

Metalworking fluids and cancer mortality in a US autoworker cohort (1941–2015)¹

by Sadie Costello, PhD,² Kevin Chen, MPH, Sally Picciotto, PhD, Liza Lutzker, MPH, Ellen Eisen, ScD

1. Appendix
2. Correspondence to: Sadie Costello, PhD, Environmental Health Science, School of Public Health, University of California, Berkeley, 2121 Berkeley Way #5302, Berkeley, CA 94720-7360, USA. [E-mail: Sadie@berkeley.edu]

Table S1. International Classification of Diseases (ICD) codes used to define cases. Deaths prior to 1999 were defined with respect to the 9th revision. Deaths in or after 1999 were defined with respect to the 10th.

| Cause of death | ICD 9 | ICD 10 |
|---|---|---|
| All causes | – | – |
| All natural causes | 001–799 | A00–R99, U00–Z99 |
| All cancers | 140–239 | C00–C99, D00–D49 |
| Esophageal cancer | 150 | C15 |
| Stomach cancer | 151 | C16 |
| Intestinal cancer | 152–153 | C17–C18 |
| Rectal cancer | 154 | C19–C21 |
| Kidney cancer | 189.0, 189.2 | C64–C66 |
| Bladder and urinary organ cancers | 188, 189.3–189.9 | C67–C68 |
| Bile duct, liver, and gallbladder cancers | 155–156 | C22–C24 |
| Pancreatic cancer | 157 | C25 |
| Laryngeal cancer | 161 | C32 |
| Lung cancer | 162 | C33–C34 |
| Skin cancer | 172–173 | C43–C44, C46.0, C46.9 |
| Prostate cancer | 185 | C61 |
| Brain and nervous system cancers | 191–192 | C47, C70–C72 |
| Leukemia | 204–208 | C91.0–C91.3, C91.5–C91.9, C92–C95 |
| Breast cancer | 174–175 | C50 |
| All nonmalignant respiratory diseases | 460–466, 470–478, 480–487, 490–495, 496–519 | A48.1, J00–J01, J02.8–J02.9, J03.8–J03.9, J04–J06, J10–J18, J20–J22, J40–J46, J30–J33, J34.1–J34.8, J35–J39, J47, J60:J95, J98, R09.1 |
| Chronic obstructive pulmonary disease | 490–492, 496 | J40–J44 |
| Pneumonia | 480–486 | A48.1, J12–J18 |

| | | |
|---|--|--|
| Cirrhosis and other chronic liver disease | 571 | K70, K73–K74, K76.0 |
| All heart diseases | 390–398, 402, 404, 410–414, 420–429 | I00–I09, I11–I13, I20–I22, I24–I25, I30–I38, I40, I42, I44–I52, I97.0–I97.1, I97.8–I97.9, R00.1, R00.8 |
| Ischemic heart disease | 410–414 | I20–I22, I24–I25, I51.3, I51.6 |
| Rheumatic heart disease | 390–398 | I00–I09 |
| Cerebrovascular disease | 430–438 | G45.0–G45.2, G45.4–G45.9, I60–I69 |
| All external causes | E800–E848, E850–E888, E929–E978, E980–E999 | V00–V99, W00–W99, X00–X84, X85–X99, Y00–Y36, Y40–Y89 |

Table S2. Cox model estimates of the hazard ratio for selected cancer outcomes associated with exposure to straight metalworking fluids, controlling for other fluid types, calendar year, calendar year of hire, age, race, sex, and plant.

| | | Number of cases | HR | 95% CI |
|-------------------------------|--------------------------|-----------------|-----|-------------|
| Laryngeal cancer (73 cases) | | | | |
| 0 | mg/m ³ ·years | 40 | 1.0 | – |
| > 0 to 0.5 | mg/m ³ ·years | 17 | 1.1 | (0.59–2.37) |
| > 0.5 | mg/m ³ ·years | 16 | 0.8 | (0.41–1.59) |
| Lung cancer (1891 cases) | | | | |
| 0 | mg/m ³ ·years | 964 | 1.0 | – |
| > 0 to 0.3 | mg/m ³ ·years | 309 | 1.0 | (0.92–1.25) |
| > 0.3 to 1.6 | mg/m ³ ·years | 309 | 0.9 | (0.82–1.12) |
| > 1.6 | mg/m ³ ·years | 309 | 0.9 | (0.78–1.05) |
| Esophageal cancer (176 cases) | | | | |
| 0 | mg/m ³ ·years | 83 | 1.0 | – |
| > 0 to 0.4 | mg/m ³ ·years | 31 | 1.1 | (0.71–1.91) |
| > 0.4 to 2.1 | mg/m ³ ·years | 32 | 1.1 | (0.74–1.92) |
| > 2.1 | mg/m ³ ·years | 30 | 1.1 | (0.73–1.85) |

| | | | | | |
|-------------------------------|--------------------------|-----|-----|-------------|----|
| Stomach cancer (192 cases) | | | | | |
| 0 | mg/m ³ ·years | 103 | 1.0 | – | |
| | | | 0 | | |
| > 0 to 0.3 | mg/m ³ ·years | 30 | 1.1 | (0.70–1.91) | |
| | | | 6 | | |
| > 0.3 to 2.9 | mg/m ³ ·years | 29 | 0.8 | (0.49–1.32) | |
| | | | 0 | | |
| > 2.9 | mg/m ³ ·years | 30 | 1.8 | (1.17–2.97) | ⌊* |
| | | | 6 | | |
| Colon cancer (407 cases) | | | | | |
| 0 | mg/m ³ ·years | 211 | 1.0 | – | |
| | | | 0 | | |
| > 0 to 0.5 | mg/m ³ ·years | 66 | 0.8 | (0.64–1.23) | |
| | | | 9 | | |
| > 0.5 to 2.1 | mg/m ³ ·years | 65 | 0.9 | (0.67–1.29) | |
| | | | 3 | | |
| > 2.1 | mg/m ³ ·years | 65 | 0.9 | (0.68–1.25) | |
| | | | 2 | | |
| Rectal cancer (83 cases) | | | | | |
| 0 | mg/m ³ ·years | 44 | 1.0 | – | |
| | | | 0 | | |
| > 0 to 1 | mg/m ³ ·years | 20 | 0.7 | (0.40–1.51) | |
| | | | 8 | | |
| > 1 | mg/m ³ ·years | 19 | 0.8 | (0.47–1.68) | |
| | | | 9 | | |
| Bladder cancer (138 cases) | | | | | |
| 0 | mg/m ³ ·years | 73 | 1.0 | – | |
| | | | 0 | | |
| > 0 to 0.3 | mg/m ³ ·years | 20 | 0.9 | (0.51–1.61) | |
| | | | 0 | | |
| > 0.3 to 1.8 | mg/m ³ ·years | 22 | 0.6 | (0.37–1.13) | |
| | | | 5 | | |
| > 1.8 | mg/m ³ ·years | 23 | 0.7 | (0.42–1.16) | |
| | | | 0 | | |
| Liver cancer (123 cases) | | | | | |
| 0 | mg/m ³ ·years | 55 | 1.0 | – | |
| | | | 0 | | |
| > 0 to 0.5 | mg/m ³ ·years | 22 | 1.0 | (0.58–1.89) | |
| | | | 5 | | |
| > 0.5 to 1.6 | mg/m ³ ·years | 23 | 1.9 | (1.09–3.31) | ⌊* |
| | | | 0 | | |
| > 1.6 | mg/m ³ ·years | 23 | 1.2 | (0.72–2.13) | |
| | | | 4 | | |
| Pancreatic cancer (315 cases) | | | | | |
| 0 | mg/m ³ ·years | 154 | 1.0 | – | |
| | | | 0 | | |

| | | | | | | |
|---|--------------|--------------------------|-----|----------|-------------|----|
| | > 0 to 0.3 | mg/m ³ ·years | 54 | 1.2 5 | (0.87–1.81) | |
| | > 0.3 to 1.1 | mg/m ³ ·years | 53 | 1.1 7 | (0.80–1.70) | |
| | > 1.1 | mg/m ³ ·years | 54 | 0.8 5 | (0.60–1.21) | |
| Skin cancer (69 cases) | | | | | | |
| | 0 | mg/m ³ ·years | 32 | 1.0 0 | – | |
| | > 0 to 0.9 | mg/m ³ ·years | 18 | 1.1 7 | (0.58–2.34) | |
| | > 0.9 | mg/m ³ ·years | 19 | 1.3 2 | (0.67–2.58) | |
| Prostate cancer (417 cases) | | | | | | |
| | 0 | mg/m ³ ·years | 192 | 1.0 0 | – | |
| | > 0 to 0.5 | mg/m ³ ·years | 75 | 1.1 5 | (0.84–1.57) | |
| | > 0.5 to 2 | mg/m ³ ·years | 75 | 1.1 1 | (0.81–1.52) | |
| | > 2 | mg/m ³ ·years | 75 | 1.0 5 | (0.78–1.41) | |
| Brain and nervous system cancers (128 cases) | | | | | | |
| | 0 | mg/m ³ ·years | 74 | 1.0 0 | – | |
| | > 0 to 1 | mg/m ³ ·years | 27 | 0.6 1 | (0.35–1.05) | |
| | > 1 | mg/m ³ ·years | 27 | 0.7 3 | (0.44–1.22) | |
| Leukemia (200 cases) | | | | | | |
| | 0 | mg/m ³ ·years | 100 | 1.0 0 | – | |
| | > 0 to 0.3 | mg/m ³ ·years | 34 | 1.0 9 | (0.69–1.75) | |
| | > 0.3 to 2.3 | mg/m ³ ·years | 33 | 0.7 7 | (0.48–1.23) | |
| | > 2.3 | mg/m ³ ·years | 33 | 0.9 4 | (0.60–1.48) | |
| Breast cancer (76 cases) | | | | | | |
| | 0 | mg/m ³ ·years | 43 | 1.0 0 | – | |
| | > 0 to 0.7 | mg/m ³ ·years | 16 | 1.3 4 | (0.64–2.82) | |
| | > 0.7 | mg/m ³ ·years | 17 | 2.1 3 | (1.04–4.39) | ⊥* |

Table S3. Cox model estimates of the hazard ratio for selected cancer outcomes associated with exposure to soluble metalworking fluids, controlling for other fluid types, calendar year, calendar year of hire, age, race, sex, and plant.

| | | Number of cases | HR | 95% CI |
|-------------------------------|--------------------------|-----------------|-----|-------------|
| Laryngeal cancer (73 cases) | | | | |
| 0 to 0.05 | mg/m ³ ·years | 18 | 1.0 | – |
| > 0.05 to 7.3 | mg/m ³ ·years | 28 | 0.7 | (0.39–1.58) |
| > 7.3 | mg/m ³ ·years | 27 | 0.8 | (0.42–1.83) |
| Lung cancer (1891 cases) | | | | |
| 0 to 0.05 | mg/m ³ ·years | 432 | 1.0 | – |
| > 0.05 to 3.3 | mg/m ³ ·years | 487 | 0.9 | (0.84–1.12) |
| > 3.3 to 11.2 | mg/m ³ ·years | 486 | 0.9 | (0.77–1.04) |
| > 11.2 | mg/m ³ ·years | 486 | 1.0 | (0.85–1.17) |
| Esophageal cancer (176 cases) | | | | |
| 0 to 0.05 | mg/m ³ ·years | 34 | 1.0 | – |
| > 0.05 to 3.3 | mg/m ³ ·years | 46 | 1.0 | (0.64–1.74) |
| > 3.3 to 10.8 | mg/m ³ ·years | 47 | 1.0 | (0.62–1.74) |
| > 10.8 | mg/m ³ ·years | 49 | 1.1 | (0.68–2.04) |
| Stomach cancer (192 cases) | | | | |
| 0 to 0.05 | mg/m ³ ·years | 58 | 1.0 | – |
| > 0.05 to 4.2 | mg/m ³ ·years | 45 | 0.6 | (0.42–1.07) |
| > 4.2 to 10 | mg/m ³ ·years | 44 | 1.0 | (0.66–1.74) |
| > 10 | mg/m ³ ·years | 45 | 0.7 | (0.42–1.18) |
| Colon cancer (407 cases) | | | | |
| 0 to 0.05 | mg/m ³ ·years | 80 | 1.0 | – |
| > 0.05 to 3.5 | mg/m ³ ·years | 109 | 1.1 | (0.83–1.57) |
| > 3.5 to 12 | mg/m ³ ·years | 109 | 0.9 | (0.69–1.35) |

| | | | | | | |
|-------------------------------|---------------|--------------------------|-----|----------|-------------|----|
| | > 12 | mg/m ³ ·years | 109 | 0.9 4 | (0.66–1.33) | |
| Rectal cancer (83 cases) | | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 20 | 1.0 0 | – | |
| | > 0.05 to 4.6 | mg/m ³ ·years | 19 | 0.8 5 | (0.41–1.76) | |
| | > 4.6 to 8.6 | mg/m ³ ·years | 23 | 2.1 8 | (1.07–4.48) | ⌊* |
| | > 8.6 | mg/m ³ ·years | 21 | 0.8 6 | (0.40–1.84) | |
| Bladder cancer (138 cases) | | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 26 | 1.0 0 | – | |
| | > 0.05 to 3.7 | mg/m ³ ·years | 37 | 1.1 0 | (0.63–1.91) | |
| | > 3.7 to 11.1 | mg/m ³ ·years | 36 | 1.1 8 | (0.67–2.07) | |
| | > 11.1 | mg/m ³ ·years | 39 | 1.1 3 | (0.63–2.02) | |
| Liver cancer (123 cases) | | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 22 | 1.0 0 | – | |
| | > 0.05 to 2.3 | mg/m ³ ·years | 34 | 1.2 9 | (0.71–2.33) | |
| | > 2.3 to 9.2 | mg/m ³ ·years | 32 | 0.7 6 | (0.41–1.40) | |
| | > 9.2 | mg/m ³ ·years | 35 | 0.9 3 | (0.50–1.74) | |
| Pancreatic cancer (315 cases) | | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 70 | 1.0 0 | – | |
| | > 0.05 to 3.4 | mg/m ³ ·years | 82 | 0.8 1 | (0.56–1.16) | |
| | > 3.4 to 9.3 | mg/m ³ ·years | 81 | 0.9 2 | (0.63–1.34) | |
| | > 9.3 | mg/m ³ ·years | 82 | 0.8 0 | (0.54–1.19) | |
| Skin cancer (69 cases) | | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 15 | 1.0 0 | – | |
| | > 0.05 to 4.7 | mg/m ³ ·years | 26 | 1.6 9 | (0.77–3.70) | |
| | > 4.7 | mg/m ³ ·years | 28 | 1.6 4 | (0.71–3.80) | |
| Prostate cancer (417 cases) | | | | | | |

| | | | | | |
|--|---------------|--------------------------|-----|-----|-------------|
| | 0 to 0.05 | mg/m ³ ·years | 68 | 1.0 | – |
| | > 0.05 to 5.1 | mg/m ³ ·years | 117 | 0.7 | (0.54–1.05) |
| | > 5.1 to 15.6 | mg/m ³ ·years | 116 | 0.7 | (0.57–1.11) |
| | > 15.6 | mg/m ³ ·years | 116 | 0.8 | (0.57–1.14) |
| Brain and nervous system cancers (128 cases) | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 32 | 1.0 | – |
| | > 0.05 to 2.7 | mg/m ³ ·years | 32 | 1.5 | (0.86–2.65) |
| | > 2.7 to 9.2 | mg/m ³ ·years | 32 | 1.4 | (0.82–2.68) |
| | > 9.2 | mg/m ³ ·years | 32 | 1.5 | (0.82–2.90) |
| Leukemia (200 cases) | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 48 | 1.0 | – |
| | > 0.05 to 3.3 | mg/m ³ ·years | 51 | 1.0 | (0.65–1.64) |
| | > 3.3 to 9.7 | mg/m ³ ·years | 50 | 1.0 | (0.67–1.76) |
| | > 9.7 | mg/m ³ ·years | 51 | 0.8 | (0.53–1.45) |
| Breast cancer (76 cases) | | | | | |
| | 0 to 0.05 | mg/m ³ ·years | 36 | 1.0 | – |
| | > 0.05 to 2.9 | mg/m ³ ·years | 22 | 0.5 | (0.30–1.14) |
| | > 2.9 | mg/m ³ ·years | 18 | 0.5 | (0.26–1.21) |

Table S4. Cox model estimates of the hazard ratio for selected cancer outcomes associated with exposure to synthetic metalworking fluids, controlling for other fluid types, calendar year, calendar year of hire, age, race, sex, and plant.

| | | | Number of cases | HR | 95% CI |
|-----------------------------|-----|--------------------------|-----------------|-----|-------------|
| Laryngeal cancer (73 cases) | | | | | |
| | 0 | mg/m ³ ·years | 54 | 1.0 | – |
| | > 0 | mg/m ³ ·years | 19 | 1.3 | (0.67–2.78) |
| Lung cancer (1891 cases) | | | | | |
| | 0 | mg/m ³ ·years | 1374 | 1.0 | – |

| | | | | | |
|-------------------------------|--------------|--------------------------|-----|----------|-------------|
| | > 0 to 0.3 | mg/m ³ ·years | 173 | 0.9 3 | (0.77–1.12) |
| | > 0.3 to 1.4 | mg/m ³ ·years | 172 | 1.0 7 | (0.89–1.29) |
| | > 1.4 | mg/m ³ ·years | 172 | 1.0 0 | (0.84–1.20) |
| Esophageal cancer (176 cases) | | | | | |
| | 0 | mg/m ³ ·years | 126 | 1.0 0 | – |
| | > 0 to 0.7 | mg/m ³ ·years | 25 | 1.1 3 | (0.66–1.96) |
| | > 0.7 | mg/m ³ ·years | 25 | 1.3 9 | (0.84–2.30) |
| Stomach cancer (192 cases) | | | | | |
| | 0 | mg/m ³ ·years | 149 | 1.0 0 | – |
| | > 0 to 0.5 | mg/m ³ ·years | 22 | 1.0 6 | (0.61–1.84) |
| | > 0.5 | mg/m ³ ·years | 21 | 0.9 0 | (0.53–1.56) |
| Colon cancer (407 cases) | | | | | |
| | 0 | mg/m ³ ·years | 310 | 1.0 0 | – |
| | > 0 to 0.4 | mg/m ³ ·years | 33 | 0.7 9 | (0.52–1.21) |
| | > 0.4 to 1.7 | mg/m ³ ·years | 32 | 0.9 8 | (0.65–1.50) |
| | > 1.7 | mg/m ³ ·years | 32 | 0.9 2 | (0.62–1.38) |
| Rectal cancer (83 cases) | | | | | |
| | 0 | mg/m ³ ·years | 59 | 1.0 0 | – |
| | > 0 to 0.8 | mg/m ³ ·years | 12 | 1.4 9 | (0.67–3.27) |
| | > 0.8 | mg/m ³ ·years | 12 | 1.6 4 | (0.79–3.41) |
| Bladder cancer (138 cases) | | | | | |
| | 0 | mg/m ³ ·years | 104 | 1.0 0 | – |
| | > 0 to 0.5 | mg/m ³ ·years | 17 | 0.9 1 | (0.49–1.70) |
| | > 0.5 | mg/m ³ ·years | 17 | 0.6 7 | (0.37–1.21) |
| Liver cancer (123 cases) | | | | | |
| | 0 | mg/m ³ ·years | 89 | 1.0 0 | – |

| | | | | | |
|--|--------------|--------------------------|-----|----------|-------------|
| | > 0 to 0.4 | mg/m ³ ·years | 17 | 1.1 7 | (0.60–2.26) |
| | > 0.4 | mg/m ³ ·years | 17 | 0.8 8 | (0.48–1.63) |
| Pancreatic cancer (315 cases) | | | | | |
| | 0 | mg/m ³ ·years | 227 | 1.0 0 | – |
| | > 0 to 0.3 | mg/m ³ ·years | 30 | 0.9 8 | (0.62–1.55) |
| | > 0.3 to 0.9 | mg/m ³ ·years | 29 | 1.2 6 | (0.80–2.00) |
| | > 0.9 | mg/m ³ ·years | 29 | 0.8 7 | (0.56–1.34) |
| Skin cancer (69 cases) | | | | | |
| | 0 | mg/m ³ ·years | 52 | 1.0 0 | – |
| | > 0 | mg/m ³ ·years | 17 | 0.6 7 | (0.34–1.31) |
| Prostate cancer (417 cases) | | | | | |
| | 0 | mg/m ³ ·years | 300 | 1.0 0 | – |
| | > 0 to 0.5 | mg/m ³ ·years | 39 | 1.0 1 | (0.67–1.50) |
| | > 0.5 to 2 | mg/m ³ ·years | 39 | 1.1 3 | (0.76–1.68) |
| | > 2 | mg/m ³ ·years | 39 | 1.3 0 | (0.89–1.89) |
| Brain and nervous system cancers (128 cases) | | | | | |
| | 0 | mg/m ³ ·years | 94 | 1.0 0 | – |
| | > 0 to 0.6 | mg/m ³ ·years | 17 | 1.5 2 | (0.80–2.91) |
| | > 0.6 | mg/m ³ ·years | 17 | 1.3 6 | (0.75–2.47) |
| Leukemia (200 cases) | | | | | |
| | 0 | mg/m ³ ·years | 142 | 1.0 0 | – |
| | > 0 to 0.9 | mg/m ³ ·years | 29 | 1.1 1 | (0.67–1.82) |
| | > 0.9 | mg/m ³ ·years | 29 | 1.3 7 | (0.86–2.19) |
| Breast cancer (76 cases) | | | | | |
| | 0 | mg/m ³ ·years | 60 | 1.0 0 | – |
| | > 0 | mg/m ³ ·years | 16 | 0.7 6 | (0.38–1.53) |
