Impact of occupational pesticide exposure assessment method on risk estimates for prostate cancer, non-Hodgkin's lymphoma and Parkinson's disease: results of three meta-analyses

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ABSTRACT
Assessment of occupational pesticide exposure in epidemiological studies of chronic diseases is challenging. Biomonitoring of current pesticide levels might not correlate with past exposure relevant to disease aetiology, and indirect methods often rely on workers' imperfect recall of exposures, or job titles. We investigated how the applied exposure assessment method influenced risk estimates for some chronic diseases. In three meta-analyses the influence of exposure assessment method type on the summary risk ratio (sRR) of prostate cancer (PC) (25 articles), non-Hodgkin's lymphoma (NHL) (29 articles) and Parkinson's disease (PD) (32 articles) was investigated. Exposure assessment method types analysed were: group-level assessments (eg, job titles), self-reported exposures, expert-level assessments (eg, job-exposure matrices) and biomonitoring (eg, blood, urine). Additionally, sRRs were estimated by study design, publication year period and geographic location where the study was conducted. Exposure assessment method types were not associated with statistically significant different sRRs across any of the health outcomes. Heterogeneity in results varied from high in cancer studies to moderate and low in PD studies. Overall, case–control designs showed significantly higher sRR estimates than prospective cohort designs. Later NHL publications showed significantly higher sRR estimates than earlier. For PC, studies from North America showed significantly higher sRR estimates than studies from Europe. We conclude that exposure assessment method applied in studies of occupational exposure to pesticides appears not to have a significant effect on risk estimates for PC, NHL and PD. In systematic reviews of chronic health effects of occupational exposure to pesticides, epidemiological study design, publication year and geographic location, should primarily be considered.

INTRODUCTION
Retrospective assessment of occupational pesticide exposure in epidemiological studies of chronic diseases is challenging. The most specific exposure assessment method is biomonitoring, which primarily relies on sampling of biomarkers or metabolites in blood, urine or skin, or on personal sampling of workers' breathing zone or skin.[1] However, (bio)monitoring is complicated; exposures vary over time and in space,[2] many pesticides have short half-lives and multiple types of pesticides are often applied simultaneously.[3] Consequently, besides the case of persistent pesticides (mainly organochlorines), biomonitoring of current exposures may not correlate well with past exposures relevant to chronic disease aetiology. Therefore, long-term pesticide exposure might be better assessed using indirect methods such as assessments by job titles, workers' self-reported exposure or job-exposure matrices (JEMs). The choice of exposure assessment method is further heavily influenced by the type of study design and the composition and size of the study population.

We showed recently in a systematic review of epidemiological studies on occupational pesticide exposure that indirect methods comprise the majority of applied exposure assessment methods, and that prostate cancer (PC), non-Hodgkin's lymphoma (NHL) and Parkinson's disease (PD) are the most frequently studied health outcomes.[4] Thus, occupational pesticide exposure in relation to chronic diseases is assessed by several different, often indirect exposure assessment methods, complicating the interpretation of synthesised study results.

In meta-analyses of PC,[5–11] NHL[12–19] and PD,[20–27] bias resulting from heterogeneity associated with the use of different pesticide exposure assessment methods is often discussed, although seldom systematically quantified and analysed in relation to disease risk. Nevertheless, regarding PC, Lewis-Mikhael *et al*[9] reported that group-based exposure assessment methods yielded much higher risk estimates than measured serum pesticide levels. In contrast, Van Maele-Fabry and colleagues[5] found in studies of pesticide manufacturing workers that biomonitoring of serum, blood, fat and/or urine yielded the highest estimated risks, followed by assessments based on job title/work area. Smith and colleagues[19] evaluated NHL risk associated with 2,4-D exposure in (mainly) occupational studies, and found higher risks by expert assessments (informed by job titles, records, questionnaires and hygiene monitoring) compared with use of self-reported exposures. Regarding PD, van der Mark *et al*[24] found that job title assessments (including additional

Key messages

What is already known about this subject?

- ⇒ Retrospective assessment of occupational pesticide exposure in epidemiological studies of chronic diseases is challenging.
- ⇒ Exposure assessments are occasionally made using direct measurements by biomonitoring, but more frequently by indirect exposure assessment methods, such as assessments based on job titles and job-exposure matrices.
- ⇒ Previous studies have suggested that exposure assessment method might be related to different risk estimates of chronic diseases.

What are the new findings?

- ⇒ We conducted three meta-analyses to specifically investigate how the type of exposure assessment method influenced summary risk estimates of prostate cancer (PC), non-Hodgkin's lymphoma (NHL) and Parkinson's disease.
- ⇒ Exposure assessment method was not associated with significantly different summary risk estimates for any of the analysed health outcomes.
- ⇒ Study design (for cancer studies), publication year (for studies on NHL) and geographic region where the study was conducted (for PC), showed a larger effect on the summary risk estimates than the applied exposure assessment method.

How might this impact on policy or clinical practice in the foreseeable future?

- ⇒ These meta-analyses will inform researchers in the field of occupational pesticide epidemiology about the potential dependence of chronic disease risk estimates on different exposure assessment methods applied.
- ⇒ The results will guide the methodological improvement of studies on chronic disease in relation to occupational exposure to pesticides, and inform about potential sources of heterogeneity (including epidemiological study design, time period of publication and region where the study was conducted) regarding systematic reviews and meta-analyses.

incorporation of JEMs and expert assessments) resulted in the highest risks in occupational and non-occupational populations, and Yan *et al*[22] reported no difference in PD risk for exposures assessed by questionnaires and face-to-face interviews.

Thus, synthesised data suggest that occupational pesticide exposure assessments informed by workers' job title generally yield the highest risk estimates for PC, NHL and PD. We aimed to further analyse how the applied exposure assessment method influences assessed risks of these three chronic diseases.

METHODS

Within the IMPRESS project (www.impress-project.org) we conducted separate meta-analyses to systematically investigate how exposure assessment method applied in studies of strictly occupational pesticide exposure influences risk estimates of PC, NHL and PD, respectively. The meta-analyses were informed by articles retrieved in a recent systematic review performed by the authors, described elsewhere,[4] plus by a few new articles. Briefly, within the IMPRESS project a systematic review of articles on associations between occupational pesticide exposure and any type of health outcome published from 1 January 1993 to 31 December 2017 was performed (search syntax and retrieved articles were published as supplementary material).[4] The systematic review resulted in 1271 articles from which the lead author of this manuscript (JO) extracted exposure assessment method(s), study design, study location (country), health outcome, authors of article, year of publication and journal.[4] A second independent reviewer (HK) assessed a random selection of 5% of included articles for eligibility and extracted data, and a random selection of 1% of excluded articles for eligibility.[4]

Article selection

For the meta-analyses we extracted from the systematic review all articles on PC, NHL and PD or Parkinsonism. Additionally, the search syntax from the systematic review was reapplied (without limiting searches to articles published between 1 January 1993 to 31 December 2017) to retrieve relevant articles published before 1993 and after 2017 until end of 2020. Moreover, relevant articles in the bibliography of retrieved articles and published meta-analyses on named health outcomes were considered. The following eligibility criteria were applied to each article for inclusion into the meta-analyses:

- ► Peer-reviewed original publications on at least one of the three named chronic diseases in relation to occupational pesticide exposure.
- ► Case–control or cohort studies (prospective, retrospective). Cross-sectional and ecological studies were excluded to limit bias of pooled risk estimates in the meta-analyses.
- ► A reported relative risk (RR), HR, standardised incidence ratios (SIR), or OR associated with a defined exposure assessment method. Articles reporting (cause-specific) mortality rates were excluded as mortality rates might not properly reflect disease risk.
- ► Analyses based on at least five exposed cases.

Data extraction from articles

In addition to data from the systematic review, we extracted for the meta-analyses from each article the reported risk estimate, study population, sample size, number of cases and controls, type of pesticide(s) and type of exposure variable (eg, cumulative exposure). Included articles and extracted data are provided in online supplemental file 1. References to included articles and applied exposure assessment method(s) are described in online supplemental file 2.

For data extraction the following a priori determined criteria were applied:

- ► We extracted risk estimates corresponding to all applied exposure assessment methods in the included articles. As some articles reported risk estimates for more than one exposure assessment method the number of extracted risk estimates exceeds the number of included articles.
- ► The most fully adjusted risk estimate(s) in each article were preferred to less adjusted or crude risk estimates.
- ► We extracted risk estimates according to the following hierarchy of exposure variable categorisation: (a) cumulative exposure (including duration of exposure as a surrogate for cumulative exposure); (b) level of exposure by categories, for example, none/low/medium/high; (c) dichotomised exposure categories based on level, for example, low/high; (d) dichotomised categories based on prevalence of exposure, for example, never/ever.
- ► Where exposure assessment methods produced multiple risk estimates for different levels of (cumulative) exposure, we extracted the result for the highest exposure group, as this was based on the highest exposure contrast and, hence, most likely identify any effect of exposure, and less likely result

from chance, bias or confounding. Additionally, exposure assessment methods that generate risk estimates by level of exposure, for example, JEM, would lose an intrinsic methodological feature had risk estimates by different exposure levels been collapsed according to pesticide exposure (never/ever).

- We preferred risk estimates based on an unexposed control group instead of a low-exposed control group.
- For case–control studies, we preferred estimates based on population controls over hospital controls.
- When several risk estimates originated from the same study population, we selected the estimate based on the highest number of cases (often corresponding to the most recent publication).
- When risk estimates were reported by several different pesticide categories, risk estimates based on the exposure category 'pesticides in general/any pesticide' were preferred over estimates based on pesticide types (eg, insecticides), pesticide classes (eg, organochlorines) and specific pesticides. This approach maximised our number of exposed cases per exposure assessment method. If multiple risks by pesticide types, chemical classes or specific pesticides were reported we extracted the highest risk estimate.

Statistical analysis

Meta-analyses were performed using the R-package 'Metagen'. Risk estimates were pooled using the inverse variance method, expressed as a summary risk ratio (sRR). Heterogeneity was quantified using I^2 with its recommended cut-offs 25% (low), 50% (moderate) and 75% (high),[28] and with Cochran's Q statistics. Due to a relatively large heterogeneity of the results for most health outcomes (PC I^2=87.3%, NHL I^2=66.8%, PD I^2=42.4%) we used random effects models for pooling effects, according to DerSimonian and Laird.[29]

The influence of exposure assessment method on the sRR of selected health outcomes was investigated using subgroup analyses by exposure assessment method type in the meta-analyses. The following categories of exposure assessment method types were applied in the analyses:

- Group-level assessments (job titles, self-reported job histories, exposure registers, registers of licensed pesticide appliers).
- Self-reported exposures (by questionnaires or interviews).
- Expert level assessments (expert case-by-case assessments, JEMs, crop-exposure matrices (CEM), algorithms).
- Biomonitoring (blood, urine, adipose tissue).

Exposure assessment methods were categorised by the level of specificity of exposure assessment. Thus, although job titles inform for example, JEM assignments, these were considered different types of exposure assessment method. Further, categorisation was made by the highest level of specificity of exposure assessment applied, meaning that, for example, expert-based exposure assessments based on self-reports were categorised as expert-level assessments. For the subgroup analyses a mixed-effects model was applied; random effects for pooling effects within each subgroup, and fixed effects for comparing sRR between subgroups. Additionally, sRR estimates were calculated by study design (prospective cohort studies, retrospective cohort studies and case–control studies), time period of publication (before and after the median publication year per health outcome) and by study location (Europe, North America or other countries).

As exposure assessment method and study design are closely related[4] we additionally analysed the influence of exposure assessment method type on sRR estimates within case–control studies only. The sample size was insufficient to conduct (meaningful) similar analyses in prospective and retrospective cohort studies, respectively.

For PD, sensitivity analyses were made through excluding some few eligible articles that did not report on the number of exposed cases. Moreover, as a sensitivity analysis for NHL, we excluded articles that used a combination of NHL and chronic lymphocytic leukaemia as health outcome. Finally, to analyse the impact of each study on the overall sRR we performed for each health outcome leave-one-out analyses among all included studies.

RESULTS

Prostate cancer

In total 25 articles were included in the meta-analysis of occupational pesticide exposure and PC (online supplemental files S1 and S2). Of these, 17 originated from our systematic review, 1 article was published after 2017[30] and 7 articles were not previously retrieved in the systematic review (these were not captured by the search algorithm as they did not mention pesticide-related terms in title/abstract or index terms, or were previously not accessible to the authors).[31–37] The articles were published between 1995 and 2019 and described prospective cohort studies (n=5), retrospective cohort studies (n=8) and case–control studies (n=12). The included articles reported studies from North America (n=12), Europe (n=11) and other countries (n=2).

In the 25 articles, a total of 27 risk estimates for PC were reported for the following exposure assessment methods (online supplemental file 2): job titles (n=5), self-reported job histories (n=1), exposure registers (n=3), records of pesticide licenses (n=4), self-reported exposures (n=5), JEM (n=2), expert assessments (n=6) and biomonitoring of blood (n=1).

Sub-group analyses and sensitivity analyses

Subgroup meta-analysis of the 27 risk estimates of PC by exposure assessment method showed no statistically significant differences in sRR (table 1, online supplemental figure S3.1). The heterogeneity in risk estimates was high for all exposure assessment methods.

Subgroup analyses by study design showed a significantly higher sRR for case–control studies compared with prospective cohort studies (sRR=1.63 vs sRR=1.08) (table 1, online supplemental figure S3.2). There was no difference in sRR estimates between studies from earlier years compared with later years (sRR=1.12 vs sRR=1.11) (table 1, online supplemental figure S3.3). Studies from North America showed a significantly higher sRR compared with studies from Europe (sRR=1.28 vs sRR=1.03) (table 1, online supplemental figure S3.4).

Within case–control studies of PC, no significant differences in sRR estimates by exposure assessment method were observed (table 1).

In the publication period 2007–2019, the sRR by expert-level and self-reported assessments were higher than the sRR estimate by group-level (sRR=2.00 and sRR=1.57 vs sRR=1.08) (table 1).

The leave-one-out analysis showed throughout all iterations a similar significant increased overall sRR (data not shown).

Table 1 Pooled risk estimates for prostate cancer by exposure assessment method, study design, publication year period and geographic region, based on meta-analysis of articles on occupational pesticide exposure published between 1995 and 2019.

	Number of risk estimates	sRR	95% CI	Heterogeneity measures I^2 (%)	P value	Q	P value
Exposure assessment method						3.28	0.35
Group-level	13	1.09	1.00 to 1.20	92	<0.01		
Self-reported exposure	5	1.35	0.95 to 1.94	76	<0.01		
Expert-level	8	1.41	0.99 to 2.01	79	<0.01		
Biomonitoring	1	1.32	0.75 to 2.33	.	.		
Study design						7.59	<0.02
Cohort (prospective)	5	1.08	1.03 to 1.14	64	<0.01		
Cohort (retrospective)	8	1.09	0.90 to 1.31	95	<0.01		
Case–control	12	1.63	1.22 to 2.18	79	<0.01		
Publication year period						0.01	0.93
1995–2006	14	1.12	0.94 to 1.35	92	<0.01		
2007–2019	13	1.11	1.04 to 1.19	77	<0.01		
Geographic region						9.15	<0.01
Europe	12	1.03	0.96 to 1.11	66	<0.01		
North America	13	1.28	1.13 to 1.45	92	<0.01		
Other	2	2.17	0.42 to 11.4	86	<0.01		
Case–control studies only							
Exposure assessment method						1.15	0.56
Group-level	1	2.37	1.22 to 4.61	.	.		
Self-reported exposure	4	1.53	0.89 to 2.62	68	0.02		
Expert-level	7	1.63	1.11 to 2.40	79	<0.01		
Exposure assessment method during publication year periods							
1995–2006							
Exposure assessment method						0.53	0.91
Group-level	7	1.16	0.87 to 1.55	95	<0.01		
Self-reported exposure	2	1.02	0.45 to 2.33	67	0.08		
Expert-level	4	1.04	0.69 to 1.57	70	0.02		
Biomonitoring	1	1.32	0.75 to 2.33	.	.		
2007–2019							
Exposure assessment method						5.8	0.05
Group-level	6	1.08	1.02 to 1.14	73	<0.01		
Self-reported exposure	3	1.57	0.96 to 2.56	85	<0.01		
Expert-level	4	2.00	1.07 to 3.75	76	<0.01		

I^2=percentage of variation across studies due to heterogeneity
Q=Cochran's Q.
sRR, summary risk ratio.

NON-HODGKIN'S LYMPHOMA

In total 29 articles were included in the meta-analysis of NHL (online supplemental files S1 and S2). Of these 24 articles originated from our systematic review, 2 articles were published before 1993[38 39] and 3 studies were not retrieved in our systematic review (these were not captured by the search algorithm as they did not mention work-related terms in title/abstract, or were previously not accessible to authors).[40–42] The articles were published between 1987 and 2017 and described prospective cohort studies (n=5), retrospective cohort studies (n=3) and case–control studies (n=21).

The 29 articles reported in total 40 risk estimates according to the following exposure assessment methods (online supplemental file S2): job titles (n=10), self-reported job histories (n=4), exposure registers (n=3), self-reported exposures (n=13), JEM (n=2), CEM (n=1), expert assessments (n=6) and exposure algorithm (n=1).

Subgroup analyses and sensitivity analyses

Subgroup meta-analysis of the 40 NHL risk estimates by exposure assessment method did not show significant differences in sRR estimates (table 2, online supplemental figure S3.5). However, expert-level assessments showed the highest sRR (sRR=1.74), followed by self-reported exposure (sRR=1.49) and group-level assessment (sRR=1.21). The sRR for all exposure assessment methods were significantly raised, and showed no heterogeneity for expert-level assessments, and moderate to high heterogeneity for group-level assessments and self-reported exposures (I^2=0%–76%). Case–control studies of NHL had a significantly higher sRR than prospective cohort studies (sRR=1.66 vs sRR=1.04) (table 2, online supplemental figure S3.6). The sRR for NHL in studies published as of 2006 was significantly higher than for studies published before 2006 (sRR=1.59 vs sRR=1.15) (table 2, online supplemental figure S3.7). Geographical region showed no statistically significant differences in sRR; all regions had sRR estimates that were significantly raised varying between (sRR=1.27–1.77) (table 2, online supplemental figure S3.8).

Within case–control studies the sRR estimates by exposure assessment method were very similar (table 2).

In the period 2006–2017, the sRR by expert-level and self-reported assessments were slightly higher than the sRR estimate by group-level (sRR=1.88 and sRR=1.94 vs sRR=1.35) (table 2).

All results remained largely unaffected when excluding two studies that analysed NHL and chronic lymphocytic leukaemia combined (data not shown). The leave-one-out analysis showed throughout all iterations a significant increased overall sRR.

Parkinson's disease

In total 32 articles were included for the meta-analysis of exposure assessment method and risk of PD (online supplemental files S1 and S2). Of these 23 originated from our systematic review, 2 articles were published before 1993,[43 44] 2 were published after 2017,[45 46] 4 articles were not retrieved in our systematic review (these were not captured by the search algorithm as they did not mention occupational terms in title/abstract, or any pesticide related terms in title/abstract or index terms)[47–50] and 1 article was at the time of systematic review analysis not accessible to the authors in full text.[51] Included articles were published between 1990 and 2020 and described prospective cohort studies (n=7), retrospective cohort studies (n=1) and case–control studies (n=24).

Table 2 Pooled risk estimates for non-Hodgkin's lymphoma by exposure assessment method, study design, publication year period and geographic region, based on meta-analysis of articles on occupational pesticide exposure published between 1987 and 2017.

	Number of risk estimates	sRR	95% CI	Heterogeneity measures			
				I^2 (%)	P value	Q	P value
Exposure assessment method						6.23	0.07
Group-level	17	1.21	1.05 to 1.40	63	<0.01		
Self-reported exposure	13	1.49	1.16 to 1.91	76	<0.01		
Expert-level	10	1.74	1.39 to 2.19	0	0.68		
Study design						22.1	<0.01
Cohort (prospective)	8	1.04	0.96 to 1.13	23	0.24		
Cohort (retrospective)	4	1.11	0.89 to 1.39	11	0.34		
Case–control	28	1.66	1.39 to 1.98	57	<0.01		
Publication year period							
1987–2005	19	1.15	1.00 to 1.32	21	0.2	8.5	<0.01
2006–2017	21	1.59	1.34 to 1.87	78	<0.01		
Geographic region						3.89	0.14
Europe	18	1.42	1.13 to 1.77	55	<0.01		
North America	18	1.27	1.10 to 1.47	70	<0.01		
Other	4	1.77	1.31 to 2.39	38	0.18		
Case–control studies only							
Exposure assessment method						0.1	0.95
Group-level	9	1.63	1.20 to 2.21	61	<0.01		
Self-reported exposure	11	1.67	1.21 to 2.31	71	<0.01		
Expert-level	8	1.73	1.33 to 2.27	0	0.47		
Exposure assessment method during publication year periods							
1987–2005							
Exposure assessment method						2.30	0.32
Group-level	8	1.04	0.83 to 1.28	31	0.18		
Self-reported exposure	8	1.26	1.05 to 1.51	0	0.51		
Expert-level	3	1.37	0.86 to 2.17	0	0.51		
2006–2017							
Exposure assessment method						4.68	0.1
Group-level	9	1.35	1.11 to 1.64	74	<0.01		
Self-reported exposure	5	1.94	1.14 to 3.30	91	<0.01		
Expert-level	7	1.88	1.45 to 2.24	0	0.7		

I^2=percentage of variation across studies due to heterogeneity. Q=Cochran's Q.
sRR, summary risk ratio.

Table 3 Pooled risk estimates for Parkinson's disease by exposure assessment method, study design, publication year period and geographic region, based on meta-analysis of articles on occupational pesticide exposure published between 1990 and 2020.

	Number of risk estimates	sRR	95% CI	Heterogeneity measures			
				I^2 (%)	P value	Q	P value
Exposure assessment method						1.20	0.55
Group-level	6	1.34	1.16 to 1.54	0	0.54		
Self-reported exposure	22	1.45	1.18 to 1.76	56	<0.01		
Expert level	9	1.56	1.21 to 2.01	18	0.28		
Study design						2.82	0.24
Cohort (prospective)	8	1.28	0.95 to 1.73	63	<0.01		
Cohort (retrospective)	1	1.14	0.77 to 1.68	.	.		
Case–control	28	1.54	1.34 to 1.77	27	0.09		
Publication year period						1.49	0.22
1990–2006	19	1.58	1.32 to 1.89	36	0.06		
2007–2020	18	1.34	1.12 to 1.62	48	0.01		
Geographic region						1.92	0.38
Europe	14	1.47	1.21 to 1.79	37	0.08		
USA	19	1.53	1.24 to 1.88	51	<0.01		
Other	4	1.17	0.85 to 1.62	30	0.23		
Case–control studies only							
Exposure assessment method						0.60	0.74
Group-level	3	1.48	1.02 to 2.15	0	0.39		
Self-reported exposure	20	1.51	1.24 to 1.83	42	0.02		
Expert level	5	1.70	1.31 to 2.2	0	0.88		
Exposure assessment method during publication year periods							
1990–2006							
Exposure assessment method						1.24	0.54
Group-level	3	1.57	1.09 to 2.27	37	0.20		
Self-reported exposure	13	1.52	1.2 to 1.93	37	0.09		
Expert level	3	2.38	1.12 to 5.03	28	0.25		
2007–2020							
Exposure assessment method						0.62	0.73
Group-level	3	1.23	0.93 to 1.62	0	0.83		
Self-reported exposure	9	1.34	0.95 to 1.88	70	>0.01		
Expert level	6	1.42	1.12 to 1.81	0	0.49		

I^2=percentage of variation across studies due to heterogeneity. Q=Cochran's Q.
sRR, summary risk ratio.

In the 32 articles in total 37 risk estimates for PD were reported for the following exposure assessment methods (online supplemental file S2): job titles (n=4), self-reported job histories (n=2), self-reported exposures (n=22), JEM (n=7) and expert assessments (n=2).

Sub-group analyses and sensitivity analyses

Subgroup meta-analysis of the 37 PD risk estimates by exposure assessment method showed no significant differences in sRR estimates (table 3, online supplemental figure S3.9). The sRR for all exposure assessment methods were significantly raised (varying between 1.34 and 1.56), and showed low to moderate degrees of heterogeneity (I^2=0%–56%).

Type of study design, publication year period and geographic region showed no significant differences in sRR estimates for PD (table 3, online supplemental figures S3.10–S3.12).

Further, no difference in sRR estimates by exposure assessment method was found when analysed by publication year periods.

Within case–control studies the sRR were similar for the different exposure assessment methods, with slightly higher sRR for expert-level assessments (sRR=1.70) compared with self-reported exposure (sRR=1.51) and group-level assessments (sRR=1.48) (table 3).

All results remained largely unaffected (data not shown) when excluding the four PD studies that did not report the number of exposed cases (online supplemental file S1). The leave-one-out analysis showed throughout all iterations a significantly increased overall sRR (data not shown).

DISCUSSION

In three meta-analyses of the association between occupational exposure to pesticides and PC, NHL and PD, we found no statistically significant differences in sRRs estimates for applied exposure assessment methods. The heterogeneity in risk estimates varied from high in cancer studies, to moderate and low in PD studies. For cancer studies, study design appeared to be the most significant source of heterogeneity, with significantly higher sRR in case–control studies compared with prospective cohort studies. Further analyses by publication year periods showed higher sRR estimates in later NHL publications, and analyses by geographic location where the study was conducted showed significantly higher sRR estimates for PC studies conducted in North America compared with those conducted in Europe. Finally, slightly higher sRRs for PC and NHL were found for self-reported exposures and expert-level assessments in the later publication year periods.

Prostate cancer

Based on 25 studies (27 risk estimates) published 1995–2019 we found no significant differences in sRRs for PC by different exposure assessment methods. In contrast, Lewis-Mikhael *et al*[9] reported based on 25 studies published between 1985 and 2014 that group-based exposure assessments resulted in the highest risk (pooled OR=2.24 95% CI 1.36 to 3.11). Our group-level estimate (sRR=1.09 95% CI 1.00 to 1.20) was, however, based on 12 studies (13 risk estimates), whereas that of Lewis-Mikhael was based on only three studies. Our results also differ from those of Van Maele-Fabry,[5] who in 18 studies of pesticide manufacturing workers published between 1984 and 2004 found the highest risk by biomonitoring of serum, blood, fat and/or urine (sRR=1.59 95% CI 1.05 to 2.41), followed by assessments by job title/history of work area (sRR=1.22 95% CI 0.86 to 1.72), JEM (sRR=1.19 95% CI 0.86 to 1.67) and model-based estimates of cumulative dose (sRR=1.1 95% CI 0.3 to 2.8). Nevertheless, comparability with our results is limited as we included also pesticide applicators in agriculture. Additionally, we used a different categorisation of exposure assessment methods, and excluded studies analysing mortality rates of which many were biomonitoring studies.

Further, PC studies conducted in North America showed higher sRR than those conducted in Europe. This difference might be partly attributable to the large difference in bans of specific pesticides in the USA and the European Union (EU). Donley[52] showed that pesticides banned in the EU accounted for more than 25% of agricultural pesticides applied in the USA in 2016. These included, for example, terbufos which has been linked to increased PC risks.[53]

Non-Hodgkin's lymphoma

For NHL, we found based on 29 articles (40 risk estimates) published between 1987 and 2017 the highest and uniform sRR in studies applying expert-level assessments (sRR=1.74 95% CI 1.39 to 2.18). Overall, however, differences in sRR by exposure assessment method were not statistically significant. In their meta-analysis of 23 studies of occupational and non-occupational 2,4-D exposure, Smith and colleagues[19] also reported the highest pooled risk from expert assessments (informed by job titles, records, questionnaires and hygiene monitoring) (pooled RR=2.17 95% CI 1.03 to 4.58), followed by self-reported exposures (pooled RR=1.47 95% CI 0.89 to 2.44). Interestingly, our meta-analysis and that of Smith *et al*[19] produced sRR estimates based on the highest level of exposure available in each included article. In individual studies, Nanni *et al* compared self-reported exposures with assessments by CEM and found almost the same risk estimates of NHL and CLL for the two methods (OR=1.74 vs. OR=1.70).[54]

Parkinson's disease

Also for PD we found, based on 32 studies (37 risk estimates), no difference in sRR estimates by exposure assessment method. In contrast, van der Mark *et al*[24] reported in a meta-analysis of 39 studies of occupational and non-occupational pesticide exposure and PD the highest sRR in studies that assigned exposure informed by job titles (applied exposure assessment methods were expert assessments, and JEM) (sRR=2.50 95% CI 1.54 to 4.05). However, their finding[24] was based on three studies whereas our estimate was based on seven studies. Moreover, the sRR estimates in our meta-analysis for PD varied the least with respect to exposure assessment method. The lower heterogeneity might be related to that, in contrast to PC and NHL, we found no significant influence by study design, publication year periods or geographic location in PD studies. Regarding individual studies, van der Mark *et al*[55] compared PD risk in a hospital-based case–control study by JEM (assessing pesticides in general, and classes of pesticides), exposure algorithm (assessing classes of pesticides) and CEM (assessing specific pesticides), and found generally no significant differences in risk estimates. Rugbjerg *et al*,[56] however, found in a population-based case–control study that PD risk based on self-reported exposures were reduced when restricted to subjects considered exposed according to hygiene-reviews.

Exposure misclassification

Cancer studies applied most frequently group-level assignments. Generally, one would expect a lower degree of exposure misclassification in studies that apply higher quality assessment, such as JEM.[57] However, whether for example, group-level assignments will misclassify workers' exposure depends on factors including analysed exposure, completeness of job histories and type of group-level assessment applied.[58] For example, exposure misclassification resulting from assessments based on registers of licensed pesticide users should be lower compared with using farm-related job titles, which might over-estimate workers' exposure.[59] Generally, differential exposure misclassification is assumed to be relatively low when assessments are informed by job titles, which is mainly the case for group-level assessment and expert-level assessments. Thus, the overall lack of statistically significant differences in sRR between group-level assessment and expert-level assessments might be partly related to that assessments informed by job titles on average quite well capture and classify long-term pesticide exposure relevant for the development of analysed chronic diseases. In PD studies self-reported exposures were most frequently applied. In the Agricultural Health Study, self-reports regarding use and use duration have been shown to assign accurate, somewhat underestimated, exposures.[60] However, recall bias from self-reports particularly in case–control studies within the general population might generate false-positive associations, or, particularly in PD studies, possibly also false-negative associations as cases might under-report exposure due to cognitive deficits.

Analyses by study design

Regarding all analysed health outcomes, a large part of the observed study heterogeneity was driven by study design rather than by differences in applied exposure assessment method. For PC and NHL, case–control studies showed significantly higher sRR estimates than prospective cohort studies. For NHL, similar results were found in studies of organophosphate pesticides with increased risks in case–control studies (pooled OR=1.44 95% CI 1.14 to 1.81) and nested case–control studies (pooled OR=1.57 95% CI 1.04 to 2.39), but not in cohort studies (pooled OR=1.00 95% CI 0.85 to 1.17).[18] Similarly, in occupational and some non-occupational studies of organochlorine pesticides and NHL consistently higher pooled risks estimates were found in case–control studies (pooled OR=1.40 95% CI 1.22 to 1.59) and in nested case–control studies (pooled OR=1.54 95% CI 1.27 to 1.87), compared with case-cohort designs (pooled OR=1.13 95% CI 0.82 to 1.55).[61] Generally, the lower sRR estimates in prospective cohort studies compared with case–control studies might result from agricultural cohort studies (66% of our analysed prospective cohort studies) not having completely unexposed control groups, as indicated by generally higher risks of, for example, PC compared with the general population,[62] which potentially dilutes the pooled effect in agricultural cohort studies. Additionally, the higher sRR in case–control studies might be related to recall bias resulting from cases' potential over-reporting of exposure compared with controls.

Sensitivity analyses in case–control studies

Throughout all health outcomes, no significant differences in sRR by exposure assessment method were seen in case–control studies only. However, although not significant, expert-level assessments yielded for PD case–control studies a higher sRR estimate than self-reported exposures. This difference might be related to the aforementioned low degree of differential exposure misclassification associated with assessments informed by job titles (eg, in expert-level assessments). JEM, for example, assign exposure in a standardised group-based approach with exposure misclassification expected to be non-differential, and due to Berkson-type error classification will result in little or no bias in risk estimates.[58] Thus, the comparatively higher sRR estimates from expert-level assessments should not result from bias away from the null. Instead, as suggested by van der Mark,[24] who reported similar results in studies of PD, the comparatively lower sRR estimate from self-reported exposures might rather result from workers' inability to reliably remember and report exposure (especially at the level of specific pesticides), which is expected to result in non-differential misclassification of exposure and bias towards the null.[24] The lower sRR by self-reported exposures might also be related to PD cases' potential underestimation of exposure due to aforementioned cognitive deficits.

Analyses by publication year periods

Studies of NHL showed higher sRR estimates in later publication years. Additionally, slightly higher sRR for PC and NHL were found for self-reported exposures and expert-level assessments in later publication years. These changes are not explained by concurrent changes in type of study design; case–control studies, which showed the highest sRR regardless health outcome, were less frequently applied in later NHL studies and equally applied in early and late PC publications (results not shown). Publication year will partly correlate with years of pesticide exposure, and might thus reflect changes in used active ingredients and levels of exposure over time (although year of banning certain pesticides differ between countries[52]). Nevertheless, publication year correlates better with time of outcome assessment for chronic diseases (particularly for case–control studies). As the disease classification system for NHL changed in 2000 to cover subtypes of NHL,[63] the inclusion of more specific health outcomes in recent studies might have enabled the detection of associations previously undiscovered. Moreover, in present analyses later NHL studies applied less frequently group-level assessments and/or self-reported exposures, and more frequently expert-level assessments. Thus, higher sRR estimates seen in later NHL publications might partly reflect an increased probability of less error-prone (expert-level) exposure assessment methods to yield less towards-the-null biased associations. However, the superiority of expert-level assignments is dependent on the (quality of) exposure information available.

Study strengths

Presumably, this is the most comprehensive analysis of how estimated chronic disease risk depends on exposure assessment method applied in epidemiological studies of occupational exposure to pesticides, comprising three frequently analysed chronic diseases and four types of exposure assessment methods. As the objective of this meta-analysis was not to re-analyse the estimated risk of PC, NHL and PD, respectively, associated with occupational pesticide exposure, we extracted all risk estimates associated with all exposure assessment methods documented in the selected publications. This maximised the contrast in our subgroup analyses by exposure assessment method type. As the sRR in subgroup-analyses by exposure assessment method types were based partly on risk estimates generated from the same study population, these should be less influenced by between-study characteristics that evidently contribute to heterogeneity of results in meta-analyses. Additionally, we extracted risk estimates associated with the highest level of exposure, a method less prone to chance findings.[64] Assessment and classification of workers by level of (cumulative) exposure is a feature related to exposure assessment method, and is more common in more refined methods (mainly in those applying expert-level assessments). We did not collapse risk estimates within a study into pesticide exposure (never/ever), as this would have omitted an inherent methodological advantage of more refined exposure assessment methods.

Study limitations

The level of specificity at which each exposure assessment method assesses exposure, and its effect on the association between exposure assessment method type and risk of chronic disease, was not specifically considered in our analyses. We extracted primarily risk estimates according to populations exposed to 'pesticides in general'/'any pesticide', which enabled analyses of more exposed cases than had we extracted risk estimates by categories of pesticide exposure, for example, by specific pesticides. Nevertheless, inclusion of studies that assessed exposure at different levels of specificity might have contributed to a more representative estimate of how, for example, the exposure assessment method 'self-reported exposures' is associated with chronic disease risk. Further, we only included one study that assigned exposure based on biomonitoring. This partly resulted from biomonitoring studies being almost only applied in cross-sectional studies, and rarely in studies of cancer or doctor-diagnosed neurological health outcomes (notably PD).[4]

CONCLUSION

The method for assigning workers' occupational pesticide exposure appears not to result in different sRR estimates for PC, NHL and PD. Overall, study design, publication year and geographic region where the study was conducted, showed larger effects on estimated sRRs than exposure assessment method. When performing systematic reviews of studies on chronic health effects of occupational pesticide exposure, epidemiological study design, publication year and region where the study was performed, should primarily be considered.

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Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Demers 2006. Exp. AI	Cancer and occupational exposure to pentachlorophenol and tetrachlorophenol (Canada)	2006	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Retrospective cohort	Sawmill workers	27464	92		17	5+ exposure years of cumulative dermal pentachlorophenol exposure.	RR	1.71	0.91	3.24	Pentachlorophenol	Canada
Demers 2006. JT. GenP	Cancer and occupational exposure to pentachlorophenol and tetrachlorophenol (Canada)	2006	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Retrospective cohort	Sawmill workers	27464	92		92	Standardized incidence rates calculated based on comparison with British Columbia provincial rates.	SIR	0.99	0.81	1.21	Pesticides in general	Canada
Lynge 1998. Class	Cancer incidence in Danish phenoxy herbicide workers, 1947-1993	1998	Non-Hodgkin's lymphoma	Registers	Group-based assessment	Retrospective cohort	Pesticide manufacturers	2119	6		6	Workers exposure classified based on their work area listed in personnel files.	SIR	1.10	0.4	2.6	Phenoxy herbicides	Denmark
Alavanja 2014. AI	Non-hodgkin lymphoma risk and insecticide, fungicide and fumigant use in the agricultural health study	2014	Non-Hodgkin's lymphoma	Algorithm/model	Expert-level assessment	Prospective cohort	Pesticide applicators from AHS	54306	523		14	Intensity-weighted lifetime days.	RR	1.8	1.0	3.2	Lindane	USA
Kachuri 2017. M. GenP	Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)	2017	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Agricultural workers	70570	500		500	Agricultural worker versus not agricultural worker in all other members of the cohort.	HR	1.10	1.00	1.21	Pesticides in general	Canada
Kachuri 2017.W. GenP	Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)	2017	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Agricultural workers	70570	135		135	Agricultural worker versus not agricultural worker in all other members of the cohort.	HR	1.02	0.86	1.22	Pesticides in general	Canada
Lemarchand 2017. M. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Prospective cohort	Farmers (as insured by MSA in France)	98794	644		310	Pesticide use on crops (yes versus no)	SIR	1.01	0.90	1.12	Pesticides in general	USA
Lemarchand 2017. W. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Prospective cohort	Farmers (as insured by MSA in France)	98794	367		48	Pesticide use on crops (yes versus no)	SIR	1.10	0.81	1.45	Pesticides in general	USA
Burns 2011. AI	Cancer incidence of 2,4-D production workers	2011	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Retrospective cohort	Pesticide manufacturers (male)	1256	14		14	Pesticide manufacturers versus rates for white males as comparison.	SIR	1.36	0.74	2.29	2.4D	USA
Wiklund 1987. Class	Risk of malignant lymphoma in Swedish pesticide appliers	1987	Non-Hodgkin's lymphoma	Self-reported job history	Group-based assessment	Prospective cohort	Pesticide applicators (mainly agricultural)	20245	21		12	Number of years since pesticide license. Highest category >10 years. Standardized incidence rates calculated for number of years since obtained pesticide license.	SIR	1.16	0.60	2.02	Phenoxy herbicides	Sweden
Kristensen 1996. M. GenP	Incidence and risk factors of cancer among men and women in Norwegian agriculture	1996	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Farmers	66080	69	NA	69	Incidence rates for working as a farmer compared with rural reference population.	SIR	0.82	0.64	1.03	Pesticides in general	Norway
Kristensen 1996. W. GenP	Incidence and risk factors of cancer among men and women in Norwegian agriculture	1996	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Farmers	30218	20	NA	20	Incidence rates for working as a farmer compared with rural reference population.	SIR	1.04	0.64	1.56	Pesticides in general	Norway
Kogevinas 1995. Class	Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: two nested case-control studies	1995	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Nested Case-control study	Pesticide manufacturers	21183	32		7	Level of exposure by categories (nonexposed, low, medium, high). Cumulative exposure lagged 5 years.	OR	1.36	0.46	4.03	Phenoxy herbicides	International
Hardell 2002. SRE. Type	Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies	2002	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Cases from cancer registries	1656	515	1141	18	Exposed versus non-exposed. Minimum exposure of 8 hours (one working day).	OR	2.02	0.97	4.23	Fungicides	Sweden
Ferri 2017. JEM. AI	Risk of lymphoma subtypes by occupational exposure in Southern Italy	2017	Non-Hodgkin's lymphoma	Job exposure matrix	Expert-level assessment	Case-control study	Population base	310	128	76	7	Medium-high cumulative exposure verus none.	OR	1.27	0.3	5.41	Paraquat	Italy
Ferri 2017. JT. GenP	Risk of lymphoma subtypes by occupational exposure in Southern Italy	2017	Non-Hodgkin's lymphoma	Self-reported job history	Group-based assessment	Case-control study	Population base	310	117	72	14	Agricultural worker versus not agricultural worker	OR	2.7	0.7	10.1	Pesticides in general	Italy
Balasubramaniam 2013. GenP	Case-control study of risk factors for Non-Hodgkin lymphoma in Mumbai, India	2013	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1771	388	1383	29	Ever versus never exposure.	OR	6.1	3.3	11.2	Pesticides in general	Canada
Zakerinia 2012. GenP	The relationship between exposure to pesticides and the occurrence of lymphoid neoplasm	2012	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Hospital base	400	200	200	34	Duration of exposure. High exposure is defined as >median number of years for exposed subjects.	OR	2.12	1.2	3.7	Pesticides in general	Iran
Wong 2010. SRE. Type	A hospital-based case-control study of non-Hodgkin lymphoid neoplasms in Shanghai: analysis of environmental and occupational risk factors by subtypes of the WHO classification	2010	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1947	649	1298	25	Ever exposure to pesticides	OR	1.77	1.02	3.05	Herbicides	China

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Wong 2010. JT. Type	A hospital-based case-control study of non-Hodgkin lymphoid neoplasms in Shanghai: analysis of environmental and occupational risk factors by subtypes of the WHO classification	2010	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Hospital base	1947	649	1298	195	Farmworker (all types)	OR	1.43	1.14	1.78	Pesticides in general	China
Orsi 2009. GenP	Occupational exposure to pesticides and lymphoid neoplasms among men: results of a French case-control study	2009	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Hospital base	680	244	436	32	Occupational pesticide use verified by experts.	OR	1.5	0.9	2.5	Pesticides in general	France
Richardson 2008. Type	Occupational risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Northern Germany	2008	Non-Hodgkin's lymphoma	Job exposure matrix	Expert-level assessment	Case-control study	Population base	767	242	525	23	Cumulative exposure defined as the product of cumulative hours worked in each exposed job, and the respective exposure intensity and probability scores.	OR	2.08	1.15	3.77	Herbicides	Germany
Orsi 2007. GenP	Occupation and lymphoid malignancies: results from a French case-control study	2007	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1100	399	701	14	Use of pesticides for crops at least once per week	OR	3.6	1.5	8.6	Pesticides in general	France
Rafnsson 2006. AI	Risk of non-Hodgkin's lymphoma and exposure to hexachlorocyclohexane, a nested case-control study	2006	Non-Hodgkin's lymphoma	Registers	Group-based assessment	Case-control study	Sheep owners	266	45	221	15	Number of dipped sheep (200-683). Proxy for the highest exposed.	OR	3.44	1.31	9.04	Hexachlorocyclohexane	Iceland
Miligi 2006. AI	Cancer and pesticides: an overview and some results of the Italian multicenter case-control study on hematolymphopoietic malignancies.	2006	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	2377	1145	1232	9	Probability of use >low and lack of protective equipment	OR	4.4	1.1	29.1	2.4D	Italy
Fritschi 2005. GenP	Occupational exposure to pesticides and risk of non-Hodgkin's lymphoma	2005	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1388	694	694	26	Substantial exposure versus none exposure.	OR	3.09	1.42	6.70	Pesticides in general	Australia
Mills 2005. AI	Lymphohematopoietic cancers in the United Farm Workers of America (UFW), 1988-2001	2005	Non-Hodgkin's lymphoma	Registers	Group-based assessment	Case-control study	Members of farmers union	360	60	300	60	The distribution of the 15 most commonly used pesticides (in pounds of active ingredient applied in counties where farm workers were employed) was examined, and cut points were created to construct categories in dichotomies of low versus high use or tertiles of use.	OR	3.8	1.85	7.81	2.4D	USA
Chiu 2004. Type	Agricultural pesticide use, familial cancer, and risk of non-Hodgkin lymphoma	2004	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	3790	937	2853	77	Ever versus never use.	OR	1.3	1.0	1.8	Fungicides	USA
Kato 2004. JT. GenP	Pesticide product use and risk of non-Hodgkin lymphoma in women	2004	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Population base	839	376	463	27	Highest number of years in any occupation with pesticide exposure.	OR	1.8	0.93	3.48	Pesticides in general	USA
Kato 2004. SRE. GenP	Pesticide product use and risk of non-Hodgkin lymphoma in women	2004	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	839	376	463	43	Applied pesticides on a farm (yes-no)	OR	1.18	0.59	2.38	Pesticides in general	USA
Briggs 2003. Afr.Am. GenP	Occupational risk factors for selected cancers among African American and White men in the United States	2003	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	2073	66	132	5	Ever versus never use.	OR	1.2	0.4	4.0	Pesticides in general	USA
Briggs 2003. White. GenP	Occupational risk factors for selected cancers among African American and White men in the United States	2003	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	2073	893	1488	92	Ever versus never use.	OR	0.9	0.6	1.7	Pesticides in general	USA
Fabbro-Peray. 2001. SRE. GenP	Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France	2001	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	1470	445	1025	41	Handling of pesticides	OR	1.0	0.7	1.6	Pesticides in general	France
Fabbro-Peray. 2001. JT. GenP	Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France	2001	Non-Hodgkin's lymphoma	Self-reported job history	Self-reported exposure	Case-control study	Population base	1470	445	1025	40	Agricultural occupation	OR	1.5	0.9	2.3	Pesticides in general	France
Fritschi 1996. GenP	Lymphoma, myeloma and occupation: results of a case-control study	1996	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1358	215	NA	6	Degree of expousre: non-exposed, non-substantial, substantial expousure.	OR	0.9	0.4	2.3	Pesticides in general	Canada
Nanni 1996. CEM. AI	Chronic lymphocytic leukaemias and non-Hodgkin's lymphomas by histological type in farming-animal breeding workers: a population case-control study based on a priori exposure matrices	1996	Non-Hodgkin's lymphoma	Crop exposure matrix	Expert-level assessment	Case-control study	Farmers	1164	187	977	28	Exposure to DDT according to crop exposure matrix.	OR	1.70	0.91	3.17	DDT	Italy
Nanni 1996. SRE. AI	Chronic lymphocytic leukaemias and non-Hodgkin's lymphomas by histological type in farming-animal breeding workers: a population case-control study based on a priori exposure matrices	1996	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Farmers	1164	187	977	27	Exposure to DDT (yes/no)	OR	1.74	0.93	3.27	DDT	Italy

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Hardell 1994. GenP	Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma.	1994	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Hospital base	94	20	74	20	Farmer (yes/no)	OR	0.7	0.4	1.4	Pesticides in general	Sweden
Woods 1989. JT. GenP	Non-Hodgkin's lymphoma among phenoxy herbicide-exposed farm workers in western Washington state	1989	Non-Hodgkin's lymphoma	Self-reported job history	Group-based assessment	Case-control study	Agricultural workers	377	181	196	181	Duration of work as a farmer.	OR	0.92	0.5	1.6	Pesticides in general	USA
Woods 1989. SRE.AI	Non-Hodgkin's lymphoma among phenoxy herbicide-exposed farm workers in western Washington state	1989	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Agricultural workers	377	181	196	NA	Regular work with DDT (yes/no)	OR	1.68	0.9	3.3	DDT	USA
Lerro 2019. Private. JT.GenP	Cancer incidence in the Agricultural Health Study after 20 years of follow-up	2019	Prostate cancer	Job title	Group-based assessment	Prospective cohort	Pesticide applicators (private) (agricultural)	51165	3169		3169	Incidence rates of prostate cancer for private applicators compared with rates for other cancers.	SIR	1.15	1.11	1.19	Pesticides in general	USA
Lerro 2019. Commercial. JT. GenP	Cancer incidence in the Agricultural Health Study after 20 years of follow-up	2019	Prostate cancer	Job title	Group-based assessment	Prospective cohort	Pesticide applicators (commercial) (agricultural)	4708	149		149	Incidence rates of prostate cancer for commercial applicators compared with rates for other cancers.	SIR	1.02	0.86	1.19	Pesticides in general	USA
Kachuri 2017. GenP	Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)	2017	Prostate cancer	Job title	Group-based assessment	Retrospective cohort	Agricultural workers	70570	2625		2625	Agricultural work compared with other employed members of the cohort.	HR	1.11	1.06	1.16	Pesticides in general	Canada
Lemarchand 2017. JT. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Prostate cancer	Self-reported job history	Group-based assessment	Prospective cohort	Farmers	98794	2538		2032	Work on farm (yes/no).	SIR	1.07	1.03	1.12	Pesticides in general	France
Lemarchand 2017. SRE. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Prostate cancer	Self-reported exposure	Self-reported exposure	Prospective cohort	Farmers	98794	2538		1345	Pesticide use on crops (yes versus no).	SIR	1.09	1.03	1.15	Pesticides in general	France
Burns 2011. AI	Cancer incidence of 2,4-D production workers	2011	Prostate cancer	Job title	Group-based assessment	Prospective cohort	Pesticide manufacturers (male)	1108	62		62	Pesticide manufacturers versus rates for white males as comparison.	SIR	0.74	0.57	0.94	2.4D	USA
Boers 2004. GenP	The influence of occupational exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil on prostate cancer: a prospective cohort study	2005	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Prospective cohort	Population base	58279	1376		27	Cumulative exposure. Third tertile versus no exposure.	RR	0.60	0.37	0.95	Pesticides in general	Netherlands
Fleming 1999. GenP	Cancer incidence in a cohort of licensed pesticide applicators in Florida	1999	Prostate cancer	Pesticide licence	Group-based assessment	Retrospective cohort	Pesticide applicators	33658	353		353	Incidence rates for applicators compared with that of the Florida general population.	SIR	1.91	1.72	2.13	Pesticides in general	USA
Dich 1998. GenP	Prostate cancer in pesticide applicators in Swedish agriculture	1998	Prostate cancer	Pesticide licence	Group-based assessment	Retrospective cohort	Pesticide applicators (agricultural)	20025	401		401	Incidence rates in applicators versus expected rate in Swedish male population.	SIR	1.13	1.02	1.24	Pesticides in general	Sweden
Frost 2011. GenP	Mortality and cancer incidence among British agricultural pesticide users	2011	Prostate cancer	Pesticide licence	Group-based assessment	Prospective cohort	Certified pesticide users (agricultural)	65910	205		205	Incidence rates in applicators verus that in the Great Britain population.	SIR	1.07	0.93	1.22	Pesticides in general	Great Britain
Rafnsson 2006. AI	Cancer incidence among farmers exposed to lindane while sheep dipping	2006	Prostate cancer	Registers	Group-based assessment	Retrospective cohort	Sheep owners	8311	541		541	Incidence rates in sheep owners versus that of the Icelanding male and female population.	SIR	0.92	0.85	1.00	Lindane	Iceland
Lynge 1998. GenP	Cancer incidence in Danish phenoxy herbicide workers, 1947-1993	1998	Prostate cancer	Registers	Group-based assessment	Retrospective cohort	Pesticide manufacturers	2119	15		15	Workers exposure classified based on their work area listed in personnel files.	SIR	1.00	0.6	1.7	Pesticides in general	Denmark
Zhong 1996. GenP	Cancer incidence among Icelandic pesticide users	1996	Prostate cancer	Pesticide licence	Group-based assessment	Prospective cohort	Certified pesticide users	2449	10		10	Incidence rates in pesticide users versus that of Icelanding male and femal population.	SIR	0.70	0.33	1.29	Pesticides in general	Iceland
Kristensen 1996. GenP	Incidence and risk factors of cancer among men and women in Norwegian agriculture	1996	Prostate cancer	Job title	Group-based assessment	Retrospective cohort	Farmers	66080	129		129	Incidence rates in farmers verus in the rural population of Norway.	SIR	0.90	0.75	1.07	Pesticides in general	Norway
Hessel 2004. AI	A nested case-control study of prostate cancer and atrazine exposure	2004	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Nested case-control	Population base	142	12	130	12	Cumulative exposure applied as continous variable.	OR	1.01	0.95	1.07	Atrazine	USA
Mills 2003. AI	Prostate cancer risk in California farm workers	2003	Prostate cancer	Registers	Group-based assessment	Nested case-control	Farmers	1332	222	1110	33	Exposure according to quartiles of chemical use according to a pesicide use reporting system in California.	OR	2.37	1.22	4.61	Lindane	USA
Band 2011. AI	Prostate cancer risk and exposure to pesticides in British Columbia farmers	2011	Prostate cancer	Job exposure matrix	Expert-level assessment	Case-control study	Farmers	5152	1153	3999	14	Cumulative exposure above median compared with no exposure.	OR	2.31	1.09	4.88	MCPA	Canada

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Fritschi 2007. GenP	Occupational risk factors for prostate cancer and benign prostatic hyperplasia: a case-control study in Western Australia	2007	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1008	606	402	68	Non-substantial exposure to any pesticides versus not exposed.	OR	1.02	0.69	1.50	Pesticides in general	Australia
Pavuk 2006. Type	Prostate cancer in US Air Force veterans of the Vietnam war	2006	Prostate cancer	Biomonitoring (blood)	Biomonitoring	Retrospective cohort	US Air Force veterans	2578	62	2516	28	Highest cumulative exposure verus lowest.	RR	1.32	0.75	2.34	Herbicedes (Agent Orange)	USA
Meyer 2007. GenP	A case-control study of farming and prostate cancer in African-American and Caucasian men	2007	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Population base	797	405	392	177	Farmes who ever mixed/applied pesticides versus non-farmers.	OR	1.6	1.2	2.2	Pesticides in general	USA
Settimi 2003. Class	Prostate cancer and exposure to pesticides in agricultural settings	2003	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Hospital base	783	124	659	10	Duration of exposure. More than 15 years of exposure verus non-exposed farmers and non-farmers.	OR	2.7	1.2	6.3	Organochlorine pesticides	Italy
Van der Gulden 1995. GenP	Work environment and prostate cancer risk	1995	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Cases from cancer registries	2341	469	1872	22	Frequently exposed versus non-exposed.	OR	1.47	0.88	2.46	Pesticides in general	Netherlands
Parent 2009. GenP	Does exposure to agricultural chemicals increase the risk of prostate cancer among farmers?	2009	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Farmers	124			17	Substantial level of exposure compared with unexposed farmers.	OR	2.3	1.1	5.1	Pesticides in general	Canada
Subahir 2009. GenP	Risk factors for prostate cancer in Universiti Kebangsaan Malaysia Medical Centre: a case-control study	2009	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	224	112	112	9	Exposure to pesticides (yes verus no).	OR	5.57	1.74	17.8	Pesticides in general	Malaysia
Strom 2008. GenP	Prostate cancer in Mexican-Americans: identification of risk factors	2008	Prostate cancer	Job exposure matrix	Expert-level assessment	Case-control study	Population base	350	176	174	48	High exposure versus no exposure.	OR	3.44	1.84	6.44	Pesticides in general	USA
Aronson 1996. GenP	Occupational risk factors for prostate cancer: results from a case-control study in Montreal, Quebec, Canada	1996	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1999	449	1550	19	Substantial pesticide exposure versus exposure in pool of cancer controls and population controls.	OR	1.09	0.57	2.08	Pesticides in general	Canada
Ewings 1996. GenP	A case-control study of cancer of the prostate in Somerset and east Devon	1996	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	146	40	106	15	Pesticide use (yes versus no).	OR	0.63	0.28	1.42	Pesticides in general	Great Britain
Petrovitch 2002. GenP	Plantation work and risk of Parkinson disease in a population-based longitudinal study	2002	Parkinson's disease	Self-reported job history	Group-based assessment	Prospective cohort	Honolulu Hearth Program cohort.	7986	116		12	Plantation work versus no plantation work.	RR	1.9	1.00	3.5	Pesticides in general	USA
Ascherio 2006. GenP	Pesticide exposure and risk for Parkinson's disease	2006	Parkinson's disease	Self-reported exposure	Self-reported exposure	Prospective cohort	Participants of the Cancer Prevention Study II Nutrition Cohort.	143325	30		13	Farmer exposed to pesticides versus unexposed non-farmer.	RR	1.6	0.9	2.7	Pesticides in general	USA
Shrestha 2020. GenP	Pesticide use and incident Parkinson's disease in a cohort of farmers and their spouses	2020	Parkinson's disease	Self-reported exposure	Self-reported exposure	Prospective cohort	Male pesticide applicators in AHS.	66110	183		82	Highest number of lifetime days of ever use of pesticides compared with lowest number of lifetime days.	RR	0.79	0.59	1.06	Pesticides in general	USA
Baldi 2003b. M. GenP	Neurodegenerative Diseases and Exposure to Pesticides in the elderly	2003	Parkinson's disease	Job exposure matrix	Expert-level assessment	Prospective cohort	Elderly French population	1507	10		NA	Occupational pesticide exposure according to job-exposure-matrix.	RR	5.63	1.47	21.57	Pesticides in general	France
Baldi 2003b. W. GenP	Neurodegenerative Diseases and Exposure to Pesticides in the elderly	2003	Parkinson's disease	Job exposure matrix	Expert-level assessment	Prospective cohort	Elderly French population	1507	14		NA	Occupational pesticide exposure according to job-exposure-matrix.	RR	1.02	0.22	4.82	Pesticides in general	France
Feldman 2011. GenP	Occupational exposure in parkinsonian disorders: a 43-year prospective cohort study in men	2011	Parkinson's disease	Job exposure matrix	Expert-level assessment	Prospective cohort	Population base	14169	204		21	Highest exposure probability level of pesticide exposure verus the lowest.	HR	0.9	0.5	1.4	Pesticides in general	Sweden
Kenborg 2012. GenP	Parkinson's disease among gardeners exposed to pesticides--a Danish cohort study	2012	Parkinson's disease	Job title	Group-based assessment	Retrospective cohort	Professional male gardeners	3124	28		28	Hospitalization rate due to Parkinson's disease in gardeners verus that of the general population.	SHR	1.14	0.76	1.65	Pesticides in general	Denmark
Pouchieu 2018. AI	Pesticide use in agriculture and Parkinson's disease in the AGRICAN cohort study	2018	Parkinson's disease	Crop exposure matrix	Expert-level assessment	Prospective cohort	Farmers	149810	1732	148078	28	Highest duration of use verus unexposed.	OR	1.58	0.48	5.25	Maneb	France
Tuchsen 2000. GenP	Agricultural work and the risk of Parkinson's disease in Denmark, 1981-1993	2000	Parkinson's disease	Job title	Group-based assessment	Prospective cohort	Agricultural workers	128935	134		134	All men and women in agriculture and horticulture.	SHR	1.32	1.11	1.56	Pesticides in general	Denmark
Koller 1990. GenP	Environmental risk factors in Parkinson's disease	1990	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	hospital_based	300	150	150	39	Pesticide use (yes versus no).	OR	1.08	0.69	1.69	Pesticides in general	USA
Baldi 2003a. GenP	Association between Parkinson's disease and exposure to pesticides in southwestern France	2003	Parkinson's disease	Job exposure matrix	Expert-level assessment	Case-control study	Inhabitants of agricultural region	336	84	252	19	Occupational pesticide exposure verus non-exposed.	OR	2.2	1.11	4.34	Pesticides in general	France
Chan 1998. GenP	Genetic and environmental risk factors for Parkinson's disease in a Chinese population	1998	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	528	215	313	19	Pesticide exposure in farming versus no pesticide exposure in farming.	OR	0.75	0.26	2.22	Pesticides in general	China
Dhillon 2008. Type	Pesticide/environmental exposures and Parkinson's disease in East Texas	2008	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	184	100	84	5	Insecticide applications to farm animals/animal areas.	OR	4.4	0.5	38.1	Insecticides	USA

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Dick 2007. GenP	Occupational titles as risk factors for Parkinson's disease	2007	Parkinson's disease	Job title	Group-based assessment	Case-control study	Population base	590	170	420	49	Agricultural work (yes versus no) as defined by ISIC.	OR	1.3	0.84	2.02	Pesticides in general	International
Duzcan 2003. GenP	Familial influence on parkinsonism in a rural area of Turkey (Kızılcaboluk–Denizli): A community-based case-control study	2003	Parkinsonism	Self-reported exposure	Self-reported exposure	Case-control study	Population base	144	36	108	15	Pesticide exposure (yes versus no)	OR	2.96	1.31	6.69	Pesticides in general	Turkey
Elbaz 2009. GenP	Professional exposure to pesticides and Parkinson disease	2009	Parkinson's disease	Expert case-by-case assessment	Expert-level assessment	Case-control study	Inhabitants of agricultural region	781	224	557	19	Number of years of professional exposure. More than 38 years of exposure versus no exposure.	OR	2.00	1.00	3.5	Pesticides in general	France
Fall 1999. GenP	Nutritional and occupational factors influencing the risk of Parkinson's disease: a case-control study in southeastern Sweden	1999	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	376	113	263	10	Handling pesticides within any occupation.	OR	3.3	1.00	10.0	Pesticides in general	Sweden
Firestone 2010. JT. M. GenP	Occupational factors and risk of Parkinson's disease: A population-based case-control study	2010	Parkinson's disease	Self-reported job history	Group-based assessment	Case-control study	Population base	578	252	326	8	Pesticide worker compared with subject never exposed.	OR	1.53	0.54	4.35	Pesticides in general	USA
Firestone 2010. SRE. M. GenP	Occupational factors and risk of Parkinson's disease: A population-based case-control study	2010	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	578	252	326	12	Pesticide exposure compared with subject never exposed.	OR	0.6	0.3	1.29	Pesticides in general	USA
Fong 2007. GenP	Pesticide exposure on southwestern Taiwanese with MnSOD and NQO1 polymorphisms is associated with increased risk of Parkinson's disease	2007	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	308	153	155	85	Pesticide use (yes versus no).	OR	1.68	1.03	2.76	Pesticides in general	Taiwan
Frigerio 2006. GenP	Chemical exposures and Parkinson's disease: a population-based case-control study	2006	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	278	149	129	14	Pesticide use in farming (yes versus no).	OR	1.3	0.6	3.1	Pesticides in general	USA
Gorell 1998. SRE. Type	The risk of Parkinson's disease with exposure to pesticides, farming, well water, and rural living	1998	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	608	144	464	NA	Ever versus never exposure to herbicides.	OR	4.1	1.37	12.24	Herbicides	USA
Gorell 1998. JT. GenP	The risk of Parkinson's disease with exposure to pesticides, farming, well water, and rural living	1998	Parkinson's disease	Job title	Group-based assessment	Case-control study	Population base	608	144	464	NA	Farming (yes versus no).	OR	2.79	1.03	7.55	Pesticides in general	USA
Hetzman 1994. M. GenP	A case-control study of Parkinson's disease in a horticultural region of British Columbia	1994	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	131	71	60	33	Pesticide use (yes versus no).	NA	2.32	1.1	4.88	Pesticides in general	Canada
Hetzman 1994. W. GenP	A case-control study of Parkinson's disease in a horticultural region of British Columbia	1994	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	120	56	64	9	Pesticide use (yes versus no).	NA	1.36	0.48	3.85	Pesticides in general	Canada
Kuopio 1999. Type	Environmental Risk Factors in Parkinson's Disease	1999	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	369	123	246	39	Regular and occational use of herbicides verus regular.	OR	1.02	0.63	1.65	Herbicides	Finland
Liew 2014. GenP	Job exposure matrix (JEM)-derived estimates of lifetime occupational pesticide exposure and the risk of Parkinson's disease	2014	Parkinson's disease	Job exposure matrix	Expert-level assessment	Case-control study	Population base	1107	357	750	43	High cumulative pesticide exposure versus no exposure.	OR	1.55	0.96	2.51	Pesticides in general	USA
McCann 1998. GenP	The Epidemiology of Parkinson's Disease in an Australian population	1998	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Cases and controls from hospitals, residential cares, and community groups.	534	224	310	NA	Exposure to herbicides and pesticides (daily or weekly exposure to industrial herbicides or pesticides for a cumulative period of greater than 6 months).	OR	1.2	0.8	1.5	Herbicides and pesticides	Australia
Moisan 2015. GenP	Association of Parkinson's Disease and Its Subtypes with Agricultural Pesticide Exposures in Men: A Case-Control Study in France	2015	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Farmers	431	133	298	43	Highest quartile verus lowest quartile of cumulative exposure (as defined by cumulative number of applications).	OR	2.31	1.09	4.9	Pesticides in general	France
Narayan 2017. GenP	Occupational pesticide use and Parkinson's disease in the Parkinson Environment Gene (PEG) study	2017	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	1187	360	827	40	Duration of use of pesticides. More than 10 years versus no occupational pesticide use.	OR	1.69	1.01	2.83	Pesticides in general	USA
Rugbjer 2011. Exp. GenP	Pesticide exposure and risk of Parkinson's disease--a population-based case-control study evaluating the potential for recall bias	2011	Parkinson's disease	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	808	403	405	37	Pesticide exposure beyond background.	OR	1.51	0.85	2.69	Pesticides in general	Canada
Rugbjer 2011. SRE. GenP	Pesticide exposure and risk of Parkinson's disease--a population-based case-control study evaluating the potential for recall bias	2011	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	808	403	405	74	Use or exposure to pesticides.	OR	1.76	1.15	2.7	Pesticides in general	Canada
Semchuk 1992. GenP	Parkinson's disease and exposure to agricultural work and pesticide chemicals	1992	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	390	130	260	NA	Pesticide use (yes versus no).	OR	2.25	1.27	3.99	Pesticides in general	Canada
Tanaka 2011. GenP	Occupational risk factors for Parkinson's disease: a case-control study in Japan	2011	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	618	249	369	15	Pesticide exposure (yes versus no).	OR	0.75	0.37	1.46	Pesticides in general	Japan

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Tanner 2009. GenP	Occupation and risk of parkinsonism: a multicenter case-control study	2009	Parkinsonism	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1030	519	511	44	Pesticide use (yes versus no).	OR	1.9	1.12	3.21	Pesticides in general	USA/Canada
Van der Mark 2014. JEM. GenP	Occupational exposure to pesticides and endotoxin and Parkinson disease in the Netherlands	2014	Parkinson's disease	Job exposure matrix	Expert-level assessment	Case-control study	Hospital base	1320	444	876	38	Highest cumulative exposure verus never exposed.	OR	1.56	0.86	2.83	Pesticides in general	Netherlands
Wright 2005. GenP	Environmental determinants of Parkinson's disease	2005	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	235	102	133	9	Occupational pesticide use (yes versus no).	OR	1.2	0.3	4.8	Pesticides in general	USA

JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. EXP=expert case-by-case assessment. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men. NA=not available.

Supplementary File S2.

Reference list and applied exposure assessment methods of included studies.

Prostate cancer

In total 25 articles were included in the meta-analysis of occupational pesticide exposure and prostate cancer. In these, 27 risk estimates for prostate cancer were reported for the following exposure assessment methods (EAM): job titles (n=5) (1-4), self-reported job histories (n=1) (5), exposure registers (n=3) (6-8), records of pesticide licenses (n=4) (9-12), self-reported exposures (n=5) (5, 13-16), JEM (n=2) (17, 18), expert assessments (n=6) (19-24), and biomonitoring of blood (n=1) (25). One article reported risk estimates for several EAMs applied within the same study population (5), and one article reported separate risk estimates based on job title for private and commercial pesticide applicators (2).

Non-Hodgkin's Lymphoma

In total 29 articles were included in the meta-analysis of Non-Hodgkin's Lymphoma. The articles reported 40 risk estimates according to the following EAM: job titles (n=10) (1, 3, 4, 26-30), self-reported job histories (n=4) (31-34), exposure registers (n=3) (7, 8, 35), self-reported exposures (n=13) (5, 28, 30, 32-34, 36-41), JEM (n=2) (31, 42), CEM (n=1) (39), expert assessments (n=6) (43-47), and exposure algorithm (n=1) (48). Four articles reported risk estimates for several different EAMs (28, 31, 32, 39). Three articles reported risk estimates separately for women and men (1, 4, 5), and one article applied self-reported exposures to estimate NHL risk separately for African American and white men, respectively (38).

Parkinson's disease

In total 32 articles were included in the meta-analysis of Parkinson's Disease. The articles reported 37 risk estimates according to the following EAM: job titles (n=4) (49-52), self-reported job histories (n=2) (53, 54), self-reported exposures (n=22) (50, 54-72), JEM (n=7) (73-77), and expert assessments (n=2) (64, 78). Three articles reported separate risk estimates for different EAMs (50, 54, 64). Two articles reported risk estimates separately for women and men (59, 73). Two articles (63, 76) presented partly overlapping study populations. However, we extracted risks estimates associated with different types of EAM; JEM in (76) and self-reported use in (63).

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Supplementary File S3 (figures S3.1-3.12)

Subgroup-analyses by type of exposure assessment method (EAM), study design, publication year period, and geographic location of the studies.

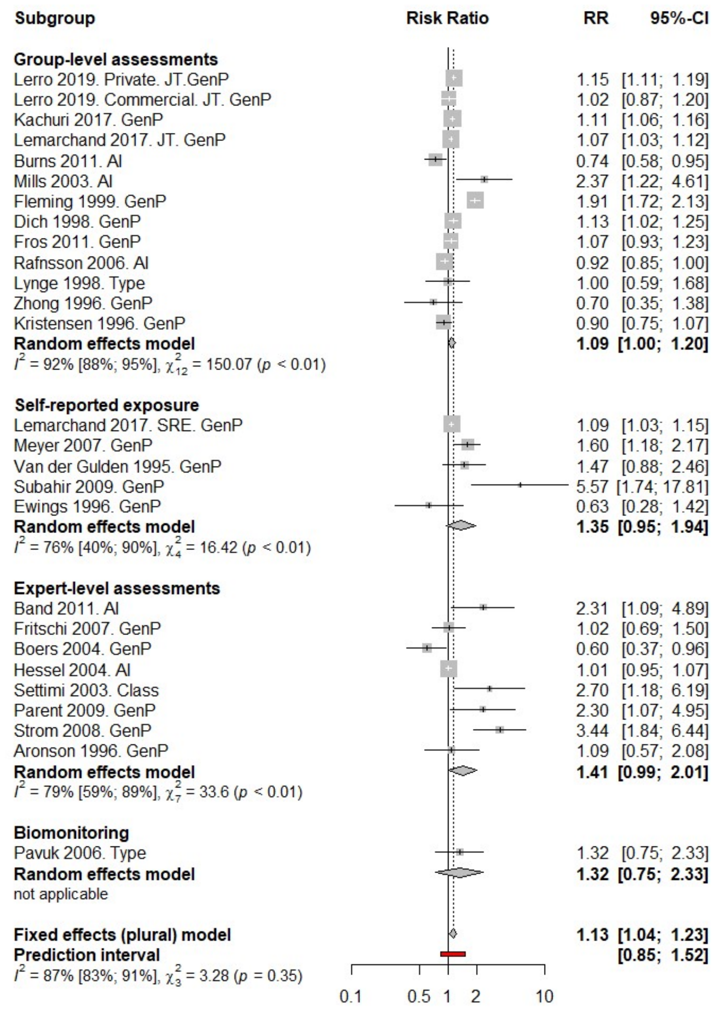

Figure S3.1. *Summary risk ratios for prostate cancer by EAM type based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I²=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

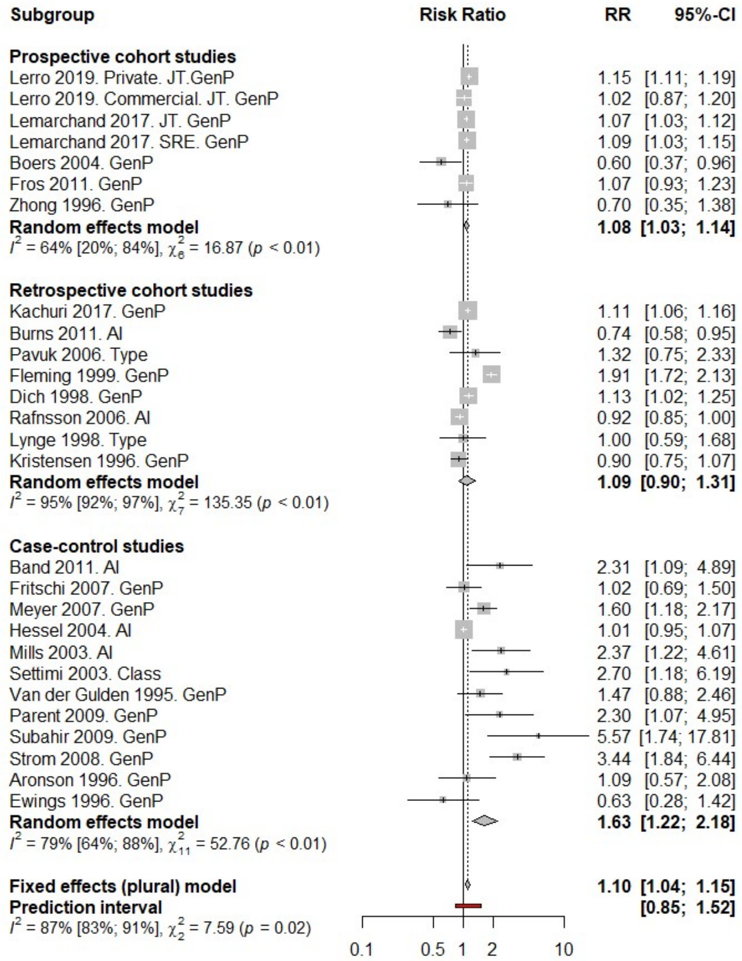

Figure S3.2. *Summary risk ratios for prostate cancer by study design based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I^2=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

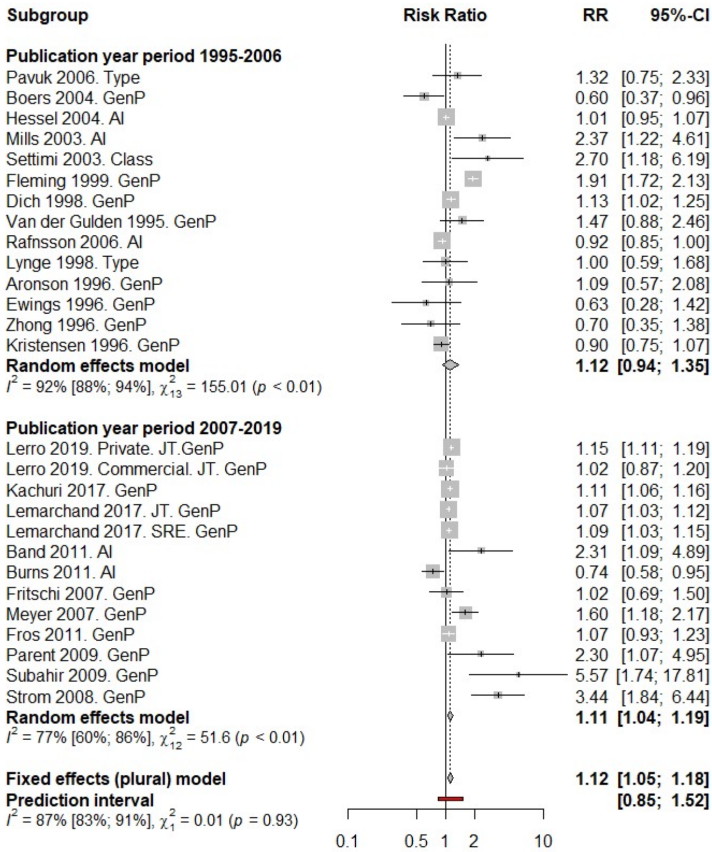

Figure S3.3. *Summary risk ratios for prostate cancer by publication year period based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I²=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

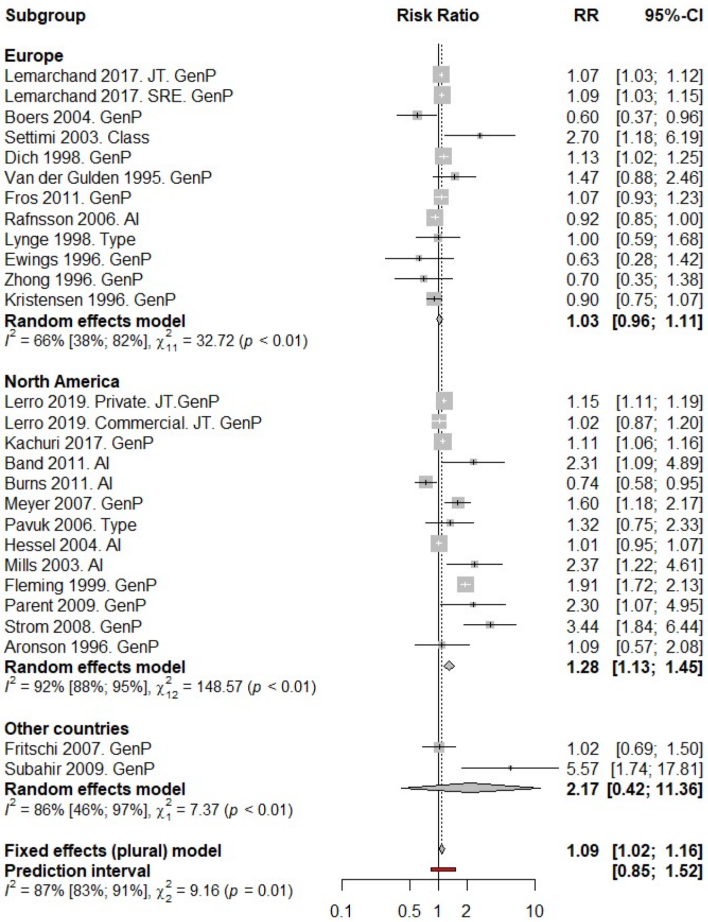

Figure S3.4. *Summary risk ratios for prostate cancer by geographic location where the study was performed based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I^2=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

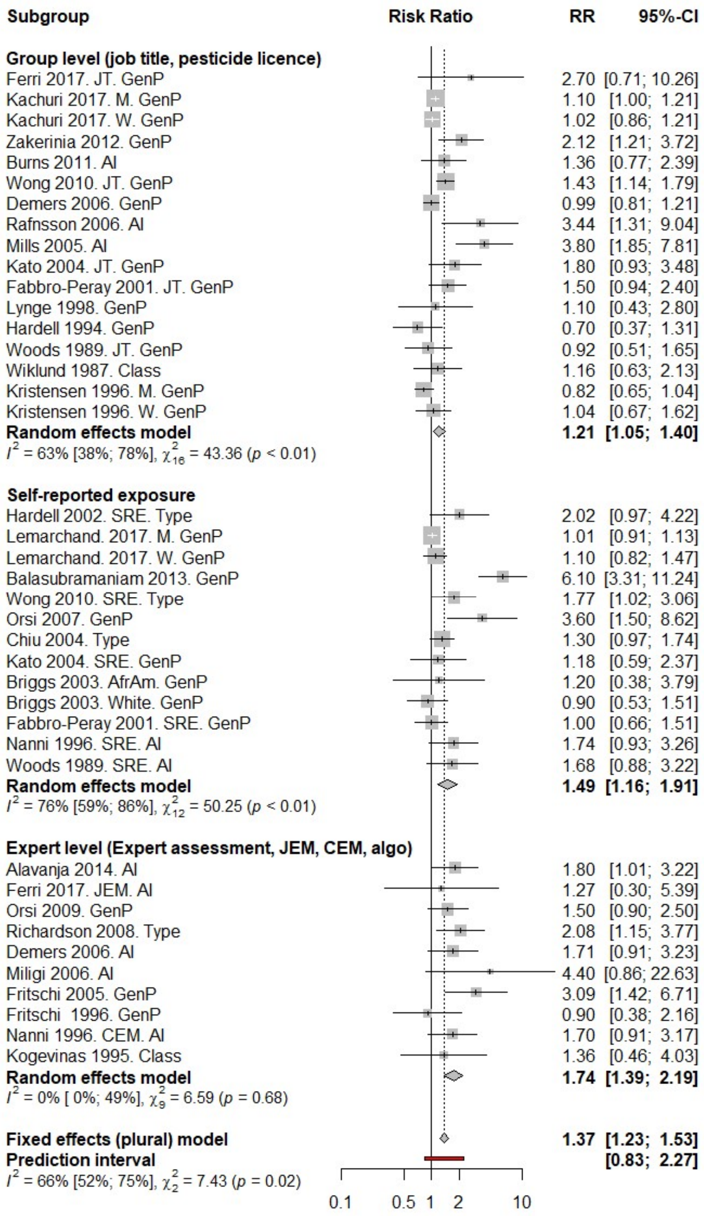

Figure S3.5 *Summary risk ratios for Non-Hodgkin's lymphoma by EAM type based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. Algo=exposure algorithm. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

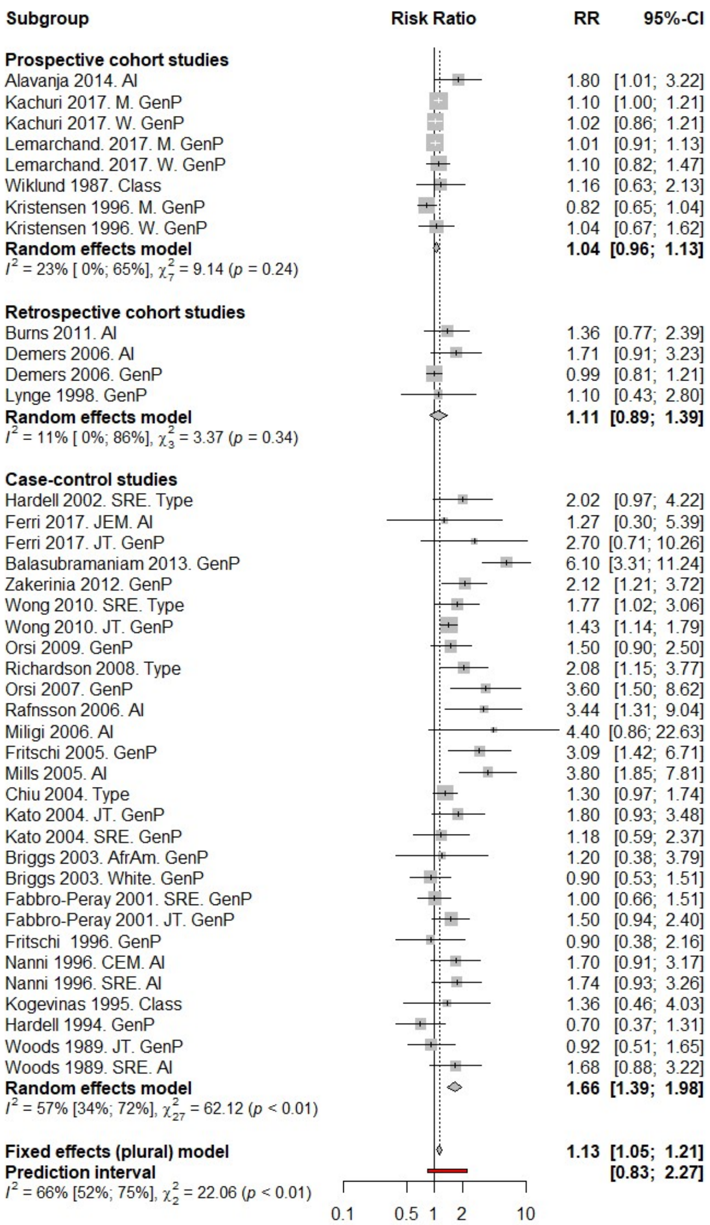

Figure S3.6 *Summary risk ratios for Non-Hodgkin's lymphoma by study design based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I²=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

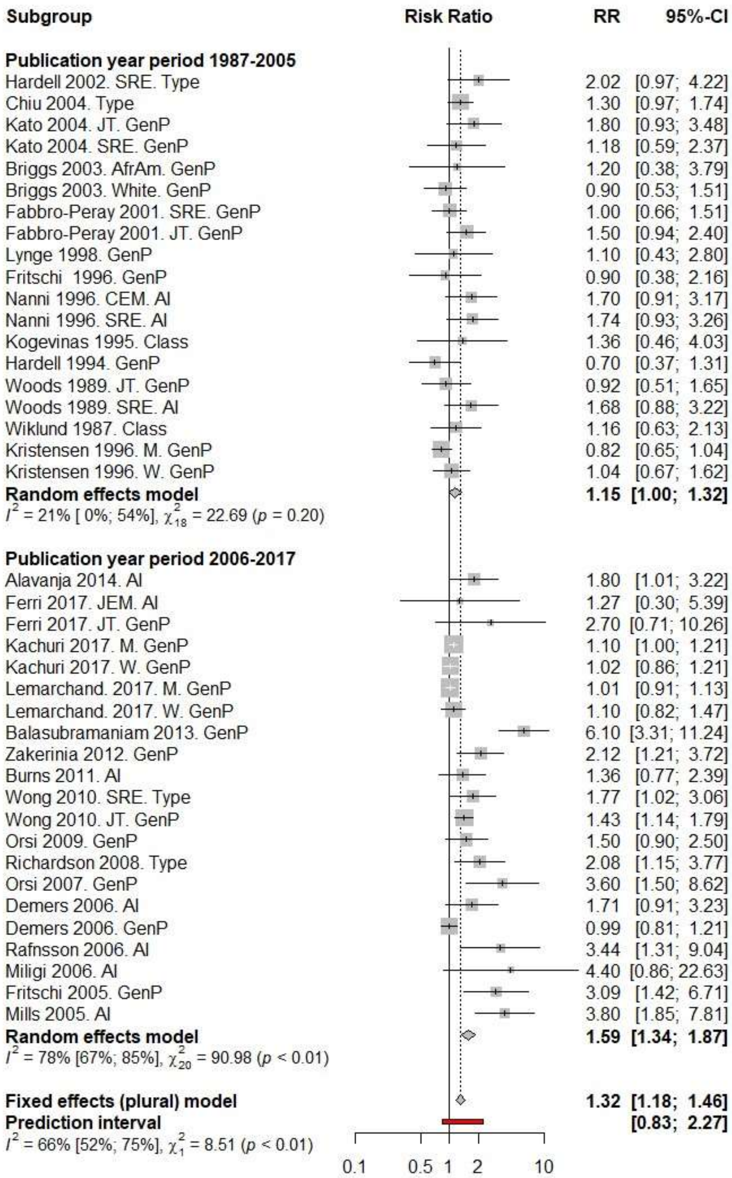

Figure S3.7 *Summary risk ratios for Non-Hodgkin's lymphoma by publication year period based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

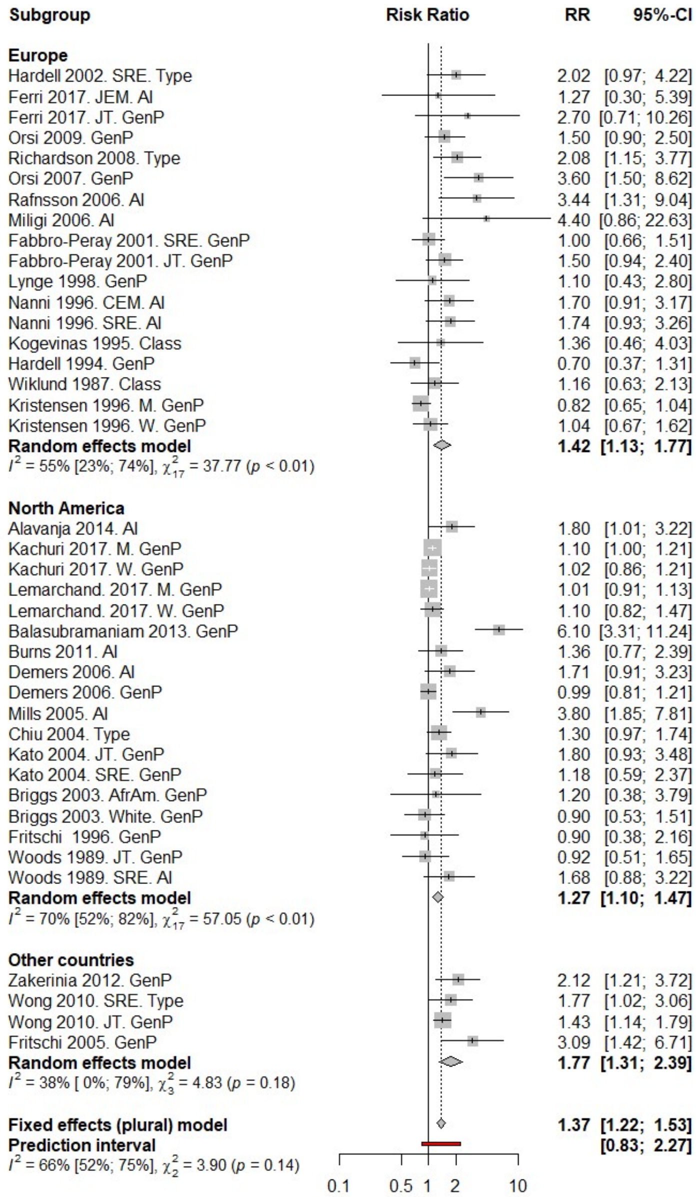

Figure S3.8 *Summary risk ratios for Non-Hodgkin's lymphoma by geographic location where the study was performed based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

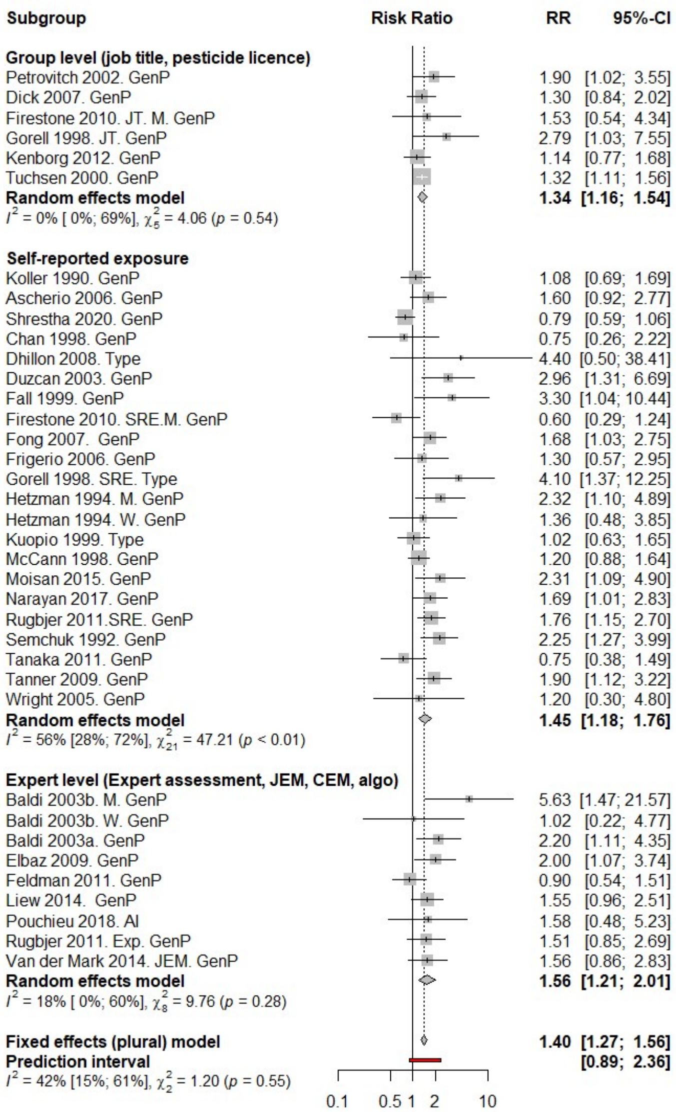

Figure S3.9. *Summary risk ratios for Parkinson's disease by EAM type based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR= relative risk. I²=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

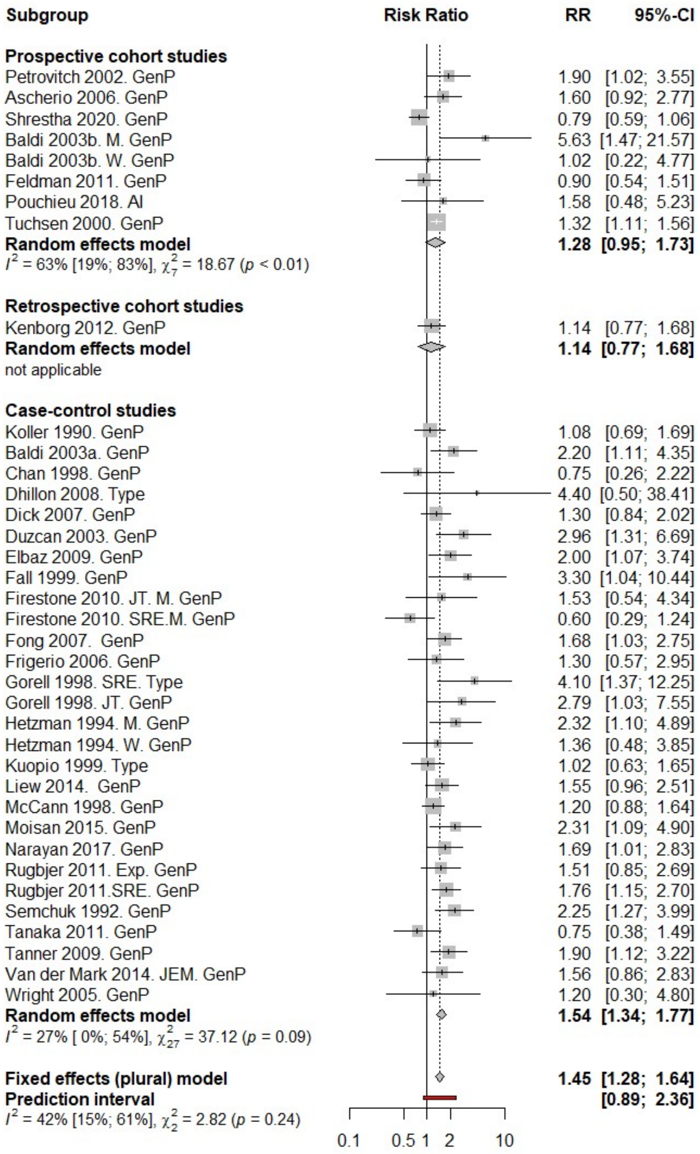

Figure S3.10. *Summary risk ratios for Parkinson's disease by study design based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR= relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

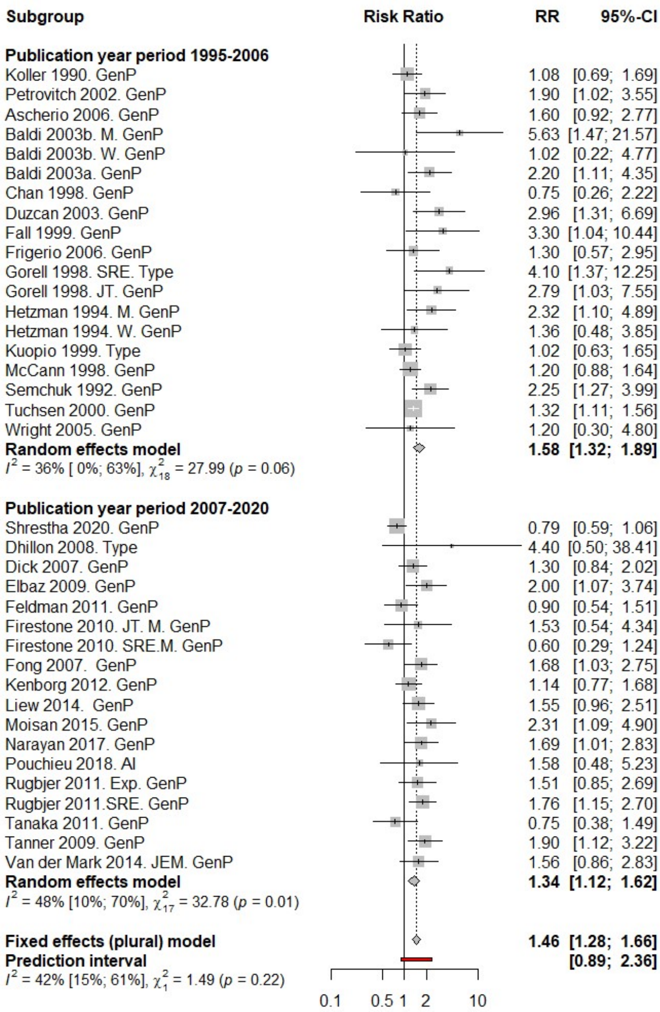

Figure S3.11. *Summary risk ratios for Parkinson's disease by publication year period based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR= relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

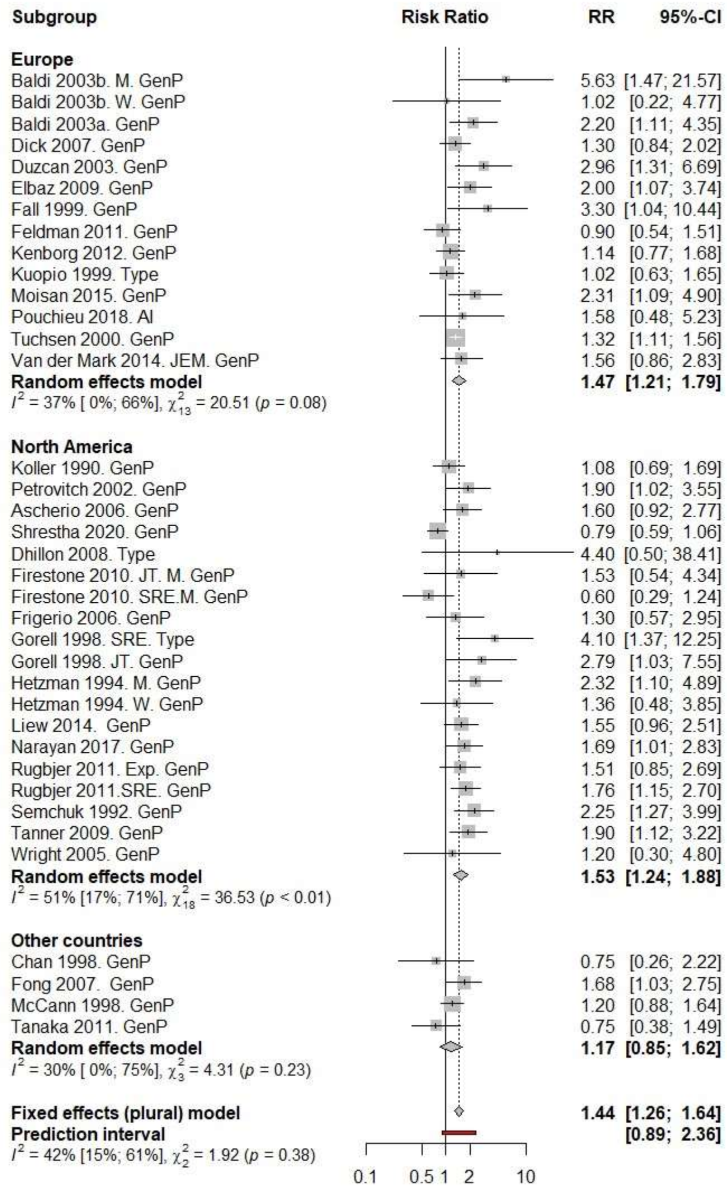

Figure S3.12. *Summary risk ratios for Parkinson's disease by geographic location where the study was performed based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR= relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Demers 2006. Exp. AI	Cancer and occupational exposure to pentachlorophenol and tetrachlorophenol (Canada)	2006	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Retrospective cohort	Sawmill workers	27464	92		17	5+ exposure years of cumulative dermal pentachlorophenol exposure.	RR	1.71	0.91	3.24	Pentachlorophenol	Canada
Demers 2006. JT. GenP	Cancer and occupational exposure to pentachlorophenol and tetrachlorophenol (Canada)	2006	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Retrospective cohort	Sawmill workers	27464	92		92	Standardized incidence rates calculated based on comparison with British Columbia provincial rates.	SIR	0.99	0.81	1.21	Pesticides in general	Canada
Lynge 1998. Class	Cancer incidence in Danish phenoxy herbicide workers, 1947-1993	1998	Non-Hodgkin's lymphoma	Registers	Group-based assessment	Retrospective cohort	Pesticide manufacturers	2119	6		6	Workers exposure classified based on their work area listed in personnel files.	SIR	1.10	0.4	2.6	Phenoxy herbicides	Denmark
Alavanja 2014. AI	Non-hodgkin lymphoma risk and insecticide, fungicide and fumigant use in the agricultural health study	2014	Non-Hodgkin's lymphoma	Algorithm/model	Expert-level assessment	Prospective cohort	Pesticide applicators from AHS	54306	523		14	Intensity-weighted lifetime days.	RR	1.8	1.0	3.2	Lindane	USA
Kachuri 2017. M. GenP	Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)	2017	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Agricultural workers	70570	500		500	Agricultural worker versus not agricultural worker in all other members of the cohort.	HR	1.10	1.00	1.21	Pesticides in general	Canada
Kachuri 2017.W. GenP	Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)	2017	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Agricultural workers	70570	135		135	Agricultural worker versus not agricultural worker in all other members of the cohort.	HR	1.02	0.86	1.22	Pesticides in general	Canada
Lemarchand 2017. M. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Prospective cohort	Farmers (as insured by MSA in France)	98794	644		310	Pesticide use on crops (yes versus no)	SIR	1.01	0.90	1.12	Pesticides in general	USA
Lemarchand 2017. W. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Prospective cohort	Farmers (as insured by MSA in France)	98794	367		48	Pesticide use on crops (yes versus no)	SIR	1.10	0.81	1.45	Pesticides in general	USA
Burns 2011. AI	Cancer incidence of 2,4-D production workers	2011	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Retrospective cohort	Pesticide manufacturers (male)	1256	14		14	Pesticide manufacturers versus rates for white males as comparison.	SIR	1.36	0.74	2.29	2.4D	USA
Wiklund 1987. Class	Risk of malignant lymphoma in Swedish pesticide appliers	1987	Non-Hodgkin's lymphoma	Self-reported job history	Group-based assessment	Prospective cohort	Pesticide applicators (mainly agricultural)	20245	21		12	Number of years since pesticide license. Highest category >10 years. Standardized incidence rates calculated for number of years since obtained pesticide license.	SIR	1.16	0.60	2.02	Phenoxy herbicides	Sweden
Kristensen 1996. M. GenP	Incidence and risk factors of cancer among men and women in Norwegian agriculture	1996	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Farmers	66080	69	NA	69	Incidence rates for working as a farmer compared with rural reference population.	SIR	0.82	0.64	1.03	Pesticides in general	Norway
Kristensen 1996. W. GenP	Incidence and risk factors of cancer among men and women in Norwegian agriculture	1996	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Prospective cohort	Farmers	30218	20	NA	20	Incidence rates for working as a farmer compared with rural reference population.	SIR	1.04	0.64	1.56	Pesticides in general	Norway
Kogevinas 1995. Class	Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: two nested case-control studies	1995	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Nested Case-control study	Pesticide manufacturers	21183	32		7	Level of exposure by categories (nonexposed, low, medium, high). Cumulative exposure lagged 5 years.	OR	1.36	0.46	4.03	Phenoxy herbicides	International
Hardell 2002. SRE. Type	Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies	2002	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Cases from cancer registries	1656	515	1141	18	Exposed versus non-exposed. Minimum exposure of 8 hours (one working day).	OR	2.02	0.97	4.23	Fungicides	Sweden
Ferri 2017. JEM. AI	Risk of lymphoma subtypes by occupational exposure in Southern Italy	2017	Non-Hodgkin's lymphoma	Job exposure matrix	Expert-level assessment	Case-control study	Population base	310	128	76	7	Medium-high cumulative exposure verus none.	OR	1.27	0.3	5.41	Paraquat	Italy
Ferri 2017. JT. GenP	Risk of lymphoma subtypes by occupational exposure in Southern Italy	2017	Non-Hodgkin's lymphoma	Self-reported job history	Group-based assessment	Case-control study	Population base	310	117	72	14	Agricultural worker versus not agricultural worker	OR	2.7	0.7	10.1	Pesticides in general	Italy
Balasubramaniam 2013. GenP	Case-control study of risk factors for Non-Hodgkin lymphoma in Mumbai, India	2013	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1771	388	1383	29	Ever versus never exposure.	OR	6.1	3.3	11.2	Pesticides in general	Canada
Zakerinia 2012. GenP	The relationship between exposure to pesticides and the occurrence of lymphoid neoplasm	2012	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Hospital base	400	200	200	34	Duration of exposure. High exposure is defined as >median number of years for exposed subjects.	OR	2.12	1.2	3.7	Pesticides in general	Iran
Wong 2010. SRE. Type	A hospital-based case-control study of non-Hodgkin lymphoid neoplasms in Shanghai: analysis of environmental and occupational risk factors by subtypes of the WHO classification	2010	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1947	649	1298	25	Ever exposure to pesticides	OR	1.77	1.02	3.05	Herbicides	China

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Wong 2010. JT. Type	A hospital-based case-control study of non-Hodgkin lymphoid neoplasms in Shanghai: analysis of environmental and occupational risk factors by subtypes of the WHO classification	2010	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Hospital base	1947	649	1298	195	Farmworker (all types)	OR	1.43	1.14	1.78	Pesticides in general	China
Orsi 2009. GenP	Occupational exposure to pesticides and lymphoid neoplasms among men: results of a French case-control study	2009	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Hospital base	680	244	436	32	Occupational pesticide use verified by experts.	OR	1.5	0.9	2.5	Pesticides in general	France
Richardson 2008. Type	Occupational risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Northern Germany	2008	Non-Hodgkin's lymphoma	Job exposure matrix	Expert-level assessment	Case-control study	Population base	767	242	525	23	Cumulative exposure defined as the product of cumulative hours worked in each exposed job, and the respective exposure intensity and probability scores.	OR	2.08	1.15	3.77	Herbicides	Germany
Orsi 2007. GenP	Occupation and lymphoid malignancies: results from a French case-control study	2007	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1100	399	701	14	Use of pesticides for crops at least once per week	OR	3.6	1.5	8.6	Pesticides in general	France
Rafnsson 2006. AI	Risk of non-Hodgkin's lymphoma and exposure to hexachlorocyclohexane, a nested case-control study	2006	Non-Hodgkin's lymphoma	Registers	Group-based assessment	Case-control study	Sheep owners	266	45	221	15	Number of dipped sheep (200-683). Proxy for the highest exposed.	OR	3.44	1.31	9.04	Hexachlorocyclohexane	Iceland
Miligi 2006. AI	Cancer and pesticides: an overview and some results of the Italian multicenter case control study on hematolymphopoietic malignancies.	2006	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	2377	1145	1232	9	Probability of use >low and lack of protective equipment	OR	4.4	1.1	29.1	2.4D	Italy
Fritschi 2005. GenP	Occupational exposure to pesticides and risk of non-Hodgkin's lymphoma	2005	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1388	694	694	26	Substantial exposure versus none exposure.	OR	3.09	1.42	6.70	Pesticides in general	Australia
Mills 2005. AI	Lymphohematopoietic cancers in the United Farm Workers of America (UFW), 1988-2001	2005	Non-Hodgkin's lymphoma	Registers	Group-based assessment	Case-control study	Members of farmers union	360	60	300	60	The distribution of the 15 most commonly used pesticides (in pounds of active ingredient applied in counties where farm workers were employed) was examined, and cut points were created to construct categories in dichotomies of low versus high use or tertiles of use.	OR	3.8	1.85	7.81	2.4D	USA
Chiu 2004. Type	Agricultural pesticide use, familial cancer, and risk of non-Hodgkin lymphoma	2004	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	3790	937	2853	77	Ever versus never use.	OR	1.3	1.0	1.8	Fungicides	USA
Kato 2004. JT. GenP	Pesticide product use and risk of non-Hodgkin lymphoma in women	2004	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Population base	839	376	463	27	Highest number of years in any occupation with pesticide exposure.	OR	1.8	0.93	3.48	Pesticides in general	USA
Kato 2004. SRE. GenP	Pesticide product use and risk of non-Hodgkin lymphoma in women	2004	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	839	376	463	43	Applied pesticides on a farm (yes-no)	OR	1.18	0.59	2.38	Pesticides in general	USA
Briggs 2003. Afr.Am. GenP	Occupational risk factors for selected cancers among African American and White men in the United States	2003	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	2073	66	132	5	Ever versus never use.	OR	1.2	0.4	4.0	Pesticides in general	USA
Briggs 2003. White. GenP	Occupational risk factors for selected cancers among African American and White men in the United States	2003	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	2073	893	1488	92	Ever versus never use.	OR	0.9	0.6	1.7	Pesticides in general	USA
Fabbro-Peray. 2001. SRE. GenP	Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France	2001	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Population base	1470	445	1025	41	Handling of pesticides	OR	1.0	0.7	1.6	Pesticides in general	France
Fabbro-Peray. 2001. JT. GenP	Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France	2001	Non-Hodgkin's lymphoma	Self-reported job history	Self-reported exposure	Case-control study	Population base	1470	445	1025	40	Agricultural occupation	OR	1.5	0.9	2.3	Pesticides in general	France
Fritschi 1996. GenP	Lymphoma, myeloma and occupation: results of a case-control study	1996	Non-Hodgkin's lymphoma	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1358	215	NA	6	Degree of expousre: non-exposed, non-substantial, substantial expousure.	OR	0.9	0.4	2.3	Pesticides in general	Canada
Nanni 1996. CEM. AI	Chronic lymphocytic leukaemias and non-Hodgkin's lymphomas by histological type in farming-animal breeding workers: a population case-control study based on a priori exposure matrices	1996	Non-Hodgkin's lymphoma	Crop exposure matrix	Expert-level assessment	Case-control study	Farmers	1164	187	977	28	Exposure to DDT according to crop exposure matrix.	OR	1.70	0.91	3.17	DDT	Italy
Nanni 1996. SRE. AI	Chronic lymphocytic leukaemias and non-Hodgkin's lymphomas by histological type in farming-animal breeding workers: a population case-control study based on a priori exposure matrices	1996	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Farmers	1164	187	977	27	Exposure to DDT (yes/no)	OR	1.74	0.93	3.27	DDT	Italy

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Hardell 1994. GenP	Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma.	1994	Non-Hodgkin's lymphoma	Job title	Group-based assessment	Case-control study	Hospital base	94	20	74	20	Farmer (yes/no)	OR	0.7	0.4	1.4	Pesticides in general	Sweden
Woods 1989. JT. GenP	Non-Hodgkin's lymphoma among phenoxy herbicide-exposed farm workers in western Washington state	1989	Non-Hodgkin's lymphoma	Self-reported job history	Group-based assessment	Case-control study	Agricultural workers	377	181	196	181	Duration of work as a farmer.	OR	0.92	0.5	1.6	Pesticides in general	USA
Woods 1989. SRE.AI	Non-Hodgkin's lymphoma among phenoxy herbicide-exposed farm workers in western Washington state	1989	Non-Hodgkin's lymphoma	Self-reported exposure	Self-reported exposure	Case-control study	Agricultural workers	377	181	196	NA	Regular work with DDT (yes/no)	OR	1.68	0.9	3.3	DDT	USA
Lerro 2019. Private. JT.GenP	Cancer incidence in the Agricultural Health Study after 20 years of follow-up	2019	Prostate cancer	Job title	Group-based assessment	Prospective cohort	Pesticide applicators (private) (agricultural)	51165	3169		3169	Incidence rates of prostate cancer for private applicators compared with rates for other cancers.	SIR	1.15	1.11	1.19	Pesticides in general	USA
Lerro 2019. Commercial. JT. GenP	Cancer incidence in the Agricultural Health Study after 20 years of follow-up	2019	Prostate cancer	Job title	Group-based assessment	Prospective cohort	Pesticide applicators (commercial) (agricultural)	4708	149		149	Incidence rates of prostate cancer for commercial applicators compared with rates for other cancers.	SIR	1.02	0.86	1.19	Pesticides in general	USA
Kachuri 2017. GenP	Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)	2017	Prostate cancer	Job title	Group-based assessment	Retrospective cohort	Agricultural workers	70570	2625		2625	Agricultural work compared with other employed members of the cohort.	HR	1.11	1.06	1.16	Pesticides in general	Canada
Lemarchand 2017. JT. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Prostate cancer	Self-reported job history	Group-based assessment	Prospective cohort	Farmers	98794	2538		2032	Work on farm (yes/no).	SIR	1.07	1.03	1.12	Pesticides in general	France
Lemarchand 2017. SRE. GenP	Cancer incidence in the AGRICAN cohort study (2005-2011)	2017	Prostate cancer	Self-reported exposure	Self-reported exposure	Prospective cohort	Farmers	98794	2538		1345	Pesticide use on crops (yes versus no).	SIR	1.09	1.03	1.15	Pesticides in general	France
Burns 2011. AI	Cancer incidence of 2,4-D production workers	2011	Prostate cancer	Job title	Group-based assessment	Prospective cohort	Pesticide manufacturers (male)	1108	62		62	Pesticide manufacturers versus rates for white males as comparison.	SIR	0.74	0.57	0.94	2.4D	USA
Boers 2004. GenP	The influence of occupational exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil on prostate cancer: a prospective cohort study	2005	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Prospective cohort	Population base	58279	1376		27	Cumulative exposure. Third tertile versus no exposure.	RR	0.60	0.37	0.95	Pesticides in general	Netherlands
Fleming 1999. GenP	Cancer incidence in a cohort of licensed pesticide applicators in Florida	1999	Prostate cancer	Pesticide licence	Group-based assessment	Retrospective cohort	Pesticide applicators	33658	353		353	Incidence rates for applicators compared with that of the Florida general population.	SIR	1.91	1.72	2.13	Pesticides in general	USA
Dich 1998. GenP	Prostate cancer in pesticide applicators in Swedish agriculture	1998	Prostate cancer	Pesticide licence	Group-based assessment	Retrospective cohort	Pesticide applicators (agricultural)	20025	401		401	Incidence rates in applicators versus expected rate in Swedish male population.	SIR	1.13	1.02	1.24	Pesticides in general	Sweden
Frost 2011. GenP	Mortality and cancer incidence among British agricultural pesticide users	2011	Prostate cancer	Pesticide licence	Group-based assessment	Prospective cohort	Certified pesticide users (agricultural)	65910	205		205	Incidence rates in applicators verus that in the Great Britain population.	SIR	1.07	0.93	1.22	Pesticides in general	Great Britain
Rafnsson 2006. AI	Cancer incidence among farmers exposed to lindane while sheep dipping	2006	Prostate cancer	Registers	Group-based assessment	Retrospective cohort	Sheep owners	8311	541		541	Incidence rates in sheep owners versus that of the Icelanding male and female population.	SIR	0.92	0.85	1.00	Lindane	Iceland
Lynge 1998. GenP	Cancer incidence in Danish phenoxy herbicide workers, 1947-1993	1998	Prostate cancer	Registers	Group-based assessment	Retrospective cohort	Pesticide manufacturers	2119	15		15	Workers exposure classified based on their work area listed in personnel files.	SIR	1.00	0.6	1.7	Pesticides in general	Denmark
Zhong 1996. GenP	Cancer incidence among Icelandic pesticide users	1996	Prostate cancer	Pesticide licence	Group-based assessment	Prospective cohort	Certified pesticide users	2449	10		10	Incidence rates in pesticide users versus that of Icelanding male and femal population.	SIR	0.70	0.33	1.29	Pesticides in general	Iceland
Kristensen 1996. GenP	Incidence and risk factors of cancer among men and women in Norwegian agriculture	1996	Prostate cancer	Job title	Group-based assessment	Retrospective cohort	Farmers	66080	129		129	Incidence rates in farmers verus in the rural population of Norway.	SIR	0.90	0.75	1.07	Pesticides in general	Norway
Hessel 2004. AI	A nested case-control study of prostate cancer and atrazine exposure	2004	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Nested case-control	Population base	142	12	130	12	Cumulative exposure applied as continous variable.	OR	1.01	0.95	1.07	Atrazine	USA
Mills 2003. AI	Prostate cancer risk in California farm workers	2003	Prostate cancer	Registers	Group-based assessment	Nested case-control	Farmers	1332	222	1110	33	Exposure according to quartiles of chemical use according to a pesicide use reporting system in California.	OR	2.37	1.22	4.61	Lindane	USA
Band 2011. AI	Prostate cancer risk and exposure to pesticides in British Columbia farmers	2011	Prostate cancer	Job exposure matrix	Expert-level assessment	Case-control study	Farmers	5152	1153	3999	14	Cumulative exposure above median compared with no exposure.	OR	2.31	1.09	4.88	MCPA	Canada

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Fritschi 2007. GenP	Occupational risk factors for prostate cancer and benign prostatic hyperplasia: a case-control study in Western Australia	2007	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1008	606	402	68	Non-substantial exposure to any pesticides versus not exposed.	OR	1.02	0.69	1.50	Pesticides in general	Australia
Pavuk 2006. Type	Prostate cancer in US Air Force veterans of the Vietnam war	2006	Prostate cancer	Biomonitoring (blood)	Biomonitoring	Retrospective cohort	US Air Force veterans	2578	62	2516	28	Highest cumulative exposure versus lowest.	RR	1.32	0.75	2.34	Herbicedes (Agent Orange)	USA
Meyer 2007. GenP	A case-control study of farming and prostate cancer in African-American and Caucasian men	2007	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Population base	797	405	392	177	Farmes who ever mixed/applied pesticides versus non-farmers.	OR	1.6	1.2	2.2	Pesticides in general	USA
Settimi 2003. Class	Prostate cancer and exposure to pesticides in agricultural settings	2003	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Hospital base	783	124	659	10	Duration of exposure. More than 15 years of exposure versus non-exposed farmers and non-farmers.	OR	2.7	1.2	6.3	Organochlorine pesticides	Italy
Van der Gulden 1995. GenP	Work environment and prostate cancer risk	1995	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Cases from cancer registries	2341	469	1872	22	Frequently exposed versus non-exposed.	OR	1.47	0.88	2.46	Pesticides in general	Netherlands
Parent 2009. GenP	Does exposure to agricultural chemicals increase the risk of prostate cancer among farmers?	2009	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Farmers	124			17	Substantial level of exposure compared with unexposed farmers.	OR	2.3	1.1	5.1	Pesticides in general	Canada
Subahir 2009. GenP	Risk factors for prostate cancer in Universiti Kebangsaan Malaysia Medical Centre: a case-control study	2009	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	224	112	112	9	Exposure to pesticides (yes verus no).	OR	5.57	1.74	17.8	Pesticides in general	Malaysia
Strom 2008. GenP	Prostate cancer in Mexican-Americans: identification of risk factors	2008	Prostate cancer	Job exposure matrix	Expert-level assessment	Case-control study	Population base	350	176	174	48	High exposure versus no exposure.	OR	3.44	1.84	6.44	Pesticides in general	USA
Aronson 1996. GenP	Occupational risk factors for prostate cancer: results from a case-control study in Montreal, Quebec, Canada	1996	Prostate cancer	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	1999	449	1550	19	Substantial pesticide exposure versus exposure in pool of cancer controls and population controls.	OR	1.09	0.57	2.08	Pesticides in general	Canada
Ewings 1996. GenP	A case-control study of cancer of the prostate in Somerset and east Devon	1996	Prostate cancer	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	146	40	106	15	Pesticide use (yes versus no).	OR	0.63	0.28	1.42	Pesticides in general	Great Britain
Petrovitch 2002. GenP	Plantation work and risk of Parkinson disease in a population-based longitudinal study	2002	Parkinson's disease	Self-reported job history	Group-based assessment	Prospective cohort	Honolulu Hearth Program cohort.	7986	116		12	Plantation work versus no plantation work.	RR	1.9	1.00	3.5	Pesticides in general	USA
Ascherio 2006. GenP	Pesticide exposure and risk for Parkinson's disease	2006	Parkinson's disease	Self-reported exposure	Self-reported exposure	Prospective cohort	Participants of the Cancer Prevention Study II Nutrition Cohort.	143325	30		13	Farmer exposed to pesticides versus unexposed non-farmer.	RR	1.6	0.9	2.7	Pesticides in general	USA
Shrestha 2020. GenP	Pesticide use and incident Parkinson's disease in a cohort of farmers and their spouses	2020	Parkinson's disease	Self-reported exposure	Self-reported exposure	Prospective cohort	Male pesticide applicators in AHS.	66110	183		82	Highest number of lifetime days of ever use of pesticides compared with lowest number of lifetime days.	RR	0.79	0.59	1.06	Pesticides in general	USA
Baldi 2003b. M. GenP	Neurodegenerative Diseases and Exposure to Pesticides in the elderly	2003	Parkinson's disease	Job exposure matrix	Expert-level assessment	Prospective cohort	Elderly French population	1507	10		NA	Occupational pesticide exposure according to job-exposure-matrix.	RR	5.63	1.47	21.57	Pesticides in general	France
Baldi 2003b. W. GenP	Neurodegenerative Diseases and Exposure to Pesticides in the elderly	2003	Parkinson's disease	Job exposure matrix	Expert-level assessment	Prospective cohort	Elderly French population	1507	14		NA	Occupational pesticide exposure according to job-exposure-matrix.	RR	1.02	0.22	4.82	Pesticides in general	France
Feldman 2011. GenP	Occupational exposure in parkinsonian disorders: a 43-year prospective cohort study in men	2011	Parkinson's disease	Job exposure matrix	Expert-level assessment	Prospective cohort	Population base	14169	204		21	Highest exposure probability level of pesticide exposure verus the lowest.	HR	0.9	0.5	1.4	Pesticides in general	Sweden
Kenborg 2012. GenP	Parkinson's disease among gardeners exposed to pesticides--a Danish cohort study	2012	Parkinson's disease	Job title	Group-based assessment	Retrospective cohort	Professional male gardeners	3124	28		28	Hospitalization rate due to Parkinson's disease in gardeners versus that of the general population.	SHR	1.14	0.76	1.65	Pesticides in general	Denmark
Pouchieu 2018. AI	Pesticide use in agriculture and Parkinson's disease in the AGRICAN cohort study	2018	Parkinson's disease	Crop exposure matrix	Expert-level assessment	Prospective cohort	Farmers	149810	1732	148078	28	Highest duration of use verus unexposed.	OR	1.58	0.48	5.25	Maneb	France
Tuchsen 2000. GenP	Agricultural work and the risk of Parkinson's disease in Denmark, 1981-1993	2000	Parkinson's disease	Job title	Group-based assessment	Prospective cohort	Agricultural workers	128935	134		134	All men and women in agriculture and horticulture.	SHR	1.32	1.11	1.56	Pesticides in general	Denmark
Koller 1990. GenP	Environmental risk factors in Parkinson's disease	1990	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	hospital_based	300	150	150	39	Pesticide use (yes versus no).	OR	1.08	0.69	1.69	Pesticides in general	USA
Baldi 2003a. GenP	Association between Parkinson's disease and exposure to pesticides in southwestern France	2003	Parkinson's disease	Job exposure matrix	Expert-level assessment	Case-control study	Inhabitants of agricultural region	336	84	252	19	Occupational pesticide exposure verus non-exposed.	OR	2.2	1.11	4.34	Pesticides in general	France
Chan 1998. GenP	Genetic and environmental risk factors for Parkinson's disease in a Chinese population	1998	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	528	215	313	19	Pesticide exposure in farming versus no pesticide exposure in farming.	OR	0.75	0.26	2.22	Pesticides in general	China
Dhillon 2008. Type	Pesticide/environmental exposures and Parkinson's disease in East Texas	2008	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	184	100	84	5	Insecticide applications to farm animals/animal areas.	OR	4.4	0.5	38.1	Insecticides	USA

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Dick 2007. GenP	Occupational titles as risk factors for Parkinson's disease	2007	Parkinson's disease	Job title	Group-based assessment	Case-control study	Population base	590	170	420	49	Agricultural work (yes versus no) as defined by ISIC.	OR	1.3	0.84	2.02	Pesticides in general	International
Duzcan 2003. GenP	Familial influence on parkinsonism in a rural area of Turkey (Kızılcaboluk–Denizli): A community-based case-control study	2003	Parkinsonism	Self-reported exposure	Self-reported exposure	Case-control study	Population base	144	36	108	15	Pesticide exposure (yes versus no)	OR	2.96	1.31	6.69	Pesticides in general	Turkey
Elbaz 2009. GenP	Professional exposure to pesticides and Parkinson disease	2009	Parkinson's disease	Expert case-by-case assessment	Expert-level assessment	Case-control study	Inhabitants of agricultural region	781	224	557	19	Number of years of professional exposure. More than 38 years of exposure versus no exposure.	OR	2.00	1.00	3.5	Pesticides in general	France
Fall 1999. GenP	Nutritional and occupational factors influencing the risk of Parkinson's disease: a case-control study in southeastern Sweden	1999	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	376	113	263	10	Handling pesticides within any occupation.	OR	3.3	1.00	10.0	Pesticides in general	Sweden
Firestone 2010. JT. M. GenP	Occupational factors and risk of Parkinson's disease: A population-based case-control study	2010	Parkinson's disease	Self-reported job history	Group-based assessment	Case-control study	Population base	578	252	326	8	Pesticide worker compared with subject never exposed.	OR	1.53	0.54	4.35	Pesticides in general	USA
Firestone 2010. SRE. M. GenP	Occupational factors and risk of Parkinson's disease: A population-based case-control study	2010	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	578	252	326	12	Pesticide exposure compared with subject never exposed.	OR	0.6	0.3	1.29	Pesticides in general	USA
Fong 2007. GenP	Pesticide exposure on southwestern Taiwanese with MnSOD and NQO1 polymorphisms is associated with increased risk of Parkinson's disease	2007	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	308	153	155	85	Pesticide use (yes versus no).	OR	1.68	1.03	2.76	Pesticides in general	Taiwan
Frigerio 2006. GenP	Chemical exposures and Parkinson's disease: a population-based case-control study	2006	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	278	149	129	14	Pesticide use in farming (yes versus no).	OR	1.3	0.6	3.1	Pesticides in general	USA
Gorell 1998. SRE. Type	The risk of Parkinson's disease with exposure to pesticides, farming, well water, and rural living	1998	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	608	144	464	NA	Ever versus never exposure to herbicides.	OR	4.1	1.37	12.24	Herbicides	USA
Gorell 1998. JT. GenP	The risk of Parkinson's disease with exposure to pesticides, farming, well water, and rural living	1998	Parkinson's disease	Job title	Group-based assessment	Case-control study	Population base	608	144	464	NA	Farming (yes versus no).	OR	2.79	1.03	7.55	Pesticides in general	USA
Hetzman 1994. M. GenP	A case-control study of Parkinson's disease in a horticultural region of British Columbia	1994	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	131	71	60	33	Pesticide use (yes versus no).	NA	2.32	1.1	4.88	Pesticides in general	Canada
Hetzman 1994. W. GenP	A case-control study of Parkinson's disease in a horticultural region of British Columbia	1994	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	120	56	64	9	Pesticide use (yes versus no).	NA	1.36	0.48	3.85	Pesticides in general	Canada
Kuopio 1999. Type	Environmental Risk Factors in Parkinson's Disease	1999	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	369	123	246	39	Regular and occational use of herbicides verus regular.	OR	1.02	0.63	1.65	Herbicides	Finland
Liew 2014. GenP	Job exposure matrix (JEM)-derived estimates of lifetime occupational pesticide exposure and the risk of Parkinson's disease	2014	Parkinson's disease	Job exposure matrix	Expert-level assessment	Case-control study	Population base	1107	357	750	43	High cumulative pesticide exposure versus no exposure.	OR	1.55	0.96	2.51	Pesticides in general	USA
McCann 1998. GenP	The Epidemiology of Parkinson's Disease in an Australian population	1998	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Cases and controls from hospitals, residential cares, and community groups.	534	224	310	NA	Exposure to herbicides and pesticides (daily or weekly exposure to industrial herbicides or pesticides for a cumulative period of greater than 6 months).	OR	1.2	0.8	1.5	Herbicides and pesticides	Australia
Moisan 2015. GenP	Association of Parkinson's Disease and Its Subtypes with Agricultural Pesticide Exposures in Men: A Case-Control Study in France	2015	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Farmers	431	133	298	43	Highest quartile verus lowest quartile of cumulative exposure (as defined by cumulative number of applications).	OR	2.31	1.09	4.9	Pesticides in general	France
Narayan 2017. GenP	Occupational pesticide use and Parkinson's disease in the Parkinson Environment Gene (PEG) study	2017	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	1187	360	827	40	Duration of use of pesticides. More than 10 years versus no occupational pesticide use.	OR	1.69	1.01	2.83	Pesticides in general	USA
Rugbjer 2011. Exp. GenP	Pesticide exposure and risk of Parkinson's disease--a population-based case-control study evaluating the potential for recall bias	2011	Parkinson's disease	Expert case-by-case assessment	Expert-level assessment	Case-control study	Population base	808	403	405	37	Pesticide exposure beyond background.	OR	1.51	0.85	2.69	Pesticides in general	Canada
Rugbjer 2011. SRE. GenP	Pesticide exposure and risk of Parkinson's disease--a population-based case-control study evaluating the potential for recall bias	2011	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	808	403	405	74	Use or exposure to pesticides.	OR	1.76	1.15	2.7	Pesticides in general	Canada
Semchuk 1992. GenP	Parkinson's disease and exposure to agricultural work and pesticide chemicals	1992	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	390	130	260	NA	Pesticide use (yes versus no).	OR	2.25	1.27	3.99	Pesticides in general	Canada
Tanaka 2011. GenP	Occupational risk factors for Parkinson's disease: a case-control study in Japan	2011	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	618	249	369	15	Pesticide exposure (yes versus no).	OR	0.75	0.37	1.46	Pesticides in general	Japan

Article	Article name	Publication year	Health outcome	Exposure assessment method	Exposure assessment method type	Study design	Study population	Sample size	Number of cases	Number of controls	Number of exposed cases	Exposure definition and comparison	Risk measure	Risk estimate	Lower CI	Upper CI	Type of pesticide	Study location
Tanner 2009. GenP	Occupation and risk of parkinsonism: a multicenter case-control study	2009	Parkinsonism	Self-reported exposure	Self-reported exposure	Case-control study	Hospital base	1030	519	511	44	Pesticide use (yes versus no).	OR	1.9	1.12	3.21	Pesticides in general	USA/Canada
Van der Mark 2014. JEM. GenP	Occupational exposure to pesticides and endotoxin and Parkinson disease in the Netherlands	2014	Parkinson's disease	Job exposure matrix	Expert-level assessment	Case-control study	Hospital base	1320	444	876	38	Highest cumulative exposure verus never exposed.	OR	1.56	0.86	2.83	Pesticides in general	Netherlands
Wright 2005. GenP	Environmental determinants of Parkinson's disease	2005	Parkinson's disease	Self-reported exposure	Self-reported exposure	Case-control study	Population base	235	102	133	9	Occupational pesticide use (yes versus no).	OR	1.2	0.3	4.8	Pesticides in general	USA

JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. EXP=expert case-by-case assessment. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men. NA=not available.

Supplementary File S2.

Reference list and applied exposure assessment methods of included studies.

Prostate cancer

In total 25 articles were included in the meta-analysis of occupational pesticide exposure and prostate cancer. In these, 27 risk estimates for prostate cancer were reported for the following exposure assessment methods (EAM): job titles (n=5) (1-4), self-reported job histories (n=1) (5), exposure registers (n=3) (6-8), records of pesticide licenses (n=4) (9-12), self-reported exposures (n=5) (5, 13-16), JEM (n=2) (17, 18), expert assessments (n=6) (19-24), and biomonitoring of blood (n=1) (25). One article reported risk estimates for several EAMs applied within the same study population (5), and one article reported separate risk estimates based on job title for private and commercial pesticide applicators (2).

Non-Hodgkin's Lymphoma

In total 29 articles were included in the meta-analysis of Non-Hodgkin's Lymphoma. The articles reported 40 risk estimates according to the following EAM: job titles (n=10) (1, 3, 4, 26-30), self-reported job histories (n=4) (31-34), exposure registers (n=3) (7, 8, 35), self-reported exposures (n=13) (5, 28, 30, 32-34, 36-41), JEM (n=2) (31, 42), CEM (n=1) (39), expert assessments (n=6) (43-47), and exposure algorithm (n=1) (48). Four articles reported risk estimates for several different EAMs (28, 31, 32, 39). Three articles reported risk estimates separately for women and men (1, 4, 5), and one article applied self-reported exposures to estimate NHL risk separately for African American and white men, respectively (38).

Parkinson's disease

In total 32 articles were included in the meta-analysis of Parkinson's Disease. The articles reported 37 risk estimates according to the following EAM: job titles (n=4) (49-52), self-reported job histories (n=2) (53, 54), self-reported exposures (n=22) (50, 54-72), JEM (n=7) (73-77), and expert assessments (n=2) (64, 78). Three articles reported separate risk estimates for different EAMs (50, 54, 64). Two articles reported risk estimates separately for women and men (59, 73). Two articles (63, 76) presented partly overlapping study populations. However, we extracted risks estimates associated with different types of EAM; JEM in (76) and self-reported use in (63).

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Supplementary File S3 (figures S3.1-3.12)

Subgroup-analyses by type of exposure assessment method (EAM), study design, publication year period, and geographic location of the studies.

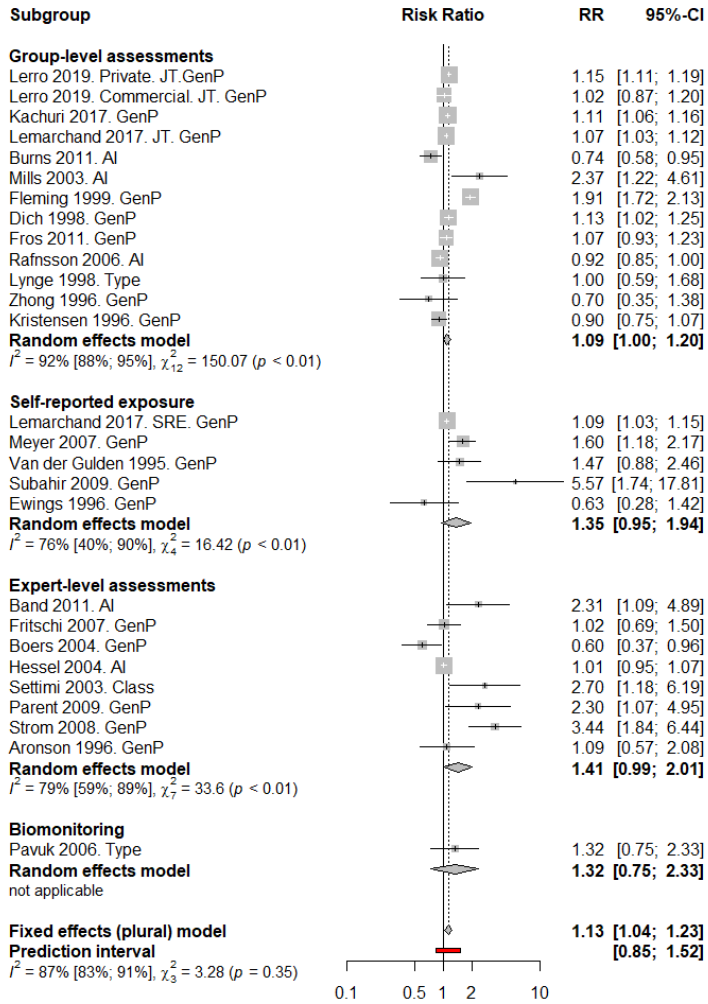

Figure S3.1. *Summary risk ratios for prostate cancer by EAM type based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I^2=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

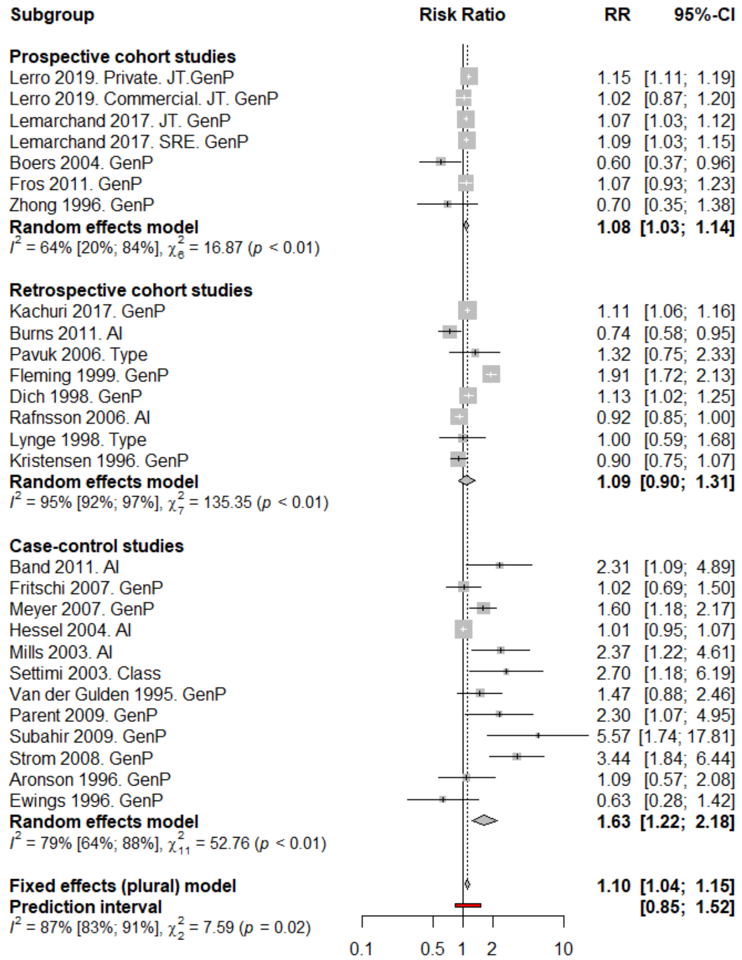

Figure S3.2. *Summary risk ratios for prostate cancer by study design based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I^2=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

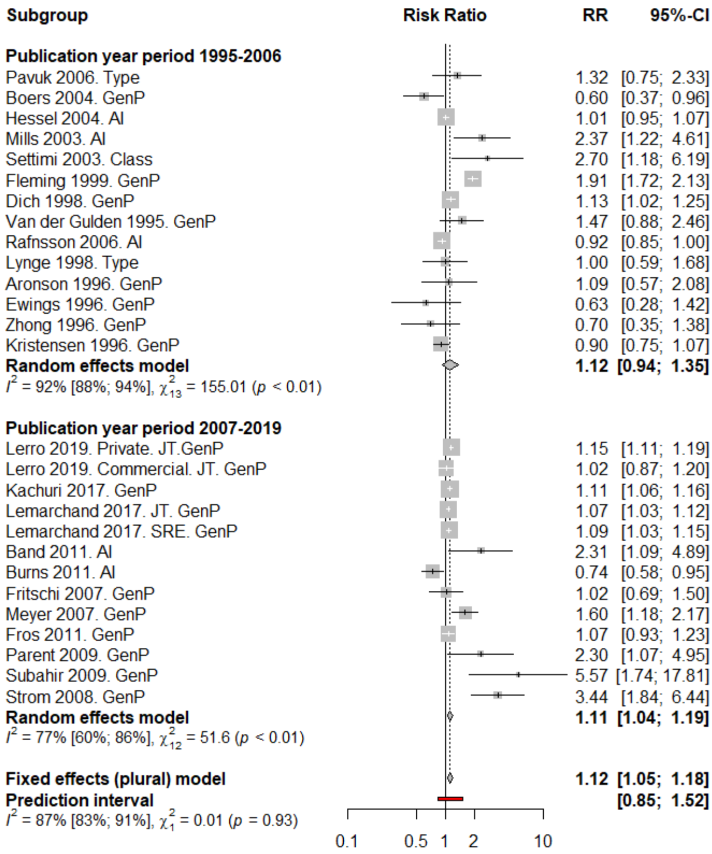

Figure S3.3. *Summary risk ratios for prostate cancer by publication year period based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I²=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

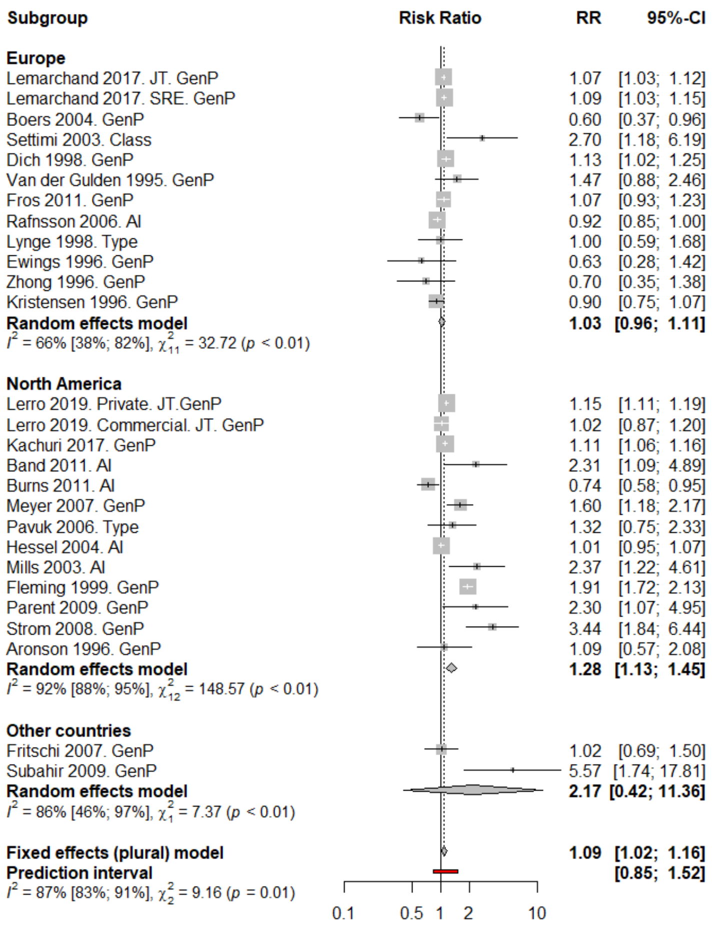

Figure S3.4. *Summary risk ratios for prostate cancer by geographic location where the study was performed based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1995-2019. RR=relative risk. I^2=percentage of variation across studies that is due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. Private=private pesticide applicator. Commercial=commercial pesticide applicator.*

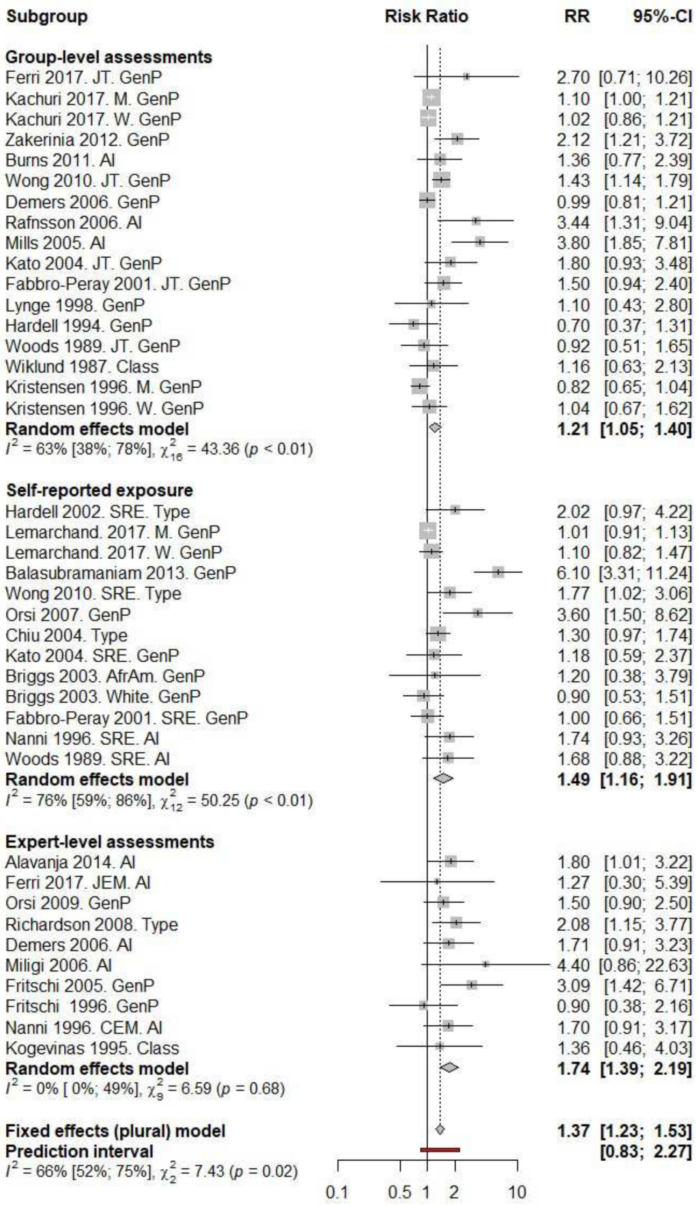

Figure S3.5 *Summary risk ratios for Non-Hodgkin's lymphoma by EAM type based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk.* I^2*=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. Algo=exposure algorithm. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

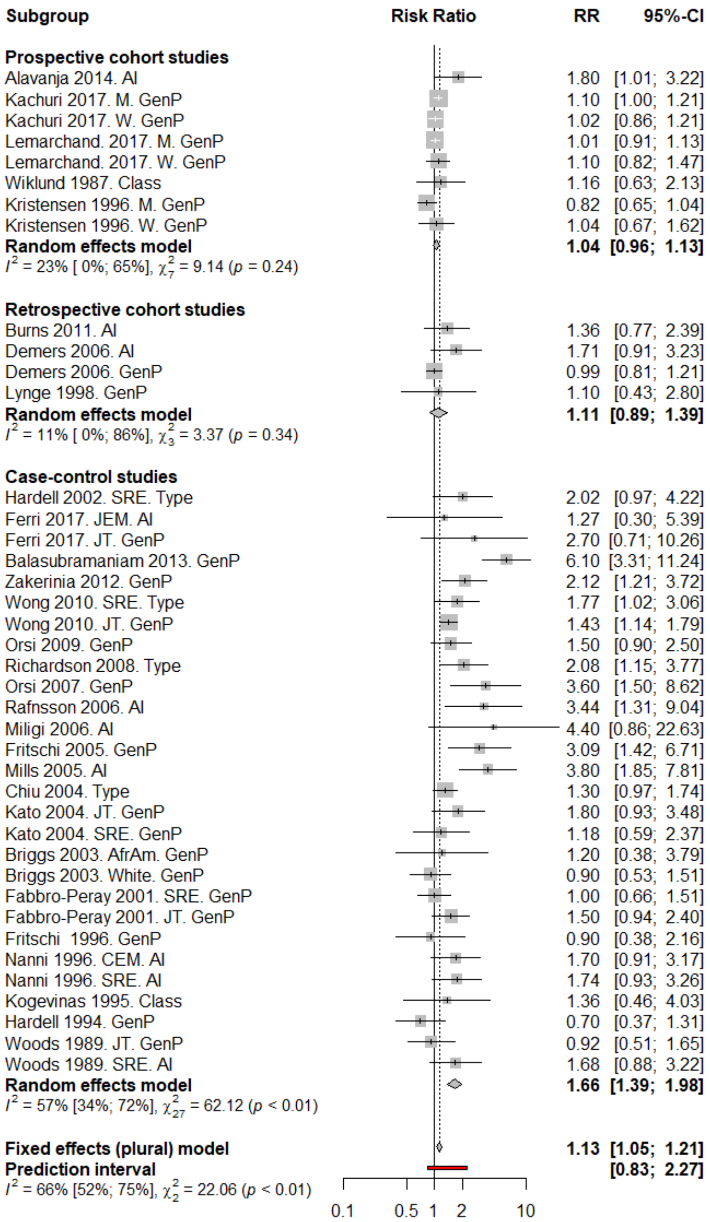

Figure S3.6 *Summary risk ratios for Non-Hodgkin's lymphoma by study design based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I²=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

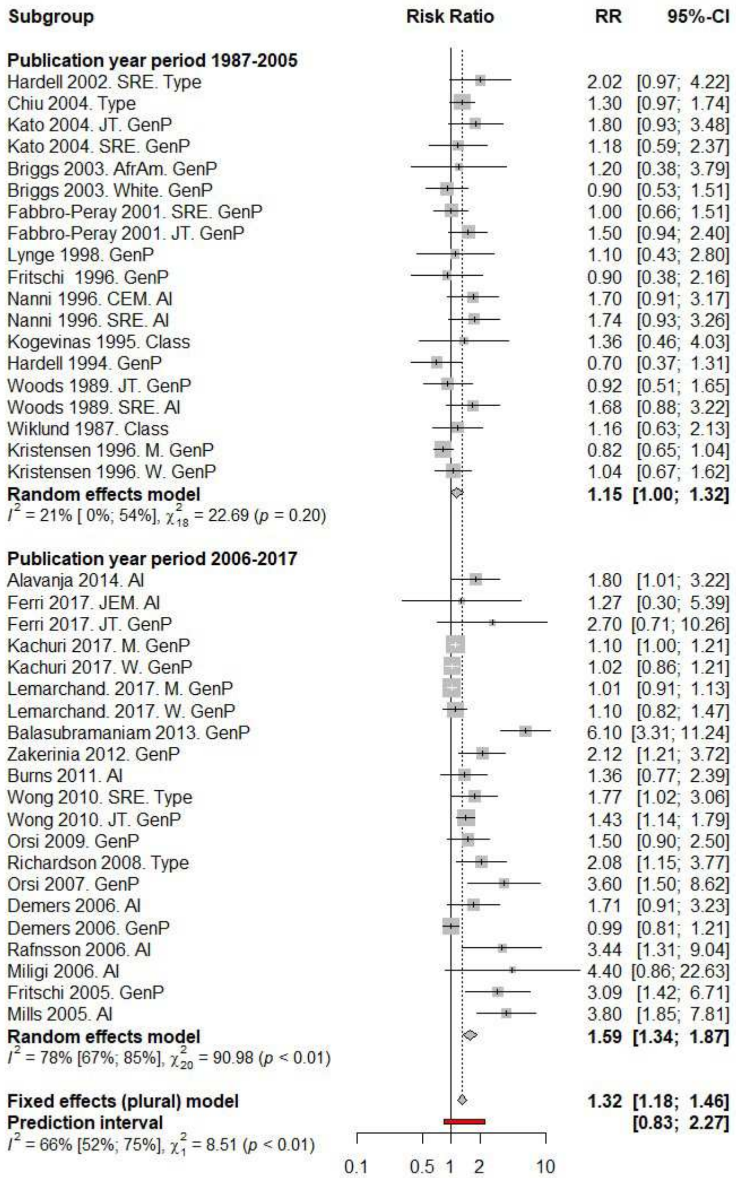

Figure S3.7 *Summary risk ratios for Non-Hodgkin's lymphoma by publication year period based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

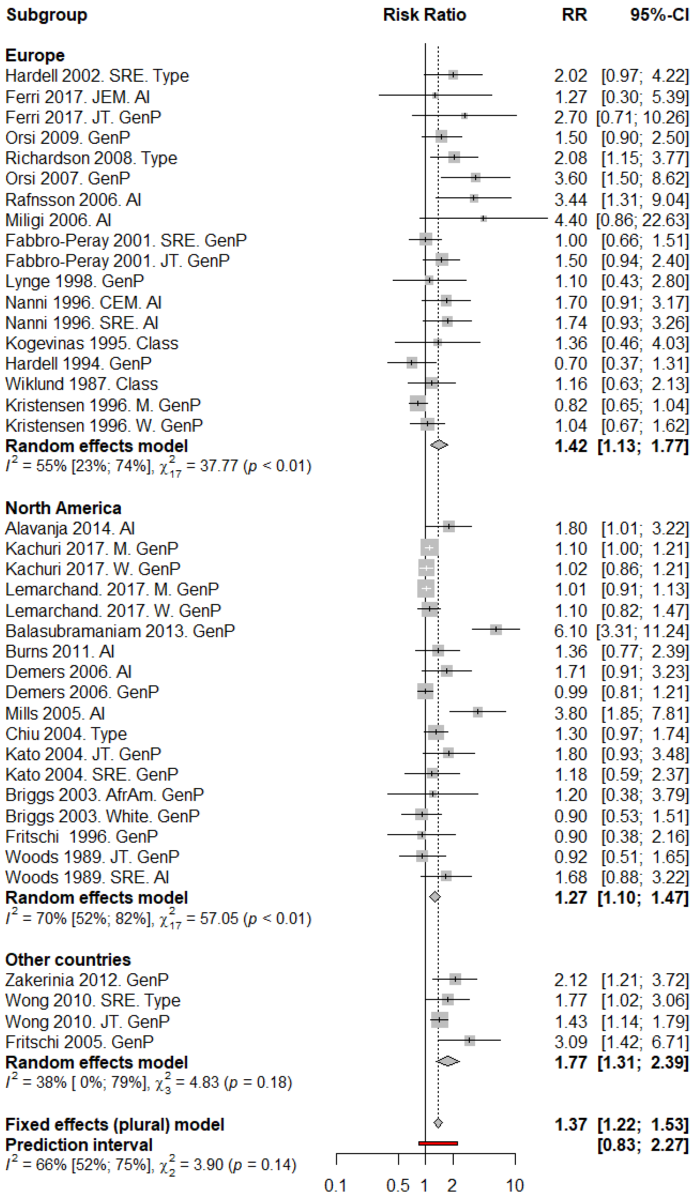

Figure S3.8 *Summary risk ratios for Non-Hodgkin's lymphoma by geographic location where the study was performed based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1987-2017. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. JEM=job-exposure matrix. CEM=crop-exposure matrix. GenP=general pesticides. Type=type of pesticide. Class=class of pesticides. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

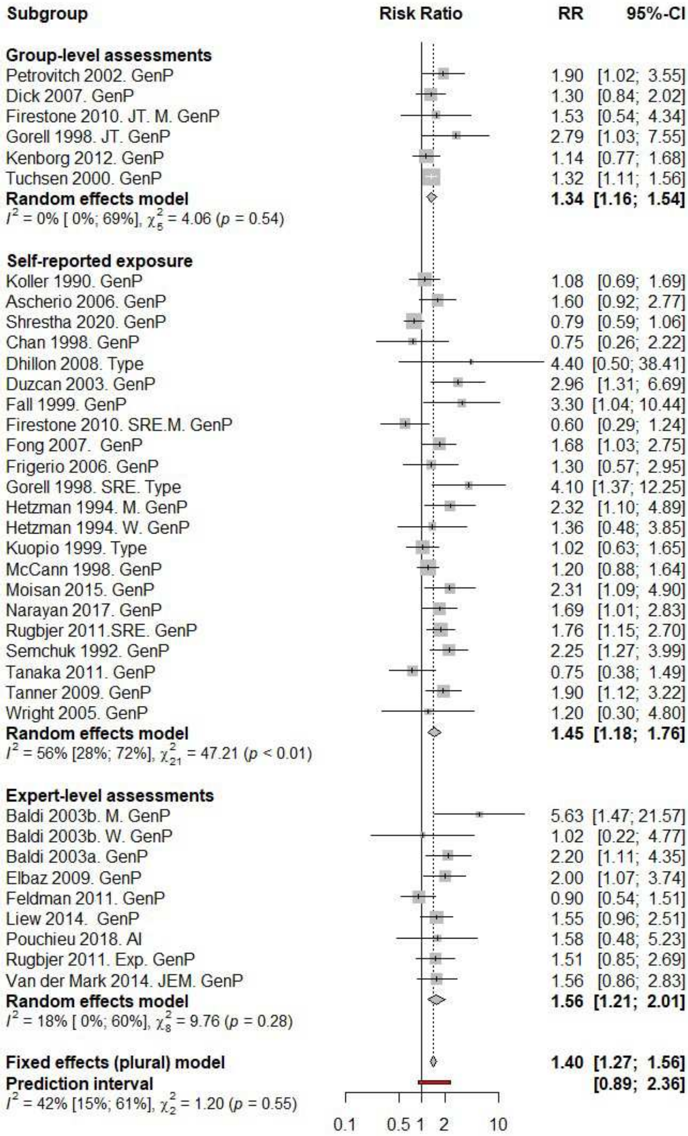

Figure S3.9. *Summary risk ratios for Parkinson's disease by EAM type based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1990-2020. RR=relative risk. I²=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

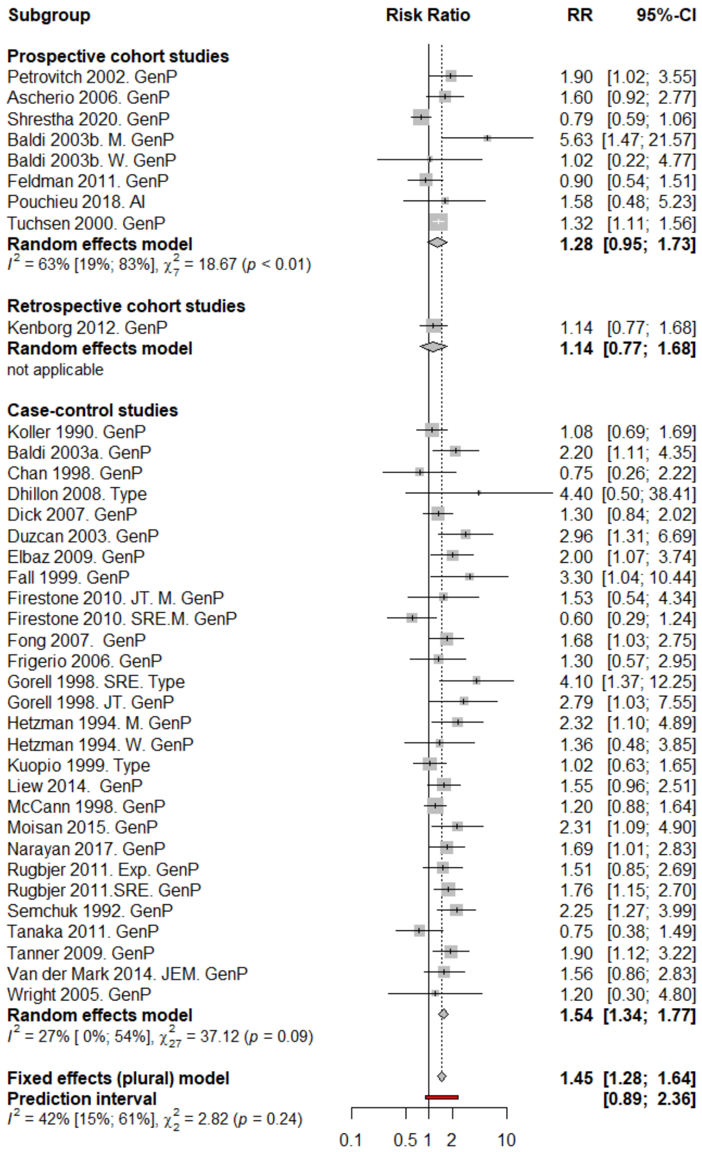

Figure S3.10. *Summary risk ratios for Parkinson's disease by study design based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1990-2020. RR=relative risk. I²=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

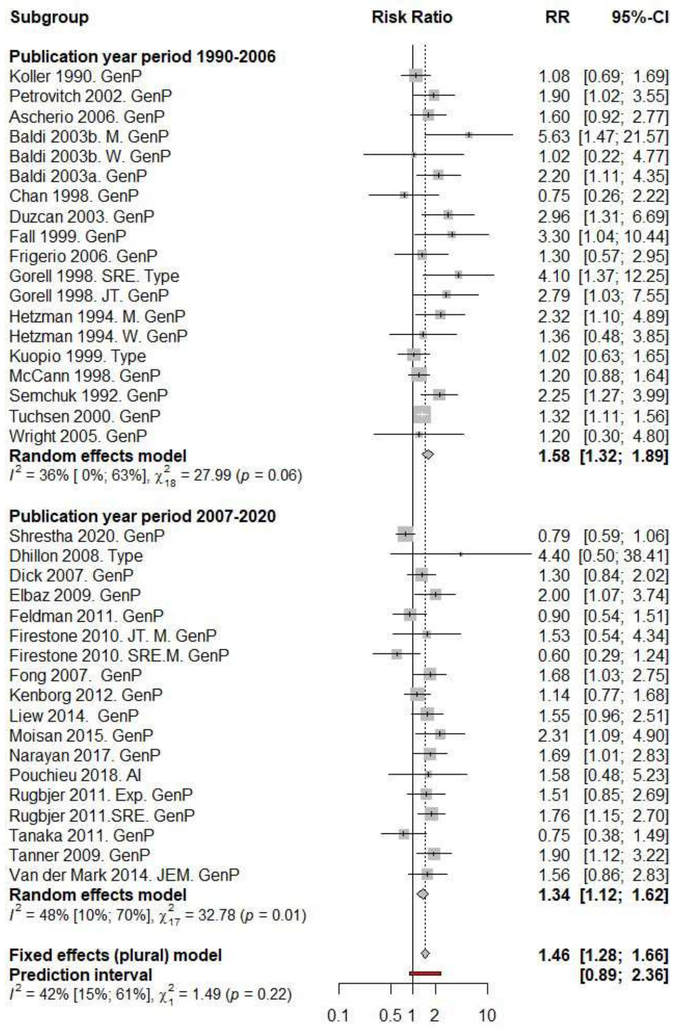

Figure S3.11. *Summary risk ratios for Parkinson's disease by publication year period based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1990-2020. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*

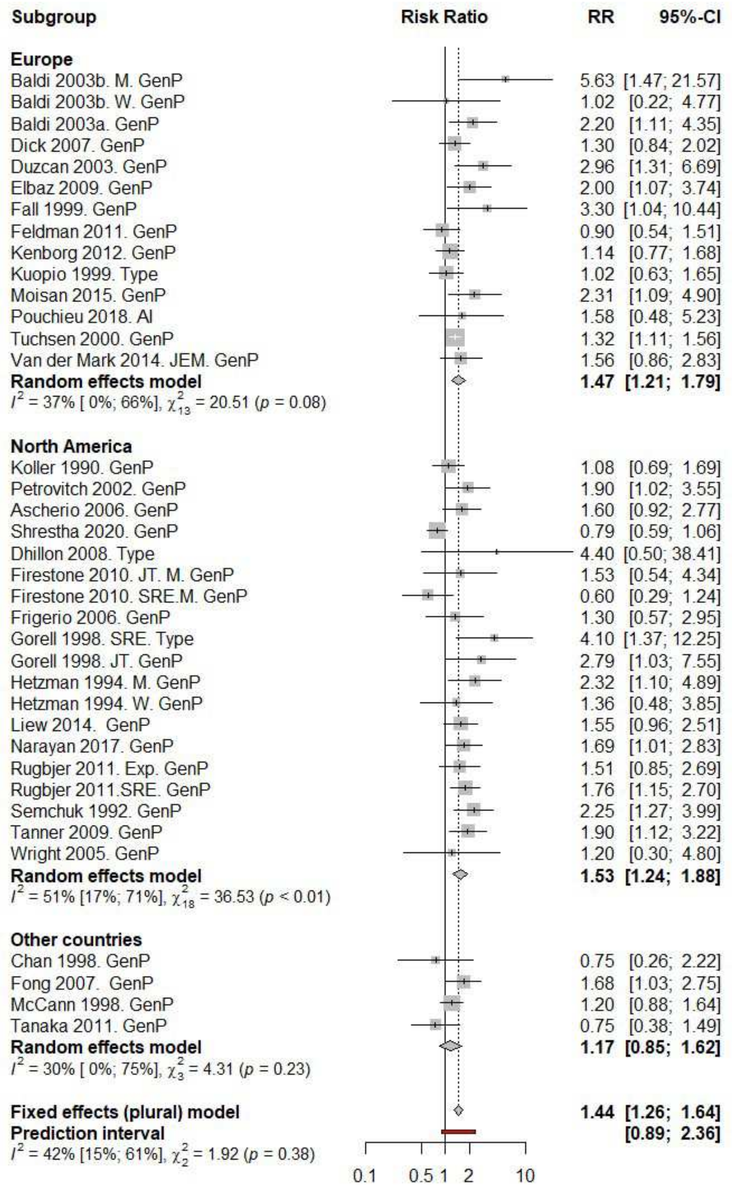

Figure S3.12. *Summary risk ratios for Parkinson's disease by geographic location where the study was performed based on random-effects meta-analysis of articles on occupational pesticide exposure published between 1990-2020. RR=relative risk. I^2=percentage of variation across studies due to heterogeneity. JT=job title. SRE=self-reported exposure. GenP=general pesticides. Type=type of pesticide. AI=active ingredient. AfrAm=Afro-American. W=women. M=men.*