Risk Assessment for Metalworking Fluids

Supplemental Materials

1. Cancer Mortality: Published Studies

From analyses of mortality at three auto manufacturing plants, using different study designs and analytical methods, relative risk estimates are available (Table S1). Some of these results duplicated other analyses and were excluded from further consideration.

Table S1 Estimates of cancer associations from studies at three plants in the auto industry

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author | Paper ID | site | β,RR | β,LCL | β,UCL | MWFtype | MeancumX  | Spec.cumX | scen | use |
| Agalliu | 3 | prostate | 2.3800 | 1.310 | 4.330 | str | 0.130 | 10.000 | 2 | 0 |
| Agalliu | 4 | prostate | 1.0600 | 1.010 | 1.110 | sol |  | 10.000 | 2 | 1 |
| Agalliu | 4 | prostate | 1.1200 | 1.040 | 1.200 | strl |  | 10.000 | 2 | 1 |
| Agalliu | 4 | prostate | 1.1000 | 0.840 | 1.430 | sol |  | 10.000 | 2 | 1 |
| Agalliu | 4 | prostate | 1.2900 | 1.000 | 1.460 | sol |  | 50.000 | 2 | 1 |
| Agalliu | 4 | prostate | 1.4100 | 0.990 | 2.000 | sol |  | 100.000 | 2 | 1 |
| Agalliu | 4 | prostate | 3.4100 | 1.050 | 11.100 | sol |  | 270.000 | 2 | 1 |
| Bardin | 12 | pancreas | 1.0050 | 1.000 | 1.010 | str | 4.660 |  | 1 | 1 |
| Bardin | 12 | pancreas | 1.0050 | 1.000 | 1.010 | sol | 29.560 |  | 1 | 1 |
| Bardin | 12 | pancreas | 1.0500 | 0.970 | 1.140 | syn | 0.290 |  | 1 | 1 |
| Bardin | 12 | pancreas | 1.0500 | 0.970 | 1.140 | syn,G | 0.290 |  | 1 | 1 |
| Bardin | 12 | pancreas | 1.0050 | 1.000 | 1.010 | sol,G | 19.100 |  | 1 | 1 |
| Bardin | 13 | bil.trct | 3.8800 | 0.880 | 19.960 | chl | 2.200 |  | 1 | 0 |
| Bardin | 13 | bil.trct | 1.0900 | 0.970 | 1.220 | str | 4.400 |  | 1 | 1 |
| Betenia | 18 | cervical | 2.9600 | 2.110 | 4.020 | sol | 1.530 |  | 3 | 1 |
| Costello | 33 | melanoma | 1.0700 | 0.540 | 2.100 | str | 0.410 |  | 3 | 1 |
| Costello | 33 | melanoma | 1.1400 | 0.590 | 2.200 | str | 1.910 |  | 3 | 1 |
| Costello | 33 | melanoma | 1.3900 | 0.620 | 3.110 | sol | 2.590 |  | 3 | 1 |
| Costello | 33 | melanoma | 1.1700 | 0.530 | 2.610 | sol | 6.320 |  | 3 | 1 |
| Eisen | 42 | brain | 0.8800 | 0.490 | 1.590 | str | 0.500 |  | 3 | 1 |
| Eisen | 42 | brain | 1.1200 | 0.550 | 2.260 | str | 1.730 |  | 3 | 1 |
| Eisen | 42 | brain | 0.7100 | 0.340 | 1.480 | str | 5.000 |  | 3 | 1 |
| Eisen | 42 | brain | 1.7600 | 0.880 | 3.490 | sol,G | 1.000 |  | 3 | 0 |
| Eisen | 42 | brain | 2.0800 | 1.050 | 4.110 | sol,G | 4.900 |  | 3 | 0 |
| Eisen | 42 | brain | 1.5800 | 0.740 | 3.380 | sol,G | 15.000 |  | 3 | 0 |
| Eisen | 42 | brain | 1.0000 | 0.430 | 2.270 | syn | 0.500 |  | 3 | 1 |
| Eisen | 42 | brain | 1.2800 | 0.590 | 2.780 | syn | 2.000 |  | 3 | 1 |
| Eisen | 42 | colon | 0.9500 | 0.690 | 1.320 | str | 0.500 |  | 3 | 0 |
| Eisen | 42 | colon | 1.1500 | 0.730 | 1.680 | str | 1.730 |  | 3 | 0 |
| Eisen | 42 | colon | 0.7500 | 0.510 | 1.090 | str | 5.000 |  | 3 | 0 |
| Eisen | 42 | colon | 0.9000 | 0.620 | 1.290 | sol,G | 1.000 |  | 3 | 0 |
| Eisen | 42 | colon | 1.2100 | 0.870 | 1.690 | sol,G | 4.900 |  | 3 | 0 |
| Eisen | 42 | colon | 0.9100 | 0.630 | 1.300 | sol,G | 15.000 |  | 3 | 0 |
| Eisen | 42 | colon | 0.6100 | 0.340 | 1.070 | syn | 0.500 |  | 3 | 0 |
| Eisen | 42 | colon | 1.0300 | 0.660 | 1.620 | syn | 2.000 |  | 3 | 0 |
| Eisen | 42 | lymphopoietic | 0.8500 | 0.540 | 1.320 | str | 0.500 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 1.2200 | 0.740 | 2.010 | str | 1.730 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 1.2300 | 0.720 | 1.750 | str | 5.000 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 1.1500 | 0.730 | 1.800 | sol,G | 1.000 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 1.0600 | 0.670 | 1.660 | sol,G | 4.900 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 0.9600 | 0.600 | 1.550 | sol,G | 15.000 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 1.0200 | 0.540 | 1.910 | syn | 0.500 |  | 3 | 1 |
| Eisen | 42 | lymphopoietic | 1.0200 | 0.550 | 1.900 | syn | 2.000 |  | 3 | 1 |
| Eisen | 42 | rectum | 1.3000 | 0.710 | 2.390 | str | 0.500 |  | 3 | 1 |
| Eisen | 42 | rectum | 1.7700 | 0.900 | 3.480 | str | 1.730 |  | 3 | 1 |
| Eisen | 42 | rectum | 2.0100 | 1.150 | 3.520 | str | 5.000 |  | 3 | 1 |
| Eisen | 42 | rectum | 1.1100 | 0.560 | 2.160 | sol,G | 1.000 |  | 3 | 1 |
| Eisen | 42 | rectum | 1.2800 | 0.690 | 2.390 | sol,G | 4.900 |  | 3 | 1 |
| Eisen | 42 | rectum | 1.3600 | 0.810 | 2.760 | sol,G | 15.000 |  | 3 | 1 |
| Eisen | 42 | rectum | 0.5800 | 0.190 | 1.750 | syn | 0.500 |  | 3 | 1 |
| Eisen | 42 | rectum | 1.3500 | 0.660 | 1.620 | syn | 2.000 |  | 3 | 1 |
| Eisen | 42 | stomach | 1.2000 | 0.820 | 1.740 | str | 0.500 |  | 3 | 1 |
| Eisen | 42 | stomach | 0.6500 | 0.360 | 1.160 | str | 1.730 |  | 3 | 1 |
| Eisen | 42 | stomach | 1.1000 | 0.750 | 1.700 | str | 5.000 |  | 3 | 1 |
| Eisen | 42 | stomach | 0.8800 | 0.570 | 1.360 | sol,G | 1.000 |  | 3 | 1 |
| Eisen | 42 | stomach | 1.1700 | 0.780 | 1.770 | sol,G | 4.900 |  | 3 | 1 |
| Eisen | 42 | stomach | 1.0500 | 0.680 | 1.630 | sol,G | 15.000 |  | 3 | 1 |
| Eisen | 42 | stomach | 1.1100 | 0.650 | 1.900 | syn | 0.500 |  | 3 | 1 |
| Eisen | 42 | stomach | 0.5600 | 0.280 | 1.150 | syn | 2.000 |  | 3 | 1 |
| Eisen | 44 | larynx | 1.5400 | 0.860 | 2.780 | str | 0.220 |  | 3 | 1 |
| Eisen | 44 | larynx | 1.2200 | 0.520 | 2.860 | sol | 3.460 |  | 3 | 1 |
| Eisen | 44 | larynx | 0.8500 | 0.460 | 1.550 | gnd | 1.220 |  | 3 | 1 |
| Friesen | 50 | bladder | 1.4000 | 0.820 | 2.380 | str | 0.075 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.2200 | 0.710 | 2.090 | str | 0.280 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.1300 | 0.670 | 6.690 | str | 0.980 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.5100 | 0.880 | 2.610 | str | 4.090 |  | 3 | 0 |
| Friesen | 50 | bladder | 2.0700 | 1.190 | 3.620 | str | 15.000 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.2000 | 0.690 | 2.080 | sol | 0.500 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.0800 | 0.610 | 1.890 | sol | 1.720 |  | 3 | 0 |
| Friesen | 50 | bladder | 0.9000 | 0.520 | 1.570 | sol | 4.360 |  | 3 | 0 |
| Friesen | 50 | bladder | 0.8900 | 0.500 | 1.600 | sol | 10.700 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.0200 | 0.560 | 1.880 | sol | 20.000 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.1400 | 0.560 | 2.310 | syn | 0.035 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.0800 | 0.520 | 2.230 | syn | 0.120 |  | 3 | 0 |
| Friesen | 50 | bladder | 1.1800 | 0.570 | 2.420 | syn | 0.290 |  | 3 | 0 |
| Friesen | 50 | bladder | 0.6100 | 0.290 | 1.260 | syn | 0.960 |  | 3 | 0 |
| Friesen | 50 | bladder | 0.7800 | 0.380 | 1.161 | syn | 4.000 |  | 3 | 0 |
| Malloy  | 92 | rectum | 1.4000 | 0.600 | 3.600 | sol | 27.500 |  | 3 | 1 |
| Malloy  | 92 | rectum | 1.8000 | 0.600 | 5.700 | syn | 1.840 |  | 3 | 1 |
| Malloy  | 92 | rectum | 1.2000 | [1] |  | str |  | 5.000 | 2 | 1 |
| Malloy  | 92 | rectum | 1.5000 | [1] |  | str |  | 10.000 | 2 | 1 |
| Malloy  | 92 | rectum | 2.5000 | [1] |  | str |  | 25.000 | 2 | 1 |
| Malloy  | 92 | rectum | 3.2000 | [1] |  | str |  | 40.000 | 2 | 1 |
| Malloy  | 92 | rectum | 1.5000 | 0.800 | 2.800 | str | 4.410 |  | 3 | 1 |
| Malloy  | 92 | rectum | 1.9000 | 0.800 | 4.600 | sol | 10.060 |  | 3 | 1 |
| Malloy  | 92 | rectum | 1.3000 | 0.400 | 4.000 | syn | 0.835 |  | 3 | 1 |
| Malloy  | 92 | rectum | 1.6000 | 0.900 | 3.200 | str | 1.146 |  | 3 | 1 |
| Mehta | 94 | lung | 1.0800 | 0.920 | 1.250 | syn |  | 10.000 | 2 | 1 |
| Schroeder | 126 | lung | 2.2500 | 1.140 | 4.440 | Al |  |  | 0 | 0 |
| Schroeder | 126 | lung | 2.8500 | 1.430 | 5.680 | Al |  |  | 0 | 0 |
| Sullivan | 137 | esoph | 1.4000 | 0.500 | 4.000 | str | 0.319 |  | 3 | 1 |
| Sullivan | 137 | esoph | 1.3000 | 0.500 | 3.600 | str | 1.284 |  | 3 | 1 |
| Sullivan | 137 | esoph | 3.9000 | 1.100 | 14.300 | syn | 2.700 |  | 3 | 1 |
| Sullivan | 137 | esoph | 3.7000 | 1.200 | 11.100 | nta |  |  | 3 | 0 |
| Sullivan | 137 | esoph | 2.1000 | 0.600 | 7.800 | sol | 6.300 |  | 3 | 1 |
| Sullivan | 137 | esoph | 3.5000 | 0.900 | 13.100 | sol | 16.400 |  | 3 | 1 |
| Thompson | 145 | breast | 1.3300 | 1.050 | 1.670 | sol |   | 4.000 | 2 | 1 |
| Thurston | 146 | brain | 1.6300 | 0.770 | 3.430 | sol | 0.400 |  | 3 | 1 |
| Thurston | 146 | brain | 1.5500 | 0.840 | 2.880 | sol | 1.280 |  | 3 | 1 |
| Thurston | 146 | brain | 1.9900 | 1.090 | 3.620 | sol | 3.330 |  | 3 | 1 |

where,

 Mean cumX – average cumulative exposure in stratum analyzed

Spec. cumX – specified cumulative exposure in evaluation of spline prediction

scen – type of analytical model design scenario:

|  |  |
| --- | --- |
| scen | Original model formin published study |
| 1 | Logistic regression, loglinear, on continuous cumulative exposure |
| 2 | Proportional hazard regression, spline, on continuous cumulative exposure |
| 3 | Logistic regression, loglinear, on categorical strata of cumulative exposure |

use=0 – excluded: non MWF exposure or insufficient evidence of causation or duplicated studies

Al – aluminum machining

nta – nitrosamines

chl – chlorinated compounds

1. p-value =0.025 estimated from reported p<0.05
2. Calculation of excess lifetime risk for aggregate cancer mortality

A national life-table constructed from Social Security data [[SSA 2005](#_ENREF_50)] was used combining both sexes and assuming the national distribution with respect to race. The surviving population was calculated starting at age 20 for a 45 yr exposure, and lifetime risk was calculated through age 85. The number of MWF-associated deaths in each year of age was calculated by applying to the surviving population and the corresponding hypothetical cumulative exposure at the achieved age, the excess relative rates of mortality for the attributable outcomes (Table S2), as derived from the data in Table S1, and the baseline rates, using age- and site-specific national death rates (NIOSH LTAS 1992). Table S3 displays a lifetable calculation for a specific exposure level (0.05 mg/m3 and a 20 yr lag for all MWF results). Excess deaths begin to appear only after age 40 and continue to accrue until age 85 due to the 20 yr lag except for the breast cancer cases where the exposure metric was calculated from a time window in the 10 years prior to observation.

Table S2 Example of lifetime risk calculation for X=0.05, lag=20, MWF=all

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| age | SrvPop | sdths | cumx | ncasex | tcasex | sdthx | SrvPox | xltr |
| 20 | 98591 | 85 | 0.00 | 0.0 | 0 | 85 | 98591 | 0.0000 |
| 21 | 98502 | 90 | 0.00 | 0.0 | 0 | 90 | 98502 | 0.0000 |
| 22 | 98409 | 93 | 0.00 | 0.0 | 0 | 93 | 98409 | 0.0000 |
| 23 | 98316 | 93 | 0.00 | 0.0 | 0 | 93 | 98316 | 0.0000 |
| 24 | 98225 | 92 | 0.00 | 0.0 | 0 | 91 | 98224 | 0.0000 |
| … |   |
| 38 | 96648 | 166 | 0.00 | 1.8 | 11 | 166 | 96637 | 0.0001 |
| 39 | 96469 | 180 | 0.00 | 1.8 | 13 | 179 | 96456 | 0.0001 |
| 40 | 96274 | 195 | 0.03 | 3.2 | 16 | 194 | 96258 | 0.0002 |
| 41 | 96064 | 210 | 0.08 | 3.5 | 20 | 210 | 96044 | 0.0002 |
| 42 | 95836 | 227 | 0.13 | 3.7 | 23 | 227 | 95813 | 0.0002 |
| … |   |
| 64 | 82477 | 1228 | 1.23 | 31.6 | 360 | 1223 | 82142 | 0.0037 |
| 65 | 81153 | 1324 | 1.28 | 38.5 | 399 | 1319 | 80785 | 0.0040 |
| 66 | 79725 | 1427 | 1.33 | 39.4 | 438 | 1421 | 79325 | 0.0044 |
| 67 | 78191 | 1534 | 1.38 | 40.1 | 478 | 1527 | 77758 | 0.0048 |
| 68 | 76547 | 1643 | 1.43 | 40.8 | 519 | 1634 | 76082 | 0.0053 |
| … |   |
| 81 | 44163 | 3209 | 2.08 | 47.9 | 1161 | 3158 | 43415 | 0.0118 |
| 82 | 40861 | 3302 | 2.13 | 45.7 | 1207 | 3246 | 40123 | 0.0122 |
| 83 | 37487 | 3374 | 2.18 | 43.2 | 1250 | 3313 | 36767 | 0.0127 |
| 84 | 34069 | 3418 | 2.23 | 40.5 | 1290 | 3352 | 33374 | 0.0131 |
| 85 | 30640 | 3429 | 2.28 | 40.5 | 1331 | 3359 | 29974 | 0.0135 |

where,

SrvPop = surviving population of 100,000 without exposure effects

sdths = deaths expected without exposure effects

cumX = cumulative exposure (lagged) with age at constant exposure X

ncasex = excess deaths predicted with exposure (includes deaths from breast cancer based on non-lagged 10 yr window model specification; Thompson et al., 2005)

tcasex = cumulative excess deaths with age

sdthx = non-attributable deaths expected in population with exposure effects

SrvPox = surviving population of 100,000 with exposure effects

Xltr = excess lifetime risk (final: 1331/98591 = 0.0135 = 14/1000)

1. Published Paper IDs

|  |  |
| --- | --- |
| Paper ID | Paper |
| 3 | Agalliu, I., Eisen, E. A., Kriebel, D., Quinn, M. M., Wegman, D. H. (2005). A biological approach to characterizing exposure to metalworking fluids and risk of prostate cancer (United States). *Cancer Causes & Control* 16:323 -331. |
| 4 | Agalliu, I., Kriebel, D., Quinn, M. M., Wegman, D. H., & Eisen, E. A. (2005). Prostate cancer incidence in relation to time windows of exposure to metalworking fluids in the auto industry. *Epidemiology, 16*(5), 664-671.  |
| 12 | Bardin, J. A., Eisen, E. A., Tolbert, P. E., Hallock, M. F., Hammond, S. K., Woskie, S. R., . . . Monson, R. R. (1997). Mortality studies of machining fluid exposure in the automobile industry. V: A case-control study of pancreatic cancer. *Am.J.Ind.Med, 32*(3), 240-247.  |
| 13 | Bardin, J. A., Gore, R. J., Wegman, D. H., Kriebel, D., Woskie, S. R., & Eisen, E. A. (2005). Registry-based case-control studies of liver cancer and cancers of the biliary tract nested in a cohort of autoworkers exposed to metalworking fluids. *Scand.J.Work Environ.Health, 31*(3), 205-211.  |
| 18 | Betenia, N., Costello, S., & Eisen, E. A. (2012). Risk of cervical cancer among female autoworkers exposed to metalworking fluids. *Scand J Work Environ Health, 38*(1), 78-83. doi: 10.5271/sjweh.3193 |
| 33 | Costello, S., Friesen, M. C., Christiani, D. C., & Eisen, E. A. (2011). Metalworking fluids and malignant melanoma in autoworkers. *Epidemiology, 22*(1), 90-97.  |
| 42 | Eisen, E. A., Bardin, J., Gore, R., Woskie, S. R., Hallock, M. F., & Monson, R. R. (2001). Exposure-response models based on extended follow-up of a cohort mortality study in the automobile industry. *Scand.J.Work Environ.Health, 27*(4), 240-249.  |
| 44 | Eisen, E. A., Tolbert, P. E., Hallock, M. F., Monson, R. R., Smith, T. J., & Woskie, S. R. (1994). Mortality Studies of Machining Fluid Exposure in the Automobile Industry III: A Case-Control Study of Larynx Cancer *Am.J.Ind.Med, 26*(2), 185-202.  |
| 50 | Friesen, M. C., et al. (2009). Quantitative exposure to metalworking fluids and bladder cancer incidence in a cohort of autoworkers. *American Journal of Epidemiology* 169: 1471-1478. |
| 92 | Malloy, E. J., Miller, K. L., & Eisen, E. A. (2007). Rectal cancer and exposure to metalworking fluids in the automobile manufacturing industry. *Occup.Environ.Med, 64*(4), 244-249.  |
| 94 | Mehta, A. J., Malloy, E. J., Applebaum, K. M., Schwartz, J., Christiani, D. C., & Eisen, E. A. (2010). Reduced lung cancer mortality and exposure to synthetic fluids and biocide in the auto manufacturing industry. *Scand.J.Work Environ.Health, 36*(6), 499-508.  |
| 126 | Schroeder, J. C., et al. (1997). "Mortality studies of machining fluid exposure in the automobile industry. IV: A case-control study of lung cancer." Am.J.Ind.Med 31(5): 525-533. |
| 137 | Sullivan, P. A., Eisen, E. A., Woskie, S. R., Kriebel, D., Wegman, D. H., Hallock, M. F., . . . Monson, R. R. (1998). Mortality studies of metalworking fluid exposure in the automobile industry: VI. A case-control study of esophageal cancer. *Am.J.Ind.Med, 34*(1), 36-48.  |
| 145 | Thompson, D., Kriebel, D., Quinn, M. M., Wegman, D. H., & Eisen, E. A. (2005). Occupational exposure to metalworking fluids and risk of breast cancer among female autoworkers. *Am.J.Ind.Med, 47*(2), 153-160.  |
| 146 | Thurston, S. W., Eisen, E. A., & Schwartz, J. (2002). Smoothing in survival models: an application to workers exposed to metalworking fluids. *Epidemiology, 13*(6), 685-692.  |