	1.0 (ref)	145	1.0 (ref)
low	50	1.2 (0.8-1.6)	49	1.1(0.8-1.5)
medium	54	1.2 (0.8-1.7)	49	1.3(0.9-1.9)
high	44	1.0 (0.7-1.4)	48	0.98(0.7-1.4)
		P trend (full)=0.90		P trend (full)=0.81
Metribuzin				
None	94	1.0 (ref)	94	1.0 (ref)
low	28	1.0(0.6-1.5)	21	1.0 (0.6-1.7)
medium	15	0.8(0.4-1.3)	23	0.91 (0.6-1.5)
high	20	1.4(0.8-2.3)	19	1.1 (0.7-1.9)
		P trend (full)=0.29		P trend (full)=0.66
Paraquat				
None	127	1.0 (ref)	127	1.0 (ref)
low	10	1.6(0.8-3.0)	10	2.0 (1.0-3.7)
medium	10	0.9(0.5-1.7)	9	0.6 (0.3-1.3)
high	8	1.2(0.6-2.5)	9	1.9 (0.9-3.9)
		P trend (full)=0.72		P trend (full)=0.08
Pendimethalin				
None	96	1.0 (ref)	96	1.0 (ref)

low	32	1.0(0.6-1.5)	25	0.9 (0.5-1.6)
medium	23	1.0(0.6-1.8)	26	0.9 (0.6-1.4)
high	20	1.0(0.6-1.5)	24	1.1 (0.7-1.8)
		P trend (full)=0.72		P trend (full)=0.60
Trifluralin				
None	140	1.0 (ref)	140	1.0 (ref)
low	51	0.9(0.7-1.3)	50	0.9 (0.6-1.2)
medium	58	1.0(0.7-1.3)	52	1.0 (0.7-1.4)
high	43	0.8(0.6-1.2)	48	0.8 (0.6-1.1)
		P trend (full)=0.41		P trend (full)=0.30
2,4,5 T				
None	71	1.0 (ref)	71	1.0 (ref)
low	30	1.6(1.0-2.4)	17	1.6 (0.9-2.6)
medium	4	1.1(0.4-3.0)	16	1.7 (1.0-2.9)
high	15	1.1(0.7-2.0)	16	1.0 (0.6-1.7)
		P trend (full)=0.78		P trend (full)=0.23

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70), smoking status(current, former, never), number of livestock (0,<100,100-999,>999), drove diesel tractor(<weekly,≥weekly), state (NC, IA)

Supplemental Table 1A. Chlorinated Insecticide exposure (in total days and intensity weighted days) and NHL age-adjusted relative risk(1993 through 2008).				
	Total exposure days		Intensity weight exposure days	
	NHL cases	RR (95% CI)[1]	NHL cases	RR (95% CI)
Aldrin				
None	232	1.0 (ref)	232	1.0 (ref)
low	14	0.8 (0.5-1.4)	12	0.9 (0.5-1.6)
medium	14	1.6 (0.8-3.4)	12	1.0 (0.6-1.9)
high	7	0.9 (0.7-1.2)	11	0.9 (0.7-1.2)
		P for trend=0.42		P for trend=0.95
		P for trend (full)=0.34		P for trend (full)=0.60
Dieldrin				
None	278	1.0 (ref)	278	1.0 (ref)
low	4	0.7 (0.2-1.8)	3	1.1 (0.3-3.3)
medium	4	2.0 (0.8-5.5)	4	1.2 (0.5-3.4)
high	1	0.6 (0.1-4.4)	2	0.6 (0.1-2.2)
		P for trend=0.91		P for trend=0.59
		P trend (full)=0.61		P trend (full)=0.84
Heptachlor				
None	240	1.0 (ref)	240	1.0 (ref)
low	11	0.9 (0.5-1.6)	11	0.9 (0.5-1.7)
medium	15	2.1 (1.3-3.6)	10	2.8 (1.5-5.3)
high	5	0.9 (0.4-2.1)	10	1.0 (0.5-1.9)
		P for trend=0.11		P for trend=0.41
		P for trend (full)=0.19		P for trend (full)=0.16

2,4,5 TP				
None	276	1.0 (ref)	276	1.0 (ref)
low	8	1.8 (0.9-3.7)	4	1.6 (0.6-4.3)
medium	0	0.6 (0.2-1.9)	4	1.4 (0.5-3.8)
high	3	0.9 (0.6-1.2)	3	0.8 (0.2-2.4)
		P for trend=0.40		P for trend=0.75
		P for trend (full)=0.27		P for trend (full)=0.74
Toxaphene				
None	250	1.0 (ref)	250	1.0 (ref)
low	10	3.4 (1.4-8.3)	7	1.6 (0.8-3.5)
medium	5	0.6 (0.3-1.3)	8	0.8 (0.4-1.6)
high	6	1.0 (0.7-1.3)	6	0.7 (0.3-1.6)
		P for trend=0.33		P for trend=0.31
		P for trend (full)= 0.12		P for trend (full)=0.69

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

Supplemental Table 2A. Chlorinated Insecticide exposure (in total days and intensity weighted days) and NHL fully adjusted relative risk(1993 through 2008).

	Life-time exposure days		Intensity weight exposure days	
	NHL cases	RR (95% CI)[1]	NHL cases	RR (95% CI)
Aldrin				
None	232	1.0 (ref)	232	1.0 (ref)
low	14	0.7 (0.4-1.3)	12	0.8 (0.5-1.5)

medium	14	0.7 (0.4-1.2)	12	0.7 (0.4-1.3)
high	7	1.4 (0.7)	11	0.9 (0.5-1.7)
		P for trend (full)=0.34		P for trend (full)=0.60
Chlordane				
None	223	1.0 (ref)	223	1.0 (ref)
low	23	1.0 (0.6-1.6)	13	1.2 (0.7-2.2)
medium	6	1.8 (0.8-4.2)	13	0.9 (0.5-1.7)
high	9	0.4 (0.4-1.7)	12	1.0 (0.6-1.8)
		P for trend (full)=0.63		P for trend (full)=0.90
DDT				
None	194	1.0 (ref)	194	1.0 (ref)
low	20	0.8 (0.5-1.3)	19	0.9 (0.6-1.5)
medium	18	1.0 (0.6-1.6)	18	0.9 (0.5-1.4)
high	17	1.5 (0.9-2.5)	18	1.4 (0.9-2.4)
		P for trend (full)=0.48		P for trend (full)=0.61
Dieldrin				
None	278	1.0 (ref)	278	1.0 (ref)
low	4	0.6 (0.2-1.7)	3	1.0 (0.3-3.1)
medium	4	1.8 (0.6-4.8)	4	1.1 (0.4-3.1)
high	1	0.6 (0.1-4.1)	2	0.5 (0.1-2.0)
		P trend (full)=0.61		P trend (full)=0.84
Heptachlor				
None	240	1.0 (ref)	240	1.0 (ref)
low	11	0.8 (0.4-1.5)	11	0.8 (0.5-1.6)
medium	15	1.9 (1.1-3.3)	10	2.4 (1.3-4.7)
high	5	0.8 (0.3-1.9)	10	0.9 (0.5-1.8)
		P for trend (full)=0.19		P for trend (full)=0.16

Lindane				
None	122	1.0 (ref)	122	1.0 (ref)
low	11	0.9 (0.5-1.8)	10	1.0(0.5-1.8)
medium	10	1.0 (0.5-2.0)	11	1.2(0.6-2.3)
high	10	2.4 (1.2-4.5)	9	1.7(0.9-3.3)
		P for trend (full)=0.01		P for trend (full)=0.12
2,4,5 TP				
None	276	1.0 (ref)	276	1.0 (ref)
low	8	1.8 (0.9-3.8)	4	1.6 (0.6-4.4)
medium	0	0.6 (0.2-2.0)	4	1.4 (0.5-3.9)
high	3	0.9 (0.6-1.2)	3	0.8 (0.3-2.5)
		P for trend (full)=0.27		P for trend (full)=0.74
Toxaphene				
None	250	1.0 (ref)	250	1.0 (ref)
low	10	0.91 (0.5-1.7)	7	1.6 (0.7-3.3)
medium	5	3.4 (1.4-8.3)	8	0.8 (0.4-1.6)
high	6	0.6 (0.3-1.3)	6	0.7 (0.3-1.7)
		P for trend (full)= 0.12		P for trend (full)=0.69

Supplemental Table 3. Herbicide exposures (Life-time days) and age-adjusted NHL risk by cell type (1993 through 2008).								
Pesticide (chemical class)	CLL, SLL, PLL, MCL		Diffuse Large B-cell		Follicular B-cell		Other B-cell types	
	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n
Alachlor (acetanilide)								
None	1.0 (ref)	53	1.0 (ref)	43	1.0 (ref)	22	1.0 (ref)	9
low	0.9(0.6-1.5)	23	0.9(0.5-1.6)	13	1.3(0.6-2.6)	10	1.6 (0.6-4.4)	7
medium	0.8(0.5-1.4)	18	0.7(0.4-1.3)	14	0.8(0.3-1.6)	9	2.1 (0.8-5.3)	10
high	1.1(0.6-2.1)	14	0.8(0.4-1.6)	10	1.1(0.4-2.7)	6	4.0 (1.2-13.0)	4
	LD P =0.67		LD P trend=0.52		LD P trend=0.99		LD P trend=0.02	
	IWLD P=0.49		IWLD P trend=0.092		IWLD P trend=0.97		IWLD P trend= 0.20	
Atrazine (triazine)								
None	1.0 (ref)	34	1.0 (ref)	26	1.0 (ref)	12	1.0 (ref)	5
low	1.0 (0.6-1.7)	29	1.1(0.6-2.0)	21	1.7(0.7-3.9)	17	2.4 (0.9-6.8)	13
medium	1.2 (0.7-2.0)	25	1.1(0.6-2.2)	23	1.3(0.5-3.4)	10	1.7(0.5-5.9)	6
high	1.0 (0.6-1.7)	26	0.9(0.5-1.7)	19	1.4(0.6-3.4)	13	3.6 (1.2-10.8)	9
	LD P trend=0.90		LD P trend=0.62		LD P trend=0.83		LD P trend=0.06	
	IWLD P trend=0.75		IWLD P trend=0.87		IWLD P trend=0.76		IWLD P trend=0.22	

Butylate (thio-carbamate-)								
None	1.0 (ref)	40	1.0 (ref)	33	1.0 (ref)	14	1.0 (ref)	8
low	0.8(0.4-1.9)	7	1.1(0.4-3.0)	4	0.8(0.2-2.9)	3	3.0 (0.8-11.3)	3
medium	3.5(1.6-7.6)	8	1.2(0.4-3.5)	4	6.3(2.1-19.3)	4	4.0(1.2-13.7)	4
high	1.3(0.4-4.3)	3	0.8(0.2-2.5)	3	1.0(0.1-7.9)	1	2.4 (0.3-19.7)	1
	LD P trend=0.04		LD P trend=0.69		LD P trend=0.07		LD P trend=0.05	
	IWLD P trend=0.19		IWLD P trend=0.89		IWLD P trend=0.12		IWLD P trend=0.13	
Chlorimuron-ethyl (Sulfonylurea)								
None	1.0 (ref)	38	1.0 (ref)	29	1.0 (ref)	14	1.0 (ref)	14
low	1.3(0.7-2.6)	11	1.4(0.7-3.0)	9	0.9(0.3-3.1)	3	-	1
medium	2.9(1.4-6.6)	9	1.2(0.4-4.0)	3	2.8(0.9-8.7)	4	-	1
high	0.3(0.1-2.5)	1	1.4(0.5-3.9)	4	0.7(0.9-5.1)	1	-	0
	LD P for trend=0.91		LD P trend=0.21		LD P trend=0.56		LD P for trend=xx	
	IWLD P trend=0.56		IWLD P trend=0.92		IWLD P trend=0.62		IWLD P trend=	
Cyanazine (triazine)								
None	1.0 (ref)	65	1.0 (ref)	46	1.0 (ref)	24	1.0 (ref)	10
low	1.2 (0.7-2.2)	15	1.4 (0.8-2.4)	16	1.9(0.9-3.8)	12	3.7(1.4-9.7)	7
medium	0.9 (0.5-1.6)	16	0.8 (0.4-1.8)	8	1.7(0.8-3.6)	9	2.9 (1.5-7.5)	8
high	1.1(0.6-2.0)	14	1.0 (0.5-2.1)	8	0.8(0.3-2.2)	4	2.6(0.9-7.5)	5
	LD P trend=0.93		LD P trend=0.93		LD P trend=0.87		LD P trend=0.17	

	IWLD P trend=0.35		IWLD P trend=0.47		IWLD P trend=0.68		IWLD P trend=0.15	
2,4-D **(Chlorinated Phenoxy)**								
None	1.0 (ref)	25	1.0 (ref)	23	1.0 (ref)	9	1.0 (ref)	5
low	0.90(0.5-1.5)	31	0.9(0.5-1.7)	23	1.8(0.8-4.4)	14	1.9 (0.6-6.2)	10
medium	1.2(0.7-2.0)	29	1.0(0.6-1.9)	21	1.0(0.4-2.4)	14	1.7 (0.5-5.6)	9
high	1.3(0.7-2.2)	29	0.7(0.4-1.3)	21	1.4(0.6-3.4)	12	2.2 (0.7-7.2)	9
	LD P trend=0.20		LD P trend=0.23		LD P trend=0.84		LD P trend=0.35	
	IWLD P trend=0.83		IWLD P trend=0.41		IWLD P trend=0.22		IWLD P trend=0.75	
Dicamba **(benzoic acid)**								
None	1.0 (ref)	39	1.0 (ref)	40	1.0 (ref)	22	1.0 (ref)	6
low	1.5 (0.9-2.6)	23	1.1 (0.6-2.1)	12	1.5(0.7-3.4)	9	3.2 (1.0-9.9)	8
medium	1.5 (0.9-3.4)	20	1.1 (0.6-2.1)	13	1.8(0.90-4.0)	10	5.2(1.6-16.6)	7
high	2.0 (1.1-3.4)	20	0.7 (0.4-1.4)	11	0.7(0.3-1.5)	8	5.1(1.6-16.1)	7
	LD P trend=0.03		LD P trend=0.26		LD P trend=0.32		LD P trend=0.02	
	IWLD P trend=0.04		IWLD P trend=0.35		IWLD P trend=0.22		IWLD P trend=0.02	
EPTC **(thio-carbamate)**								
None	1.0 (ref)	86	1.0 (ref)	62	1.0 (ref)	40	1.0 (ref)	19
low	1,2(0.6-2.3)	9	1.2(0.6-2.7)	7	-	3	2.1 (0.7-6.0)	4
medium	1.2(0.6-2.5)	8	1.7(0.7-4.2)	5	-	0	2.1 (0.6-7.1)	3
high	1.4(0.6-3.4)	5	0.8(0.3-2.3)	4	-	1	4.9 (1.4-16.7)	3
	LD P trend= 0.41		LD P trend=0.98		LD P trend=0.10		LD P trend=0.01	
	IWLD P trend=0.43		IWLD P trend=0.59		IWLD P trend=0.14		IWLD P trend=0.15	

Glyphosate (isopropyl-amine)								
None	1.0 (ref)	25	1.0 (ref)	19	1.0 (ref)	13	1.0 (ref)	10
low	0.6(0.4-1.1)	32	1.3(0.7-2.6)	23	0.7(0.3-1.7)	15	0.4 (0.1-1.2)	9
medium	1.1(0.6-1.9)	29	1.1(0.5-2.1)	23	0.6(0.2-1.4)	11	0.6 (0.2-1.6)	7
high	1.1(0.6-1.8)	29	0.7(0.4-1.3)	22	0.7(0.3-1.8)	12	0.6 (0.2-1.8)	7
	LD P trend=0.21		LD P trend=0.05		LD P trend=0.66		LD P trend=0.98	
	IWLD P trend=0.18		IWLD P trend=0.19		IWLD P trend=0.83		IWLD P trend=0.75	
Herbicide Oil (petroleum oil)								
None	1.0 (ref)	42	1.0 (ref)	35	1.0 (ref)	17	1.0 (ref)	14
low	1.8(0.8-4.3)	7	1.0(0.4-2.5)	6	1.4(0.3-5.9)	2	-	1
medium	2.6(1.0-6.7)	5	2.8(0.7-11.9)	2	1.1(0.1-8.4)	1	-	1
high	1.0(0.4-2.6)	5	1.4(0.4-4.5)	3	0.5(0.1-3.6)	1	0	0
	LD P trend=0.76		LD P trend=0.55		LD P trend=0.46		LD P trend=xxx	
	IWLD P trend=0.88		IWLD P trend=0.16		IWLD P trend=0.40		IWLD P trend=xxx	
Imazethapry (imid-azolinone)								
None	1.0 (ref)	68	1.0 (ref)	57	1.0 (ref)	29	1.0 (ref)	12
low	1.0(0.6-1.8)	16	0.7(0.3-1.4)	10	0.7(0.3-1.7)	6	1.6 (0.6-3.8)	8
medium	0.8(0.4-1.6)	11	0.6(0.3-1.4)	6	1.1(0.3-3.5)	6	5.2 (1.6-16.6)	4
high	1.2(0.6-2.2)	12	0.5(0.2-1.2)	3	1.0(0.4-2.8)	5	3.2 (1.0-10.0)	4
	LD P trend=0.71		Ld P trend=0.16		LD P trend=0.90		LD P trend=0.03	
	IWLD P trend=0.95		IWLD P trend=0.34		IWLD P trend=0.83		IWLD P trend=0.03	

Metolachlor (chlor-acetanilide)								
None	1.0 (ref)	52	1.0 (ref)	48	1.0 (ref)	20	1.0 (ref)	10
low	1.2(0.7-2.0)	23	0.9(0.4-2.1)	11	1.4(0.6-3.2)	9	2.7 (1.0-7.0)	9
medium	1.7(0.95-3.2)	17	1.3(0.7-2.4)	12	1.4(0.6-3.7)	9	2.1 (0.6-7.7)	4
high	1.3(0.8-2.3)	18	0.4(0.2-0.9)	9	1.5(0.7-3.6)	8	2.6 (0.9-7.2)	6
	LD P trend=0.19		LD P trend=0.02		LD P trend=0.43		LD P trend=0.19	
	IWLD P trend=0.20		IWLD P trend=0.23		IWLD P trend=0.33		IWLD P trend=0.64	
Metribuzin (Triazinone)								
None	1.0 (ref)	30	1.0 (ref)	35	1.0 (ref)	13	1.0 (ref)	9
low	1.5(0.7-2.9)	11	0.5(0.2-1.4)	5	1.4(0.5-3.9)	5	1.0 (0.2-4.9)	3
medium	2.1(1.1-4.0)	13	0.5(0.1-2.0)	3	0.8(0.2-2.9)	3	2.8 (0.9-8.9)	5
high	1.8(0.6-5.2)	4	0.4(0.1-1.6)	2	1.3(0.2-9.8)	1	-	0
	LD P trend=0.06		LD P trend=0.13		LD P trend=0.88		LD P trend=0.60	
	IWLD P trend=0.03		IWLD P trend=0.21		IWLD P trend=0.10		IWLD P trend=0.43	
Paraquat (bi-pyridylium)								
None	1.0 (ref)	48	1.0 (ref)	37	1.0 (ref)	15	1.0 (ref)	14
low	1.0(0.4-2.4)	5	2.4(0.9-6.7)	4	2.9(0.7-12.7)	2	-	1
medium	1.0(0.2-4.0)	2	0.7-0.2-2.3)	3	1.2(0.3-5.3)	2	-	1
high	1.0(0.3-3.2)	3	0.8(0.2-3.4)	2	1.0(0.1-7.6)	1	-	0
	Ld P trend=0.99		LD P trend=0.23		LD P trend=0.94		LD P trend=xxx	
	IWLD P trend=0.44		IWLD P trend=0.78		IWLD P trend=0.75		IWLD P trend=xxx	

Pendi-methalin (dinitro-aniline)								
None	1.0 (ref)	38	1.0 (ref)	28	1.0 (ref)	11	1.0 (ref)	8
low	1.2(0.6-2.2)	12	1.0(0.4-2.2)	9	1.4(0.5-4.2)	6	1.8 (0.5-6.2)	5
medium	1.2(0.6-2.7)	8	0.92(0.3-2.6)	6	1.5(0.4-5.4)	4	2.3 (0.6-8.9)	4
high	0.8(0.3-1.9)	6	0.8(0.3-2.1)	5	1.4(0.5-4.5)	4	1.8 (0.5-6.9)	3
	LD P trend=0.66		LD P trend=0.66		LD P trend=0.57		LD P trend=0.42	
	IWLD P trend=0.44		IWLD P trend= 0.88		IWLD P trend=0.49		IWLD P trend=0.70	
Trifluralin (dinitro-aniline)								
None	1.0 (ref)	45	1.0 (ref)	43	1.0 (ref)	25	1.0 (ref)	10
low	1.1(0.7-1.9)	23	0.9(0.5-1.7)	14	0.9(0.4-1.9)	8	1.2 (0.4-3.2)	7
medium	1.6(0.9-2.6)	21	0.8(0.4-1.7)	11	0.8(0.4-1.8)	8	2.7 (1.0-7.0)	7
high	1.1(0.6-1.9)	15	0.6(0.3-1.2)	11	0.8(0.3-1.9)	7	3.3 (1.2-9.1)	6
	LD P trend= 0.08		LD P trend=0.13		LD P trend=0.62		LD P trend=0.01	
	IWLD P trend=0.80		IWLD P trend=0.11		IWLD P trend=0.65		IWLD P trend=0.08	
2,4,5 T								
None	1.0 (ref)	37	1.0 (ref)	33	1.0 (ref)	14	1.0 (ref)	12
low	2.1(1.1-3.9)	14	1.3(0.6-3.0)	7	4.6(1.3-16.1)	3	-	3
medium	2.4(0.7-7.00	3	0.9(0.2-3.7)	2	2.1(0.6-7.2)	3	-	0
high	1.1(0.4-2.8)	5	1.3(0.4-4.3)	3	1.1(0.2-4.8)	2	-	1
	LD P trend= 0.33		LD P trend=0.71		LD P trend=0.73		LD P trend=xxx	
	IWLD P trend=0.83		IWLD P trend=0.90		IWLD P trend=0.80		IWLD P trend=0.97	

[1] Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

[2] Numbers do not sum to NHL subtype totals due to missing data

Supplemental Table 4. Insecticides, fungicide and fumigant exposure (life-time days) and age-adjusted risk of NHL by cell type (1993 through 2008).

	CLL, SLL, PLL, MCL		Diffuse Large B-cell		Follicular B-cell		Other B-cell types	
	RR (95% CI)	**n**	**RR (95% CI)**	**n**	**RR (95% CI)**	**n**	**RR (95% CI)**	n
Aldicarb								
None	1.0 (ref)	51	1.0 (ref)	40	1.0 (ref)	19	1.0 (ref)	15
low	1.9(0.3-13.4)	1	1.7(0.4-7.2)	2	6.1(0.8-45.7)	1	-	1
medium	0.95(0.1-6.9))	1	4.8(1.2-19.8)	2	1.2(0.2-9.4)	2	-	1
high	-	0	0.5(0.1-4.1)	1	-	0	-	0
	LD P trend=0.15		LD P trend=0.72		LD P trend=0.63		LD P trend=xxx	
	IWLD P trend=0.14		IWLD P trend=0.89		IWLD P trend=0.64		IWLD P trend=xxx	
Benomyl								
None	1.0 (ref)	52	1.0 (ref)	36	1.0 (ref)	18	1.0 (ref)	15
low	-	4	10.9(3.6-35.4)	3	1.3(0.2-9.7)	1		1
medium	-	0	1.2(0.4-3.4)	3	1.9(0.3-14.5)	1		0
high	-	0	3.4(0.8-14.1)	2	-	0		0
	LD P trend=		LD P trend=		LD P trend=		LD P trend=	
	IWLD P trend=		IWLD P trend=0.15		IWLD P trend=0.73		IWLD P trend=	
Carbaryl								
None	1.0 (ref)	32	1.0 (ref)	23	1.0 (ref)	9	1.0 (ref)	9
low	1.1(0.5-2.2)	15	0.7(0.3-1.5)	10	1.1(0.3-4.0)	5	xxx-	6

medium	1.0(0.2-4.2)	2	1.3(0.6-3.0)	8	1.8(0.6-5.9)	4	xxx-	0
high	0.4(0.2-0.8)	8	1.5(0.7-3.5)	8	1.3(0.4-4.1)	4	xxx-	1
	LD P trend=0.007		LD P trend=0.19		LD P trend=0.66		LD P trend=xxx	
	IWLD P trend=0.02		IWLD P trend=0.27		IWLD P trend=0.81		IWLD P trend=xxx	
Carbofuran								
None	1.0 (ref)	67	1.0 (ref)	58	1.0 (ref)	33	1.0 (ref)	19
low	1.4(0.8-2.5)	15	0.9(0.4-1.9)	8	0.96(0.4-2.5)	5	1.0 (0.4-2.7)	5
medium	1.2(0.6-2.4)	10	0.9(0.4-1.8)	9	1.6(0.7-3.9)	6	1.4(0.2-10.7)	1
high	1.3(0.7-2.4)	12	1.1(0.5-2.9)	5	0.6(0.2-2.0)	3	0.94(0.2-4.1)	2
	LD P trend=0.36		LD P trend=0.81		LD P trend=0.79		LD P trend=0.99	
	IWLD P trend=0.79		IWLD P trend=0.71		IWLD P trend=0.72		IWLD P trend=xxx	
Chlorpyrifos								
None	1.0 (ref)	69	1.0 (ref)	55	1.0 (ref)	26	1.0 (ref)	18
low	0.9(0.5-1.7)	15	1.2(0.6-2.1)	13	1.4(0.7-3.1)	10	0.9(0.3-2.6)	5
medium	1.1(0.7-2.0)	16	1.0(0.5-1.7)	15	1.2(0.5-2.9)	7	4.2(1.7-10.6)	6
high	1.0(0.5-1.7)	14	0.9(0.6-4.0)	7	1.4(0.6-3.4)	6	0.8(0.3-2.3)	4
	LD P trend=0.99		LD P trend=0.66		LD P trend=0.56		LD P trend=0.97	
	IWLD P trend=0.88		IWLD P trend=0.67		IWLD P trend=0.22		IWLD P trend=	
Chlorthalonil								
None	1.0 (ref)	107	1.0 (ref)	84	1.0 (ref)	45	1.0 (ref)	32
low	0.9(0.3-2.9)	3	1.6(0.4-6.6)	2	3.1(0.7-12.6)	2	-	1
medium	0.7(0.2-2.7)	2	1.4(0.3-5.6)	2	1.2(0.3-4.8)	2	-	0

high	0.7(0.2-2.7)	2	0.2(0.1-1.4)	1	0.6(0.1-4.4)	1	-	0
	LD P trend=0.46		LD P trend=0.11		LD P trend=0.61		LD P trend=xxx	
	IWLD P trend=0.96		IWLD P trend=0.17		IWLD P trend=0.41		IWLD P trend=xxx	
Coumaphos								
None	1.0 (ref)	92	1.0 (ref)	72	1.0 (ref)	42	1.0 (ref)	22
low	1.1(0.4-3.1)	4	0.7(0.2-2.3)	3	1.9(0.6-6.0)	3	xxx-	4
medium	2.0(0.8-4.9)	5	2.1(0.5-8.5)	2	0.5(0.1-4.0)	1	xxx-	0
high	1.3(0.4-4.0)	3	1.5(0.4-5.9)	2	2.2(0.3-16.3)	1	-	1
	LD P trend=0.36		LD P trend=0.47		LD P trend=0.43		LD P trend=xxx	
	IWLD P trend=0.53		IWLD P trend=0.74		IWLD P trend=0.82		IWLD P trend=xxx	
Diazinon								
None	1.0 (ref)	40	1.0 (ref)	33	1.0 (ref)	13	1.0 (ref)	12
low	1.5(0.7-3.1)	9	1.2(0.4-3.1)	5	1.6(0.4-5.5)	3	xxx-	2
medium	1.2(0.4-3.6)	5	0.9(0.3-2.8)	4	1.6(0.4-7.4)	3	xxx-	1
high	1.2(0.5-3.0)	5	1.2(0.4-3.8)	3	2.0(0.4-10.0)	2	xxx-	0
	LD P trend=0.72		LD P trend=0.84		LD P trend=0.35		LD P trend=xxx	
	IWLD P trend=0.60		IWLD P trend=0.84		IWLD P trend=0.53		IWLD P trend=xxx	
DDVP								
None	1.0 (ref)	95	1.0 (ref)	74	1.0 (ref)	43	1.0 (ref)	24
low	1.3(0.5-3.5)	4	4.1(1.0-16.9)	2	0.7(0.2-3.1)	2	xxx-	1
medium	1.4(0.6-3.4)	5	0.5(0.1-1.9)	2	2.2(0.3-16.1)	1	xxx-	2
high	0.3(0.1-2.1)	3	0.3(0.1-2.2)	1	0.5(0.1-	1	-xxx	0

					3.9)			
	LD P trend=0.46		LD P trend=0.25		LD P trend=0.54		LD P trend=xxx	
	IWLD P trend=0.85		IWLD P trend=0.54		IWLD P trend=0.53		IWLD P trend=xxx	
Fonofos								
None	1.0 (ref)	79	1.0 (ref)	61	1.0 (ref)	40	1.0 (ref)	17
low	1.6(.8-2.9)	12	1.5(0.8-3.1)	9	-	5	2.2(0.8-5.9)	5
medium	1.2(0.5-2.9)	5	1.0(0.4-2.3)	6	-	0	2.0(0.6-6.7)	3
high	0.9(0.5-2.0)	8	1.3(0.5-3.2)	5	-	2	2.3(0.3-17.0)	1
	LD P trend=0.88		LD P trend=0.62		LD P trend=0.20		LD P trend=0.19	
	IWLD P trend=0.94		IWLD P trend=0.77		IWLD P trend=0.18		IWLD P trend=xxx	
Lindane								
None	1.0 (ref)	41	1.0 (ref)	39	1.0 (ref)	14	1.0 (ref)	14
low	1.6(0.7-3.6)	8	0.7(0.2-3.0)	9	2.7(0.8-9.4)	3	xxx-	1
medium	1.1(0.3-4.8)	3	1.1(0.3-3.7)	6	3.6(0.8-15.9)	2	xxx-	0
high	3.8(1.5-9.6)	5	1.3(0.2-9.7)	5	2.4(0.5-10.4)	2	xxx-	0
	LD P trend=0.005		LD P trend=0.25		LD P trend=0.25		LD P trend=xxx	
	IWLD P trend=0.04		IWLD P trend=0.29		IWLD P trend=0.18		IWLD P trend=xxx	
Malathion								
None	1.0 (ref)	21	1.0 (ref)	16	1.0 (ref)	5	1.0 (ref)	6
low	0.94(0.5-1.8)	17	0.8(0.4-1.7)	16	1.0(0.3-3.6)	6	-xxx	8
medium	0.8(0.4-1.7)	11	0.9(0.4-2.1)	8	1.2(0.3-4.3)	5	-xxx	0
high	0.8(0.4-1.7)	11	1.7(0.8-3.8)	11	1.5(0.4-4.9)	5	-xxx	3
	LD P trend=0.52		LD P trend=0.07		LD P trend=0.48		LD P trend=xxx	

	IWLD P trend=0.24		IWLD P trend=0.33		IWLD P trend=0.56		IWLD P trend=xxx	
Maneb								
None	1.0 (ref)	52	1.0 (ref)	37	1.0 (ref)	19	1.0 (ref)	16
low	2.9(0.9-9.4)	3	2.6(0.6-10.9)	2	2.6(0.4-19.8)	1	-xxx	0
medium	1.6(0.4-6.6)	2	1.3(0.4-4.2)	3	1.1(0.1-8.0)	1	-xxx	0
high	0.3(0.1-2.4)	1	3.5(0.5-25.4)	1	-	0	-xxx	0
	LD P trend=0.43		LD P trend=0.19		LD P trend=0.55		LD P trend=xxx	
	IWLD P trend=0.49		IWLD P trend=0.17		IWLD P trend=0.66		IWLD P trend=xxx	
Metalaxyl								
None	1.0 (ref)	46	1.0 (ref)	34	1.0 (ref)	18	1.0 (ref)	
Low	3.9(1.7-9.3)	6	1.1(0.3-3.6)	4	0.8(0.2-3.4)	2	-xxx	
medium	1.3(0.3-5.4)	2	1.4(0.5-3.9)	5	2.1(0.5-9.2)	2	-xxx	
high	0.4(0.1-1.2)	3	0.9(0.2-4.0)	2	0.9(0.1-6.4)	1	-xxx	
	LD P trend=0.08		LD P trend=0.92		LD P trend=0.81		LD P trend=xxx	
	IWLD P trend=0.04		IWLD P trend=0.85		IWLD P trend=0.83		IWLD P trend=xxx	
Methylbromide								
None	1.0 (ref)	101	1.0 (ref)	65	1.0 (ref)	45	1.0 (ref)	14
low	0.8(0.3-2.1)	4	4.8(2.5-9.3)	10	1.4(0.3-5.8)	2	-xxx	1
medium	0.7(0.3-1.6)	5	1.3(0.6-3.1)	6	1.2(0.4-4.0)	3	-xxx	1
high	0.4(0.1-1.3)	3	1.2(0.5-2.6)	7	-	0	-xxx	0
	LD P trend=0.09		LD P trend=0.71		LD P trend=0.08		LD P trend=xxx	
	IWLD P trend=0.02		IWLD P trend=0.57		IWLD P trend=0.09		IWLD P trend=xxx	
Permethrin								

animals								
None	1.0 (ref)	95	1.0 (ref)	78	1.0 (ref)	38	1.0 (ref)	25
low	1.3(0.5-3.3)	5	0.2(0.1-1.3)	1	2.8(1.1-7.0)	5	-xxx	1
medium	0.9(0.2-3.7)	3	0.5(0.1-3.4)	1	2.9(0.7-12.0)	2	-xxx	2
high	0.8(0.3-2.5)	3	-	0	0.8(0.2-3.5)	2	-xxx	0
	LD P trend=0.75		LD P trend=0.19		LD P trend=0.93		LD P trend=0.87	
	IWLD P trend=0.70		IWLD P trend=0.29		IWLD P trend=0.73		IWLD P trend=xxx	
Permethrin crops								
None	1.0 (ref)	86	1.0 (ref)	72	1.0 (ref)	39	1.0 (ref)	23
low	1.9(0.6-5.4)	6	0.6(0.1-2.2)	3	1.1(0.3-3.5)	3	-xxx	4
medium	0.8(0.4-1.9)	6	2.7(0.7-10.6)	2	1.5(0.4-6.4)	2	-xxx	0
high	1.2(0.4-4.0)	4	0.4(0.1-1.8)	2	0.5(0.1-3.9)	2	-xxx	0
	LD P trend=0.76		LD P trend=0.28		LD P trend=0.57		LD P trend=0.37	
	IWLD P trend=0.70		IWLD P trend=0.33		IWLD P trend=0.45		IWLD P trend=xxx	
Phorate								
None	1.0 (ref)	36	1.0 (ref)	29	1.0 (ref)	15	1.0 (ref)	10
low	1.4(0.7-3.0)	9	1.0(0.4-2.6)	5	0.6(0.1-2.7)	2	1.4 (0.4-4.6)	4
medium	1.4(0.6-3.2)	6	2.0(0.9-4.7)	7	2.9(0.96-8.7)	4	1.5 (0.2-11.6)	1
high	0.94(0.4-2.4)	5	0.7(0.2-2.4)	3	-	0	1.4 (0.2-11.2)	1
	LD P trend=0.90		LD P trend=0.92		LD P trend=0.82		LD P trend=XXX	
	IWLD P trend=0.53		IWLD P trend=0.98		IWLD P trend=0.33		IWLD P trend=xxx	
Terbufos								

None	1.0 (ref)	53	1.0 (ref)	47	1.0 (ref)	26	1.0 (ref)	10
low	1.8(1.0-3.1)	17	0.9(0.4-1.7)	12	2.5(1.1-5.4)	8	2.3 (0.8-6.6)	6
medium	2.2(1.3-3.6)	21	2.2(1.2-4.2)	12	1.8(0.7-4.3)	7	3.1(1.1-9.2)	5
high	1.4(0.8-2.6)	13	1.1(0.5-2.3)	10	0.7(0.3-1.8)	6	4.1(1.4-11.9)	5
	LD P trend=0.16		LD P trend=0.34		LD P trend=0.54		LD P trend=0.01	
	IWLD P trend=0.14		IWLD P trend=0.40		IWLD P trend=0.18		IWLD P trend=xxx	

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)

Supplemental Table 5. Estimated individual and joint effects of pesticide combinations and age-adjusted risk of NHL		
Individual and joint pesticide exposures	**Exposed cases**	**Poisson Regression RR (95% CI)[1]**
Chlordane and DDT		
--Neither	174	1.0 (reference)
--Chlordane only	19	0.6 (0.4-1.0)
--DDT only	49	0.8(0.6-1.2)
--Both	56	0.9 (0.7-1.3)
Chlordane and Lindane		
--Neither	200	1.0 (reference)
--Chlordane only	47	0.8(0.6-1.2)
--Lindane only	23	1.0(0.6-1.5)
--both	28	1.0(0.7-1.6)
Lindane and dicamba		
--Neither	113	1.0 (reference)
--Lindane only	15	1.0 (0.6-1.7)
--dicamba only	120	1.3 (0.98-1.6)
--both	32	1.2 (0.8-1.8)
Atrazine and Chlordane		
--Neither	58	1.0 (reference)
--atrazine only	162	1.3(0.97-1.8)
--Chlordane only	19	1.0(0.6-1.7)
--Both	57	1.1(0.8-1.6)
2,4,5 t and Lindane		
--Neither	190	1.0 (reference)
--2,4,5-t only	57	1.1(0.9-1.6)

--Lindane only	27	1.1(0.7-1.6)
--Both	25	1.2 (0.8-1.8)
Atrazine and Lindane		
--Neither	73	1.0 (reference)
--Atrazine only	173	1.1 (0.9-1.5)
--Lindane only	4	0.5 (0.2-1.3)
--both	47	1.3 (0.9-1.9)
Atrazine and Dicamba		
--Neither	61	1.0 (reference)
--Atrazine only	72	1.0 (0.7-1.4)
--Dicamba only	17	1.0 (0.6-1.7)
--both	140	1.3 (0.97-1.8)
Atrazine and Carbofuran		
--Neither	68	1.0 (reference)
--Atrazine only	132	1.1 (0.9-1.5)
--Carbofuran only	9	0.9 (0.4-1.8)
--Both	81	1.2 (0.9-1.6)
Atrazine and Diazinon		
--Neither	58	1.0 (reference)
--atrazine only	163	1.2 (0.9-1.7)
--Diazinon only	20	0.9 (0.5-1.5)
--Both	59	1.1 (0.8-1.6)
Atrazine and alachlor		
--Neither	65	1.0 (reference)
--atrazine only	73	1.1 (0.8-1.5)

--alachlor only	16	0.8 (0.5-1.4)
--Both	146	1.1 (0.8-1.5)
2,4, 5 t and dicamba		
--Neither	94	1.0 (reference)
--2,4,5-t only	32	1.3 (0.9-1.9)
--dicamba only	107	1.4 (1.0-1.8)
--Both	45	1.3 (0.9-1.8)
2,4-D and Chlordane		
--Neither	55	1.0 (reference)
--2,4-D only	164	1.1(0.8-1.5)
--Chlordane only	7	0.7(0.3-1.5)
--Both	70	1.0 (0.7-1.5)
Glyphosate and atrazine		
--Neither	30	1.0 (reference)
--Glyphosate only	60	0.96(0.6-1.5)
--atrazine only	63	1.4(0.9-2.1)
--Both	171	1.1(0.7-1.6)
Glyphosate and 2,4-D		
--Neither	32	1.0 (reference)
--Glyphosate only	44	1.1(0.7-1.7)
--2,4-D only	61	1.4(0.9-2.1)
--Both	188	1.1(0.7-1.5)
Glyphosate and Chlordane		
--Neither	72	1.0 (reference)
--Glyphosate only	147	0.9 (0.7-1.2)

--chlordane only	13	1.0 (0.5-1.7)
--Both	64	0.8 (0.6-1.1)
2,4-D and Lindane		
---Neither	60	1.0 (reference)
---only 2,4-D	180	1.1(0.8-1.4)
---only lindane	3	0.6(0.2-1.8)
---both	48	1.2(0.8-1.7)
2,4-D and atrazine		
---Neither	41	1.0 (reference)
---only 2,4-D	49	1.0(0.7-1.5)
---only atrazine	35	1.2(0.8-1.9)
---both	199	1.2(0.8-1.7)
2,4-D and dicamba		
---Neither	51	1.0 (reference)
---only 2,4-D	81	0.9(0.6-1.3)
---only dicamba	13	1.2(0.7-2.2)
---both	144	1.2(0.9-1.7)
2,4-D and cyanazine		
---Neither	58	1.0 (reference)
---only 2,4-D	104	0.9(0.6-1.2)
---only cyanazine	11	0.9(0.5-1.7)
---both	130	1.2(0.9-1.6)
2,4-D and terbufos		
---Neither	48	1.0 (reference)
---only 2,4-D	113	1.0(0.7-1.5)

---only terbufos	16	1.7(0.97-3.0)
---both	115	1.5(1.0-2.0)
Cyanazine and atrazine		
---Neither	72	1.0 (reference)
---only cyanazine	11	1.3(0.7-2.4)
---only atrazine	90	1.0(0.8-1.4)
---both	130	1.3(0.97-1.7)

[1]Age adjusted (<45,45-49,50-54,55-59,60-64,65-69,≥70)