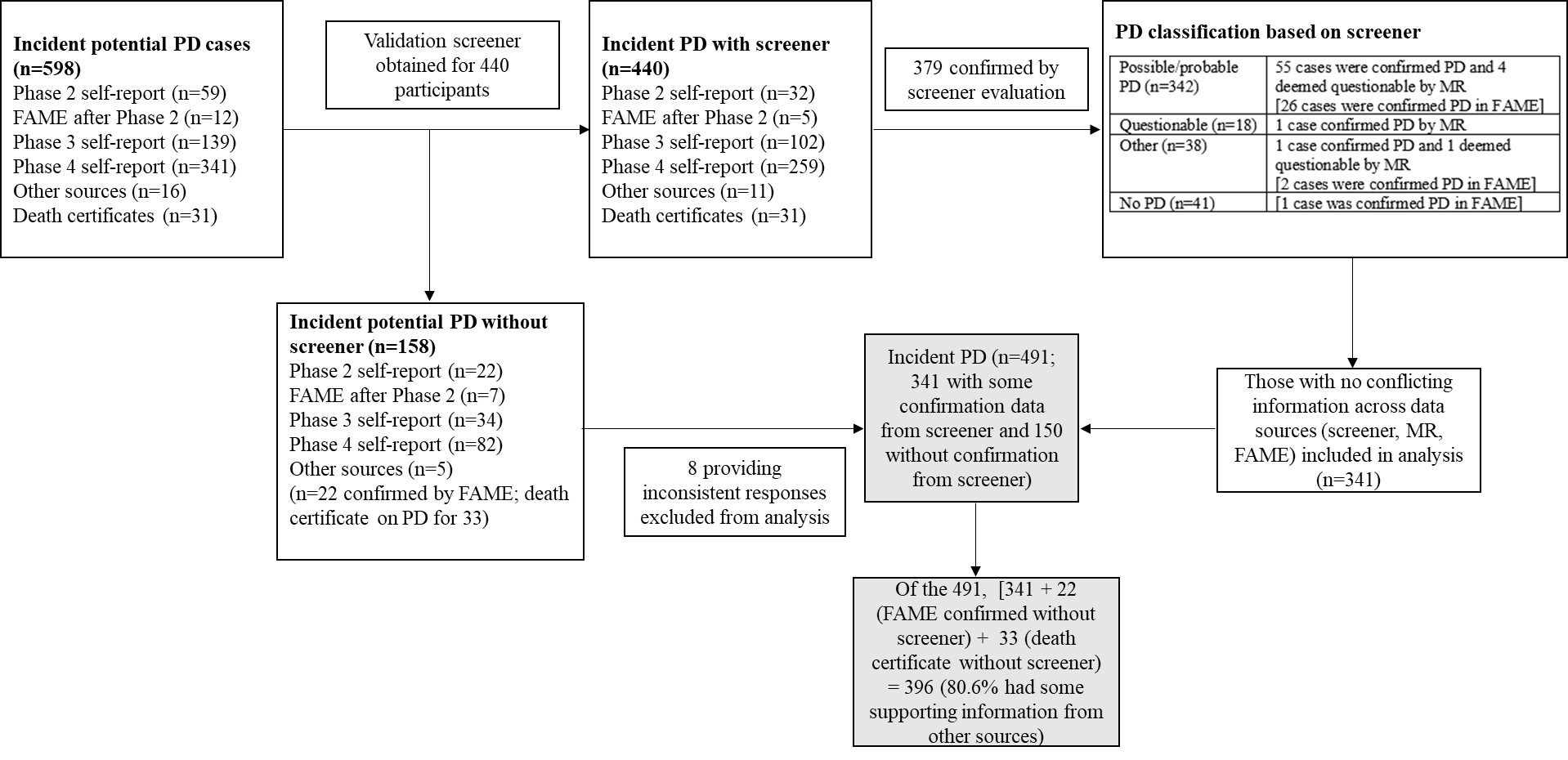
Supplemental Figure 1: Timeline of the Agricultural Health Study



Supplemental Figure 2: Selection of Parkinson’s disease cases from a pool of incident potential cases



Abbreviations: PD, Parkinson’s disease; FAME, Farming and Movement Evaluation Study; MR, Medical Record

Supplemental Table 1: Ever-use of any pesticides reported at enrollment and PD risk in male pesticide applicators and female spouses

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Incident case analysis  (n=66,110) | | Overall (incident and prevalent) case analysis (n=66,216)a | |
|  | Lifetime daysb | No PD (n(%)) | PD (n(%)) | HR (95% CI)c | PD (n(%)) | OR (95% CI)d |
| Overall samplee | Never use | 11945 (19.7) | 40 (8.8) | Ref | 56 (10) | Ref |
|  | > 0 to 39 | 12386 (20.4) | 82 (18) | 1.23 (0.81, 1.89) | 106 (19) | 1.18 (0.81, 1.71) |
|  | 40 to 179 | 14415 (23.8) | 128 (28.1) | 1.21 (0.79, 1.86) | 147 (26.3) | 1.07 (0.73, 1.56) |
|  | 180 to 370 | 10668 (17.6) | 104 (22.8) | 1.27 (0.82, 1.98) | 122 (21.9) | 1.16 (0.79, 1.72) |
|  | > 370 | 11240 (18.5) | 102 (22.4) | 1.07 (0.69, 1.67) | 127 (22.8) | 1.06 (0.72, 1.57) |
| Male applicators onlyf | 0 to 64 | 9984 (27.2) | 106 (28.6) | Ref | 133 (29.7) | Ref |
|  | 65 to 225 | 11644 (31.8) | 101 (27.3) | 0.86 (0.65, 1.13) | 118 (26.3) | 0.83 (0.64, 1.07) |
|  | 226 to 458 | 7689 (21) | 81 (21.9) | 0.98 (0.73, 1.31) | 93 (20.8) | 0.96 (0.73, 1.26) |
|  | > 458 | 7328 (20) | 82 (22.2) | 0.79 (0.59, 1.06) | 104 (23.2) | 0.88 (0.67, 1.14) |
| Female spouses onlyg | Never use | 11360 (49.7) | 38 (45.8) | Ref | 51 (48.1) | Ref |
|  | > 0 to 51 | 6047 (26.4) | 8 (9.6) | 0.47 (0.22, 1.02) | 13 (12.3) | 0.63 (0.34, 1.16) |
|  | > 51 | 5472 (23.9) | 37 (44.6) | 1.58 (1.00, 2.50) | 42 (39.6) | 1.48 (0.98, 2.25) |

Abbreviation: CI, Confidence Intervals; HR, Hazard Ratio; OR, Odds Ratio; PD, Parkinson’s disease

aIncludes prevalent cases

bLife time days calculated from questions on general pesticide use at Phase 1 enrollment questionnaire (how many years did you personally mix or apply pesticides? And during those years, how many days per year did you personally mix or apply pesticides?)

cHR adjusted for state of residence, smoking status, education

dOR adjusted for age at enrollment, state of residence, smoking status, education

eIn the overall sample, quartiles of lifetime days of use of any pesticide among users were compared with never use as the referent

fAmong male applicators, higher quartiles of lifetime days of any pesticide use were compared with the lowest quartile (note: never use was not chosen as the referent because only a few participants indicated so)

gAmong female spouses, median lifetime days of use of any pesticide among users were compared with never use as the referent

Supplemental Table 2: Ever-use of pesticides reported at enrollment and Parkinson’s disease (PD) risk in male pesticide applicators and female spouses

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Male applicators (n=37,284) | | | Female spouses (n=27,673) | | |
| Pesticide | non-PD, n(%) | PD, n (%) | HR (95% CI)a | non-PD , n (%) | PD, n (%) | HR (95% CI)a |
| **Organochlorine insecticide** |  |  |  |  |  |  |
| Aldrin (≤ 63y)b | 1472 (8.4) | 14 (16.7) | 0.86 (0.46, 1.60) |  |  |  |
| > 63y | 4839 (33) | 82 (36.4) | 0.92 (0.66, 1.28) |  |  |  |
| Chlordane | 8777 (26.7) | 122 (38.4) | 1.00 (0.78, 1.28) | *1142 (4.4)* | *6 (5.8)* | *0.85 (0.37, 1.94)* |
| Dieldrin | 2333 (7.2) | 37 (12) | 0.86 (0.58, 1.28) |  |  |  |
| DDT | 8238 (25.2) | 139 (44.3) | 0.90 (0.69, 1.17) | 977 (3.8) | 6 (5.8) | 0.77 (0.34, 1.77) |
| Heptachlor | 5291 (16.4) | 87 (28.2) | 1.09 (0.80, 1.48) |  |  |  |
| Toxaphene | 5028 (15.3) | 60 (19.1) | 0.78 (0.59, 1.04) |  |  |  |
| Lindane | 6730 (20.4) | 73 (23.3) | 0.94 (0.72, 1.23) |  |  |  |
| **Carbamate insecticide** |  |  |  |  |  |  |
| Aldicarb | 3662 (11.3) | 27 (8.7) | 0.94 (0.61, 1.46) |  |  |  |
| Carbaryl | 18622 (56.5) | 194 (62.4) | 1.10 (0.85, 1.43) | 8287 (31.6) | 36 (34) | 1.00 (0.63, 1.59) |
| Carbofuran | 9602 (28.8) | 113 (36.1) | 1.09 (0.86, 1.37) |  |  |  |
| **Organophosphate insecticide** |  |  |  |  |  |  |
| Chlorpyrifos | 15434 (42.9) | 139 (38.3) | 0.93 (0.75, 1.16) |  |  |  |
| Coumaphos | 3005 (9.2) | 32 (10.5) | 1.00 (0.69, 1.44) |  |  |  |
| Diazinon | 10821 (32.8) | 97 (31.2) | 0.75 (0.58, 0.98) | 2783 (10.7) | 7 (6.7) | 0.57 (0.27, 1.24) |
| Dichlorvos | 3662 (11) | 42 (13.7) | 1.08 (0.78, 1.51) |  |  |  |
| Fonofos | 7634 (22.8) | 73 (23.2) | 0.94 (0.71, 1.23) |  |  |  |
| Malathion | 24541 (72) | 253 (76.7) | 1.05 (0.81, 1.35) | 5274 (20.1) | 23 (21.7) | 0.90 (0.53, 1.54) |
| Parathion | 5323 (16.2) | 61 (19.5) | 0.97 (0.73, 1.3) |  |  |  |
| Phorate | 11414 (34.5) | 120 (38) | 0.97 (0.76, 1.24) |  |  |  |
| Terbufos | 13656 (40.7) | 145 (46.2) | 1.3 (1.03, 1.64) |  |  |  |
| **Permethrin insecticide** |  |  |  |  |  |  |
| Permethrin (Crops) (≤ 63y)b | 2842 (16) | 8 (9.9) | 0.6 (0.29, 1.24) |  |  |  |
| > 63y | 1764 (11.5) | 26 (11.7) | 1.2 (0.79, 1.81) |  |  |  |
| Permethrin (Animals) | 4665 (13.9) | 36 (11.7) | 1.03 (0.72, 1.47) |  |  |  |
| **Fumigant** |  |  |  |  |  |  |
| Carbon disulfide/ Carbon tetrachloride | 1922 (5.8) | 29 (9.2) | 1.01 (0.69, 1.49) |  |  |  |
| Aluminum phosphide | *1657 (5)* | *15 (4.8)* | *1.01 (0.6, 1.7)* |  |  |  |
| Ethylene dibromide | 1243 (3.8) | 5 (1.6) | 0.34 (0.14, 0.83) |  |  |  |
| Methyl bromide | 5248 (15.7) | 46 (14.4) | 0.85 (0.58, 1.25) |  |  |  |
| **Fungicide** |  |  |  |  |  |  |
| *Benomylc* | *3147 (9.8)* | *25 (8.2)* | *0.74 (0.44, 1.23)* |  |  |  |
| Captan | 3897 (11.8) | 33 (10.7) | 0.91 (0.63, 1.31) |  |  |  |
| Chlorothalonil | 2552 (7.7) | 21 (6.7) | 1.02 (0.61, 1.69) |  |  |  |
| Maneb (≤ 63y)b | 1493 (8.4) | 8 (9.3) | 1.46 (0.64, 3.33) |  |  |  |
| > 63y | 1696 (11.1) | 21 (9.3) | 0.81 (0.48, 1.37) |  |  |  |
| Metalaxyl | 7885 (23.7) | 65 (20.3) | 0.88 (0.64, 1.21) |  |  |  |
| **Herbicide** |  |  |  |  |  |  |
| Alachlor | 18551 (55) | 189 (59.6) | 1.08 (0.86, 1.35) | 1107 (4.3) | 6 (5.8) | 1.06 (0.32, 3.53) |
| Butylate | 10877 (33.2) | 108 (35) | 1.06 (0.82, 1.37) |  |  |  |
| Chlorimuron ethyl | 12715 (38.5) | 105 (33.2) | 1.02 (0.80, 1.29) |  |  |  |
| Dicamba | 17238 (52.8) | 160 (53) | 0.96 (0.74, 1.26) |  |  |  |
| EPTC | 6840 (20.7) | 53 (17.5) | 0.85 (0.63, 1.16) |  |  |  |
| Glyphosate | 27733 (76.9) | 278 (76.2) | 1.02 (0.79, 1.30) | 8867 (34) | 42 (39.6) | 1.44 (0.92, 2.25) |
| Imazethapyr | 14643 (44.9) | 128 (42.4) | 1.11 (0.85, 1.45) | 769 (3) | 4 (3.9) | 1.15 (0.28, 4.72) |
| Metolachlor | 16054 (47.7) | 127 (41) | 0.81 (0.64, 1.03) | 862 (3.3) | 5 (4.8) | 1.29 (0.36, 4.67) |
| Paraquat | 8103 (24.5) | 84 (26.3) | 1.04 (0.79, 1.35) |  |  |  |
| Pendimethalin | 15267 (45.9) | 135 (42.6) | 1.03 (0.83, 1.29) |  |  |  |
| Petroleum distillate | 16240 (49.4) | 154 (49) | 0.99 (0.79, 1.24) |  |  |  |
| Trifluralin | 17624 (54.9) | 182 (61.1) | 1.36 (1.04, 1.78) | 1339 (5.2) | 8 (7.8) | 1.42 (0.53, 3.77) |
| 2,4-D | 27778 (77.3) | 289 (79.8) | 1.02 (0.78, 1.33) | 3955 (15.2) | 21 (19.8) | 0.98 (0.56, 1.71) |
| 2,4,5-T | 7256 (22.3) | 117 (37.5) | 1.53 (1.20, 1.97) |  |  |  |
| 2,4,5-TP | 3181 (9.8) | 23 (7.4) | 0.39 (0.25, 0.61) |  |  |  |
| Atrazine | 26301 (73) | 268 (73.6) | 1.05 (0.82, 1.33) | 1172 (4.5) | 5 (4.8) | 0.46 (0.13, 1.67) |
| Cyanazine | 14546 (43.3) | 136 (43.7) | 0.96 (0.75, 1.22) | 744 (2.9) | 6 (5.8) | 2.80 (0.79, 9.95) |
| Metribuzin | 15192 (47.9) | 137 (46.9) | 0.86 (0.65, 1.13) |  |  |  |

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

aHR adjusted for state of residence, smoking status, education, and ever-use of correlated pesticides (other pesticides whose ever-use variable had Spearman correlation ≥ 0.40 with the ever-use variable of the target pesticide)

bHazard ratio allowed to vary by the median age (i.e., 63 years) for pesticides that did not meet proportional hazards assumptions (p ≤ 0.10)

cProportional hazards assumptions not met for those in italics, but there was no adequate sample size to provide stratified estimates by the median age

Supplemental Table 3: Ever-use of pesticides reported at enrollment and incident PD in all participants

Stratified by follow-up period (≤ 10 years versus > 10 years)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Hazard ratio (95% CI) | |  |
| Pesticide | Follow up ≤ 10y | Follow up > 10 y | p-heterogeneity |
| **Organochlorine insecticide** |  |  |  |
| Aldrin | 0.94 (0.64, 1.38) | 0.89 (0.63, 1.26) | 0.78 |
| Chlordane | 1.14 (0.83, 1.57) | 0.98 (0.73, 1.32) | 0.42 |
| Dieldrin | 0.74 (0.42, 1.31) | 1.00 (0.63, 1.58) | 0.39 |
| DDT | 0.94 (0.69, 1.28) | 0.80 (0.58, 1.08) | 0.34 |
| Heptachlor | 1.07 (0.72, 1.58) | 0.97 (0.68, 1.39) | 0.67 |
| Toxaphene | 0.90 (0.60, 1.35) | 0.73 (0.50, 1.08) | 0.44 |
| Lindane | 0.95 (0.65, 1.38) | 0.90 (0.65, 1.25) | 0.84 |
| **Carbamate insecticide** |  |  |  |
| Aldicarb | 0.92 (0.47, 1.78) | 1.15 (0.69, 1.91) | 0.58 |
| Carbaryl | 1.22 (0.93, 1.60) | 1.00 (0.77, 1.30) | 0.14 |
| Carbofuran | 1.00 (0.72, 1.39) | 0.91 (0.68, 1.22) | 0.63 |
| **Organophosphate insecticide** |  |  |  |
| Chlorpyrifos | 0.92 (0.69, 1.24) | 0.91 (0.71, 1.17) | 0.94 |
| Coumaphos | 1.20 (0.72, 1.98) | 0.93 (0.58, 1.48) | 0.46 |
| Diazinon | 0.77 (0.56, 1.08) | 0.71 (0.53, 0.95) | 0.66 |
| Dichlorvos | 1.17 (0.73, 1.87) | 1.09 (0.74, 1.61) | 0.82 |
| Fonofos | 1.04 (0.72, 1.50) | 0.83 (0.59, 1.16) | 0.33 |
| Malathion | 1.14 (0.85, 1.53) | 0.92 (0.69, 1.21) | 0.09 |
| Parathion | 1.17 (0.80, 1.71) | 0.84 (0.58, 1.23) | 0.20 |
| Phorate | 0.93 (0.67, 1.30) | 0.80 (0.59, 1.09) | 0.44 |
| Terbufos | 1.39 (1.01, 1.91) | 1.25 (0.94, 1.67) | 0.56 |
| **Permethrin insecticide** |  |  |  |
| Permethrin (Crops) | 0.98 (0.57, 1.67) | 0.99 (0.64, 1.53) | 0.96 |
| Permethrin (Animals) | 0.95 (0.54, 1.66) | 1.13 (0.77, 1.67) | 0.60 |
| **Fumigant** |  |  |  |
| Carbon disulfide/Carbon tetrachloride | 0.82 (0.45, 1.49) | 1.21 (0.77, 1.92) | 0.29 |
| Aluminum phosphide | 1.25 (0.59, 2.66) | 0.97 (0.50, 1.89) | 0.61 |
| Methyl bromide | 1.00 (0.62, 1.60) | 0.75 (0.47, 1.21) | 0.34 |
| **Fungicide** |  |  |  |
| Benomyl | 0.86 (0.45, 1.64) | 0.75 (0.41, 1.39) | 0.73 |
| Captan | 0.73 (0.41, 1.31) | 0.91 (0.59, 1.43) | 0.54 |
| Chlorothalonil | 1.04 (0.53, 2.05) | 0.91 (0.48, 1.74) | 0.76 |
| Maneb | 0.90 (0.49, 1.64) | 0.84 (0.48, 1.46) | 0.86 |
| Metalaxyl | 0.97 (0.63, 1.51) | 0.76 (0.51, 1.15) | 0.36 |
| **Herbicide** |  |  |  |
| Alachlor | 1.34 (0.99, 1.79) | 0.98 (0.74, 1.31) | 0.04 |
| Butylate | 1.37 (0.99, 1.90) | 0.75 (0.53, 1.05) | 0.003 |
| Chlorimuron ethyl | 1.38 (0.99, 1.92) | 0.83 (0.60, 1.16) | 0.01 |
| Dicamba | 1.11 (0.81, 1.53) | 0.82 (0.60, 1.11) | 0.06 |
| EPTC | 1.08 (0.71, 1.64) | 0.68 (0.45, 1.04) | 0.10 |
| Glyphosate | 1.22 (0.93, 1.61) | 1.02 (0.79, 1.32) | 0.14 |
| Imazethapyr | 1.23 (0.88, 1.73) | 0.92 (0.67, 1.27) | 0.11 |
| Metolachlor | 1.00 (0.73, 1.37) | 0.67 (0.49, 0.91) | 0.03 |
| Paraquat | 1.21 (0.86, 1.72) | 1.00 (0.73, 1.39) | 0.38 |
| Pendimethalin | 1.20 (0.87, 1.65) | 0.98 (0.73, 1.32) | 0.28 |
| Petroleum distillate | 1.06 (0.79, 1.44) | 0.84 (0.64, 1.12) | 0.17 |
| Trifluralin | 1.61 (1.18, 2.20) | 1.08 (0.79, 1.47) | 0.01 |
| 2,4-D | 1.21 (0.88, 1.68) | 0.95 (0.69, 1.31) | 0.06 |
| 2,4,5-T | 1.77 (1.28, 2.45) | 1.42 (1.04, 1.95) | 0.25 |
| 2,4,5-TP | 0.33 (0.16, 0.68) | 0.44 (0.26, 0.75) | 0.52 |
| Atrazine | 1.23 (0.89, 1.69) | 0.90 (0.66, 1.24) | 0.02 |
| Cyanazine | 1.05 (0.76, 1.45) | 0.81 (0.59, 1.10) | 0.14 |
| Metribuzin | 0.97 (0.69, 1.37) | 0.79 (0.57, 1.09) | 0.24 |

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; PD, Parkinson’s disease

HR adjusted for sex, state of residence, smoking status, education, and ever-use of correlated pesticides (other pesticides whose ever-use variable had Spearman correlation ≥ 0.40 with the ever-use variable of the target pesticide)

Supplemental Table 4: Ever-use of pesticides reported at enrollment and PD in all participants including prevalent cases (n=66,216)

|  |  |  |  |
| --- | --- | --- | --- |
| Pesticide | non-PD, n (%) | PD, n (%) | OR (95% CI)a |
| **Organochlorine insecticide** |  |  |  |
| Aldrin | 6507 (11.1) | 123 (24.6) | 1.01 (0.76, 1.33) |
| Chlordane | 9758 (16.5) | 147 (29) | 1.01 (0.8, 1.28) |
| Dieldrin | 2440 (4.1) | 50 (10) | 0.92 (0.65, 1.29) |
| DDT | 8954 (15.4) | 175 (35.4) | 0.9 (0.7, 1.14) |
| Heptachlor | 5442 (9.4) | 105 (21.3) | 0.99 (0.74, 1.31) |
| Toxaphene | 5160 (8.7) | 65 (12.9) | 0.74 (0.56, 0.98) |
| Lindane | 7250 (12.1) | 94 (18.5) | 1.03 (0.81, 1.3) |
| **Carbamate insecticide** |  |  |  |
| Aldicarb | 3809 (6.5) | 32 (6.5) | 1.02 (0.68, 1.53) |
| Carbaryl | 27180 (45.5) | 272 (53.9) | 1.06 (0.86, 1.31) |
| Carbofuran | 10017 (16.7) | 134 (26.4) | 1.01 (0.81, 1.26) |
| **Organophosphate insecticide** |  |  |  |
| Chlorpyrifos | 16700 (26.8) | 175 (30.9) | 0.99 (0.82, 1.21) |
| Coumaphos | 3423 (5.7) | 41 (8.1) | 1.08 (0.78, 1.5) |
| Diazinon | 13979 (23.3) | 132 (26) | 0.85 (0.68, 1.06) |
| Dichlorvos | 4425 (7.3) | 53 (10.4) | 1.14 (0.85, 1.54) |
| Fonofos | 8219 (13.6) | 89 (17.1) | 0.9 (0.7, 1.15) |
| Malathion | 28496 (48.7) | 302 (61.9) | 1.06 (0.84, 1.34) |
| Parathion | 5661 (9.5) | 76 (15) | 1.07 (0.82, 1.39) |
| Phorate | 11404 (19.9) | 134 (28.5) | 0.87 (0.69, 1.11) |
| Terbufos | 13718 (23.8) | 159 (33.5) | 1.21 (0.96, 1.52) |
| **Permethrin insecticide** |  |  |  |
| Permethrin (Crops) | 5263 (8.8) | 43 (8.5) | 1.00 (0.73, 1.39) |
| Permethrin (Animals) | 5696 (9.4) | 45 (8.8) | 1.05 (0.76, 1.44) |
| **Fumigant** |  |  |  |
| Carbon disulfide/Carbon tetrachloride | 2099 (3.5) | 40 (7.7) | 1.08 (0.77, 1.51) |
| Aluminum phosphide | 1707 (2.8) | 22 (4.3) | 1.4 (0.9, 2.16) |
| Ethylene dibromide | 1294 (2.2) | 9 (1.8) | 0.56 (0.29, 1.09) |
| Methyl bromide | 5707 (9.5) | 54 (10.5) | 0.9 (0.63, 1.27) |
| **Fungicide** |  |  |  |
| Benomyl | 3492 (6) | 34 (7) | 0.89 (0.57, 1.4) |
| Captan | 4617 (7.7) | 39 (7.7) | 0.81 (0.58, 1.14) |
| Chlorothalonil | 2899 (4.8) | 26 (5.1) | 0.95 (0.6, 1.5) |
| Maneb | 3715 (6.2) | 37 (7.3) | 0.95 (0.63, 1.42) |
| Metalaxyl | 7968 (13.6) | 68 (13.8) | 0.89 (0.65, 1.21) |
| **Herbicide** |  |  |  |
| Alachlor | 19057 (32.1) | 223 (44.8) | 1.16 (0.92, 1.46) |
| Butylate | 10995 (19) | 118 (25.1) | 0.97 (0.75, 1.24) |
| Chlorimuron | 12693 (21.8) | 122 (25.5) | 1.1 (0.86, 1.41) |
| Dicamba | 17945 (31) | 190 (40.3) | 0.95 (0.74, 1.21) |
| EPTC | 7049 (12.2) | 62 (13.2) | 0.8 (0.6, 1.08) |
| Glyphosate | 35406 (58.6) | 343 (65.7) | 1.08 (0.87, 1.34) |
| Imazethapyr | 15124 (26.3) | 148 (31.6) | 0.99 (0.76, 1.27) |
| Metolachlor | 16114 (27.9) | 153 (32.4) | 0.84 (0.66, 1.06) |
| Paraquat | 8526 (14.2) | 103 (20.1) | 1.13 (0.89, 1.44) |
| Pendimethalin | 15250 (26.1) | 155 (32.2) | 1.14 (0.91, 1.45) |
| Petroleum distillates | 16756 (28.9) | 167 (35) | 0.87 (0.69, 1.08) |
| Trifluralin | 18665 (32.2) | 216 (46) | 1.28 (0.99, 1.64) |
| 2,4-D | 28871 (49.8) | 313 (65.8) | 1.07 (0.82, 1.41) |
| 2,4,5-T | 7264 (12.5) | 134 (27.1) | 1.41 (1.1, 1.8) |
| 2,4,5-TP | 3287 (5.5) | 29 (5.7) | 0.46 (0.3, 0.69) |
| Atrazine | 25297 (42.8) | 280 (56.7) | 0.96 (0.73, 1.25) |
| Cyanazine | 14641 (25.2) | 165 (34.5) | 1.01 (0.79, 1.29) |
| Metribuzin | 15500 (26.8) | 164 (35.1) | 0.92 (0.71, 1.19) |

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; OR, Odds Ratio

aOR adjusted for sex, state of residence, smoking status, education, and ever-use of correlated pesticides (other pesticides whose ever-use variable had Spearman correlation ≥ 0.40 with the ever-use variable of the target pesticide)

Supplemental Table 5: Intensity-weighted lifetime days of pesticide use reported at enrollment and PD in male applicators (including prevalent cases, n = 37,362)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Pesticide | Lifetime days | No PD (n (%)) | PD (n (%)) | OR (95 % CI) |
| **Organochlorine insecticide** |  |  |  |  |
| Aldrin | Never use | 13397 (82.7) | 171 (75) | Ref |
|  | Tertile 1 | 992 (6.1) | 20 (8.8) | 0.82 (0.49, 1.35) |
|  | Tertile 2 | 908 (5.6) | 19 (8.3) | 0.81 (0.48, 1.37) |
|  | Tertile 3 | 900 (5.6) | 18 (7.9) | 0.73 (0.42, 1.25) |
| Chlordane | Never use | 13296 (80.9) | 177 (75.3) | Ref |
|  | Tertile 1 | 1063 (6.5) | 19 (8.1) | 0.94 (0.57, 1.53) |
|  | Tertile 2 | 1077 (6.6) | 17 (7.2) | 0.78 (0.46, 1.30) |
|  | Tertile 3 | 999 (6.1) | 22 (9.4) | 0.99 (0.62, 1.58) |
| Dieldrin | Never use | 15739 (96.2) | 217 (93.5) | Ref |
|  | ≤ Median | 307 (1.9) | 9 (3.9) | 0.97 (0.48, 1.97) |
|  | > Median | 308 (1.9) | 6 (2.6) | 0.66 (0.28, 1.53) |
| DDT | Never use | 12677 (78.6) | 137 (59.8) | Ref |
|  | Tertile 1 | 1192 (7.4) | 26 (11.4) | 0.87 (0.55, 1.37) |
|  | Tertile 2 | 1133 (7) | 41 (17.9) | 1.39 (0.93, 2.06) |
|  | Tertile 3 | 1118 (6.9) | 25 (10.9) | 0.9 (0.56, 1.43) |
| Heptachlor | Never use | 14194 (87.4) | 183 (78.9) | Ref |
|  | Tertile 1 | 670 (4.1) | 16 (6.9) | 1.21 (0.70, 2.11) |
|  | Tertile 2 | 715 (4.4) | 19 (8.2) | 1.34 (0.80, 2.24) |
|  | Tertile 3 | 653 (4) | 14 (6) | 1.03 (0.57, 1.85) |
| Toxaphene | Never use | 14905 (88.5) | 217 (89.3) | Ref |
|  | Tertile 1 | 690 (4.1) | 8 (3.3) | 0.56 (0.27, 1.14) |
|  | Tertile 2 | 637 (3.8) | 10 (4.1) | 0.75 (0.39, 1.43) |
|  | Tertile 3 | 614 (3.6) | 8 (3.3) | 0.56 (0.27, 1.16) |
| Lindane | Never use | 15591 (86.3) | 231 (86.2) | Ref |
|  | Tertile 1 | 823 (4.6) | 8 (3) | 0.57 (0.28, 1.17) |
|  | Tertile 2 | 839 (4.6) | 19 (7.1) | 1.3 (0.8, 2.1) |
|  | Tertile 3 | 815 (4.5) | 10 (3.7) | 0.73 (0.39, 1.39) |
| **Carbamate insecticide** |  |  |  |  |
| Carbaryl | Never use | 9518 (57.9) | 137 (58.5) | Ref |
|  | Tertile 1 | 2426 (14.8) | 34 (14.5) | 0.81 (0.55, 1.2) |
|  | Tertile 2 | 2391 (14.5) | 32 (13.7) | 0.7 (0.46, 1.07) |
|  | Tertile 3 | 2099 (12.8) | 31 (13.2) | 0.62 (0.38, 1) |
| Carbofuran | Never use | 23484 (72) | 240 (65.6) | Ref |
|  | Tertile 1 | 3025 (9.3) | 47 (12.8) | 1.18 (0.85, 1.64) |
|  | Tertile 2 | 3095 (9.5) | 47 (12.8) | 1.13 (0.81, 1.56) |
|  | Tertile 3 | 2998 (9.2) | 32 (8.7) | 0.81 (0.55, 1.19) |
| **Organophosphate insecticide** |  |  |  |  |
| Chlorpyrifos | Never use | 18439 (54.9) | 223 (57.3) | Ref |
|  | Tertile 1 | 4991 (14.9) | 62 (15.9) | 1.17 (0.88, 1.56) |
|  | Tertile 2 | 5152 (15.3) | 45 (11.6) | 0.81 (0.58, 1.12) |
|  | Tertile 3 | 4982 (14.8) | 59 (15.2) | 1.19 (0.89, 1.60) |
| Coumaphos | Never use | 29725 (91.2) | 333 (90.5) | Ref |
|  | Tertile 1 | 955 (2.9) | 11 (3) | 0.95 (0.52, 1.75) |
|  | Tertile 2 | 979 (3) | 13 (3.5) | 1.11 (0.63, 1.94) |
|  | Tertile 3 | 938 (2.9) | 11 (3) | 1 (0.54, 1.84) |
| Diazinon | Never use | 13412 (79.2) | 192 (79.7) | Ref |
|  | Tertile 1 | 1194 (7.1) | 17 (7.1) | 0.92 (0.55, 1.53) |
|  | Tertile 2 | 1209 (7.1) | 20 (8.3) | 1 (0.62, 1.62) |
|  | Tertile 3 | 1120 (6.6) | 12 (5) | 0.67 (0.36, 1.22) |
| Dichlorvos | Never use | 29516 (89.2) | 324 (87.3) | Ref |
|  | Tertile 1 | 1182 (3.6) | 8 (2.2) | 0.57 (0.28, 1.15) |
|  | Tertile 2 | 1205 (3.6) | 23 (6.2) | 1.72 (1.11, 2.66) |
|  | Tertile 3 | 1169 (3.5) | 16 (4.3) | 1.21 (0.72, 2.02) |
| Fonofos | Never use | 25838 (77.6) | 296 (78.3) | Ref |
|  | Tertile 1 | 2467 (7.4) | 27 (7.1) | 0.93 (0.62, 1.4) |
|  | Tertile 2 | 2526 (7.6) | 32 (8.5) | 1.05 (0.72, 1.53) |
|  | Tertile 3 | 2463 (7.4) | 23 (6.1) | 0.74 (0.48, 1.15) |
| Malathion | Never use | 5557 (34.5) | 78 (34.8) | Ref |
|  | Tertile 1 | 3547 (22) | 51 (22.8) | 1.01 (0.7, 1.47) |
|  | Tertile 2 | 3645 (22.6) | 45 (20.1) | 0.85 (0.57, 1.24) |
|  | Tertile 3 | 3359 (20.9) | 50 (22.3) | 0.89 (0.6, 1.3) |
| Parathion | Never use | 16605 (92.1) | 245 (91.1) | Ref |
|  | ≤ Median | 718 (4) | 12 (4.5) | 0.93 (0.51, 1.68) |
|  | > Median | 697 (3.9) | 12 (4.5) | 0.98 (0.54, 1.79) |
| Phorate | Never use | 10665 (67.6) | 134 (61.5) | Ref |
|  | Tertile 1 | 1713 (10.9) | 28 (12.8) | 1.07 (0.69, 1.66) |
|  | Tertile 2 | 1755 (11.1) | 37 (17) | 1.4 (0.94, 2.08) |
|  | Tertile 3 | 1640 (10.4) | 19 (8.7) | 0.72 (0.43, 1.19) |
| Terbufos | Never use | 18415 (59.4) | 192 (56.1) | Ref |
|  | Tertile 1 | 4184 (13.5) | 46 (13.5) | 1.18 (0.84, 1.66) |
|  | Tertile 2 | 4293 (13.8) | 60 (17.5) | 1.44 (1.06, 1.97) |
|  | Tertile 3 | 4108 (13.3) | 44 (12.9) | 1.13 (0.79, 1.6) |
| **Permethrin insecticide** |  |  |  |  |
| Permethrin (Crops) | Never use | 28383 (86.5) | 328 (89.4) | Ref |
|  | Tertile 1 | 1470 (4.5) | 19 (5.2) | 1.46 (0.91, 2.34) |
|  | Tertile 2 | 1492 (4.5) | 12 (3.3) | 0.94 (0.52, 1.69) |
|  | Tertile 3 | 1466 (4.5) | 8 (2.2) | 0.66 (0.32, 1.35) |
| Permethrin (Animals) | Never use | 28783 (86.3) | 336 (89.6) | Ref |
|  | Tertile 1 | 1574 (4.7) | 11 (2.9) | 0.82 (0.45, 1.52) |
|  | Tertile 2 | 1508 (4.5) | 10 (2.7) | 0.79 (0.41, 1.49) |
|  | Tertile 3 | 1490 (4.5) | 18 (4.8) | 1.52 (0.93, 2.46) |
| **Fumigant** |  |  |  |  |
| Carbon disulphide/Carbon tetrachloride | Never use | 17467 (95.8) | 250 (94) | Ref |
|  | ≤ Median | 398 (2.2) | 7 (2.6) | 0.74 (0.34, 1.6) |
|  | > Median | 364 (2) | 9 (3.4) | 1.08 (0.55, 2.14) |
| Ethylene Dibromide | Never use | 17442 (95.6) | 258 (95.2) | Ref |
|  | ≤ Median | 397 (2.2) | 8 (3) | 1.3 (0.63, 2.71) |
|  | > Median | 411 (2.3) | 5 (1.8) | 0.76 (0.31, 1.9) |
| Methyl Bromide | Never use | 28072 (84.9) | 328 (86.1) | Ref |
|  | Tertile 1 | 1613 (4.9) | 15 (3.9) | 0.81 (0.47, 1.41) |
|  | Tertile 2 | 1670 (5.1) | 23 (6) | 1.31 (0.8, 2.12) |
|  | Tertile 3 | 1706 (5.2) | 15 (3.9) | 0.77 (0.43, 1.37) |
| **Fungicide** |  |  |  |  |
| Benomyl | Never use | 14990 (92.8) | 206 (91.2) | Ref |
|  | ≤ Median | 592 (3.7) | 5 (2.2) | 0.53 (0.21, 1.37) |
|  | > Median | 573 (3.5) | 15 (6.6) | 1.48 (0.77, 2.83) |
| Captan | Never use | 29167 (89.8) | 334 (91.5) | Ref |
|  | Tertile 1 | 1224 (3.8) | 9 (2.5) | 0.69 (0.35, 1.36) |
|  | Tertile 2 | 1046 (3.2) | 6 (1.6) | 0.54 (0.24, 1.21) |
|  | Tertile 3 | 1060 (3.3) | 16 (4.4) | 1.21 (0.72, 2.04) |
| Chlorothalonil | Never use | 30547 (92.8) | 351 (94.4) | Ref |
|  | Tertile 1 | 750 (2.3) | 8 (2.2) | 0.98 (0.47, 2.04) |
|  | Tertile 2 | 787 (2.4) | 8 (2.2) | 1.01 (0.47, 2.15) |
|  | Tertile 3 | 816 (2.5) | 5 (1.3) | 0.69 (0.27, 1.76) |
| Maneb/Mancozeb | Never use | 15485 (92.5) | 224 (93.3) | Ref |
|  | Tertile 1 | 422 (2.5) | 5 (2.1) | 0.61 (0.24, 1.52) |
|  | Tertile 2 | 428 (2.6) | 5 (2.1) | 0.58 (0.23, 1.47) |
|  | Tertile 3 | 399 (2.4) | 6 (2.5) | 0.68 (0.28, 1.62) |
| Metalaxyl | Never use | 13387 (82.1) | 193 (83.5) | Ref |
|  | Tertile 1 | 986 (6) | 17 (7.4) | 1.31 (0.78, 2.18) |
|  | Tertile 2 | 1005 (6.2) | 15 (6.5) | 1.31 (0.73, 2.36) |
|  | Tertile 3 | 936 (5.7) | 6 (2.6) | 0.67 (0.28, 1.61) |
| **Herbicide** |  |  |  |  |
| Alachlor | Never use | 14805 (46.3) | 150 (42.3) | Ref |
|  | Tertile 1 | 5731 (17.9) | 72 (20.3) | 1.19 (0.88, 1.62) |
|  | Tertile 2 | 5827 (18.2) | 67 (18.9) | 1.12 (0.82, 1.54) |
|  | Tertile 3 | 5641 (17.6) | 66 (18.6) | 1.2 (0.87, 1.65) |
| Butylate | Never use | 11339 (71.3) | 163 (74.8) | Ref |
|  | Tertile 1 | 1520 (9.6) | 25 (11.5) | 1.18 (0.75, 1.85) |
|  | Tertile 2 | 1564 (9.8) | 15 (6.9) | 0.7 (0.4, 1.22) |
|  | Tertile 3 | 1477 (9.3) | 15 (6.9) | 0.76 (0.44, 1.33) |
| Chlorimuron Ethyl | Never use | 10728 (67) | 159 (72.9) | Ref |
|  | Tertile 1 | 1803 (11.3) | 23 (10.6) | 1.15 (0.73, 1.83) |
|  | Tertile 2 | 1825 (11.4) | 18 (8.3) | 0.9 (0.54, 1.49) |
|  | Tertile 3 | 1660 (10.4) | 18 (8.3) | 1 (0.6, 1.66) |
| Dicamba | Never use | 14415 (46.8) | 156 (47) | Ref |
|  | Tertile 1 | 5407 (17.5) | 54 (16.3) | 0.86 (0.61, 1.22) |
|  | Tertile 2 | 5621 (18.2) | 53 (16) | 0.84 (0.59, 1.19) |
|  | Tertile 3 | 5368 (17.4) | 69 (20.8) | 1.23 (0.88, 1.71) |
| EPTC | Never use | 24585 (79.2) | 279 (83) | Ref |
|  | Tertile 1 | 2149 (6.9) | 21 (6.3) | 0.85 (0.54, 1.35) |
|  | Tertile 2 | 2182 (7) | 15 (4.5) | 0.6 (0.35, 1.03) |
|  | Tertile 3 | 2116 (6.8) | 21 (6.3) | 0.94 (0.59, 1.5) |
| Glyphosate | Never use | 7709 (23.1) | 95 (24.7) | Ref |
|  | Tertile 1 | 8396 (25.1) | 106 (27.6) | 1.08 (0.81, 1.44) |
|  | Tertile 2 | 8738 (26.2) | 98 (25.5) | 0.99 (0.73, 1.34) |
|  | Tertile 3 | 8545 (25.6) | 85 (22.1) | 0.93 (0.67, 1.28) |
| Imazethapyr | Never use | 16671 (54.5) | 195 (59.1) | Ref |
|  | Tertile 1 | 4730 (15.4) | 49 (14.8) | 0.96 (0.67, 1.36) |
|  | Tertile 2 | 4620 (15.1) | 42 (12.7) | 0.89 (0.62, 1.29) |
|  | Tertile 3 | 4594 (15) | 44 (13.3) | 1.05 (0.73, 1.53) |
| Metolachlor | Never use | 16056 (52) | 195 (58.4) | Ref |
|  | Tertile 1 | 4970 (16.1) | 45 (13.5) | 0.73 (0.52, 1.03) |
|  | Tertile 2 | 5057 (16.4) | 42 (12.6) | 0.7 (0.49, 1) |
|  | Tertile 3 | 4770 (15.5) | 52 (15.6) | 0.98 (0.7, 1.36) |
| Paraquat | Never use | 15305 (84.1) | 232 (83.2) | Ref |
|  | Tertile 1 | 961 (5.3) | 15 (5.4) | 1 (0.59, 1.71) |
|  | Tertile 2 | 973 (5.3) | 21 (7.5) | 1.4 (0.87, 2.24) |
|  | Tertile 3 | 962 (5.3) | 11 (3.9) | 0.74 (0.39, 1.39) |
| Pendimethalin | Never use | 10014 (62.2) | 151 (67.4) | Ref |
|  | Tertile 1 | 2078 (12.9) | 30 (13.4) | 1.1 (0.73, 1.66) |
|  | Tertile 2 | 2064 (12.8) | 27 (12.1) | 1.12 (0.72, 1.72) |
|  | Tertile 3 | 1954 (12.1) | 16 (7.1) | 0.81 (0.47, 1.4) |
| Petroleum | Never use | 12420 (77.9) | 184 (82.9) | Ref |
|  | Tertile 1 | 1168 (7.3) | 10 (4.5) | 0.58 (0.3, 1.1) |
|  | Tertile 2 | 1194 (7.5) | 13 (5.9) | 0.85 (0.48, 1.51) |
|  | Tertile 3 | 1158 (7.3) | 15 (6.8) | 0.93 (0.54, 1.59) |
| Trifluralin | Never use | 14086 (45.7) | 137 (41.6) | Ref |
|  | Tertile 1 | 5481 (17.8) | 69 (21) | 1.27 (0.92, 1.75) |
|  | Tertile 2 | 5745 (18.6) | 52 (15.8) | 0.93 (0.65, 1.34) |
|  | Tertile 3 | 5498 (17.8) | 71 (21.6) | 1.38 (0.98, 1.93) |
| 2,4-D | Never use | 6722 (21.6) | 58 (17.1) | Ref |
|  | Tertile 1 | 7680 (24.7) | 78 (22.9) | 1.13 (0.79, 1.62) |
|  | Tertile 2 | 8428 (27.1) | 97 (28.5) | 1.12 (0.78, 1.61) |
|  | Tertile 3 | 8294 (26.6) | 107 (31.5) | 1.05 (0.73, 1.52) |
| 2,4,5 T | Never use | 13132 (81.1) | 171 (72.2) | Ref |
|  | Tertile 1 | 1034 (6.4) | 22 (9.3) | 1.1 (0.68, 1.75) |
|  | Tertile 2 | 1045 (6.5) | 21 (8.9) | 1.06 (0.66, 1.71) |
|  | Tertile 3 | 973 (6) | 23 (9.7) | 1.26 (0.79, 2.01) |
| 2,4,5 T P | Never use | 15731 (94.9) | 228 (95) | Ref |
|  | ≤ Median | 429 (2.6) | 5 (2.1) | 0.59 (0.24, 1.46) |
|  | > Median | 408 (2.5) | 7 (2.9) | 0.87 (0.4, 1.89) |
| Atrazine | Never use | 8359 (26.2) | 89 (25.4) | Ref |
|  | Tertile 1 | 7622 (23.9) | 87 (24.8) | 1.07 (0.77, 1.49) |
|  | Tertile 2 | 8102 (25.4) | 84 (23.9) | 0.89 (0.63, 1.25) |
|  | Tertile 3 | 7829 (24.5) | 91 (25.9) | 0.97 (0.69, 1.37) |
| Cyanazine | Never use | 17558 (56.5) | 189 (55.6) | Ref |
|  | Tertile 1 | 4497 (14.5) | 43 (12.6) | 0.81 (0.56, 1.16) |
|  | Tertile 2 | 4631 (14.9) | 53 (15.6) | 0.95 (0.68, 1.33) |
|  | Tertile 3 | 4399 (14.2) | 55 (16.2) | 1.15 (0.82, 1.61) |
| Metribuzin | Never use | 9363 (59.5) | 136 (61.8) | Ref |
|  | Tertile 1 | 2123 (13.5) | 33 (15) | 1.14 (0.75, 1.73) |
|  | Tertile 2 | 2167 (13.8) | 24 (10.9) | 0.83 (0.52, 1.33) |
|  | Tertile 3 | 2089 (13.3) | 27 (12.3) | 0.97 (0.62, 1.53) |

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; OR,Odds Ratio

aOR adjusted for sex, state of residence, smoking status, education, and ever-use of correlated pesticides (other pesticides whose ever-use variable had Spearman correlation ≥ 0.40 with the ever-use variable of the target pesticide)

Supplemental Table 6: Ever-use of pesticide reported at enrollment and PD risk in all participants using inverse probability weights

|  |  |
| --- | --- |
| Pesticide | HR (95% CI) |
| **Organochlorine insecticide** |  |
| Aldrin | 0.90 (0.66, 1.23) |
| Chlordane | 1.08 (0.83, 1.40) |
| Dieldrin | 0.83 (0.57, 1.21) |
| DDT | 0.82 (0.63, 1.08) |
| Heptachlor | 1.06 (0.77, 1.45) |
| Toxaphene | 0.79 (0.58, 1.08) |
| Lindane | 0.92 (0.70, 1.20) |
| **Carbamate insecticide** |  |
| Aldicarb | 1.10 (0.70, 1.71) |
| Carbaryl | 1.14 (0.90, 1.44) |
| Carbofuran | 0.96 (0.75, 1.21) |
| **Organophosphate insecticide** |  |
| Chlorpyrifos | 0.89 (0.71, 1.10) |
| Coumaphos | 1.05 (0.74, 1.49) |
| Diazinon | 0.72 (0.56, 0.93) |
| Dichlorvos | 1.15 (0.84, 1.56) |
| Fonofos | 0.91 (0.70, 1.19) |
| Malathion | 1.05 (0.80, 1.38) |
| Parathion | 0.98 (0.74, 1.31) |
| Phorate (≤ 63y) | 1.30 (0.84, 2.00) |
| > 63y | 0.72 (0.53, 0.98) |
| Terbufos | 1.30 (1.02, 1.67) |
| **Permethrin insecticide** |  |
| Permethrin (Crops) | 1.00 (0.70, 1.43) |
| Permethrin (Animals) | 1.10 (0.79, 1.54) |
| **Fumigant** |  |
| Carbon disulfide/Carbon tetrachloride | 1.03 (0.70, 1.53) |
| Aluminum phosphide | 1.11 (0.67, 1.85) |
| Ethylene dibromide | 0.37 (0.15, 0.90) |
| Methyl bromide | 0.86 (0.58, 1.27) |
| **Fungicide** |  |
| Benomyl (overall) | 0.82 (0.51, 1.31) |
| (≤ 63y) | 0.37 (0.13, 1.08) |
| > 63y | 0.97 (0.58, 1.62) |
| Captan | 0.88 (0.61, 1.28) |
| Chlorothalonil | 0.96 (0.60, 1.54) |
| Maneb (≤ 63y) | 1.35 (0.63, 2.91) |
| > 63y | 0.71 (0.42, 1.18) |
| Metalaxyl | 0.85 (0.61, 1.18) |
| **Herbicide** |  |
| Alachlor | 1.16 (0.89, 1.50) |
| Butylate (≤ 63y) | 1.23 (0.81, 1.88) |
| > 63y | 0.88 (0.64, 1.20) |
| Chlorimuron | 1.03 (0.78, 1.36) |
| Dicamba | 0.96 (0.73, 1.27) |
| EPTC | 0.83 (0.60, 1.14) |
| Glyphosate | 1.15 (0.89, 1.48) |
| Imazethapyr | 1.05 (0.80, 1.39) |
| Metolachlor | 0.77 (0.60, 0.99) |
| Paraquat | 1.19 (0.92, 1.55) |
| Pendimethalin | 1.11 (0.86, 1.43) |
| Petroleum | 0.97 (0.76, 1.23) |
| Trifluralin | 1.32 (0.99, 1.77) |
| 2,4-D | 1.08 (0.80, 1.47) |
| 2,4,5-T | 1.61 (1.22, 2.12) |
| 2,4,5-TP | 0.38 (0.24, 0.62) |
| Atrazine | 1.08 (0.81, 1.44) |
| Cyanazine | 0.87 (0.66, 1.14) |
| Metribuzin | 0.86 (0.65, 1.13) |

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; OR,Odds Ratio

aHR adjusted for sex, state of residence, smoking status, education, and ever-use of correlated pesticides (other pesticides whose ever-use variable had Spearman correlation ≥ 0.40 with the ever-use variable of the target pesticide)

Supplemental table 7: Ever-use of pesticide reported through Phase 2 and PD risk in applicators (n=37,284)

|  |  |  |  |
| --- | --- | --- | --- |
| Pesticide | No PD (n (%)) | PD (n (%)) | HR (95% CI)a |
| **Organochlorine insecticide** |  |  |  |
| Aldrin | 6311 (19.6) | 96 (31.1) | 0.91 (0.67, 1.23) |
| Chlordane | 8556 (26.2) | 119 (37.9) | 1.03 (0.8, 1.33) |
| Dieldrin | 2333 (7.2) | 37 (12) | 0.86 (0.59, 1.26) |
| DDT | 8238 (25.2) | 139 (44.3) | 0.9 (0.7, 1.16) |
| Heptachlor | 5291 (16.4) | 87 (28.2) | 1.09 (0.79, 1.49) |
| Toxaphene | 5456 (16.6) | 65 (20.6) | 0.82 (0.62, 1.08) |
| Lindane | 6733 (20.4) | 73 (23.3) | 0.94 (0.72, 1.23) |
| **Carbamate insecticide** |  |  |  |
| Aldicarb | 3747 (11.5) | 27 (8.7) | 0.92 (0.6, 1.41) |
| Carbaryl | 19211 (58.2) | 199 (64) | 1.11 (0.85, 1.43) |
| Carbofuran | 9795 (29.4) | 115 (36.6) | 1.08 (0.86, 1.36) |
| **Organophosphate insecticide** |  |  |  |
| Chlorpyrifos | 16197 (45) | 142 (39.1) | 0.90 (0.73, 1.11) |
| Coumaphos | 3059 (9.3) | 32 (10.5) | 0.98 (0.68, 1.42) |
| Diazinon | 11287 (34.2) | 99 (31.8) | 0.74 (0.56, 0.96) |
| Dichlorvos | 3781 (11.4) | 42 (13.7) | 1.07 (0.77, 1.49) |
| Fonofos | 7655 (22.8) | 73 (23.2) | 0.94 (0.71, 1.23) |
| Malathion | 25236 (73.7) | 260 (78.3) | 1.05 (0.81, 1.37) |
| Parathion | 5354 (16.3) | 62 (19.8) | 0.97 (0.73, 1.29) |
| Phorate | 11251 (35.1) | 115 (39) | 0.97 (0.75, 1.24) |
| Terbufos | 13922 (41.4) | 146 (46.3) | 1.28 (1.01, 1.62) |
| **Permethrin insecticide** |  |  |  |
| Permethrin (Crops) | 5198 (15.7) | 38 (12.5) | 0.96 (0.67, 1.36) |
| Permethrin (Animals) | 5331 (15.9) | 38 (12.3) | 0.98 (0.69, 1.38) |
| **Fumigant** |  |  |  |
| Carbon disulfide/Carbon tetrachloride | 1922 (5.8) | 29 (9.2) | 1.01 (0.68, 1.5) |
| Aluminum phosphide | 1714 (5.2) | 17 (5.4) | 1.11 (0.68, 1.82) |
| Ethylene dibromide | 1253 (3.8) | 5 (1.6) | 0.34 (0.14, 0.82) |
| Methyl bromide | 5299 (15.9) | 47 (14.6) | 0.82 (0.55, 1.21) |
| **Fungicide** |  |  |  |
| Benomyl | 3173 (9.9) | 27 (8.9) | 0.76 (0.47, 1.23) |
| Captan | 4417 (13.3) | 39 (12.6) | 0.96 (0.68, 1.36) |
| Chlorothalonil | 2740 (8.3) | 23 (7.3) | 1.05 (0.66, 1.67) |
| Maneb | 3230 (9.8) | 32 (10.3) | 1.01 (0.64, 1.6) |
| Metalaxyl | 8068 (24.2) | 71 (22) | 0.96 (0.70, 1.31) |
| **Herbicide** |  |  |  |
| Alachlor | 18743 (55.5) | 192 (60.6) | 1.11 (0.88, 1.39) |
| Butylate | 11040 (33.5) | 110 (35.4) | 1.06 (0.82, 1.38) |
| Chlorimuron Ethyl | 13088 (39.5) | 106 (33.5) | 0.99 (0.78, 1.26) |
| Dicamba | 18455 (56.3) | 171 (56.4) | 1.03 (0.78, 1.38) |
| EPTC | 6882 (20.8) | 53 (17.5) | 0.85 (0.63, 1.16) |
| Glyphosate | 31157 (85.5) | 303 (82.8) | 1.01 (0.75, 1.36) |
| Imazethapyr | 15573 (47.5) | 133 (43.9) | 1.03 (0.78, 1.35) |
| Metolachlor | 17568 (51.8) | 136 (43.7) | 0.80 (0.63, 1.02) |
| Paraquat | 8306 (25) | 85 (26.5) | 1.03 (0.79, 1.34) |
| Pendimethalin | 16680 (49.8) | 145 (45.5) | 1.00 (0.80, 1.26) |
| Petroleum | 16338 (49.7) | 155 (49.4) | 0.99 (0.79, 1.24) |
| Trifluralin | 18038 (56.1) | 185 (62.1) | 1.38 (1.04, 1.83) |
| 2,4-D | 29186 (80.7) | 294 (81.2) | 0.95 (0.72, 1.27) |
| 2,4,5-T | 7273 (22.3) | 117 (37.5) | 1.52 (1.18, 1.97) |
| 2,4,5-TP | 3181 (9.8) | 23 (7.4) | 0.39 (0.25, 0.62) |
| Atrazine | 27689 (76.5) | 276 (75.8) | 1.04 (0.80, 1.35) |
| Cyanazine | 14657 (43.6) | 137 (44.1) | 0.96 (0.75, 1.24) |
| Metribuzin | 15357 (48.3) | 138 (47.3) | 0.85 (0.64, 1.13) |

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

aHR adjusted for sex, state of residence, smoking status, education, and ever-use of correlated pesticides (other pesticides whose ever-use variable had Spearman correlation ≥ 0.40 with the ever-use variable of the target pesticide)

Supplemental Table 8: Comparison between pesticide exposure information reported at the AHS enrollment questionnaire and at FAME among FAME participants – in overall sample and by cases and control status

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | AHS exposure status at enrollment | | | | | | | | | | |
|  | Overall FAME samplea | | | FAME cases | | | | FAME controls | | | |
|  | Exposed  n (%) | Unexposed n (%) | Missing | All cases n (%) | Exposed n (%) | Unexposed n (%) | Missing | All controls | Exposed  n (%) | Unexposed n (%) | Missing |
| FAME exposure |  |  |  |  |  |  |  |  |  |  |  |
| Aldrin |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 91 (72.8) | 28 (10.4) | 7 (15.6) | 26 (28) | 16 (76.2) | 8 (13.1) | 2 (18.2) | 100 (28.9) | 75 (72.1) | 20 (9.6) | 5 (14.7) |
| Unexposed | 34 (27.2) | 241 (89.6) | 38 (84.4) | 67 (72) | 5 (23.8) | 53 (86.9) | 9 (81.8) | 246 (71.1) | 29 (27.9) | 188 (90.4) | 29 (85.3) |
| DDT |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 130 (77.4) | 65 (27.2) | 16 (44.4) | 47 (47) | 28 (75.7) | 17 (31.5) | 2 (22.2) | 164 (47.8) | 102 (77.9) | 48 (25.9) | 14 (51.9) |
| Unexposed | 38 (22.6) | 174 (72.8) | 20 (55.6) | 53 (53) | 9 (24.3) | 37 (68.5) | 7 (77.8) | 179 (52.2) | 29 (22.1) | 137 (74.1) | 13 (48.1) |
| Dieldrin |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 20 (38.5) | 22 (7) | 2 (4.2) | 12 (13.6) | 6 (60) | 5 (7.2) | 1 (11.1) | 32 (9.8) | 14 (33.3) | 17 (6.9) | 1 (2.6) |
| Unexposed | 32 (61.5) | 293 (93) | 46 (95.8) | 76 (86.4) | 4 (40) | 64 (92.8) | 8 (88.9) | 295 (90.2) | 28 (66.7) | 229 (93.1) | 38 (97.4) |
| Parathion |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 8 (15.1) | 5 (1.4) | 3 (6.3) | 6 (6) | 3 (27.3) | 3 (3.8) | 0 (0) | 10 (2.8) | 5 (11.9) | 2 (0.7) | 3 (8.1) |
| Unexposed | 45 (84.9) | 346 (98.6) | 45 (93.8) | 94 (94) | 8 (72.7) | 75 (96.2) | 11 (100) | 342 (97.2) | 37 (88.1) | 271 (99.3) | 34 (91.9) |
| Permethrin |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 19 (36.5) | 35 (9.6) | 3 (9.4) | 16 (16.2) | 3 (37.5) | 11 (13.4) | 2 (22.2) | 41 (11.7) | 16 (36.4) | 24 (8.5) | 1 (4.3) |
| Unexposed | 33 (63.5) | 330 (90.4) | 29 (90.6) | 83 (83.8) | 5 (62.5) | 71 (86.6) | 7 (77.8) | 309 (88.3) | 28 (63.6) | 259 (91.5) | 22 (95.7) |
| Benomyl |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 11 (32.4) | 10 (2.7) | 1 (2.4) | 7 (7.1) | 4 (44.4) | 3 (3.7) | 0 (0) | 15 (4.3) | 7 (28) | 7 (2.4) | 1 (3) |
| Unexposed | 23 (67.6) | 365 (97.3) | 41 (97.6) | 92 (92.9) | 5 (55.6) | 78 (96.3) | 9 (100) | 337 (95.7) | 18 (72) | 287 (97.6) | 32 (97) |
| Paraquat |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 41 (54.7) | 25 (7.5) | 6 (16.7) | 23 (23.7) | 10 (58.8) | 11 (15.5) | 2 (22.2) | 49 (14.1) | 31 (53.4) | 14 (5.3) | 4 (14.8) |
| Unexposed | 34 (45.3) | 308 (92.5) | 30 (83.3) | 74 (76.3) | 7 (41.2) | 60 (84.5) | 7 (77.8) | 298 (85.9) | 27 (46.6) | 248 (94.7) | 23 (85.2) |
| 2,4-D |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 287 (92) | 40 (30.1) | 2 (25) | 76 (73.8) | 67 (94.4) | 8 (28.6) | 1 (25) | 253 (72.3) | 220 (91.3) | 32 (30.5) | 1 (25) |
| Unexposed | 25 (8) | 93 (69.9) | 6 (75) | 27 (26.2) | 4 (5.6) | 20 (71.4) | 3 (75) | 97 (27.7) | 21 (8.7) | 73 (69.5) | 3 (75) |
| Trifluralin |  |  |  |  |  |  |  |  |  |  |  |
| Exposed | 151 (79.9) | 36 (15.7) | 5 (14.7) | 46 (45.1) | 42 (89.4) | 3 (6.7) | 1 (10) | 146 (41.7) | 109 (76.8) | 33 (17.9) | 4 (16.7) |
| Unexposed | 38 (20.1) | 193 (84.3) | 29 (85.3) | 56 (54.9) | 5 (10.6) | 42 (93.3) | 9 (90) | 204 (58.3) | 33 (23.2) | 151 (82.1) | 20 (83.3) |

Abbreviations: FAME, Farming and Movement Evaluation Study

Note: FAME asked exposure occurring prior to a reference date (cases: age at Parkinson’s disease diagnosis and controls: median age of Parkinson’s disease diagnosis for cases within the corresponding age-, sex, and state-specific stratum) whereas AHS enrollment asked ever-use of these pesticides

aFAME participants whose information on FAME exposure were excluded.