Table 2.4.1: Cohort studies on relationship of endocrine disruptors with prostatic cancer

| Region and subjects | Number of subjects | Follow-up period | Compound | Confounders considered | Relative risk (SMR, SIR, etc.) by category | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | P trend |
| Wiklund, 1986 | | | | | | | | | | | |
| Sweden<br>Farm workers born in 1981-1940 | 254,417 farm workers, 1,725,845 controls cohort | 1961-79 | Farm workers | | | 0.90 (1961-1967)<br>0.93 (1967-1973)<br>1.01 (1974-1979)<br>Significant change with time (P < 0.01) | | | | | |
| Saracci R, 1991 | | | | | | | | | | | |
| Cohorts from Australia, Austria, Canada, Denmark, Finland, Italy, Holland, New Zealand, Sweden and U.K.<br>Retrospective study | 18,390 (16,863 men, 1,527 women)<br>13,482 exposed, 416 probably exposed, 3,951 unexposed, 541 unknown | 1955-88 (varies by cohort) | Chlorophenoxy herbicides (2,4-T、2,4,5-T、2,4,5-TCP、2,4,6-TCP、2,4-DCP、2,4-DP、2,4-DB、2,3,4,6-TeCP、MCPA、MCPB、MCPP、PCP、PBA) | | | SMR (95% CI) (deaths observed)<br>Exposed: 111 (75-158) (30)<br>Probably exposed: 0 (0-671) (0)<br>Unexposed: 40 (5-143) (2)<br>Unknown: 217 (6-1211) (1) | | | | | |
| Morrison, 1993 | | | | | | | | | | | |
| Canada<br>Farm owners 45 or more years of age<br>Retrospective study | 145,383 | 1971-87 | Herbicides | Age, calendar year (adjusted) | | Herbicide spraying area (250 acre or more vs. 0 acre), mortality ratio RR<br>1.19 (0.98-1.45) | | | | | |
| Dich, 1998 | | | | | | SIR | | | | | |
| Sweden<br>Pesticide spraying operators qualified in 1965-76<br>Retrospective study | 20,025 | Up to 1991 | Pesticides (principally DDT, lindane, pentachlorophenol) phenoxyacetic acid | Year of qualification, year of birth, region | | 1.13 (1.02-1.24) | | | | | |
| Fleming, 1999 | | | | | | SIR(95%C) | | | | | |
| Florida, U.S.<br>Qualified pesticide spraying operators | 33,658 (30,155 men, 3.503 women) | 1975-93 | Pesticide spraying operators | Age, calendar year (adjusted) | | All subjects: 2.48 (1,57-3.72) (23 observed)<br>Private operators: 2.37 (1.33-3.91) (15 observed)<br>Commercial or public operators: 2.72 (1.17-5.36) (8 observed) | | | | | |
| Fleming, 1999 | | | | | | SMR(95%C) | | | | | |
| Florida, U.S.<br>Qualified pesticide spraying operators | 33,658 (30,155 men) | 1975-90 | Pesticide spraying operators | Age, calendar year (adjusted) | | 2.38 (1.83-3.04)(64 observed) | | | | | |
| Sharma-Wagner, 2000 | | | | | | SIR(95%Cl) | | | | | |
| Sweden<br>Swedish Cancer-Environment Registry<br>Nationwide | | 1961-79 | Pesticides | Age, region (adjusted) | | Farmers, stock raisers<br>Farm workers, forestry officials, gardeners | | | | | |
| MacLennan, 2002 | | | | | | | | | | | |
| Louisiana, U.S.<br>Atrazine and triazine herbicides<br>Manufacturer employees<br>Average 10 years of employment<br>Retrospective studies | 2,045 | 1985-97 | Atrazine and triazine-based herbicides | None | | l/E<br>11/6.3<br>SIR(95%Cl)<br>100 175 (87-312)<br>Current employees<br>100 300 (110-652)<br>Contract workers or employees on leave<br>100 116 (38-271) | | | | | |

Table 2.4.1: Cohort studies on relationship of endocrine disruptors with prostatic cancer

| Region and subjects | Number of subjects | Follow-up period | Compound | Confounders considered | Relative risk (SMR, SIR, etc.) by category | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | P trend |
| Alavanja, 2003 | | | | | | SIR(95%CI) | | | | | |
| North Carolina and Iowa, U.S. | 55332 | Time of registration (1993-97)-1999 | Pesticide spraying operators | Age, family history | | 1.14 (1.05-1.24) | | | | | |
| AHS cohort study | | | Alachlor | | 1 | 0.91 (0.70-1.18) | 1.11 (0.85-1.45) | 1.35 (0.95-1.92) | 0.70 (0.44-1.12) | 0.77 (0.48-1.26) | 0.52 |
| Male pesticide spraying operators | | | Atrazine | | 1 | 1.02 (0.79-1.31) | 0.91 (0.71-1.18) | 0.89 (0.65-1.23) | 0.82 (0.54-1.25) | 0.97 (0.63-1.48) | 0.34 |
| | | | Carbofuran | | 1 | 1.29 (0.95-1.74) | 1.93 (1.42-2.62) | 1.00 (0.66-1.51) | 0.68 (0.38-1.23) | 1.01 (0.58-1.77) | 0.23 |
| | | | Chlorpyrifos | | 1 | 0.95 (0.70-1.30) | 1.04 (0.75-1.42) | 0.89 (0.58-1.36) | 0.64 (0.35-1.18) | 0.73 (0.41-1.31) | 0.23 |
| | | | Permethrin | | 1 | 1.30 (0.76-2.24) | 2.31 (1.38-3.87) | 1.11 (0.54-2.25) | 1.73 (0.63-4.75) | 0.74 (0.24-2.33) | 0.63 |
| | | | Aldrin | | 1 | 1.44 (0.98-2.11) | 1.12 (0.76-1.66) | 1.56 (0.92-2.64) | 0.87 (0.38-1.99) | 1.38 (0.60-3.19) | 0.7 |
| | | | DD | | 1 | 1.18 (0.84-1.66) | 1.17 (0.81-1.69) | 0.76 (0.46-1.27) | 1.38 (0.71-2.68) | 1.14 (0.59-2.21) | 0.89 |
| | | | Heptachlor | | 1 | 1.08 (0.67-1.74) | 0.86 (0.53-1.41) | 1.00 (0.51-1.98) | 0.64 (0.20-2.03) | 0.66 (0.21-2.09) | 0.41 |
| | | | Methyl bromide | | 1 | 1.01 (0.66-1.56) | 0.76 (0.47-1.25) | 0.70 (0.38-1.28) | 2.73 (1.18-6.33) | 3.47 (1.37-8.76) | 0.004 |
| | | | Captan | | 1 | 1.07 (0.50-2.30) | 1.09 (0.48-2.48) | 1.89 (0.58-6.12) | 0.95 (0.23-3.93) | 2.79 (0.35-22.1) | 0.11 |
| Rusiecki, 2004 | | | | | | SIR(95%CI) | | | | | |
| North Carolina and Iowa, U.S. | 53943 | Survey by questionnaire | Atrazine | Age, sex, drinking habit, | | Exposure level estimated by exposure period | | | | | |
| Pesticide spraying operators cohort (53,943 subjects) | | | | farm location, smoking habit, education, family | 1 | 0.89 (0.66-1.21) | 0.75 (0.56-1.03) | 0.88 (0.63-1.23) | | | 0.26 |
| | | | | | | Exposure level estimated by exposure period and intensity | | | | | |
| 68% (36,513) with atrazine exposure history | | | | history, state, use of 10 atrazine-related pesticides | 1 | 1 1.03 (0.76-1.41) | 0.86 (0.62-1.20) | 0.89 (0.63-1.25) | | | 0.35 |

Table 2.4.2: Nested case-control studies on relationship of endocrine disruptors with prostatic cancer

| Region and number of subjects (case/control) | Compound | Detection rate from serum | | | Comparison of serum levels | | | Odds ratio by category | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Case | Control | P value | Case | Control | P value | 1.00 | 2 | 3 | 4 | P trend |
| Charles, 2003 | | | | | | | | | | | | |
| U.S.<br>Five electric companies<br>Current and ex-employees in 1987-94<br>Followed up from 1988 on<br>387 Cases, 1935 controls<br>44-92 Years of age<br>91% Whites<br>44.5% Upper blue collars | PCB(Exposed for at least 2821 hours) | | | | | | | | 1.47(0.97-2.24) | | | |
| Mills, 2003 | | | | | | | | | | | | |
| California, U.S.<br>Agricultural labor union members<br>Hispanic<br>222 Cases diagnosed in 1987-99, average 70 years of age<br>1110 Controls | Chlorothaloni | | | | | | | 1.00 | 1.04 (0.69-1.56) | 1.11 (0.65-1.89) | 1.12 (0.58-2.15) | 0.71 |
| | Diazinon | | | | | | | 1.00 | 0.89 (0.58-1.36) | 0.51 (0.29-0.91) | 0.64 (0.33-1.26) | 0.56 |
| | Dichlorvos | | | | | | | 1.00 | 1.38 (0.91-2.10) | 1.15 (0.71-1.87) | 1.64 (0.97-2.78) | 0.21 |
| | Dichloropropene | | | | | | | 1.00 | 1.08 (0.72-1.62) | 0.85 (0.51-1.42) | 0.73 (0.39-1.35) | 0.67 |
| | Dicofol | | | | | | | 1.00 | 0.86 (0.57-1.29) | 1.04 (0.64-1.67) | 1.09 (0.65-1.83) | 0.84 |
| | Heptachlor | | | | | | | 1.00 | 1.13 (0.73-1.73) | 2.07 (1.21-3.54) | 2.01 (1.12-3.60) | 0.003 |
| | Lindane | | | | | | | 1.00 | 1.14 (0.45-1.77) | 1.86 (1.10-3.17) | 2.37 (1.22-4.61) | 0.003 |
| | Malathion | | | | | | | 1.00 | 0.93 (0.62-1.39) | 1.01 (0.61-1.67) | 1.04 (0.59-1.85) | 0.89 |
| | Mancozeb | | | | | | | 1.00 | 0.91 (0.60-1.38) | 0.92 (0.54-1.55) | 1.10 (0.62-1.97) | 0.89 |
| | Maneb | | | | | | | 1.00 | 1.03 (0.68-1.55) | 1.01 (0.61-1.68) | 0.77 (0.41-1.42) | 0.58 |
| | Methyl bromide | | | | | | | 1.00 | 1.17 (0.77-1.79) | 1.20 (0.66-2.18) | 1.59 (0.77-3.30) | 0.25 |
| | Propagarite | | | | | | | 1.00 | 0.79 (0.52-1.21) | 0.92 (0.56-1.49) | 1.14 (0.71-1.83) | 0.68 |
| | Propoxur | | | | | | | 1.00 | 1.01 (0.66-1.53) | 0.99 (0.60-1.64) | 1.49 (0.88-2.52) | 0.15 |
| | Propyzamide | | | | | | | 1.00 | 0.73 (0.49-1.09) | 0.69 (0.43-1.12) | 0.54 (0.30-0.97) | 0.07 |
| | Simazine | | | | | | | 1.00 | 1.52 (1.00-2.34) | 1.56 (0.92-2.66) | 1.81 (0.93-3.53) | 0.03 |
| | Trifluralin | | | | | | | 1.00 | 0.98 (0.66-1.46) | 0.93 (0.59-1.48) | 0.77 (0.43-1.37) | 0.36 |
| Hessel, 2004 | | | | | | | | OR for all subjects (12 cases, 130 controls) | | | | |
| U.S.<br>Company workers whose medical records exist from an original cohort of a Louisiana atrazine manufacturing plant employees (2045 subjects)<br>12 Cases, 130 controls | strazine | | | | | | | 1.00 | Average exposure (continuous): 0.87 (0.46-1.30) | | | |
| | | | | | | | | 1.00 | Exposure period (continuous): 1.30 (1.06-1.66) | | | |
| | | | | | | | | 1.00 | Cumulative exposure (continuous): 1.01 (0.95-1.07) | | | |
| | | | | | | | | OR for subjects who underwent PSA test at least once (10 cases, 48 controls) | | | | |
| | | | | | | | | 1.00 | Average exposure (continuous): 0.82 (0.36-1.47) | | | |
| | | | | | | | | 1.00 | Exposure period (continuous): 0.96 (0.71-1.30) | | | |
| | | | | | | | | 1.00 | Cumulative exposure (continuous): 0.98 (0.91-1.05) | | | |

Table 2.4.3: Case-control studies on relationship of endocrine disruptors with prostatic cancer

| Region and number of subjects (case/control) | Compound | Detection rate from serum | | | Comparison of serum levels | | | Odds ratio by category | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Case | Control | P value | Case | Control | P value | 1.00 | 2 | 3 | 4 | 5 | P trend |
| Checkoway, 1987 | | | | | | | | | | | | | |
| North Carolina, U.S.<br>Whites and blacks<br>Benign prostatic hypertrophy patients as controls<br>40/64 | Pesticides and herbicides | | | | | | | | Pesticide exposure: 12.5% for cases, 7.8% for controls<br>Herbicide exposure: 10.0% for cases, 6.3% for controls<br>Agricultural job experience: 75/0% for cases, 37.5% for controls<br>(No statistical analysis was attempted) | | | | |
| van der Gulden, 1995 | | | | | Average use of pesticides (day/year) | | | | | | | | |
| Holland<br>Population-based<br>345/1346 | Pesticides | | | | 11.400 | 7.500 | 0.03 | 1.00<br>1.00<br>1.00<br>1.00 | Agriculture: 0.85 (0.57-1.25)<br>Farmers: 0.78 (0.51-1.18)<br>Farm workers: 2.74 (0.94-7.98)<br>Pesticides: 0.84 (0.63-1.13) (occasional and frequent users), 1.47 (0.88-46) for frequent users | | | | |
| Krstev, 1998 | | | | | | | | | | | | | |
| Atlanta, Georgia; Detroit, Michigan; New Jersey, U.S.<br>Whites and blacks<br>Population-based<br>981 Cases (479 blacks. 502 whites)<br>1315 Controls (594 blacks, 721 whites) | Agriculture | | | | | | | <br>1.00<br>1.00<br><br>1.00<br>1.00 | Farm workers:<br>All subjects: 2.17 (1.18-3.98)<br>Blacks: 1.97 (0.91-4.25)、白人; 2.71 (1.00-7.38)<br>Farmers:<br>All subjects: 1.63 (1.04-2.54)<br>Blacks: 1.59 (0.90-2.80)、白人; 1.90 (0.91-3.95) | | | | |
| Settimi, 2001 | | | | | | | | Non-agriculture | | | | | |
| 5 Rural areas in Italy<br>Hospital-based<br>1990-92<br>140 Cases, 897 controls | Agriculture<br><br><br>Pesticides | | | | | | | 1.00<br>1.00<br>Non-agriculture<br>1.00<br>Non-agriculture<br>1.00 | 1.4 (1.0-2.1)<br>1.4 (0.4-4.9)<br>pesticide use<br>1.7 (1.2-2.6)<br>no pesticide use<br>1.1 (0.5-2.2) | 1.3 (0.6-2.5)<br><br>1.3 (0.5-2.9) | 1.5 (1.0-2.1)<br><br>1.9 (1.2-2.9) | By period of farm working<br><br>By period of pesticide use | |
| Settimi, 2003 | | | | | | | | | | | | | |
| 5 Rural areas in Italy<br>Hospital-based<br>1990-92<br>124 Cases (average 66.1 years of age)<br>897 Controls (average 64.1 years of age) | Agriculture<br><br>Carbamates<br>Organochlorine pesticides<br>DDT<br>Dicofol & Tetradifon<br>Dithocarbamates<br>Ziram | | | | | | | 1.00<br><br>1.00<br>1.00<br>1.00<br>1.00<br>1.00<br>1.00 | 1.4 (0.9-2.0)<br><br>1.2 (0.4-2.4)<br>2.5 (1.4-4.2)<br>2.1 (1.2-3.8)<br>2.8 (1.5-5.0)<br>1.0 (0.6-1.7)<br>1.2 (0.5-3.0) | | | | |

| Region and number of subjects (case/control) | Compound | Detection rate from serum | | | Comparison of serum levels | | | Odds ratio by category | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Case | Control | P value | Case | Control | P value | 1.00 | 2 | 3 | 4 | 5 | P trend |
| Ritchie, 2003 | | (%) | (%) | | Median serum level ( $\mu$ g/g fat) | | | | | | | | |
| Iowa, U.S. | $\beta$ -HCH | 14 | 15 | 0.82 | | | | | | | | | |
| 98-99% Whites | p,p'-DDE | 100 | 99 | 0.99 | 0.290 | 0.270 | 0.68 | 1.00 | 0.72 (0.31-1.71) | 1.08 (0.47-2.50) | | | |
| Hospital-based | p,p'-DDT | 0 | 2 | 0.53 | | | | | | | | | |
| 58 Cases (47-85 years of age) | dieldrin | 29 | 38 | 0.25 | | | | 1.00 | 0.97 (0.40-2.36) | 0.28 (0.09-0.88) | | | |
| 99 Controls (44-85 years of age) | heptachlor epoxide | 24 | 34 | 0.18 | | | | 1.00 | 0.58 (0.21-1.64) | 0.33 (0.10-1.03) | | | |
| | HCB | 5 | 4 | 0.71 | | | | | | | | | |
| | trans-nonachlor | 98 | 88 | 0.03 | 0.033 | 0.033 | 0.38 | 1.00 | 1.96 (0.83-4.66) | 1.18 (0.45-3.08) | | | |
| | oxychlordane | 91 | 82 | 0.10 | 0.027 | 0.026 | 0.58 | 1.00 | 3.11 (1.27-7.63) | 1.23 (0.42-3.55) | | | |
| | PCB18 | 2 | 0 | 0.37 | | | | | | | | | |
| | PCB28 | 2 | 1 | 0.99 | | | | | | | | | |
| | PCB99 | 12 | 11 | 0.86 | | | | | | | | | |
| | PCB118 | 7 | 6 | 0.99 | | | | | | | | | |
| | PCB138 | 0 | 1 | 0.99 | | | | | | | | | |
| | PCB146 | 0 | 1 | 0.99 | | | | | | | | | |
| | PCB153 | 88 | 84 | 0.48 | 0.040 | 0.033 | 0.41 | 1.00 | 1.76 (0.76-4.07) | 0.98 (0.37-2.59) | | | |
| | PCB170 | 4 | 5 | 0.99 | | | | | | | | | |
| | PCB180 | 54 | 38 | 0.07 | 0.022 | 0.009 | 0.10 | 1.00 | 3.13 (1.33-7.34) | 1.47 (0.58-3.73) | | | |
| | PCB187 | 10 | 7 | 0.55 | | | | | | | | | |
| | PCB194 | 5 | 7 | 0.75 | | | | | | | | | |
| | PCB201 | 0 | 1 | 0.99 | | | | | | | | | |
| | Total PCBs | | | | 0.055 | 0.042 | 0.18 | 1.00 | 1.36 (0.56-3.32) | 1.67 (0.66-4.22) | | | |

Table 2.4.4: Ecological studies on relationship of endocrine disruptors with prostatic cancer

| Region and number of subjects | Compound | Comparison of serum levels | | P value | Odds ratio by category | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Case | Control | | 1(Low) | 2 | 3 | 4(High) | P trend |
| Wilkinson, 1997 | | | | | | | | | |
| U.K.<br>Residents around a pesticide plant<br>Local cancer prevalence and mortality | Pesticides | | | | | O/E 1.37 (95%Cl: 0.89-2.02) (0-1 km radius)<br>O/E 1.10 (95%Cl: 1.02-1.18) (0-7.5 km radius) | | | |
| Schreinemacher, 1999 | | | | | | | | | |
| 4 Regions in Minnesota, U.S.<br>1980-89<br>Whites | Ethylenebisdithiocarbamates and other herbicides (?) | | | | SRR (95% CI) (compared with urban and forest areas)<br>Region 1 (corn, soybean)<br>Region 2 (wheat, corn, soybean)<br>Region 3 (potato, wheat, sugar beet; heavy use of pesticides) | | | | |
| Schreinemacher, 2000 | | | | | | | | | |
| U.S.<br>Whites<br>152 Counties in Minnesota, North Dakota, South Dakota and Montana producing spring wheat and durum wheat treated with chlorophenoxy herbicides<br>1980-89<br>Ecological study | Chlorophenoxy herbicides | | | | SRR (95% CI) for counties with acreage < 23,000 acres<br>23,000-110,999 acres<br>≥ 111,000 acres | | | | |
| Janssens, 2001 | | | | | | | | | |
| 589 Communities in Belgium<br>Acreage and pesticide use in 1998<br>Mortality statistics in 1985-94 | Pesticides | Defoliant use correlated with mortality (P = 0.01)<br>Growth regulator use correlated with mortality (P = 0.02)<br>No correlation for other pesticides | | | | | | | |
| Koifman, 2002 | | | | | | | | | |
| 11 States of Brazil | Pesticides | Correlation factor between pesticide sales in 1985 and prostatic cancer mortality in 1996-98: r = 0.67 (95% CI = -0.20-0.83) | | | | | | | |

Table 2.4.5: Meta-analysis of relationship of endocrine disruptors with prostatic cancer

| Region and subject (case/control) | Compound/factor | Estimated meta-rate ratio |
|---|---|---|
| Van Maele-Fabry, 2003 | | |
| Agricultural workers<br>25 Estimated values from 22 studies (11 cohort studies, 4 PMR studies, 7 case-control studies) | Pesticides? | 1.13 (1.04-1.22) |

PMR: proportional mortality ratios