

UAW-GM Cohort Study

Clean referent group, messy exposure groups; exposure lagged 21 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 (57 cases)					
0	mg/m ³ .years	24			
> 0 to 0.5	mg/m ³ .years	17	1.09	0.84	(0.48, 2.51)
> 0.5	mg/m ³ .years	16	0.88	0.79	(0.36, 2.17)
Trend				0.32	
Lung cancer (1542 cases)					
0	mg/m ³ .years	615			
> 0 to 0.3	mg/m ³ .years	309	1.05	0.55	(0.89, 1.25)
> 0.3 to 1.6	mg/m ³ .years	309	0.95	0.57	(0.79, 1.14)
> 1.6	mg/m ³ .years	309	0.91	0.29	(0.76, 1.09)
Trend				0.26	
Esophageal cancer (146 cases)					
0	mg/m ³ .years	53			
> 0 to 0.4	mg/m ³ .years	31	1.02	0.95	(0.58, 1.80)
> 0.4 to 2.1	mg/m ³ .years	32	0.97	0.92	(0.53, 1.77)
> 2.1	mg/m ³ .years	30	0.97	0.91	(0.53, 1.75)
Trend				0.39	
Stomach cancer (160 cases)					
0	mg/m ³ .years	70			
> 0 to 0.3	mg/m ³ .years	30	1.02	0.94	(0.59, 1.77)
> 0.3 to 2.9	mg/m ³ .years	30	0.74	0.31	(0.41, 1.33)
> 2.9	mg/m ³ .years	30	1.58	0.12	(0.89, 2.78)

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				0.08		.
Colon cancer (324 cases)						
0	mg/m ³ .years	128				
> 0 to 0.5	mg/m ³ .years	66	0.85	0.40	(0.59, 1.24)	
> 0.5 to 2.1	mg/m ³ .years	65	0.88	0.53	(0.58, 1.32)	
> 2.1	mg/m ³ .years	65	0.89	0.56	(0.61, 1.31)	
Trend				0.75		
Rectal cancer (61 cases)						
0	mg/m ³ .years	22				
> 0 to 1	mg/m ³ .years	20	1.16	0.73	(0.50, 2.69)	
> 1	mg/m ³ .years	19	1.61	0.27	(0.69, 3.77)	
Trend				0.17		
Bladder cancer (105 cases)						
0	mg/m ³ .years	40				
> 0 to 0.3	mg/m ³ .years	20	1.17	0.64	(0.61, 2.22)	
> 0.3 to 1.8	mg/m ³ .years	22	0.88	0.71	(0.46, 1.71)	
> 1.8	mg/m ³ .years	23	0.85	0.62	(0.45, 1.61)	
Trend				0.41		
Liver cancer (99 cases)						
0	mg/m ³ .years	31				
> 0 to 0.5	mg/m ³ .years	22	1.26	0.51	(0.64, 2.47)	
> 0.5 to 1.6	mg/m ³ .years	23	2.45	0.01	(1.26, 4.76)	*
> 1.6	mg/m ³ .years	23	1.83	0.07	(0.96, 3.52)	.
Trend				0.76		
Pancreatic cancer (262 cases)						
0	mg/m ³ .years	101				
> 0 to 0.3	mg/m ³ .years	54	1.01	0.96	(0.67, 1.53)	
> 0.3 to 1.1	mg/m ³ .years	53	0.94	0.79	(0.60, 1.47)	
> 1.1	mg/m ³ .years	54	0.73	0.14	(0.47, 1.11)	
Trend				0.03		*
Skin cancer (57 cases)						
0	mg/m ³ .years	20				
> 0 to 0.9	mg/m ³ .years	18	2.11	0.07	(0.95, 4.68)	.
> 0.9	mg/m ³ .years	19	2.39	0.04	(1.04, 5.45)	*
Trend				0.53		
Prostate cancer (329 cases)						
0	mg/m ³ .years	103				
> 0 to 0.5	mg/m ³ .years	76	0.91	0.61	(0.62, 1.32)	
> 0.5 to 2	mg/m ³ .years	75	0.83	0.39	(0.55, 1.26)	
> 2	mg/m ³ .years	75	0.79	0.24	(0.53, 1.17)	
Trend				0.32		
Brain and nervous system cancers (104 cases)						
0	mg/m ³ .years	50				
> 0 to 1	mg/m ³ .years	27	0.69	0.27	(0.36, 1.33)	
> 1	mg/m ³ .years	27	0.88	0.71	(0.46, 1.71)	

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				0.98	
Leukemia (169 cases)					
0	mg/m ³ .years	69			
> 0 to 0.3	mg/m ³ .years	34	1.05	0.87	(0.61, 1.78)
> 0.3 to 2.3	mg/m ³ .years	33	0.75	0.32	(0.42, 1.32)
> 2.3	mg/m ³ .years	33	0.94	0.82	(0.54, 1.63)
Trend				0.96	
Breast cancer (75 cases)					
0	mg/m ³ .years	42			
> 0 to 0.7	mg/m ³ .years	16	0.87	0.72	(0.41, 1.84)
> 0.7	mg/m ³ .years	17	1.54	0.22	(0.77, 3.09)
Trend				0.13	

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	40			
> 5 to 17.9	mg/m ³ .years	16	0.79	0.45	(0.42, 1.47)
> 17.9	mg/m ³ .years	16	1.28	0.48	(0.64, 2.56)
Trend				0.30	
Lung cancer (1855 cases)					
0 to 5	mg/m ³ .years	1044			
> 5 to 9.8	mg/m ³ .years	271	0.94	0.39	(0.81, 1.08)
> 9.8 to 19.2	mg/m ³ .years	270	1.03	0.74	(0.88, 1.19)
> 19.2	mg/m ³ .years	270	1.06	0.48	(0.91, 1.24)
Trend				0.30	
Esophageal cancer (174 cases)					
0 to 5	mg/m ³ .years	91			
> 5 to 9.5	mg/m ³ .years	27	1.07	0.77	(0.68, 1.69)
> 9.5 to 16.2	mg/m ³ .years	28	1.51	0.09	(0.94, 2.41)
> 16.2	mg/m ³ .years	28	0.97	0.91	(0.59, 1.60)
Trend				0.57	
Stomach cancer (190 cases)					
0 to 5	mg/m ³ .years	110			
> 5 to 8.3	mg/m ³ .years	27	1.42	0.13	(0.91, 2.23)
> 8.3 to 17.8	mg/m ³ .years	26	0.91	0.71	(0.57, 1.47)
> 17.8	mg/m ³ .years	27	0.92	0.73	(0.56, 1.50)
Trend				0.58	
Colon cancer (400 cases)					
0 to 5	mg/m ³ .years	211			

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	
> 5 to 10.1	mg/m ³ .years	63	0.91	0.56	(0.68, 1.23)	
> 10.1 to 21.2	mg/m ³ .years	63	0.88	0.44	(0.65, 1.21)	
> 21.2	mg/m ³ .years	63	0.94	0.71	(0.68, 1.30)	
Trend				0.95		
Rectal cancer (83 cases)						
0 to 5	mg/m ³ .years	41				
> 5 to 9.3	mg/m ³ .years	22	2.19	0.01	(1.25, 3.83)	*
> 9.3	mg/m ³ .years	20	0.89	0.73	(0.48, 1.68)	
Trend				0.62		
Bladder cancer (136 cases)						
0 to 5	mg/m ³ .years	73				
> 5 to 9.3	mg/m ³ .years	20	1.01	0.98	(0.60, 1.68)	
> 9.3 to 21.3	mg/m ³ .years	21	0.84	0.51	(0.50, 1.42)	
> 21.3	mg/m ³ .years	22	1.12	0.68	(0.66, 1.91)	
Trend				0.28		
Liver cancer (120 cases)						
0 to 5	mg/m ³ .years	70				
> 5 to 12.7	mg/m ³ .years	25	0.91	0.70	(0.55, 1.49)	
> 12.7	mg/m ³ .years	25	0.84	0.53	(0.49, 1.43)	
Trend				0.38		
Pancreatic cancer (310 cases)						
0 to 5	mg/m ³ .years	174				
> 5 to 8.3	mg/m ³ .years	46	1.25	0.20	(0.89, 1.77)	
> 8.3 to 16.2	mg/m ³ .years	45	1.06	0.74	(0.74, 1.52)	
> 16.2	mg/m ³ .years	45	0.86	0.43	(0.59, 1.25)	
Trend				0.24		
Skin cancer (67 cases)						
0 to 5	mg/m ³ .years	41				
> 5 to 16.2	mg/m ³ .years	13	0.89	0.74	(0.44, 1.78)	
> 16.2	mg/m ³ .years	13	1.43	0.36	(0.66, 3.06)	
Trend				0.14		
Prostate cancer (410 cases)						
0 to 5	mg/m ³ .years	175				
> 5 to 10.9	mg/m ³ .years	79	0.98	0.89	(0.74, 1.30)	
> 10.9 to 24.2	mg/m ³ .years	78	0.88	0.40	(0.66, 1.18)	
> 24.2	mg/m ³ .years	78	1.12	0.45	(0.83, 1.52)	
Trend				0.17		
Brain and nervous system cancers (126 cases)						
0 to 5	mg/m ³ .years	76				
> 5 to 11.9	mg/m ³ .years	25	1.32	0.28	(0.80, 2.19)	
> 11.9	mg/m ³ .years	25	1.19	0.53	(0.69, 2.06)	
Trend				0.93		
Leukemia (195 cases)						
0 to 5	mg/m ³ .years	114				
> 5 to 9.2	mg/m ³ .years	27	0.99	0.96	(0.63, 1.55)	

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	
> 9.2 to 19.9	mg/m ³ .years	27	0.85	0.50	(0.54, 1.36)	
> 19.9	mg/m ³ .years	27	0.92	0.74	(0.57, 1.50)	
Trend				0.78		
Breast cancer (72 cases)						
0 to 5	mg/m ³ .years	66				
> 5	mg/m ³ .years	6	0.39	0.04	(0.16, 0.98)	*

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 (43 cases)						
0	mg/m ³ .years	24				
> 0	mg/m ³ .years	19	0.73	0.76	(0.09, 5.71)	
Lung cancer (1132 cases)						
0	mg/m ³ .years	615				
> 0 to 0.3	mg/m ³ .years	173	0.96	0.78	(0.69, 1.33)	
> 0.3 to 1.4	mg/m ³ .years	172	1.17	0.35	(0.85, 1.61)	
> 1.4	mg/m ³ .years	172	1.05	0.77	(0.77, 1.43)	
Trend				0.96		
Esophageal cancer (103 cases)						
0	mg/m ³ .years	53				
> 0 to 0.7	mg/m ³ .years	25	0.85	0.77	(0.28, 2.54)	
> 0.7	mg/m ³ .years	25	0.94	0.90	(0.32, 2.71)	
Trend				0.95		
Stomach cancer (105 cases)						
0	mg/m ³ .years	65				
> 0 to 0.5	mg/m ³ .years	21	1.25	0.71	(0.38, 4.11)	
> 0.5	mg/m ³ .years	19	0.96	0.94	(0.31, 3.00)	
Trend				0.59		
Colon cancer (225 cases)						
0	mg/m ³ .years	128				
> 0 to 0.4	mg/m ³ .years	33	0.88	0.73	(0.41, 1.86)	
> 0.4 to 1.7	mg/m ³ .years	32	0.91	0.80	(0.42, 1.93)	
> 1.7	mg/m ³ .years	32	0.95	0.88	(0.46, 1.94)	
Trend				0.83		
Rectal cancer (46 cases)						
0	mg/m ³ .years	22				
> 0 to 0.8	mg/m ³ .years	12	2.92	0.12	(0.76, 11.18)	
> 0.8	mg/m ³ .years	12	3.11	0.09	(0.85, 11.39)	
Trend				0.61		
Bladder cancer (74 cases)						

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
0	mg/m ³ .years	40			
> 0 to 0.5	mg/m ³ .years	17	2.11	0.14	(0.79, 5.68)
> 0.5	mg/m ³ .years	17	1.47	0.41	(0.59, 3.66)
Trend				0.95	
Liver cancer (65 cases)					
0	mg/m ³ .years	31			
> 0 to 0.4	mg/m ³ .years	17	0.94	0.94	(0.19, 4.65)
> 0.4	mg/m ³ .years	17	0.89	0.89	(0.19, 4.15)
Trend				0.38	
Pancreatic cancer (189 cases)					
0	mg/m ³ .years	101			
> 0 to 0.3	mg/m ³ .years	30	0.61	0.31	(0.24, 1.57)
> 0.3 to 0.9	mg/m ³ .years	29	0.77	0.59	(0.30, 1.98)
> 0.9	mg/m ³ .years	29	0.51	0.15	(0.20, 1.28)
Trend				0.33	
Skin cancer (37 cases)					
0	mg/m ³ .years	20			
> 0	mg/m ³ .years	17	1.19	0.83	(0.25, 5.75)
Prostate cancer (220 cases)					
0	mg/m ³ .years	103			
> 0 to 0.5	mg/m ³ .years	39	0.94	0.87	(0.44, 1.98)
> 0.5 to 2	mg/m ³ .years	39	0.98	0.95	(0.47, 2.06)
> 2	mg/m ³ .years	39	1.15	0.69	(0.57, 2.34)
Trend				0.04	*
Brain and nervous system cancers (84 cases)					
0	mg/m ³ .years	50			
> 0 to 0.6	mg/m ³ .years	17	1.34	0.60	(0.44, 4.05)
> 0.6	mg/m ³ .years	17	0.94	0.91	(0.31, 2.84)
Trend				0.58	
Leukemia (118 cases)					
0	mg/m ³ .years	62			
> 0 to 0.9	mg/m ³ .years	28	1.51	0.37	(0.61, 3.77)
> 0.9	mg/m ³ .years	28	1.89	0.14	(0.82, 4.37)
Trend				0.39	
Breast cancer (58 cases)					
0	mg/m ³ .years	42			
> 0	mg/m ³ .years	16	0.33	0.28	(0.04, 2.45)

Clean referent group, messy exposure groups; exposure lagged 21 years;soluble referent at 5 mg/m³.y

