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Supplemental Material

Pesticide Use and Incident Hypothyroidism in Pesticide Applicators in the Agricultural Health Study

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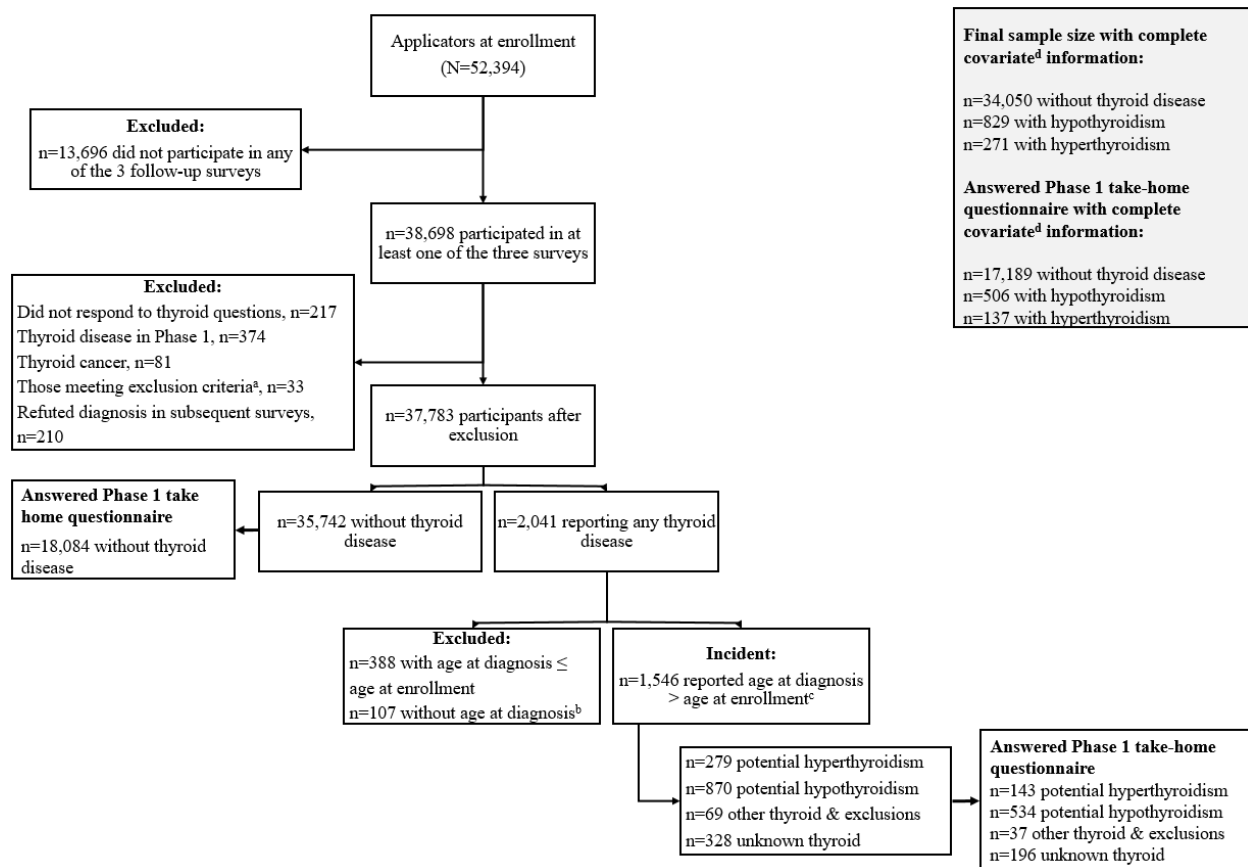


Figure S1: Selection of the participants for the study.

^aExamples – non-thyroid conditions such as pituitary tumors

^bWith no information on whether thyroid disease was diagnosed before or after enrollment

^cAge at diagnosis for n=47 thyroid cases was imputed as mid-point between the last report of no disease and when the disease was first reported

^dCovariates (age, gender, state, education, and smoking) that were included in the model were considered

Table S1: Thyroid disease information collected in the Agricultural Health Study.

Phase 1
Has a doctor ever told you that you had been diagnosed with
1) a. Goiter
b. How old were you when the doctor first told you?
2) a. Thyrotoxicosis/Grave's disease (excess thyroid hormone)
b. How old were you when the doctor first told you?
3) a. Other thyroid disease.
b. How old were you when the doctor first told you?

Phase 2
Has a doctor or other health professional ever told you that you had thyroid disease or thyroid problem?
1) Were you told you had an overactive thyroid (also called hyperthyroidism)?
a. Was it due to Graves' disease?
i. How old were you when the doctor first told you that you had this (Graves' disease)?
ii. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?
b. Was it due to thyrotoxicosis?
i. How old were you when the doctor first told you had this (thyrotoxicosis)?
ii. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?
c. Was there some other cause that was identified?
i. What was this cause?
ii. How old were you when the doctor first told you had this condition?
iii. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?
2) Were you told you had an underactive thyroid (also called hypothyroidism)?
a. Was this due to thyroiditis, Hashimoto's disease or autoimmune disease?
i. How old were you when the doctor first told you had this condition?
ii. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?
b. Was there some other cause that was identified?
i. What was this cause?
ii. How old were you when the doctor first told you had this condition?
iii. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?
3) Were you ever told you had an enlarged thyroid, thyroid nodules or Goiter?
a. How old were you when the doctor first told you had this?
b. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?
4) Were you ever told that you had some other thyroid problem?
a. What was this?
b. How old were you when the doctor first told you had this condition?
c. Do you take any medicines for this condition, or did you receive any treatment (like surgery) at the time it was diagnosed?

Phase 3
Have you ever been diagnosed with thyroid disease or thyroid problems?
1) Have you ever been diagnosed with an overactive thyroid (hyperthyroidism)?
a. Was this Graves' disease or some other type of thyroid condition that caused overactive thyroid gland?

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- i. How old were you when you were first diagnosed with an overactive thyroid condition?
 - ii. Do you currently take any prescribed medicines for this condition?
- 2) Have you ever been diagnosed with an underactive thyroid (hypothyroidism)?
- a. Was this thyroiditis (sometimes called Hashimoto's thyroiditis) or was this some other type of thyroid condition that caused underactive thyroid gland?
 - i. How old were you when participant was first diagnosed with an underactive thyroid condition?
 - ii. Do you currently take any prescribed medicines for this condition?
- 3) If participant do not know about it was over- or under-active thyroid, then they were asked about their age when they were first diagnosed with thyroid disease and if they currently take any prescribed medicines for this condition.
-

Phase 4

Have you ever been diagnosed with thyroid disease or thyroid problem?

- 1) Have you ever been diagnosed with overactive thyroid (hyperthyroidism)?
- a. How old were you when you were first diagnosed with an overactive thyroid?
 - b. Was this Graves' disease or some other type of thyroid condition that caused the overactive thyroid gland?
 - c. Do you currently take any prescribed medicines for an overactive thyroid?
- 2) Have you ever been diagnosed with an underactive thyroid (hypothyroidism)?
- a. How old were you when you were first diagnosed with an underactive thyroid?
 - b. Was this thyroiditis, sometimes called Hashimoto's thyroiditis, or some other type or thyroid condition that caused the underactive thyroid gland?
 - c. Do you currently take any prescribed medicines for an underactive thyroid?
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Table S2: Decision criteria for hyperthyroidism and hypothyroidism (N=1,546).

General exclusions		Incident cases
1	Participants responded 'yes' to 'goiter' or 'other thyroid disease' but did report whether they had hyperthyroidism or hypothyroidism in Phase 2	30
2	Participants responded to thyroid disease question in all three follow-ups but provided inconsistent responses. They reported having thyroid disease in a preceding survey but refuted in subsequent surveys. All but few cases were excluded. Please see bullets 8 and 12 for the exceptions.	13
3	Participants responded 'yes' to thyroid disease question but did not provide information if the disease was hypothyroidism or hyperthyroidism in any follow-up	328
Hyperthyroidism assigned		
4	Participants reported having hyperthyroidism, or both hyperthyroidism and hypothyroidism in the same survey but with age at hyperthyroidism diagnosis \leq age at hypothyroidism diagnosis consistently across the three follow-ups	249
5	Participants reported having both hyperthyroidism and hypothyroidism but did not report sufficient information to differentiate whether hyperthyroidism or hypothyroidism occurred first	1
6	Participants reported having hyperthyroidism in two surveys although they reported having hypothyroidism in one survey, irrespective of the response order	1
7	Participants reported having hyperthyroidism in only one of the three follow-ups, and reported hypothyroidism in other subsequent surveys but not preceding surveys	26
8	Participants reported hyperthyroidism in two surveys although refuted thyroid disease diagnosis in the third survey, irrespective of the response order	2
Total		279
Hypothyroidism assigned		
9	Participants reported hypothyroidism in any of the three follow-ups but did not report having hyperthyroidism in other phases	856
10	Participants reported having hypothyroidism in the two consecutive surveys but followed by report of hyperthyroidism or both thyroid conditions	4
11	Reports of hypothyroidism in any two surveys and both in another with hypothyroidism preceding hyperthyroidism	1
12	Participants reported hypothyroidism in two surveys but refuted hypothyroidism diagnosis (but did not report hyperthyroidism) in the third survey, irrespective of the response order	9
Total		870
Other exclusions after 1 through 12 conditions,		
13	Participants reported hypothyroidism in preceding survey and hyperthyroidism in a subsequent survey	23
14	Other inconsistencies (e.g., participants reported hypothyroidism, then hyperthyroidism, and then hypothyroidism)	3

Table S3: Ever-use of pesticide and hypothyroidism risk adjusting for correlated pesticides.

Pesticide	HR (95% CI) ^a	p-value	Correlated pesticides ^b
Organochlorine insecticide			
Aldrin ≤ 62 years ^c	0.96 (0.67, 1.37)	0.80	DDT, Dieldrin, Heptachlor
> 62 years ^c	1.15 (0.87, 1.53)	0.33	
Chlordane	1.20 (1.01, 1.42)	0.03	DDT
DDT ≤ 62 years ^c	0.88 (0.64, 1.20)	0.41	Aldrin, Chlordane
> 62 years ^c	1.03 (0.80, 1.32)	0.82	
Heptachlor ≤ 62 years ^c	0.82 (0.58, 1.16)	0.26	Aldrin, Dieldrin
> 62 years ^c	1.35 (1.04, 1.76)	0.02	
Carbamate insecticide			
Aldicarb	0.75 (0.55, 1.02)	0.07	Benomyl, Chlorothalonil Diazinon
Carbaryl	1.05 (0.89, 1.24)	0.55	
Organophosphate insecticide			
Diazinon	1.26 (1.07, 1.47)	0.01	Carbaryl
Fungicide			
Benomyl	1.03 (0.75, 1.42)	0.85	Aldicarb, Chlorothalonil, Maneb/Mancozeb
Chlorothalonil	0.98 (0.70, 1.39)	0.92	
Maneb/Mancozeb	0.95 (0.71, 1.28)	0.75	Benomyl
Metalaxyl	0.91 (0.74, 1.13)	0.40	Methyl Bromide
Fumigant			
Methyl Bromide	0.93 (0.72, 1.22)	0.61	Metalaxyl
Herbicide			
Butylate	1.08 (0.92, 1.28)	0.34	Metribuzin
Dicamba	1.31 (1.10, 1.56)	<0.01	Imazethapyr
Imazethapyr	0.96 (0.81, 1.13)	0.59	Dicamba
Trifluralin	1.13 (0.96, 1.34)	0.15	Metribuzin
2,4,5-T	1.02 (0.84, 1.23)	0.88	2,4,5-TP
Metribuzin	0.95 (0.79, 1.13)	0.53	Butylate, Trifluralin

Abbreviation: 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; DDT, Dichlorodiphenyltrichloroethane; HR, Hazard Ratio

^aAdjusted for sex, education, state, smoking, and correlated pesticides

^bPesticides correlated with Phi coefficient ≥ 0.40

^cHR allowed to vary by the median age for pesticides for which proportional hazards assumptions were not met

Table S4: Intensity-weighted lifetime days of pesticide use and hypothyroidism risk adjusting for correlated pesticides

Pesticide	Intensity-weighted days ^a	HR (95% CI) ^b	p-value	p-trend ^c	Correlated pesticides
Chlordane	> 0 – ≤238	1.35 (0.97, 1.88)	0.08	0.01	DDT
	> 238 – ≤720	1.61 (1.19, 2.18)	0.00		
	> 720	1.50 (1.08, 2.08)	0.02		
DDT	> 0 – ≤335	1.00 (0.72, 1.41)	0.98	0.53	Aldrin, Chlordane
	> 335 – ≤1599	1.04 (0.75, 1.45)	0.80		
	> 1599	1.11 (0.79, 1.56)	0.54		
Heptachlor	> 0 – ≤289	0.89 (0.58, 1.38)	0.62	0.99	Aldrin, Dieldrin
	> 289 – ≤882	0.96 (0.63, 1.47)	0.86		
	> 882	0.99 (0.65, 1.53)	0.98		
Carbaryl	> 0 – ≤380	1.24 (0.96, 1.60)	0.10	0.89	Diazinon
	> 380 – ≤2337	1.23 (0.94, 1.62)	0.13		
	> 2337	1.12 (0.80, 1.55)	0.51		
Diazinon	> 0 – ≤315	1.30 (0.95, 1.78)	0.10	0.03	Carbaryl
	> 315 – ≤1218	1.39 (1.02, 1.89)	0.04		
	> 1218	1.44 (1.03, 2.01)	0.03		
Methyl Bromide	> 0 – ≤320	1.06 (0.74, 1.52)	0.73	0.46	Metalaxyl
	> 320 – ≤1372	0.94 (0.64, 1.40)	0.78		
	> 1372	0.87 (0.58, 1.31)	0.50		
Benomyl	> 0 – ≤841	1.27 (0.78, 2.08)	0.34	0.65	Aldicarb, Chlorothalonil, Maneb/Mancozeb
	> 841	0.91 (0.49, 1.67)	0.76		
Chlorothalonil	> 0 – ≤588	1.12 (0.69, 1.82)	0.65	0.39	Aldicarb, Benomyl
	> 588 – ≤3162	1.28 (0.77, 2.13)	0.34		
	> 3162	0.73 (0.37, 1.44)	0.37		
Maneb/Mancozeb	> 0 – ≤457	0.50 (0.22, 1.13)	0.10	0.84	Benomyl
	> 457 – ≤2744	1.35 (0.78, 2.34)	0.28		
	> 2744	0.99 (0.53, 1.88)	0.99		
Metalaxyl	> 0 – ≤312	0.70 (0.45, 1.07)	0.10	0.54	Methyl Bromide
	> 312 – ≤1512	0.90 (0.58, 1.41)	0.66		
	> 1512	1.11 (0.69, 1.77)	0.68		
Butylate	> 0 – ≤455	1.10 (0.81, 1.50)	0.53	0.39	Metribuzin
	> 455 – ≤1523	0.94 (0.68, 1.31)	0.71		
	> 1523	1.17 (0.86, 1.59)	0.32		
Dicamba	> 0 – ≤572	1.27 (1.02, 1.58)	0.03	0.10	Imazethapyr
	> 572 – ≤2184	1.35 (1.09, 1.68)	0.01		
	> 2184	1.32 (1.06, 1.65)	0.01		
Imazethapyr	> 0 – ≤341	0.93 (0.74, 1.16)	0.52	0.81	Dicamba
	> 341 – ≤1015	0.99 (0.79, 1.24)	0.92		

Pesticide	Intensity-weighted days ^a	HR (95% CI) ^b	p-value	p-trend ^c	Correlated pesticides		
Trifluralin	> 1015	0.96 (0.76, 1.21)	0.70	0.74	Metribuzin		
	> 0 – ≤1008	1.02 (0.78, 1.34)	0.87				
	> 1008 – ≤3828	1.16 (0.89, 1.51)	0.28				
	> 3828	0.97 (0.73, 1.29)	0.84				
2,4,5-T ^d ≤ 62 years	> 0 – ≤480	0.86 (0.53, 1.39)	0.53	0.17	2,4,5-TP		
	> 480	0.70 (0.39, 1.26)	0.24				
	> 62 years	> 0 – ≤480	1.43 (1.01, 2.02)			0.05	0.11
	> 480	1.42 (1.00, 2.01)	0.05				
Metribuzin	> 0 – ≤315	1.04 (0.77, 1.39)	0.82	0.40	Butylate, Trifluralin		
	> 315 – ≤1006	0.88 (0.64, 1.20)	0.42				
	> 1006	1.13 (0.84, 1.52)	0.40				

Abbreviation: 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; CI, Confidence Intervals; DDT, Dichlorodiphenyltrichloroethane; HR, Hazard Ratio

^a Split using tertile cut-offs or at the median of intensity-weighted lifetime days among exposed for each pesticide

^b Adjusted for sex, education, state, and smoking

^c P-trend values were obtained using an ordinal variable coded with median values for each category

^d Hazard ratio allowed to vary by the median age (i.e., 62 years) for pesticides for which proportional hazards assumptions were not met ($p \leq 0.10$)

Table S5: Ever-use of pesticides and hypothyroidism – cases restricted to those taking thyroid-related medications (N=35,073).

Pesticide	Exposed cases	HR (95% CI) ^a	P-value
Organochlorine insecticide			
Aldrin ≤ 62 years ^b	50	0.85 (0.62, 1.15)	0.29
> 62 years ^b	144	1.28 (1.01, 1.62)	0.04
Chlordane	254	1.22 (1.04, 1.43)	0.02
DDT ≤ 62 years ^b	58	0.88 (0.66, 1.18)	0.39
> 62 years ^b	191	1.22 (0.98, 1.53)	0.08
Dieldrin ≤ 62 years ^b	17	0.94 (0.58, 1.54)	0.82
> 62 years ^b	62	1.21 (0.91, 1.61)	0.19
Heptachlor ≤ 62 years ^b	42	0.86 (0.62, 1.20)	0.37
> 62 years ^b	131	1.42 (1.11, 1.80)	<0.01
Lindane ≤ 62 years ^b	84	1.04 (0.81, 1.33)	0.77
> 62 years ^b	110	1.58 (1.25, 2.00)	<0.01
Toxaphene ≤ 62 years ^b	39	0.77 (0.55, 1.08)	0.13
> 62 years ^b	77	1.13 (0.87, 1.46)	0.37
Carbamate insecticide			
Aldicarb	56	0.80 (0.59, 1.07)	0.13
Carbaryl	452	1.11 (0.95, 1.30)	0.21
Carbofuran	240	1.16 (0.99, 1.37)	0.06
Organophosphate insecticide			
Chlorpyrifos	322	1.04 (0.90, 1.20)	0.6
Coumaphos ≤ 62 years ^b	32	0.86 (0.60, 1.24)	0.42
> 62 years ^b	44	1.42 (1.03, 1.95)	0.03
Diazinon	287	1.32 (1.13, 1.54)	<0.01
Dichlorvos	122	1.45 (1.18, 1.77)	<0.01
Fonofos	191	1.17 (0.99, 1.40)	0.07
Malathion	567	1.19 (1.00, 1.42)	0.05
Parathion	130	1.20 (0.98, 1.46)	0.08
Phorate	262	1.01 (0.86, 1.19)	0.91
Terbufos	313	1.17 (1.01, 1.37)	0.04
Pyrethroid insecticide			
Permethrin (animals)	115	1.19 (0.97, 1.46)	0.10
Permethrin (crops)	110	1.27 (1.03, 1.56)	0.03
Fumigant			
Carbon tetrachloride/ Carbon disulphide 80/20 mix	57	1.09 (0.83, 1.44)	0.53
Aluminum Phosphide ≤62 years ^b	21	0.97 (0.62, 1.50)	0.88
> 62 years ^b	16	1.23 (0.74, 2.03)	0.42
Ethylene Dibromide	22	0.84 (0.55, 1.29)	0.43
Methyl Bromide	102	0.98 (0.76, 1.25)	0.86
Fungicide			
Benomyl	68	0.94 (0.71, 1.23)	0.64
Captan	76	0.87 (0.69, 1.11)	0.27
Chlorothalonil	45	0.88 (0.64, 1.21)	0.43
Maneb/Mancozeb	67	0.95 (0.72, 1.25)	0.69
Metalaxyl	143	0.92 (0.75, 1.13)	0.44

Pesticide	Exposed cases	HR (95% CI) ^a	P-value
Herbicide			
Alachlor	410	1.07 (0.92, 1.25)	0.39
Butylate	257	1.08 (0.92, 1.27)	0.34
Chlorimuron Ethyl	241	0.93 (0.80, 1.09)	0.39
Dicamba	424	1.36 (1.14, 1.62)	<0.01
EPTC	156	1.08 (0.90, 1.29)	0.43
Glyphosate	601	1.28 (1.06, 1.54)	0.01
Imazethapyr	313	0.99 (0.84, 1.18)	0.94
Metolachlor	340	1.02 (0.88, 1.19)	0.78
Paraquat	157	0.95 (0.79, 1.15)	0.6
Pendimethalin	285	0.91 (0.78, 1.06)	0.21
Petroleum Oil ≤ 62 years ^b	189	0.93 (0.76, 1.14)	0.48
> 62 years ^b	167	1.18 (0.94, 1.49)	0.15
Trifluralin	410	1.10 (0.94, 1.30)	0.23
2,4-D	617	1.37 (1.12, 1.69)	<0.01
2,4,5-T	207	1.12 (0.95, 1.33)	0.19
2,4,5-TP	89	1.17 (0.93, 1.47)	0.17
Atrazine ≤ 62 years ^b	294	0.97 (0.77, 1.23)	0.80
> 62 years ^b	258	1.11 (0.86, 1.45)	0.41
Cyanazine	327	1.06 (0.90, 1.25)	0.47
Metribuzin	348	1.03 (0.88, 1.21)	0.74

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; DDT,

Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; HR, Hazard Ratio

^aAdjusted for sex, education, state, and smoking

^bHR allowed to vary by the median age for pesticides that did not meet proportional hazards assumptions

Table S6: Ever-use of pesticides and hypothyroidism risk excluding female applicators (N=34,375).

Pesticide	Exposed cases	HR (95% CI) ^a	P-value
Organochlorine insecticide			
Aldrin ≤ 62 years ^b	57	0.88 (0.66, 1.18)	0.39
> 62 years ^b	167	1.26 (1.00, 1.58)	0.05
Chlordane	274	1.22 (1.05, 1.43)	0.01
DDT ≤ 62 years ^b	61	0.83 (0.63, 1.11)	0.22
> 62 years ^b	209	1.19 (0.95, 1.49)	0.12
Dieldrin ≤ 62 years ^b	18	0.91 (0.56, 1.46)	0.68
> 62 years ^b	72	1.21 (0.92, 1.59)	0.17
Heptachlor ≤ 62 years ^b	44	0.81 (0.59, 1.12)	0.21
> 62 years ^b	145	1.37 (1.09, 1.74)	0.01
Lindane ≤ 62 years ^b	90	1.06 (0.83, 1.34)	0.66
> 62 years ^b	125	1.58 (1.26, 1.99)	<0.01
Toxaphene ≤ 62 years ^b	44	0.79 (0.58, 1.09)	0.15
> 62 years ^b	88	1.13 (0.88, 1.45)	0.35
Carbamate insecticide			
Aldicarb	57	0.74 (0.56, 0.99)	0.05
Carbaryl	473	1.15 (0.98, 1.35)	0.08
Carbofuran	253	1.13 (0.97, 1.32)	0.11
Organophosphate insecticide			
Chlorpyrifos	339	1.02 (0.88, 1.18)	0.79
Coumaphos ≤ 62 years ^b	36	0.93 (0.66, 1.31)	0.66
> 62 years ^b	53	1.48 (1.09, 2.01)	0.01
Diazinon	294	1.30 (1.12, 1.52)	<0.01
Dichlorvos	127	1.41 (1.16, 1.72)	<0.01
Fonofos	201	1.15 (0.97, 1.37)	0.10
Malathion	600	1.25 (1.05, 1.49)	0.01
Parathion	139	1.18 (0.97, 1.43)	0.10
Phorate	286	1.04 (0.89, 1.21)	0.64
Terbufos	328	1.13 (0.97, 1.32)	0.11
Pyrethroid insecticide			
Permethrin (animals)	122	1.21 (0.99, 1.48)	0.06
Permethrin (crops)	109	1.18 (0.96, 1.45)	0.11
Fumigant			
Carbon tetrachloride/ Carbon disulphide 80/20 mix	57	1.02 (0.77, 1.34)	0.91
Aluminum Phosphide ≤ 62 years ^b	22	0.94 (0.61, 1.44)	0.77
> 62 years ^b	21	1.27 (0.79, 2.04)	0.33
Ethylene Dibromide	22	0.77 (0.5, 1.18)	0.23
Methyl Bromide	106	0.94 (0.73, 1.20)	0.60
Fungicide			
Benomyl	68	0.90 (0.69, 1.18)	0.46
Captan	81	0.90 (0.71, 1.14)	0.38
Chlorothalonil	48	0.90 (0.66, 1.23)	0.50
Maneb/Mancozeb	67	0.90 (0.68, 1.19)	0.46
Metalaxyl	145	0.88 (0.71, 1.07)	0.20
Herbicide			
Alachlor	438	1.06 (0.91, 1.23)	0.45

Pesticide	Exposed cases	HR (95% CI) ^a	P-value
Butylate	279	1.09 (0.94, 1.27)	0.26
Chlorimuron Ethyl	258	0.94 (0.80, 1.09)	0.41
Dicamba	444	1.26 (1.06, 1.49)	0.01
EPTC	167	1.09 (0.91, 1.30)	0.37
Glyphosate	625	1.27 (1.05, 1.52)	0.01
Imazethapyr	334	1.00 (0.85, 1.18)	0.96
Metolachlor	358	1.00 (0.86, 1.16)	0.98
Paraquat	167	0.93 (0.77, 1.12)	0.42
Pendimethalin	305	0.91 (0.78, 1.06)	0.21
Petroleum Oil ≤ 62 years ^b	204	0.95 (0.78, 1.16)	0.64
> 62 years ^b	193	1.24 (0.99, 1.55)	0.06
Trifluralin	436	1.11 (0.95, 1.30)	0.19
2,4-D	651	1.31 (1.07, 1.61)	0.01
2,4,5-T	217	1.05 (0.89, 1.24)	0.58
2,4,5-TP	92	1.09 (0.87, 1.36)	0.44
Atrazine ≤ 62 years ^b	306	0.86 (0.69, 1.08)	0.19
> 62 years ^b	299	1.18 (0.91, 1.53)	0.22
Cyanazine	354	1.09 (0.93, 1.27)	0.31
Metribuzin	375	1.03 (0.88, 1.20)	0.69

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; DDT,

Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; HR, Hazard Ratio

^aAdjusted for sex, education, state, and smoking

^bHR allowed to vary by the median age for pesticides that did not meet proportional hazards assumptions

Table S7: Ever-use of pesticides and hypothyroidism risk – cases restricted to those confirmed by a validation questionnaire or medical records or who reported having hypothyroidism ≥ 2 times in surveys (N=34,464).

Pesticide	Exposed cases	HR (95% CI) ^a	P-value
Organochlorine insecticide			
Aldrin	76	1.07 (0.81, 1.42)	0.62
Chlordane	112	1.36 (1.07, 1.73)	0.01
DDT	85	0.97 (0.74, 1.29)	0.84
Dieldrin	33	1.27 (0.88, 1.86)	0.21
Heptachlor	65	1.06 (0.79, 1.43)	0.68
Lindane ≤ 62 years ^b	47	1.01 (0.73, 1.39)	0.97
> 62 years ^b	45	1.78 (1.19, 2.66)	<0.01
Toxaphene	40	0.81 (0.58, 1.14)	0.23
Carbamate insecticide			
Aldicarb	20	0.61 (0.38, 0.98)	0.04
Carbaryl	206	1.13 (0.89, 1.42)	0.31
Carbofuran	112	1.25 (0.99, 1.57)	0.06
Organophosphate insecticide			
Chlorpyrifos	145	0.98 (0.79, 1.22)	0.85
Coumaphos	28	0.88 (0.60, 1.30)	0.51
Diazinon ≤ 62 years ^b	92	1.41 (1.07, 1.87)	0.02
> 62 years ^b	56	2.17 (1.47, 3.21)	<0.01
Dichlorvos	60	1.50 (1.13, 2.00)	0.01
Fonofos	90	1.20 (0.93, 1.55)	0.16
Malathion	273	1.44 (1.1, 1.88)	0.01
Parathion	57	1.25 (0.93, 1.68)	0.14
Phorate	117	0.97 (0.77, 1.24)	0.83
Terbufos	138	1.05 (0.83, 1.31)	0.70
Pyrethroid insecticide			
Permethrin (animals)	58	1.15 (0.86, 1.54)	0.34
Permethrin (crops)	56	1.30 (0.97, 1.74)	0.08
Fumigant			
Carbon tetrachloride/ Carbon disulphide 80/20 mix	21	1.01 (0.65, 1.58)	0.96
Ethylene Dibromide	10	0.9 (0.48, 1.71)	0.75
Methyl Bromide	49	1.29 (0.89, 1.87)	0.18
Fungicide			
Benomyl	30	0.96 (0.64, 1.45)	0.84
Captan	39	0.93 (0.67, 1.30)	0.68
Chlorothalonil	18	0.79 (0.48, 1.30)	0.36
Maneb/Mancozeb	28	0.95 (0.62, 1.45)	0.82
Metalaxyl ≤ 62 years ^b	50	0.97 (0.68, 1.39)	0.88
> 62 years ^b	14	0.77 (0.42, 1.41)	0.39
Herbicide			
Alachlor	187	1.03 (0.82, 1.28)	0.82
Butylate	112	0.96 (0.76, 1.21)	0.73
Chlorimuron Ethyl ≤ 62 years ^b	78	0.81 (0.61, 1.07)	0.14
> 62 years ^b	34	0.96 (0.64, 1.45)	0.85
Dicamba	197	1.28 (0.99, 1.66)	0.06

Pesticide	Exposed cases	HR (95% CI) ^a	P-value
EPTC	78	1.14 (0.87, 1.48)	0.34
Glyphosate	286	1.44 (1.08, 1.92)	0.01
Imazethapyr	156	1.06 (0.83, 1.35)	0.66
Metolachlor	156	0.97 (0.77, 1.21)	0.78
Paraquat	68	0.93 (0.70, 1.24)	0.63
Pendimethalin	139	0.95 (0.76, 1.19)	0.68
Petroleum Oil	179	1.20 (0.96, 1.49)	0.12
Trifluralin	197	1.18 (0.93, 1.49)	0.18
2,4-D	286	1.55 (1.14, 2.12)	0.01
2,4,5-T	91	1.25 (0.97, 1.61)	0.09
2,4,5-TP	42	1.31 (0.94, 1.82)	0.11
Atrazine	260	1.21 (0.92, 1.58)	0.17
Cyanazine	153	1.06 (0.83, 1.34)	0.66
Metribuzin	164	1.01 (0.80, 1.27)	0.94

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; DDT, Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; HR, Hazard Ratio

^aAdjusted for sex, education, state, and smoking

^bHR allowed to vary by the median age for pesticides that did not meet proportional hazards assumptions

Table S8: Ever-use of pesticide and hypothyroidism risk using inverse probability of censoring weights.

Pesticide	Exposed cases	HR (95% CI) ^a	p-value
Organochlorine insecticide			
Aldrin ≤ 62 years ^b	60	0.89 (0.67, 1.18)	0.42
> 62 years ^b	156	1.29 (1.03, 1.62)	0.03
Chlordane	276	1.20 (1.02, 1.40)	0.02
DDT ≤ 62 years ^b	66	0.84 (0.64, 1.12)	0.24
> 62 years ^b	199	1.22 (0.97, 1.52)	0.08
Dieldrin ≤ 62 years ^b	20	0.94 (0.60, 1.48)	0.78
> 62 years ^b	68	1.25 (0.96, 1.64)	0.10
Heptachlor ≤ 62 years ^b	47	0.82 (0.60, 1.12)	0.22
> 62 years ^b	136	1.34 (1.05, 1.70)	0.02
Lindane ≤ 62 years ^b	94	1.00 (0.79, 1.26)	1.00
> 62 years ^b	116	1.59 (1.26, 2.01)	<.0001
Toxaphene	128	1.00 (0.82, 1.22)	0.96
Carbamate insecticide			
Aldicarb	62	0.79 (0.59, 1.05)	0.11
Carbaryl	496	1.12 (0.96, 1.31)	0.15
Carbofuran	261	1.13 (0.97, 1.32)	0.12
Organophosphate insecticide			
Chlorpyrifos	350	1.02 (0.89, 1.18)	0.77
Coumaphos ≤ 62 years ^b	37	0.93 (0.66, 1.31)	0.68
> 62 years ^b	47	1.44 (1.05, 1.97)	0.02
Diazinon	313	1.27 (1.09, 1.48)	0.00
Dichlorvos	131	1.39 (1.15, 1.69)	0.00
Fonofos	203	1.14 (0.96, 1.35)	0.14
Malathion	621	1.23 (1.04, 1.46)	0.02
Parathion	142	1.21 (1.00, 1.46)	0.05
Phorate	285	0.99 (0.85, 1.15)	0.86
Terbufos	334	1.14 (0.98, 1.32)	0.10
Pyrethroid insecticide			
Permethrin (animals)	125	1.17 (0.96, 1.43)	0.12
Permethrin (crops)	114	1.14 (0.93, 1.40)	0.20
Fumigant			
Carbon tetrachloride/ Carbon disulfide 80/20 mix	57	1.02 (0.77, 1.35)	0.90
Aluminum Phosphide	41	1.05 (0.76, 1.45)	0.76
Ethylene Dibromide	24	0.80 (0.53, 1.21)	0.29
Methyl Bromide	113	0.99 (0.77, 1.26)	0.91
Fungicide			
Benomyl	74	0.93 (0.71, 1.21)	0.58

Pesticide	Exposed cases	HR (95% CI) ^a	p-value
Captan	87	0.91 (0.73, 1.14)	0.42
Chlorothalonil	50	0.87 (0.64, 1.18)	0.37
Maneb/Mancozeb	73	0.93 (0.71, 1.22)	0.60
Metalaxyl	157	0.92 (0.75, 1.12)	0.40
Herbicide			
Alachlor	442	1.04 (0.90, 1.21)	0.60
Butylate	281	1.09 (0.93, 1.27)	0.29
Chlorimuron Ethyl	259	0.94 (0.80, 1.10)	0.44
Dicamba	453	1.28 (1.08, 1.51)	0.01
EPTC	163	1.03 (0.86, 1.23)	0.74
Glyphosate	650	1.19 (0.99, 1.43)	0.07
Imazethapyr	335	0.97 (0.82, 1.13)	0.68
Metolachlor	360	0.97 (0.84, 1.12)	0.70
Paraquat	169	0.94 (0.78, 1.13)	0.52
Pendimethalin	311	0.91 (0.78, 1.05)	0.20
Petroleum Oil ≤62 years ^b	209	0.89 (0.74, 1.08)	0.25
>62 years ^b	175	1.20 (0.96, 1.51)	0.11
Trifluralin	444	1.11 (0.95, 1.30)	0.18
2,4-D	666	1.34 (1.10, 1.63)	0.00
2,4,5-T	221	1.09 (0.92, 1.28)	0.33
2,4,5-TP	96	1.14 (0.92, 1.42)	0.24
Atrazine	592	0.98 (0.83, 1.16)	0.81
Cyanazine	356	1.05 (0.90, 1.23)	0.52
Metribuzin	375	1.02 (0.88, 1.19)	0.79

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; DDT, Dichlorodiphenyltrichloroethane; HR, Hazard Ratio

^aAdjusted for sex, education, state, and smoking

^bHR allowed to vary by the median age for pesticides for which proportional hazards assumptions were not met

Note: exposed cases may differ from the main analysis because, for 25 participants, thyroid disease reports (in Phase 4) by proxy of deceased were also used to confirm hypothyroidism diagnosis in the main analysis (which were censored here assuming loss to follow up changing definition of hypothyroidism for some) and because of rounding of imputed age to create person-year data.