

UAW-GM Cohort Study

Clean referent group, messy exposure groups; exposure lagged 30 years

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Introduction

In previous survival analyses, hazard ratios associated with exposure to the three metalworking fluid types were estimated simultaneously in the same Cox proportional hazards model. There was a concern that those estimates may have been biased or misleading, as those models assumed independent covariate (statistical) effects e.g. that the effect of exposure to straight metalworking fluids was constant across levels of exposure to other metalworking fluid types. One way we attempted to address this concern was to fit independent models for each exposure-outcome pair of interest where person-time included in the analytic dataset would be restricted to those where either (1) cumulative exposure was zero or (2) cumulative exposure to the exposure of interest was nonzero. In other words, we excluded person-time satisfying both (1) zero exposure to the metalworking fluid type of interest *and* (2) nonzero exposure to some metalworking fluid other than the type in which we were interested. Coding of exposure and potential confounders was equivalent as that in the original analyses. As in the previous analyses, the category cut-points for the continuous covariates were determined in a data-adaptive way, so covariate definitions may vary from model to model. The results from the $13 \times 3 = 39$ models are presented below.

Results

Table 1: 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	<i>p</i>	95% CI
Laryngeal cancer (59 cases)					
0	mg/m ³ .years	31			
> 0 to 0.3	mg/m ³ .years	14	1.86	0.16	(0.78, 4.43)
> 0.3	mg/m ³ .years	14	1.32	0.55	(0.54, 3.23)
Trend				0.96	
Lung cancer (1619 cases)					
0	mg/m ³ .years	901			
> 0 to 0.3	mg/m ³ .years	240	1.12	0.25	(0.93, 1.34)
> 0.3 to 1.4	mg/m ³ .years	239	0.97	0.77	(0.80, 1.18)
> 1.4	mg/m ³ .years	239	0.90	0.26	(0.74, 1.08)
Trend				0.30	
Esophageal cancer (150 cases)					
0	mg/m ³ .years	80			
> 0 to 0.5	mg/m ³ .years	24	0.98	0.94	(0.53, 1.81)
> 0.5 to 2.2	mg/m ³ .years	23	1.25	0.50	(0.65, 2.38)
> 2.2	mg/m ³ .years	23	1.19	0.58	(0.64, 2.23)
Trend				0.47	
Stomach cancer (172 cases)					
0	mg/m ³ .years	103			
> 0 to 0.3	mg/m ³ .years	23	0.83	0.56	(0.45, 1.55)
> 0.3 to 2.6	mg/m ³ .years	23	0.65	0.19	(0.33, 1.25)
> 2.6	mg/m ³ .years	23	1.39	0.31	(0.73, 2.61)

Table 1: 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	<i>p</i>	95% CI	
Trend				0.21		
Colon cancer (339 cases)						
0	mg/m ³ .years	188				
> 0 to 0.3	mg/m ³ .years	51	0.77	0.20	(0.51, 1.16)	
> 0.3 to 2.4	mg/m ³ .years	50	0.56	0.01	(0.36, 0.87)	*
> 2.4	mg/m ³ .years	50	0.77	0.23	(0.50, 1.18)	
Trend				0.76		
Rectal cancer (66 cases)						
0	mg/m ³ .years	37				
> 0 to 0.6	mg/m ³ .years	15	1.50	0.34	(0.66, 3.41)	
> 0.6	mg/m ³ .years	14	1.24	0.64	(0.50, 3.10)	
Trend				0.87		
Bladder cancer (113 cases)						
0	mg/m ³ .years	58				
> 0 to 0.5	mg/m ³ .years	27	1.41	0.25	(0.79, 2.52)	
> 0.5	mg/m ³ .years	28	0.76	0.38	(0.41, 1.40)	
Trend				0.51		
Liver cancer (106 cases)						
0	mg/m ³ .years	53				
> 0 to 0.9	mg/m ³ .years	26	1.22	0.53	(0.65, 2.30)	
> 0.9	mg/m ³ .years	27	1.76	0.08	(0.94, 3.29)	.
Trend				0.19		
Pancreatic cancer (279 cases)						
0	mg/m ³ .years	152				
> 0 to 0.2	mg/m ³ .years	43	1.20	0.43	(0.77, 1.87)	
> 0.2 to 0.8	mg/m ³ .years	42	1.15	0.54	(0.73, 1.82)	
> 0.8	mg/m ³ .years	42	0.63	0.05	(0.40, 1.00)	*
Trend				0.11		
Skin cancer (60 cases)						
0	mg/m ³ .years	32				
> 0 to 0.9	mg/m ³ .years	14	1.70	0.22	(0.73, 3.95)	
> 0.9	mg/m ³ .years	14	1.80	0.20	(0.73, 4.44)	
Trend				0.54		
Prostate cancer (341 cases)						
0	mg/m ³ .years	148				
> 0 to 0.3	mg/m ³ .years	65	0.92	0.66	(0.62, 1.35)	
> 0.3 to 1.5	mg/m ³ .years	64	0.78	0.26	(0.52, 1.19)	
> 1.5	mg/m ³ .years	64	0.70	0.08	(0.47, 1.05)	.
Trend				0.25		
Brain and nervous system cancers (110 cases)						
0	mg/m ³ .years	68				
> 0 to 0.9	mg/m ³ .years	21	0.70	0.34	(0.34, 1.46)	
> 0.9	mg/m ³ .years	21	0.92	0.82	(0.45, 1.88)	
Trend				0.98		
Leukemia (174 cases)						

Table 1: 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	<i>p</i>	95% CI
0	mg/m ³ .years	93			
> 0 to 0.3	mg/m ³ .years	27	1.21	0.52	(0.68, 2.14)
> 0.3 to 1.7	mg/m ³ .years	27	1.03	0.92	(0.57, 1.87)
> 1.7	mg/m ³ .years	27	0.98	0.94	(0.54, 1.75)
Trend				0.68	
Breast cancer (76 cases)					
0	mg/m ³ .years	53			
> 0 to 0.7	mg/m ³ .years	11	0.84	0.70	(0.35, 2.01)
> 0.7	mg/m ³ .years	12	1.50	0.34	(0.65, 3.43)
Trend				0.18	

Table 2: 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	<i>p</i>	95% CI
Laryngeal cancer (72 cases)					
0 to 5	mg/m ³ .years	48			
> 5 to 13.8	mg/m ³ .years	12	1.01	0.98	(0.50, 2.03)
> 13.8	mg/m ³ .years	12	1.22	0.62	(0.56, 2.63)
Trend				0.01	*
Lung cancer (1861 cases)					
0 to 5	mg/m ³ .years	1260			
> 5 to 9	mg/m ³ .years	201	1.01	0.95	(0.86, 1.18)
> 9 to 17.6	mg/m ³ .years	200	1.05	0.61	(0.88, 1.24)
> 17.6	mg/m ³ .years	200	1.13	0.17	(0.95, 1.35)
Trend				0.05	.
Esophageal cancer (168 cases)					
0 to 5	mg/m ³ .years	107			
> 5 to 9.2	mg/m ³ .years	21	1.29	0.34	(0.76, 2.18)
> 9.2 to 14.8	mg/m ³ .years	20	1.85	0.03	(1.07, 3.20)
> 14.8	mg/m ³ .years	20	1.15	0.64	(0.64, 2.04)
Trend				0.69	
Stomach cancer (189 cases)					
0 to 5	mg/m ³ .years	128			
> 5 to 7.8	mg/m ³ .years	21	1.78	0.03	(1.07, 2.97)
> 7.8 to 17.7	mg/m ³ .years	20	1.02	0.95	(0.60, 1.73)
> 17.7	mg/m ³ .years	20	1.27	0.41	(0.72, 2.24)
Trend				0.99	
Colon cancer (403 cases)					
0 to 5	mg/m ³ .years	250			
> 5 to 10	mg/m ³ .years	51	0.99	0.93	(0.71, 1.36)
> 10 to 18.1	mg/m ³ .years	51	1.23	0.23	(0.88, 1.72)

Table 2: 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	<i>p</i>	95% CI	
> 18.1	mg/m ³ .years	51	1.00	0.98	(0.70, 1.42)	
Trend				0.69		
Rectal cancer (82 cases)						
0 to 5	mg/m ³ .years	52				
> 5 to 8.3	mg/m ³ .years	15	2.41	0.01	(1.27, 4.57)	*
> 8.3	mg/m ³ .years	15	0.96	0.91	(0.48, 1.92)	
Trend				0.65		
Bladder cancer (134 cases)						
0 to 5	mg/m ³ .years	87				
> 5 to 17.1	mg/m ³ .years	23	0.74	0.24	(0.45, 1.22)	
> 17.1	mg/m ³ .years	24	1.37	0.24	(0.81, 2.32)	
Trend				0.29		
Liver cancer (122 cases)						
0 to 5	mg/m ³ .years	87				
> 5 to 12	mg/m ³ .years	18	0.83	0.50	(0.47, 1.44)	
> 12	mg/m ³ .years	17	0.66	0.18	(0.36, 1.22)	
Trend				0.34		
Pancreatic cancer (309 cases)						
0 to 5	mg/m ³ .years	218				
> 5 to 8.4	mg/m ³ .years	31	0.98	0.94	(0.66, 1.47)	
> 8.4 to 15.9	mg/m ³ .years	30	0.91	0.66	(0.60, 1.38)	
> 15.9	mg/m ³ .years	30	0.79	0.28	(0.51, 1.22)	
Trend				0.08		
Skin cancer (68 cases)						
0 to 5	mg/m ³ .years	47				
> 5 to 14.7	mg/m ³ .years	11	1.10	0.81	(0.51, 2.35)	
> 14.7	mg/m ³ .years	10	1.39	0.45	(0.60, 3.24)	
Trend				0.14		
Prostate cancer (411 cases)						
0 to 5	mg/m ³ .years	220				
> 5 to 9.8	mg/m ³ .years	64	1.04	0.80	(0.77, 1.40)	
> 9.8 to 20.3	mg/m ³ .years	63	0.98	0.91	(0.72, 1.34)	
> 20.3	mg/m ³ .years	64	1.08	0.62	(0.79, 1.49)	
Trend				0.16		
Brain and nervous system cancers (127 cases)						
0 to 5	mg/m ³ .years	91				
> 5 to 12.4	mg/m ³ .years	18	1.19	0.55	(0.67, 2.12)	
> 12.4	mg/m ³ .years	18	1.33	0.36	(0.72, 2.46)	
Trend				0.38		
Leukemia (196 cases)						
0 to 5	mg/m ³ .years	134				
> 5 to 7.9	mg/m ³ .years	21	1.21	0.46	(0.73, 1.99)	
> 7.9 to 20.2	mg/m ³ .years	20	0.65	0.11	(0.39, 1.10)	
> 20.2	mg/m ³ .years	21	1.11	0.71	(0.65, 1.90)	
Trend				0.72		

Table 2: 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	<i>p</i>	95% CI
Breast cancer (74 cases)					
0 to 5	mg/m ³ .years	68			
> 5	mg/m ³ .years	6	0.64	0.37	(0.25, 1.67)

Table 3: 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	<i>p</i>	95% CI
Laryngeal cancer (46 cases)					
0	mg/m ³ .years	31			
> 0	mg/m ³ .years	15	0.00	0.99	(0.00, Inf)
Lung cancer (1280 cases)					
0	mg/m ³ .years	901			
> 0 to 0.2	mg/m ³ .years	127	1.14	0.49	(0.78, 1.67)
> 0.2 to 1.3	mg/m ³ .years	126	1.09	0.63	(0.76, 1.59)
> 1.3	mg/m ³ .years	126	1.13	0.50	(0.79, 1.61)
Trend				0.61	
Esophageal cancer (115 cases)					
0	mg/m ³ .years	80			
> 0 to 0.7	mg/m ³ .years	18	1.42	0.56	(0.44, 4.60)
> 0.7	mg/m ³ .years	17	1.24	0.72	(0.38, 3.99)
Trend				0.95	
Stomach cancer (135 cases)					
0	mg/m ³ .years	103			
> 0 to 0.4	mg/m ³ .years	16	1.14	0.85	(0.30, 4.32)
> 0.4	mg/m ³ .years	16	0.86	0.82	(0.24, 3.11)
Trend				0.34	
Colon cancer (255 cases)					
0	mg/m ³ .years	188			
> 0 to 0.2	mg/m ³ .years	23	0.79	0.64	(0.30, 2.08)
> 0.2 to 1.4	mg/m ³ .years	22	0.59	0.28	(0.23, 1.54)
> 1.4	mg/m ³ .years	22	0.52	0.17	(0.21, 1.33)
Trend				0.36	
Rectal cancer (54 cases)					
0	mg/m ³ .years	37			
> 0 to 0.5	mg/m ³ .years	8	3.82	0.08	(0.87, 16.73)
> 0.5	mg/m ³ .years	9	3.61	0.07	(0.89, 14.71)
Trend				0.71	
Bladder cancer (85 cases)					
0	mg/m ³ .years	58			
> 0 to 0.5	mg/m ³ .years	14	2.06	0.21	(0.67, 6.28)
> 0.5	mg/m ³ .years	13	1.74	0.27	(0.65, 4.67)

Table 3: 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	<i>p</i>	95% CI	
Trend				0.85		
Liver cancer (79 cases)						
0	mg/m ³ .years	53				
> 0 to 0.4	mg/m ³ .years	13	1.65	0.47	(0.42, 6.49)	
> 0.4	mg/m ³ .years	13	1.50	0.53	(0.42, 5.35)	
Trend				0.81		
Pancreatic cancer (218 cases)						
0	mg/m ³ .years	152				
> 0 to 0.2	mg/m ³ .years	22	0.66	0.47	(0.21, 2.05)	
> 0.2 to 0.7	mg/m ³ .years	22	0.74	0.60	(0.24, 2.26)	
> 0.7	mg/m ³ .years	22	0.52	0.23	(0.18, 1.53)	
Trend				0.31		
Skin cancer (45 cases)						
0	mg/m ³ .years	32				
> 0	mg/m ³ .years	13	0.98	0.99	(0.12, 8.34)	
Prostate cancer (250 cases)						
0	mg/m ³ .years	148				
> 0 to 0.3	mg/m ³ .years	34	1.23	0.64	(0.52, 2.88)	
> 0.3 to 1.2	mg/m ³ .years	34	1.45	0.38	(0.63, 3.32)	
> 1.2	mg/m ³ .years	34	1.07	0.88	(0.48, 2.39)	
Trend				0.61		
Brain and nervous system cancers (96 cases)						
0	mg/m ³ .years	68				
> 0 to 0.2	mg/m ³ .years	14	4.47	0.01	(1.35, 14.78)	*
> 0.2	mg/m ³ .years	14	1.13	0.84	(0.35, 3.65)	
Trend				0.69		
Leukemia (137 cases)						
0	mg/m ³ .years	93				
> 0 to 0.6	mg/m ³ .years	22	1.13	0.82	(0.38, 3.38)	
> 0.6	mg/m ³ .years	22	1.31	0.60	(0.48, 3.60)	
Trend				0.27		
Breast cancer (63 cases)						
0	mg/m ³ .years	53				
> 0	mg/m ³ .years	10	0.00	0.99	(0.00, Inf)	

Clean referent group, messy exposure groups; exposure lagged 30 years; soluble referent at 5 mg/m³.y

