

Supplementary Information

Exposure to organochlorine pesticides and non-Hodgkin lymphoma: a meta-analysis of observational studies

Dan Luo¹, Tingting Zhou¹, Yun Tao¹, Yaqian Feng¹, Xiaoli Shen¹ & Surong Mei^{1,*}

¹State Key Laboratory of Environment Health (Incubation), Key Laboratory of Environment and Health, Ministry of Education, Key Laboratory of Environment and Health (Wuhan), Ministry of Environmental Protection, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, #13 Hangkong Road, Wuhan, Hubei, 430030, China

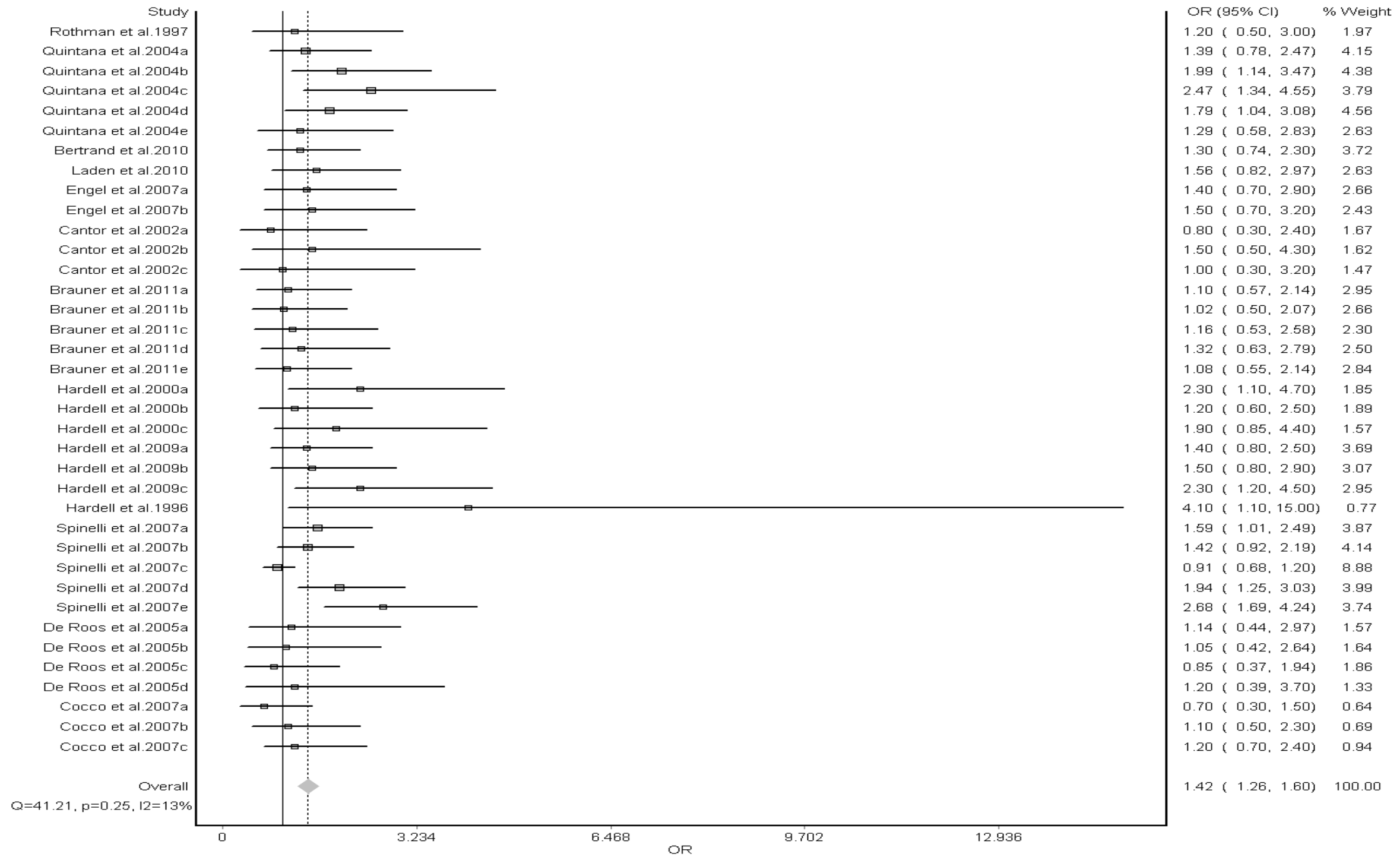
*Corresponding author:

Surong Mei; E-mail: surongmei@hust.edu.cn

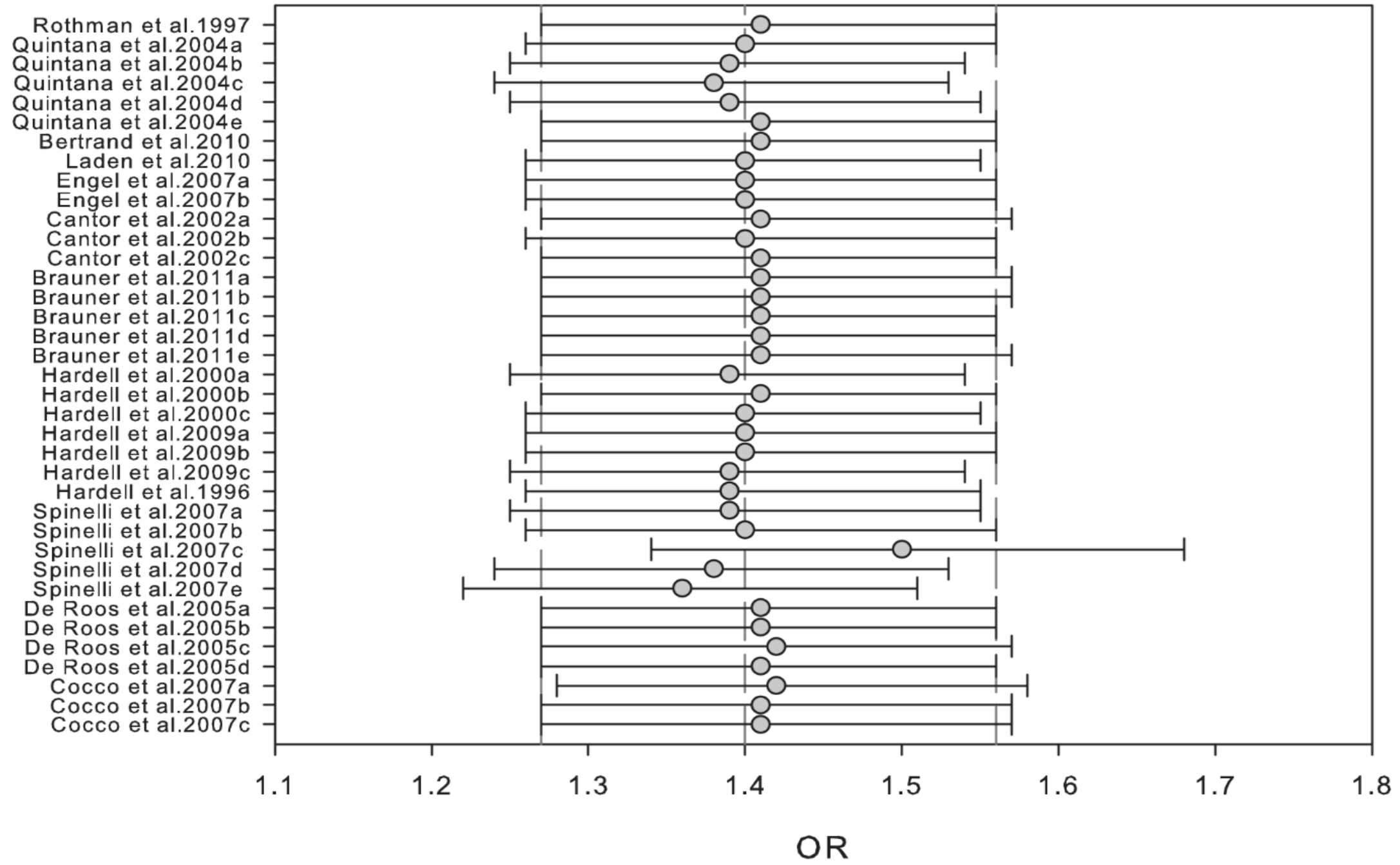
Address: School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, #13 Hangkong Road, Wuhan, Hubei, 430030, China;

Tel: +86(27)-83657849;

Fax: +86(27)-83657765.



Supplementary Figure S1. Pooled ORs with 95% CIs for the association of organochlorine pesticides and non-Hodgkin lymphoma risk based on quality-effect model. The solid diamonds and horizontal lines correspond to the study-specific ORs and 95% CIs. The gray areas reflect the study-specific weight. The hollow diamonds represent the pooled OR and 95% CI of each OCPs and the summary OR. The vertical solid lines show the OR of 1 and the vertical dashed lines indicate the corresponding pooled ORs.



Supplementary Figure S2. Results of sensitivity analysis using leave-one-out method. The gray circles and the horizontal lines represent the pooled ORs and 95% CIs after omitting studies in turn.

Supplementary Table S1. Characteristics of nested case-control studies and case-cohort studies relating organochlorine pesticides and non-Hodgkin lymphoma

Reference	Country	Cases/Controls	Objects ^a	Sample type	Gender ^b	Age (cases/controls) ^c	Unit	OR or RR(95% CI) ^d	Adjustments
Nested case-control									
Rothman et al.1997	USA	74/147	DDT	Serum	F/M	52.9/52.5 (mean)	ng/g lipid	1.2(0.50-3.00)	DDT and PCB risk estimates adjusted for each other
Quintana et al.2004a	USA	175/481	DDT	Adipose tissue	F/M	49.0 ± 22.4/50.0 ± 21.9	µg/g lipid	1.39(0.78-2.47)	Crude
Quintana et al.2004b	USA	175/481	DDE	Adipose tissue	F/M	49.0 ± 22.4/50.0 ± 21.9	µg/g lipid	1.99(1.14-3.47)	Crude
Quintana et al.2004c	USA	175/481	HCH	Adipose tissue	F/M	49.0 ± 22.4/50.0 ± 21.9	µg/g lipid	2.47(1.34-4.55)	Crude
Quintana et al.2004d	USA	175/481	Chlordane	Adipose tissue	F/M	49.0 ± 22.4/50.0 ± 21.9	µg/g lipid	1.79(1.04-3.08)	Crude
Quintana et al.2004e	USA	175/481	HCB	Adipose tissue	F/M	49.0 ± 22.4/50.0 ± 21.9	µg/g lipid	1.29(0.58-2.83)	Crude
Bertrand et al.2010	USA	205/409	DDE	Plasma	M	40-84	ng/g lipid	1.3(0.74-2.30)	BMI,smoking,alcohol intake,height
Laden et al.2010	USA	145/290	DDE	Plasma	F	44-69	ng/g lipid	1.56(0.82-2.97)	Region,BMI,smoking status,parity,breastfeeding,height
Engel et al.2007a	Norway	190/190	DDE	Serum	F/M	42.9 ± 5.3/42.9 ± 5.3	ng/g lipid	1.4(0.70-2.90)	BMI,smoking status
Engel et al.2007b	USA	74/147	DDE	Serum	F/M	52.9±13.2/52.5±13.8	ng/g lipid	1.5(0.70-3.20)	Years of education,smoking status
Cantor et al.2002a	USA	74/147	Chlordane	Serum	F/M	NA	ng/g lipid	0.8(0.30-2.40)	Crude
Cantor et al.2002b	USA	74/147	HCH	Serum	F/M	NA	ng/g lipid	1.5(0.50-4.30)	Crude
Cantor et al.2002c	USA	74/147	HCB	Serum	F/M	NA	ng/g lipid	1.0(0.30-3.20)	Crude
Case-cohort									
Brauner et al.2011a	Denmark	239/245	DDE	Adipose tissue	F/M	64/56 (median)	µg/kg lipid	1.1(0.57-2.14)	Age,sex,BMI
Brauner et al.2011b	Denmark	239/245	HCH	Adipose tissue	F/M	64/56 (median)	µg/kg lipid	1.02(0.50-2.07)	Age,sex,BMI
Brauner et al.2011c	Denmark	239/245	HCB	Adipose tissue	F/M	64/56 (median)	µg/kg lipid	1.16(0.53-2.58)	Age,sex,BMI
Brauner et al.2011d	Denmark	239/245	Chlordane	Adipose tissue	F/M	64/56 (median)	µg/kg lipid	1.32(0.63-2.79)	Age,sex,BMI
Brauner et al.2011e	Denmark	239/245	DDT	Adipose tissue	F/M	64/56 (median)	µg/kg lipid	1.08(0.55-2.14)	Age,sex,BMI

^a DDT-dichlorodiphenyltrichloroethane, DDE-dichlorodiphenyldichloroethylene, HCH-hexachlorocyclohexane, HCB-hexachlorobezene.

^b F means female, M means male, F/M means the study includes both female and male objects.

^c NA means the data is not available.

^d OR means odds ratio, and CI means confidence interval.

Supplementary Table S2. Characteristics of case-control studies relating organochlorine pesticides and non-Hodgkin lymphoma

Reference	Country	Cases/Controls	Objects ^a	Sample type	Gender ^b	Age (cases/controls)	Unit	OR or RR (95% CI) ^c	Adjustments
Hardell et al.2000a	Sweden	82/83	HCB	Adipose tissue and blood	F/M	62.5/62.3 (mean)	ng/g lipid	2.3(1.10-4.70)	Age,sex,BMI,specimen analysed (blood or adipose tissue)
Hardell et al.2000b	Sweden	82/83	DDE	Adipose tissue and blood	F/M	62.5/62.3 (mean)	ng/g lipid	1.2(0.60-2.50)	Age,sex,BMI,specimen analysed (blood or adipose tissue)
Hardell et al.2000c	Sweden	82/83	Chlordane	Adipose tissue and blood	F/M	62.5/62.3 (mean)	ng/g lipid	1.9(0.85-4.40)	Age,sex,BMI,specimen analysed (blood or adipose tissue)
Hardell et al.2009a	Sweden	99/99	HCB	Plasma	F/M	55.9/56.4(mean)	ng/g lipid	1.4(0.80-2.50)	Age,sex,BMI
Hardell et al.2009b	Sweden	99/99	DDE	Plasma	F/M	55.9/56.4(mean)	ng/g lipid	1.5(0.80-2.90)	Age,sex,BMI
Hardell et al.2009c	Sweden	99/99	Chlordane	Plasma	F/M	55.9/56.4(mean)	ng/g lipid	2.3(1.20-4.50)	Age,sex,BMI
Hardell et al.1996	Sweden	27/17	Chlordane	Adipose tissue	F/M	64.4/60.5 (mean)	ng/g lipid	4.1(1.10-150)	Crude
Spinelli et al.2007a	Canada	422/460	HCH	Plasma	F/M	20-79	ng/g lipid	1.59(1.01-2.49)	Age,ethnicity,family history of NHL
Spinelli et al.2007b	Canada	422/460	DDE	Plasma	F/M	20-79	ng/g lipid	1.42(0.92-2.19)	Age,BMI,ethnicity
Spinelli et al.2007c	Canada	422/460	DDT	Plasma	F/M	20-79	ng/g lipid	0.91(0.68-1.20)	Crude
Spinelli et al.2007d	Canada	422/460	HCB	Plasma	F/M	20-79	ng/g lipid	1.94(1.25-3.03)	Age,sex,BMI
Spinelli et al.2007e	Canada	422/460	Chlordane	Plasma	F/M	20-79	ng/g lipid	2.68(1.69-4.24)	Age,BMI
De Roos et al.2005a	USA	100/100	Chlordane	Plasma	F/M	20-74	ng/g lipid	1.14(0.44-2.97)	Sex,study site,birth date,date of blood draw
De Roos et al.2005b	USA	100/100	HCH	Plasma	F/M	20-74	ng/g lipid	1.05(0.42-2.64)	Sex,study site,birth date,date of blood draw
De Roos et al.2005c	USA	100/100	DDE	Plasma	F/M	20-74	ng/g lipid	0.85(0.37-1.94)	Sex,study site,birth date,date of blood draw
De Roos et al.2005d	USA	100/100	DDT	Plasma	F/M	20-74	ng/g lipid	1.2(0.39-3.70)	Sex,study site,birth date,date of blood draw
Cocco et al.2007a	France,Germany ,Spain	174/203	HCH	Plasma	F/M	58.0±15.6/54.7±15.6	ng/mL	0.7(0.30-1.50)	Crude
Cocco et al.2007b	France,Germany ,Spain	174/203	HCB	Plasma	F/M	58.0±15.6/54.7±15.6	ng/mL	1.1(0.50-2.30)	Crude
Cocco et al.2007c	France,Germany ,Spain	174/203	DDE	Plasma	F/M	58.0±15.6/54.7±15.6	ng/mL	1.2(0.70-2.40)	Crude

^a DDT-dichlorodiphenyltrichloroethane, DDE-dichlorodipenyldichloroethylene, HCH-hexachlorocyclohexane, HCB-hexachlorobezene.

^b F means female, M means male.

^c OR means odds ratio, and CI means confidence interval

Supplementary Table S3. Quality assessments of the nested case-control and case-cohort studies relating organochlorine pesticides and non-Hodgkin lymphoma

Study	Selection				Comparability		Exposure			Overall quality score
	1	2	3	4	5A	5B	6	7	8	
Rothman et al.1997	0	1	1	1	1	1	1	1	0	7
Quintana et al.2004a	1	1	1	1	1	1	1	1	0	8
Quintana et al.2004b	1	1	1	1	1	1	1	1	0	8
Quintana et al.2004c	1	1	1	1	1	1	1	1	0	8
Quintana et al.2004d	1	1	1	1	1	1	1	1	0	8
Quintana et al.2004e	1	1	1	1	1	1	1	1	0	8
Bertrand et al.2010	0	1	1	1	1	1	1	1	0	7
Laden et al.2010	0	1	1	1	1	1	1	0	0	6
Engel et al.2007a	0	1	1	1	1	1	1	1	0	7
Engel et al.2007b	0	1	1	1	1	1	1	1	0	7
Cantor et al.2002a	0	1	1	1	1	1	1	1	0	7
Cantor et al.2002b	0	1	1	1	1	1	1	1	0	7
Cantor et al.2002c	0	1	1	1	1	1	1	1	0	7
Brauner et al.2011a	0	1	1	1	1	1	1	1	0	7
Brauner et al.2011b	0	1	1	1	1	1	1	1	0	7
Brauner et al.2011c	0	1	1	1	1	1	1	1	0	7
Brauner et al.2011d	0	1	1	1	1	1	1	1	0	7
Brauner et al.2011e	0	1	1	1	1	1	1	1	0	7

*The study quality was assessed according to the Newcastle Ottawa Quality assessment scale for nested case-control studies. This scale awards a maximum of 9 points to each study: 4 for selection, 2 for comparability, and 3 for assessment of outcomes (for cohort study). 1 = "Yes", 0 = "No", "Unable to determine" or "Not available". For cohort studies, 1, indicates exposed cohort truly representative; 2, non-exposed cohort drawn from the same community; 3, ascertainment of exposure; 4, outcome of interest not present at start; 5A, cohorts comparable on basis of age; 5B, cohorts comparable on other factor(s); 6, quality of outcome assessment; 7, follow-up long enough for outcomes to occur; and 8, complete accounting for cohorts.

Supplementary Table S4. Quality assessment of the case-control studies relating organochlorine pesticides and non-Hodgkin lymphoma

Study	Selection				Comparability		Exposure			Overall quality score
	1	2	3	4	5A	5B	6	7	8	
Hardell et al.2000a	0	0	0	0	1	1	1	1	1	5
Hardell et al.2000b	0	0	0	0	1	1	1	1	1	5
Hardell et al.2000c	0	0	0	0	1	1	1	1	1	5
Hardell et al.2009a	1	1	1	0	1	1	1	1	0	7
Hardell et al.2009b	1	1	1	0	1	1	1	1	0	7
Hardell et al.2009c	1	1	1	0	1	1	1	1	0	7
Hardell et al.1996	1	0	0	0	1	0	1	1	0	4
Spinelli et al.2007a	0	0	1	0	1	1	1	1	0	5
Spinelli et al.2007b	0	0	1	0	1	1	1	1	0	5
Spinelli et al.2007c	0	0	1	0	1	1	1	1	0	5
Spinelli et al.2007d	0	0	1	0	1	1	1	1	0	5
Spinelli et al.2007e	0	0	1	0	1	1	1	1	0	5
De Roos et al.2005a	1	0	1	0	1	1	1	1	0	6
De Roos et al.2005b	1	0	1	0	1	1	1	1	0	6
De Roos et al.2005c	1	0	1	0	1	1	1	1	0	6
De Roos et al.2005d	1	0	1	0	1	1	1	1	0	6
Cocco et al.2007a	0	0	0	0	0	0	1	1	0	2
Cocco et al.2007b	0	0	0	0	0	0	1	1	0	2
Cocco et al.2007c	0	0	0	0	0	0	1	1	0	2

* The study quality was assessed according to the Newcastle Ottawa Quality assessment scale for case-control studies. This scale awards a maximum of 9 points to each study: 4 for selection, 2 for comparability, and 3 for assessment of outcomes (for cohort study). 1 = "Yes", 0 = "No", "Unable to determine" or "Not available". For case-control studies, 1, indicates cases independently validated; 2, cases are representative of population; 3, community controls; 4, controls have no history of Non-Hodgkin Lymphoma; 5A, study controls for age; 5B, study controls for additional factor(s); 6, ascertainment of exposure by blinded interview or record; 7, same method of ascertainment used for cases and controls; and 8, nonresponse rate the same for cases and controls.