

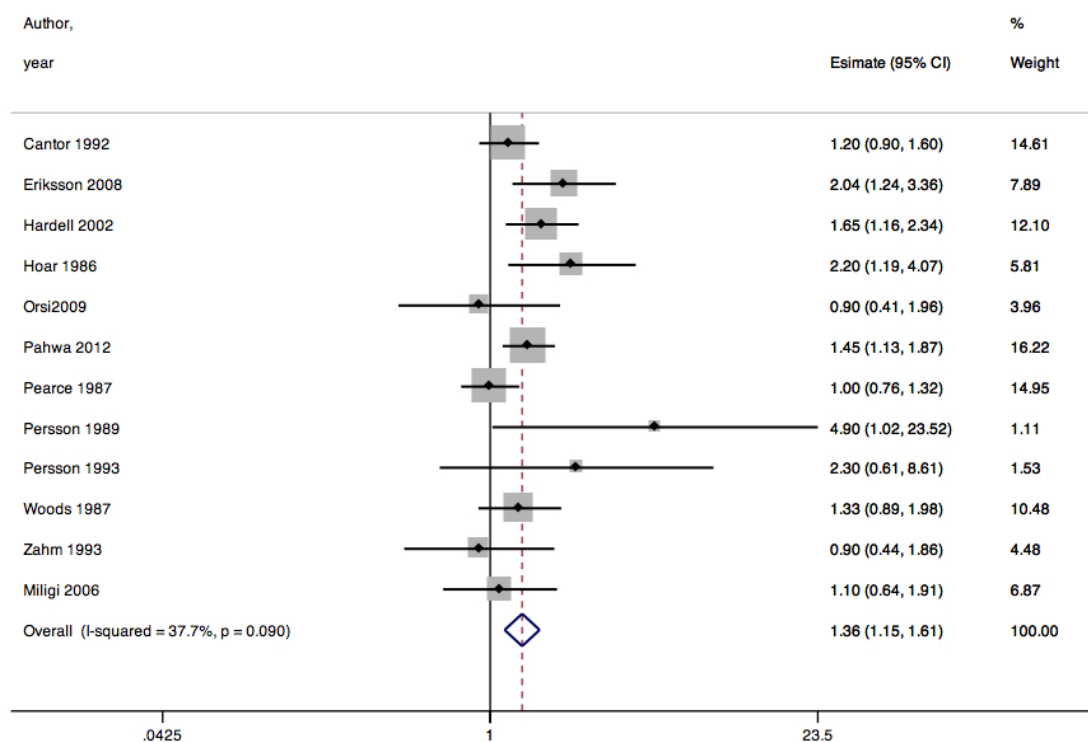
Non-Hodgkin Lymphoma and Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic Review and Meta-Analysis

S1. List of terms included in the PubMed literature search.

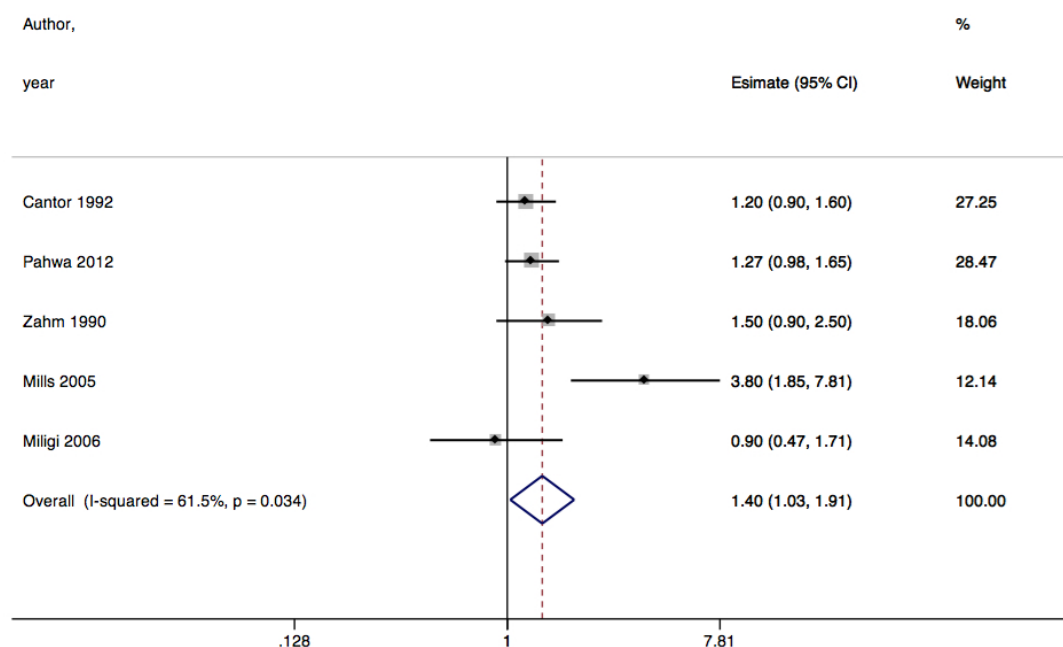
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OR "pesticides"[MeSH Terms] OR pesticides[nm] OR (insecticid[tiab] OR insecticidal[tiab] OR insecticidal/acaricidal[tiab] OR insecticidal/anthelmintic[tiab] OR insecticidal/antifeedant[tiab] OR insecticidal/irritant[tiab] OR insecticidal/larvicidal[tiab] OR insecticidal/narcotic[tiab] OR insecticidal'[tiab] OR insecticidal'b[tiab] OR insecticidally[tiab] OR insecticidation[tiab] OR insecticide[tiab] OR insecticide/acaricide[tiab] OR insecticide/antifeedant[tiab] OR insecticide/ascaricide[tiab] OR insecticide/atrazine[tiab] OR insecticide/fumigant[tiab] OR insecticide/fungicide[tiab] OR insecticide/herbicide[tiab] OR insecticide/kg[tiab] OR insecticide/lipid[tiab] OR insecticide/liter[tiab] OR insecticide/miticide[tiab] OR insecticide/mosquito[tiab] OR insecticide/nematicide[tiab] OR insecticide/nematocide[tiab] OR insecticide/organophosphrus[tiab] OR insecticide/pesticide/herbicide[tiab] OR insecticide/repellant[tiab] OR insecticide/repellent[tiab] OR insecticide'[tiab] OR insecticide's[tiab] OR insecticided[tiab] OR insecticideresistance[tiab] OR insecticideresistant[tiab] OR insecticides[tiab] OR insecticides/acaricides[tiab] OR insecticides/attract[tiab] OR insecticides/larvicides[tiab] OR insecticides/mn[tiab] OR insecticides/pesticides[tiab] OR insecticides/repellents[tiab] OR insecticides'[tiab] OR insecticidetreated[tiab] OR insecticidewise[tiab] OR insecticidal[tiab] OR insecticidic[tiab] OR insecticiding[tiab] OR insecticidity[tiab] OR insecticido[tiab]) OR "insecticides"[MeSH Terms] OR insecticides[nm] OR (herbicidal[tiab] OR herbicidally[tiab] OR herbicide[tiab] OR herbicide/binding[tiab] OR herbicide/dessicant[tiab] OR herbicide/fungicide[tiab] OR herbicide/g[tiab] OR herbicide/humic[tiab] OR herbicide/insect[tiab] OR herbicide/kg[tiab] OR herbicide/micelle[tiab] OR herbicide/ml[tiab] OR herbicide/mutation[tiab] OR herbicide/nematicide[tiab] OR herbicide/outcome[tiab] OR herbicide/pesticide[tiab] OR herbicide/substrate[tiab] OR herbicide/therapeutic[tiab] OR herbicide/tio2[tiab] OR herbicide's[tiab] OR herbicided[tiab] OR herbicideh[tiab] OR herbicideh/phytocide[tiab] OR herbicideinduced[tiab] OR herbicides[tiab] OR herbicides/chlorophenols[tiab] OR herbicides/desiccants[tiab] OR herbicides/fungicides[tiab] OR herbicides/pesticides[tiab] OR herbicides'[tiab] OR herbicidetolerant[tiab] OR herbicidies[tiab] OR herbicidin[tiab] OR herbicidins[tiab] OR herbicidovorans[tiab] OR herbicids[tiab]) OR (herbicides[nm] OR herbicidins[nm]) OR (fungicid[tiab] OR fungicidal[tiab] OR fungicidal/bactericidal[tiab] OR fungicidal/fungistatic[tiab] OR fungicidal/parasiticidal[tiab] OR fungicidally[tiab] OR fungicidals[tiab] OR fungicide[tiab] OR fungicide/algicide[tiab] OR fungicide/antioxidant[tiab] OR fungicide/bactericide[tiab] OR fungicide/disinfectant[tiab] OR fungicide/oomycetocide[tiab] OR fungicide/slimicide[tiab] OR fungicide's[tiab] OR fungicideal[tiab] OR fungicideinsensitive[tiab] OR fungicides[tiab] OR fungicides/herbicides[tiab] OR fungicides'[tiab] OR fungicidal[tiab] OR fungicidic[tiab] OR fungicidicus[tiab] OR fungicidin[tiab] OR fungicidine[tiab] OR fungicidity[tiab] OR fungicido[tiab] OR fungicidy[tiab])) AND ("1980/01/01"[PDAT] : "2013/06/31"[PDAT]) AND "humans"[MeSH Terms])) NOT News[Publication Type]) NOT Congresses[Publication Type]) NOT Review[Publication Type]) AND ("1980/01/01"[PDAT] : "2013/06/31"[PDAT]) AND "humans"[MeSH Terms]) NOT "child"[MeSH Terms] AND (("1980/01/01"[PDAT] : "2013/12/31"[PDAT]) AND "humans"[MeSH Terms]))

Figure S1. Forest plots showing estimates of association between non-Hodgkin lymphoma and occupational, agricultural exposures to (A) phenoxy herbicides, (B) 2,4-D, (C) MCPA, (D) glyphosate, (E) organochlorine insecticides, and (F) DDT.

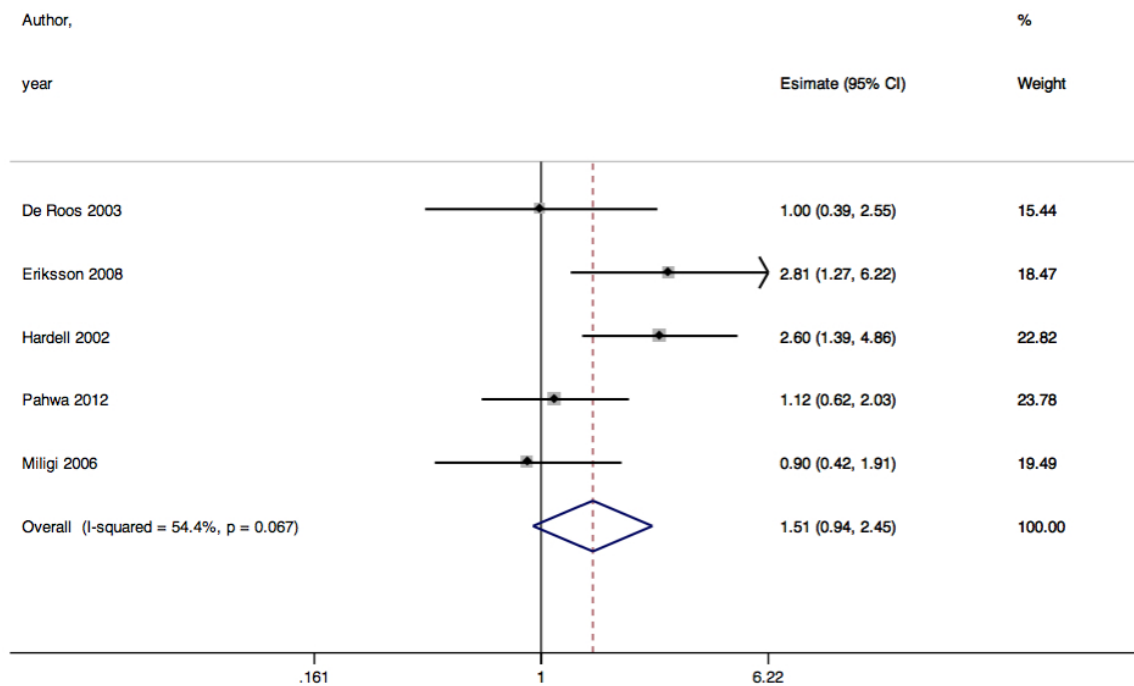


(A)

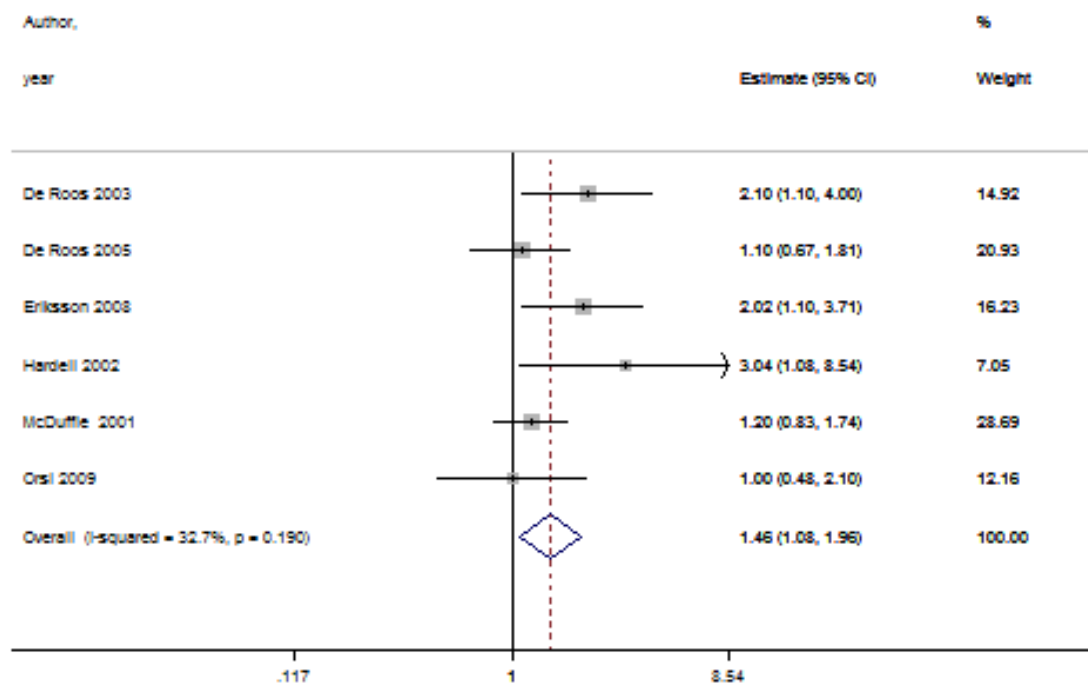


(B)

Figure S1. Cont.

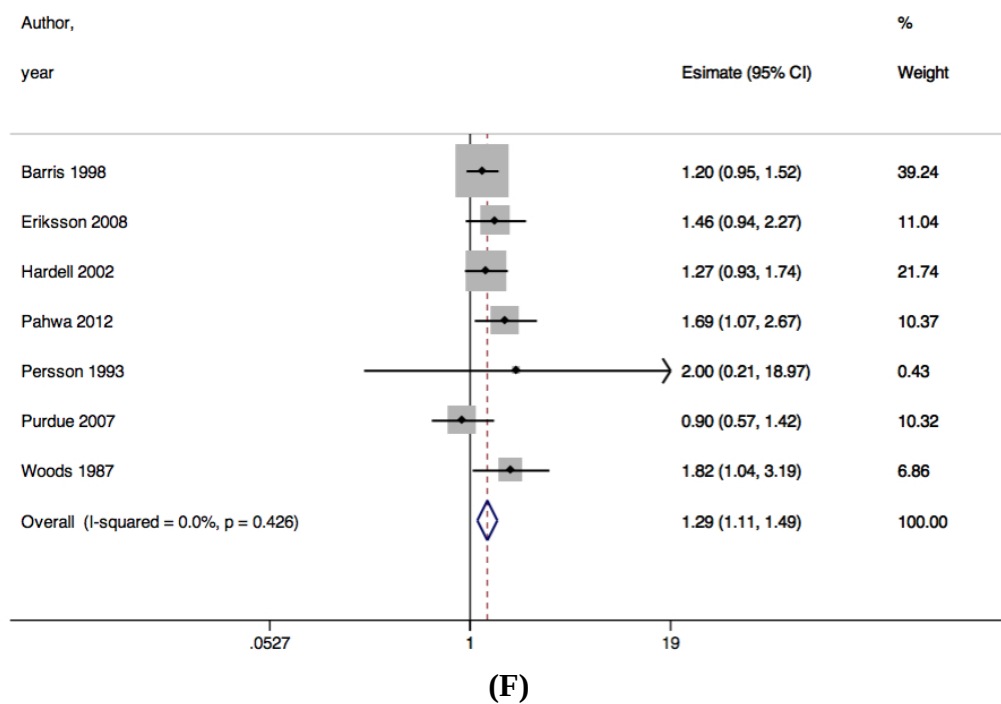
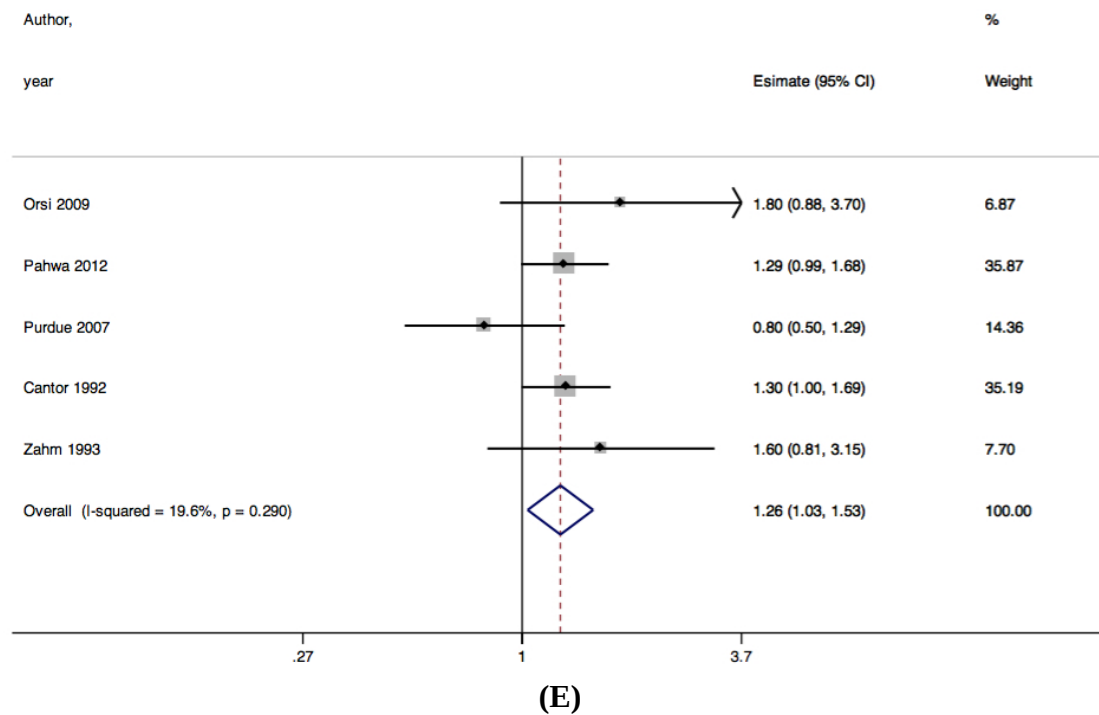


(C)



(D)

Figure S1. Cont.



Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid.

Table S1. Results of the sensitivity analysis of the effects of gender on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides

Chemical	Meta relative risk, 95% CI	I ²	Papers contributing
Male only population			
Amide herbicides	1.7, 0.7–3.8	64.0%	[1,2]
Glyphosate	1.7, 1.0–2.9	52.7%	[3–5]
Phenoxy herbicides	1.4, 1.1–1.6	44.1%	[1,2,4,6–8]
2,4–D	1.3, 1.2–1.5	0.0%	[1,6,9]
MCPA	1.5, 0.8–2.7	56.6%	[3,4,6]
Benzoic acid herbicides	1.3, 0.9–1.9	0.0%	[1,2]
Trifluralin	1.0, 0.6–1.5	0.0%	[3,5]
Triazine herbicides	1.5, 0.70–3.4	73.5%	[1,2]
OP insecticides	1.7, 1.3–2.1	39.2%	[6,10]
Diazinon	1.7, 1.2–2.3	0.0%	[5,10]
Malathion	1.8, 1.4–2.2	0.0%	[6,10]
Carbamate insecticides	1.8, 1.3–2.4	0.0%	[5,11]
OC insecticides	1.3, 1.1–1.6	0.0%	[1,6]
DDT	1.3, 1.1–1.5	27.3%	[4,6,8,12]
Aldrin	1.4, 0.2–11.1	92.0%	[3,5]
Chlordane	1.3, 0.9–1.7	0.0%	[3,5,8]
Lindane	1.9, 1.2–2.9	38.0%	[5,13,14]
Male and female population			
Phenoxy herbicides	1.6, 1.0–2.5	42.2%	[15–19]
2,4–D	1.8, 0.5–7.5	88.3%	[19,20]
MCPA	1.6, 0.5–4.8	76.0%	[15,19]
OC insecticides	1.2, 0.5–2.5	70.4%	[16,21]
DDT	1.2, 0.8–1.7	18.0%	[15,18,21]

Notes: 2,4–D, 2,4–Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2–methyl–4–chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP; Organophosphorus.

Table S2. Results of the sensitivity analysis of the effects of study design on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides, with contributing estimates restricted to case-control studies.

Chemical	Meta relative risk, 95% CI	I ²	Paper contributing
Glyphosate	1.6, 1.1–2.2	36.6%	[3–5,15,16]
Organochlorine insecticides	1.3, 1.1–1.6	0.0%	[1,6,16,22]
Aldrin	1.4, 0.2–11.1	92.0%	[3,5]
Chlordane	1.3, 0.9–1.7	0.0%	[3,5,8]
DDT	1.3, 1.1–1.6	0.0%	[4,6,8,12,15,18]
Lindane	1.9, 1.2–2.9	38.0%	[5,13,14]

Notes: DDT; dichlorodiphenyltrichloroethane.

Table S3. Results of the sensitivity analysis of the effects of diagnosis period on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides

Chemical	Meta relative risk, 95% CI	I ²	Papers contributing
Diagnosis period 1975–1989			
2,4-D	1.8, 1.0–3.1	76.6%	[1,9,20]
Amide herbicides	1.4, 0.8–2.3	43.2%	[1,2,22]
Glyphosate	2.3, 1.4–4.0	0.0%	[3,4]
MCPA	1.7, 0.7–4.4	63.8%	[3,4]
Phenoxy herbicides	1.4, 1.1–1.7	44.9%	[1,2,4,7,8,17,18,22]
Triazine herbicides	1.4, 0.9–2.2	47.3%	[1,2,23]
Carbamate insecticides	1.6, 1.1–2.4	0.0%	[11,22]
OC insecticides	1.3, 1.0–1.7	0.0%	[1,22]
OP insecticides	1.5, 1.2–1.8	0.0%	[10,22]
Diazinon	1.6, 1.2–2.2	0.0%	[10,20]
Chlordane	1.5, 1.0–2.5	0.0%	[3,8]
Trifluralin	0.9, 0.6–1.3	0.0%	[3,20,22]
Malathion	1.6, 1.3–2.1	0.0%	[10,20]
DDT	1.3, 1.1–1.5	0.0%	[4,8,12,18]
Lindane	2.0, 0.9–4.4	65.0%	[13,14]
Diagnosis period in the 1990s			
2,4-D	1.6, 0.8–3.1	79.3%	[6,19,20]
Glyphosate	1.5, 1.0–2.1	41.1%	[4,5,15,24]
MCPA	1.6, 0.9–2.9	61.9%	[4,6,15,19]
Phenoxy herbicides	1.5, 1.3–1.8	0.5%	[4,6,15,19]
Trifluralin	1.0, 0.6–1.6	0.0%	[5,20]
Aldrin	1.5, 0.2–10.1	90.0%	[5,21]
Chlordane	0.9, 0.6–1.4	42.2%	[5,21]
Diazinon	1.5, 1.0–2.4	0.0%	[5,20]
DDT	1.3, 1.0–1.6	25.4%	[4,6,15,21]
Lindane	1.9, 1.1–3.2	46.6%	[5,14,21]
Malathion	1.9, 1.5–2.5	0.0%	[6,20]
OC insecticides	1.1, 0.7–1.7	66.2%	[6,21]
Diagnosis period in the 2000s			
Glyphosate	1.3, 0.9–2.0	31.8%	[15,16,24]
Phenoxy herbicides	1.4, 0.7–3.2	66.7%	[15,16]
Lindane	2.0, 0.8–5.0	70.6%	[14, 21]
OC insecticides	1.2, 0.5–2.5	70.4%	[16,21]

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP; Organophosphorus;

¹ The first, second, and third editions of the International classification of diseases for oncology were introduced in 1976, 1990, and 2000, respectively.

Table S4. Results of the sensitivity analysis of the effects of geographic region on the meta-analytic relative risk estimates of association between non Hodgkin lymphoma and occupational exposure to agricultural pesticides

Chemical	Meta risk ratio estimate, 95% CI	I ²	Papers contributing
Only papers that report results from studies conducted in North America			
Glyphosate	1.3, 1.0–1.8	26.7%	[3,5,24]
Phenoxy herbicides	1.4, 1.1–1.6	12.9%	[1,2,6,8,22]
2,4–D	1.5, 1.1–2.1	66.5%	[1,6,9,20]
MCPA	1.1, 0.7–1.8	0.0%	[3,6]
DDT	1.3, 1.0–1.7	45.1%	[6,8,12,21]
OC insecticides	1.2, 1.0–1.5	24.7%	[1,6,21,22]
OP insecticides	1.6, 1.3–2.0	15.1%	[6,10,22]
Lindane	1.5, 1.2–1.9	0.0%	[5,13,21]
Only papers that report results from studies conducted in the United States			
2,4–D	1.8, 1.0–3.1	76.6%	[1,6,9,20]
Amide herbicides	1.4, 0.8–2.3	43.2%	[1,2,22]
Glyphosate	1.5, 0.8–2.8	58.5%	[3,24]
Phenoxy herbicides	1.3, 1.0–1.7	27.1%	[1,2,8,22]
Trifluralin	0.9, 0.6–1.3	0.0%	[3,20,22]
Triazine herbicides	1.4, 0.9–2.2	47.3%	[1,2,22]
Aldrin	0.5, 0.4–0.8	0.0%	[3,21]
Carbamate insecticides	1.6, 1.1–2.4	0.0%	[22,23]
Chlordane	1.1, 0.7–2.0	55.0%	[3,8,21]
DDT	1.2, 0.9–1.7	44.8%	[8,12,21]

Table S4. Cont.

Chemical	Meta risk ratio estimate, 95% CI	I ²	Papers contributing
Only papers that report results from studies conducted in the United States			
Diazinon	1.6, 1.2–2.2	0.0%	[10,20]
Lindane	1.4, 1.1–1.9	0.0%	[13,21]
Malathion	1.6, 1.3–2.1	0.0%	[10,20]
OC insecticides	1.2, 0.8–1.7	47.5%	[1,21,22]
OP insecticides	1.5, 1.2–1.8	0.0%	[10,22]
Only papers that report results from studies conducted in European countries			
Glyphosate	1.7, 1.0–3.1	42.8%	[4,15,16]
Phenoxy herbicides	1.6, 1.2–2.1	29.1%	[4,15–19]
MCPA	1.9, 0.9–3.8	64.8%	[4,15,19]
Only papers that report results from studies conducted in Sweden			
Glyphosate	2.2, 1.3–3.8	0.0%	[4,15]
MCPA	2.7, 1.6–4.4	0.0%	[4,15]
Phenoxy herbicides	1.9, 1.4–2.4	0.0%	[4,15,17,18]
DDT	1.3, 1.0–1.7	0.0%	[4,15,18]
Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP; Organophosphorus			

Table S5. Results of the sensitivity analysis of the effects of control source on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides, with contributing estimates restricted to those from population-based case-control studies.

Chemical	Meta risk ratio estimate, 95% CI	I ²	Papers contributing
HERBICIDES			
Amide herbicides	1.4, 0.8–2.3	43.2%	[1,2,22]
Glyphosate	1.7, 1.2–2.6	39.0%	[3,4,5,15]
Phenoxy herbicides	1.5, 1.2–1.7	20.7%	[1,2,4,6,8,15,17–19,22]
Triazine herbicides	1.4, 0.9–2.2	47.3%	[1,2,22]
INSECTICIDES			
Organochlorine insecticides	1.2, 1.0–1.5	24.7%	[1,6,21,22]
Organophosphate insecticides	1.6, 1.4–1.8	0.0%	[1,6,10,22]

Table S6. Results of the sensitivity analysis of the effects of paper contributing on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides.

Chemical	Meta estimate, 95% CI	I ²	Change	Papers contributing
HERBICIDES				
Alachlor	0.9, 0.6–1.5	69.7%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,25]
Glyphosate	1.3, 1.0–1.7	18.2%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,24]
2,4-D	1.3, 0.8–2.1	82.5%	Use De Roos 2003 [3] instead of Cantor 1992 [1] and Zahm 1990 [9]	[3,6,19,20]
Carbamate herbicides	1.2, 0.5–2.6	24.8%	Use Cantor 1992 [1] and Hoar 1986 [2] instead of Zheng 2001 [11]	[1,2,16,22]
Trifluralin	1.1, 0.7–1.8	40.0%	Use Cantor 1992 [1] and Hoar 1986 [2] instead of De Roos 2003[3]	[1,2,5,20,22]
INSECTICIDES				
OP insecticides	1.7, 1.4–2.0	0.0%	Use Cantor 1992 [1] instead of Waddell 2001 [10]	[1,6,16,22]
Diazinon	1.5, 1.1–2.1	0.0%	Use Cantor 1992 [1] instead of Waddell 2001 [10]	[1,3,5,20]
Diazinon	1.7, 1.2–2.4	0.0%	Use De Roos 2003 [3] instead of Cantor 1992 [1] and instead of Waddell 2001 [10]	[3,5,20]
Dimethoate	1.2, 0.7–2.0	0.0%	Use De Roos 2003 [3] instead of Waddell 2001 [10]	[3,5]
Malathion	1.7, 1.3–2.2	13.5%	Use Cantor 1992 [1] (use of malathion on animals) instead of Waddell 2001 [10] or De Roos 2003 [3]	[1,6,20]
Malathion	1.8, 1.4–2.4	0.0%	Use Cantor 1992 [1] (use of malathion on crops) instead of Waddell 2001 [10] or De Roos 2003 [3]	[1,6,20]
Malathion	1.6, 1.2–2.3	37.2%	Use De Roos 2003 [3] instead of Waddell 2001 [10] and Cantor 1992 [1]	[3,6,20]
Carbaryl	1.9, 1.3–2.9	0.0%	Use Cantor 1992 [1] instead of Zheng 2001 [11]	[1,5]
Carbaryl	1.5, 0.7–3.1	64.7%	Use De Roos 2003 [3] instead of Cantor 1992 [1] or Zheng 2001 [11]	[3,5]
Carbofuran	1.1, 0.7–1.8	0.0%	Use Cantor 1992 [1] instead of Zheng 2001 [11]	[1,5]

Table S6. Cont.

Chemical	Meta estimate, 95% CI	I ²	Change	Papers contributing
Carbofuran	1.1, 0.6–2.0	23.0%	Use De Roos 2003 [3] instead of Cantor 1992 [1] or Zheng 2001 [11]	[3,5]
DDT	1.3, 1.1–1.5	0.0%	Use Cantor 1992 [1] (use of DDT on animals) instead of Baris 1998 [12]	[1,4,6,8,15,18,21]
DDT	1.3, 1.2–1.6	9.1%	Use Cantor 1992 [1] (use of DDT on crops) instead of Baris 1998 [12]	[1,4,6,8,15,18,21]
Methoxychlor	1.0, 0.8–1.4	0.0%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,5]
Aldrin	1.3, 0.5–2.9	80.2%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,5,21]
Chlordane	1.2, 0.8–1.7	48.7%	Use Cantor 1992 [1] (Use of chlordane on animals) instead of De Roos 2003 [3]	[1,5,8,21]
Chlordane	1.1, 0.8–1.7	42.1%	Use Cantor 1992 [1] (Use of chlordane on crops) instead of De Roos 2003 [3]	[1,5,8,21]
Dieldrin	1.0, 0.4–2.2	50.8%	Use Cantor 1992 [1] instead of De Roos 2003[3]	[1,21]
Heptachlor	1.0, 0.7–1.7	20.5%	Use Cantor 1992 [1] instead of De Roos 2003[3]	[1,21]
Lindane	1.62, 1.16–2.27	30.6%	Use Cantor 1992 [1] (use of lindane on animals) instead of Blair 1998 [13] and De Roos 2003 [3]	[1,5,14,21]
Lindane	1.85, 1.27–2.69	23.30 %	Use Cantor 1992 [1] (use of lindane on crops) instead of Blair 1998 [13]and De Roos 2003 [3]	[1,5,14,21]
Lindane	1.62, 1.08–2.41	39.20 %	Use De Roos 2003 [3] instead of Cantor 1992 [1] or Blair 1998 [13]	[3,5,14,21]
Toxaphene	1.25, 0.72–2.19	23.50 %	Use Cantor 1992 [1] (use of toxaphene on animals) instead of De Roos 2003 [3]	[1,20,21]
Toxaphene	1.50, 0.96–2.33	0.00%	Use Cantor 1992 [1] (use of toxaphene on crops) instead of De Roos 2003 [3]	[1,20,21]

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP; Organophosphorus.

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