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	p	95% CI
Laryngeal cancer (50 cases)					
0	mg/m^3·years	17			
> 0 to 0.5	mg/m^3·years	17	0.78	0.82	(0.09, 6.47)
> 0.5	mg/m^3·years	16	0.62	0.65	(0.08, 4.88)
Trend				0.39	
Lung cancer (1314 cases)					
0	mg/m^3·years	387			
> 0 to 0.3	mg/m^3·years	309	1.12	0.51	(0.79, 1.59)
> 0.3 to 1.6	mg/m^3·years	309	1.02	0.92	(0.72, 1.45)
> 1.6	mg/m^3·years	309	0.96	0.82	(0.69, 1.35)
Trend				0.40	
Esophageal cancer (125 cases)					
0	mg/m^3·years	32			
> 0 to 0.4	mg/m^3·years	31	0.62	0.54	(0.14, 2.78)
> 0.4 to 2.1	mg/m^3·years	32	0.64	0.56	(0.14, 2.86)
> 2.1	mg/m^3·years	30	0.64	0.55	(0.15, 2.78)
Trend				0.69	
Stomach cancer (144 cases)					
0	mg/m^3·years	54			
> 0 to 0.3	mg/m^3·years	30	0.99	0.98	(0.35, 2.77)
> 0.3 to 2.9	mg/m^3·years	30	0.69	0.48	(0.24, 1.93)
> 2.9	mg/m^3·years	30	1.36	0.54	(0.51, 3.64)

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	p	95% CI	
Trend				0.17		
Colon cancer (266 cases)						
0	mg/m^3·years	70				
> 0 to 0.5	mg/m^3·years	66	0.99	0.98	(0.47, 2.11)	
> 0.5 to 2.1	mg/m^3·years	65	0.98	0.96	(0.46, 2.10)	
> 2.1	mg/m^3·years	65	1.03	0.94	(0.50, 2.13)	
Trend				0.08		·
Rectal cancer (57 cases)						
0	mg/m^3·years	18				
> 0 to 1	mg/m^3·years	20	1.20	0.82	(0.24, 5.93)	
> 1	mg/m^3·years	19	1.41	0.66	(0.30, 6.57)	
Trend				0.33		
Bladder cancer (89 cases)						
0	mg/m^3·years	24				
> 0 to 0.3	mg/m^3·years	20	0.72	0.68	(0.16, 3.37)	
> 0.3 to 1.8	mg/m^3·years	22	0.55	0.45	(0.12, 2.55)	
> 1.8	mg/m^3·years	23	0.56	0.44	(0.13, 2.45)	
Trend				0.51		
Liver cancer (85 cases)						
0	mg/m^3·years	17				
> 0 to 0.5	mg/m^3·years	22	1.78	0.32	(0.57, 5.54)	
> 0.5 to 1.6	mg/m^3·years	23	3.71	0.02	(1.22, 11.27)	*
> 1.6	mg/m^3·years	23	2.60	0.08	(0.91, 7.47)	·
Trend				0.85		
Pancreatic cancer (226 cases)						
0	mg/m^3·years	65				
> 0 to 0.3	mg/m^3·years	54	0.61	0.35	(0.21, 1.74)	
> 0.3 to 1.1	mg/m^3·years	53	0.55	0.27	(0.19, 1.59)	
> 1.1	mg/m^3·years	54	0.45	0.13	(0.16, 1.27)	
Trend				0.44		
Skin cancer (50 cases)						
0	mg/m^3·years	13				
> 0 to 0.9	mg/m^3·years	18	1.91	0.44	(0.37, 9.81)	
> 0.9	mg/m^3·years	19	2.12	0.36	(0.43, 10.47)	
Trend				0.56		
Prostate cancer (284 cases)						
0	mg/m^3·years	58				
> 0 to 0.5	mg/m^3·years	76	1.26	0.54	(0.61, 2.61)	
> 0.5 to 2	mg/m^3·years	75	1.15	0.71	(0.55, 2.40)	
> 2	mg/m^3·years	75	1.05	0.88	(0.53, 2.11)	
Trend				0.58		
Brain and nervous system cancers (75 cases)						
0	mg/m^3·years	25				
> 0 to 1	mg/m^3·years	24	0.79	0.77	(0.17, 3.71)	
> 1	mg/m^3·years	26	1.10	0.90	(0.25, 4.90)	

Clean referent group, messy exposure groups; exposure lagged 21 years;soluble referent at 0.055 mg/m^3·y

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	p	95% CI	
Trend				0.46		
Leukemia (141 cases)						
0	mg/m^3·years	41				
> 0 to 0.3	mg/m^3·years	34	1.28	0.64	(0.46, 3.59)	
> 0.3 to 2.3	mg/m^3·years	33	0.92	0.87	(0.32, 2.60)	
> 2.3	mg/m^3·years	33	1.13	0.81	(0.42, 3.06)	
Trend				0.79		
Breast cancer (64 cases)						
0	mg/m^3·years	31				
> 0 to 0.7	mg/m^3·years	16	1.85	0.27	(0.63, 5.46)	
> 0.7	mg/m^3·years	17	3.02	0.04	(1.03, 8.87)	*
Trend				0.27		

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	p	95% CI	
Laryngeal cancer (72 cases)						
0 to 0.055	mg/m^3·years	17				
> 0.1 to 7.3	mg/m^3·years	28	0.79	0.53	(0.39, 1.64)	
> 7.3	mg/m^3·years	27	0.87	0.72	(0.40, 1.89)	
Trend				0.88		
Lung cancer (1855 cases)						
0 to 0.055	mg/m^3·years	398				
> 0.1 to 3.3	mg/m^3·years	486	0.98	0.84	(0.84, 1.15)	
> 3.3 to 11.2	mg/m^3·years	485	0.91	0.23	(0.77, 1.06)	
> 11.2	mg/m^3·years	486	1.01	0.87	(0.85, 1.20)	
Trend				0.50		
Esophageal cancer (174 cases)						
0 to 0.055	mg/m^3·years	32				
> 0.1 to 3.3	mg/m^3·years	46	1.01	0.96	(0.60, 1.71)	
> 3.3 to 10.8	mg/m^3·years	47	0.98	0.96	(0.57, 1.70)	
> 10.8	mg/m^3·years	49	1.11	0.72	(0.62, 1.98)	
Trend				0.02		*
Stomach cancer (190 cases)						
0 to 0.055	mg/m^3·years	55				
> 0.1 to 4.2	mg/m^3·years	45	0.66	0.10	(0.41, 1.08)	
> 4.2 to 9.7	mg/m^3·years	45	1.10	0.71	(0.66, 1.83)	
> 9.7	mg/m^3·years	45	0.68	0.17	(0.40, 1.18)	
Trend				0.46		
Colon cancer (400 cases)						
0 to 0.055	mg/m^3·years	73				

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	p	95% CI
> 0.1 to 3.5	mg/m^3·years	109	1.15	0.40	(0.83, 1.61)
> 3.5 to 12	mg/m^3·years	109	0.98	0.89	(0.69, 1.39)
> 12	mg/m^3·years	109	0.96	0.84	(0.66, 1.39)
Trend				0.54	
Rectal cancer (83 cases)					
0 to 0.055	mg/m^3·years	20			
> 0.1 to 4.6	mg/m^3·years	19	0.75	0.44	(0.35, 1.58)
> 4.6 to 8.6	mg/m^3·years	23	1.90	0.09	(0.90, 3.98)
> 8.6	mg/m^3·years	21	0.74	0.45	(0.33, 1.63)
Trend				0.57	
Bladder cancer (136 cases)					
0 to 0.055	mg/m^3·years	24			
> 0.1 to 3.7	mg/m^3·years	37	1.09	0.77	(0.61, 1.94)
> 3.7 to 11.1	mg/m^3·years	36	1.18	0.59	(0.65, 2.12)
> 11.1	mg/m^3·years	39	1.12	0.71	(0.61, 2.05)
Trend				0.75	
Liver cancer (120 cases)					
0 to 0.055	mg/m^3·years	19			
> 0.1 to 2.3	mg/m^3·years	34	1.39	0.31	(0.74, 2.60)
> 2.3 to 9.2	mg/m^3·years	32	0.82	0.55	(0.43, 1.57)
> 9.2	mg/m^3·years	35	0.97	0.92	(0.49, 1.89)
Trend				0.78	
Pancreatic cancer (310 cases)					
0 to 0.055	mg/m^3·years	65			
> 0.1 to 3.4	mg/m^3·years	82	0.81	0.26	(0.55, 1.17)
> 3.4 to 9.3	mg/m^3·years	81	0.91	0.62	(0.61, 1.34)
> 9.3	mg/m^3·years	82	0.79	0.28	(0.53, 1.20)
Trend				0.42	
Skin cancer (67 cases)					
0 to 0.055	mg/m^3·years	13			
> 0.1 to 4.7	mg/m^3·years	26	1.93	0.13	(0.82, 4.53)
> 4.7	mg/m^3·years	28	1.97	0.15	(0.79, 4.92)
Trend				0.63	
Prostate cancer (410 cases)					
0 to 0.055	mg/m^3·years	60			
> 0.1 to 5.1	mg/m^3·years	117	0.76	0.12	(0.54, 1.07)
> 5.1 to 15.6	mg/m^3·years	116	0.78	0.18	(0.55, 1.12)
> 15.6	mg/m^3·years	117	0.81	0.25	(0.56, 1.17)
Trend				0.79	
Brain and nervous system cancers (126 cases)					
0 to 0.055	mg/m^3·years	30			
> 0.1 to 2.7	mg/m^3·years	32	1.56	0.13	(0.87, 2.77)
> 2.7 to 9.2	mg/m^3·years	32	1.53	0.17	(0.83, 2.83)
> 9.2	mg/m^3·years	32	1.62	0.15	(0.84, 3.14)
Trend				0.53	

Clean referent group, messy exposure groups; exposure lagged 21 years;soluble referent at 0.055 mg/m^3·y

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	p	95% CI
Leukemia (195 cases)					
0 to 0.055	mg/m^3·years	43			
> 0.1 to 3.3	mg/m^3·years	51	1.12	0.66	(0.68, 1.83)
> 3.3 to 9.7	mg/m^3·years	50	1.18	0.52	(0.71, 1.98)
> 9.7	mg/m^3·years	51	0.97	0.92	(0.56, 1.68)
Trend				0.38	
Breast cancer (72 cases)					
0 to 0.055	mg/m^3·years	32			
> 0.1 to 2.9	mg/m^3·years	22	0.73	0.37	(0.36, 1.47)
> 2.9	mg/m^3·years	18	0.67	0.35	(0.29, 1.55)
Trend				0.56	

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	p	95% CI
Laryngeal cancer (36 cases)					
0	mg/m^3·years	17			
> 0	mg/m^3·years	19	1.42	0.79	(0.10, 20.17)
Lung cancer (904 cases)					
0	mg/m^3·years	387			
> 0 to 0.3	mg/m^3·years	173	1.14	0.64	(0.65, 1.99)
> 0.3 to 1.4	mg/m^3·years	172	1.39	0.25	(0.79, 2.43)
> 1.4	mg/m^3·years	172	1.25	0.43	(0.72, 2.15)
Trend				0.78	
Esophageal cancer (82 cases)					
0	mg/m^3·years	32			
> 0 to 0.7	mg/m^3·years	25	0.00	0.99	(0.00, Inf)
> 0.7	mg/m^3·years	25	0.00	0.99	(0.00, Inf)
Trend				0.66	
Stomach cancer (90 cases)					
0	mg/m^3·years	50			
> 0 to 0.5	mg/m^3·years	21	0.00	0.99	(0.00, Inf)
> 0.5	mg/m^3·years	19	0.00	0.99	(0.00, Inf)
Trend				0.66	
Colon cancer (167 cases)					
0	mg/m^3·years	70			
> 0 to 0.4	mg/m^3·years	33	1.42	0.55	(0.45, 4.50)
> 0.4 to 1.7	mg/m^3·years	32	1.44	0.54	(0.45, 4.59)
> 1.7	mg/m^3·years	32	1.53	0.45	(0.50, 4.64)
Trend				0.48	
Rectal cancer (42 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	p	95% CI
0	mg/m^3·years	18			
> 0 to 0.8	mg/m^3·years	12	0.00	0.99	(0.00, Inf)
> 0.8	mg/m^3·years	12	0.00	0.99	(0.00, Inf)
Trend				0.66	
Bladder cancer (58 cases)					
0	mg/m^3·years	24			
> 0 to 0.5	mg/m^3·years	17	0.00	0.99	(0.00, Inf)
> 0.5	mg/m^3·years	17	0.00	0.99	(0.00, Inf)
Trend				0.66	
Liver cancer (51 cases)					
0	mg/m^3·years	17			
> 0 to 0.4	mg/m^3·years	17	0.00	0.99	(0.00, Inf)
> 0.4	mg/m^3·years	17	0.00	0.99	(0.00, Inf)
Trend				0.66	
Pancreatic cancer (153 cases)					
0	mg/m^3·years	65			
> 0 to 0.3	mg/m^3·years	30	0.31	0.27	(0.04, 2.51)
> 0.3 to 0.9	mg/m^3·years	29	0.37	0.36	(0.05, 3.10)
> 0.9	mg/m^3·years	29	0.26	0.20	(0.03, 2.08)
Trend				0.56	
Skin cancer (30 cases)					
0	mg/m^3·years	13			
> 0	mg/m^3·years	17	0.00	0.99	(0.00, Inf)
Prostate cancer (175 cases)					
0	mg/m^3·years	58			
> 0 to 0.5	mg/m^3·years	39	0.71	0.66	(0.16, 3.24)
> 0.5 to 2	mg/m^3·years	39	0.72	0.67	(0.16, 3.29)
> 2	mg/m^3·years	39	0.86	0.84	(0.19, 3.78)
Trend				0.84	
Brain and nervous system cancers (55 cases)					
0	mg/m^3·years	25			
> 0 to 0.6	mg/m^3·years	15	0.00	0.99	(0.00, Inf)
> 0.6	mg/m^3·years	15	0.00	0.99	(0.00, Inf)
Trend				0.66	
Leukemia (92 cases)					
0	mg/m^3·years	36			
> 0 to 0.9	mg/m^3·years	28	1.99	0.40	(0.41, 9.74)
> 0.9	mg/m^3·years	28	2.35	0.27	(0.51, 10.77)
Trend				0.49	
Breast cancer (47 cases)					
0	mg/m^3·years	31			
> 0	mg/m^3·years	16	0.00	0.99	(0.00, Inf)

Clean referent group, messy exposure groups; exposure lagged 21 years;soluble referent at 0.055 mg/m^3·y