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	p	95% CI	
Laryngeal cancer (55 cases)						
0	mg/m^3·years	27				
> 0 to 0.3	mg/m^3·years	14	1.12	0.92	(0.13, 9.52)	
> 0.3	mg/m^3·years	14	0.85	0.88	(0.11, 6.80)	
Trend				0.34		
Lung cancer (1392 cases)						
0	mg/m^3·years	674				
> 0 to 0.3	mg/m^3·years	240	1.14	0.48	(0.79, 1.66)	
> 0.3 to 1.4	mg/m^3·years	239	1.00	0.99	(0.69, 1.45)	
> 1.4	mg/m^3·years	239	0.93	0.70	(0.65, 1.33)	
Trend				0.43		
Esophageal cancer (127 cases)						
0	mg/m^3·years	57				
> 0 to 0.5	mg/m^3·years	24	2.06	0.14	(0.80, 5.34)	
> 0.5 to 2.2	mg/m^3·years	23	2.81	0.03	(1.10, 7.19)	*
> 2.2	mg/m^3·years	23	2.52	0.04	(1.03, 6.17)	*
Trend				0.55		
Stomach cancer (159 cases)						
0	mg/m^3·years	90				
> 0 to 0.3	mg/m^3·years	23	0.94	0.92	(0.30, 2.96)	
> 0.3 to 2.6	mg/m^3·years	23	0.71	0.56	(0.23, 2.25)	
> 2.6	mg/m^3·years	23	1.40	0.54	(0.48, 4.13)	

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				0.15		
Colon cancer (291 cases)						
0	mg/m^3·years	140				
> 0 to 0.3	mg/m^3·years	51	0.39	0.08	(0.13, 1.12)	·
> 0.3 to 2.4	mg/m^3·years	50	0.30	0.03	(0.10, 0.87)	*
> 2.4	mg/m^3·years	50	0.41	0.09	(0.15, 1.15)	·
Trend				0.62		
Rectal cancer (62 cases)						
0	mg/m^3·years	33				
> 0 to 0.6	mg/m^3·years	15	2.64	0.16	(0.68, 10.31)	
> 0.6	mg/m^3·years	14	2.01	0.30	(0.54, 7.48)	
Trend				0.81		
Bladder cancer (96 cases)						
0	mg/m^3·years	41				
> 0 to 0.5	mg/m^3·years	27	1.87	0.28	(0.61, 5.77)	
> 0.5	mg/m^3·years	28	0.99	0.99	(0.34, 2.92)	
Trend				0.73		
Liver cancer (86 cases)						
0	mg/m^3·years	33				
> 0 to 0.9	mg/m^3·years	26	0.90	0.89	(0.20, 4.14)	
> 0.9	mg/m^3·years	27	1.35	0.69	(0.31, 5.92)	
Trend				0.14		
Pancreatic cancer (245 cases)						
0	mg/m^3·years	118				
> 0 to 0.2	mg/m^3·years	43	0.91	0.85	(0.35, 2.39)	
> 0.2 to 0.8	mg/m^3·years	42	0.87	0.77	(0.33, 2.30)	
> 0.8	mg/m^3·years	42	0.47	0.12	(0.18, 1.21)	
Trend				0.04		*
Skin cancer (53 cases)						
0	mg/m^3·years	25				
> 0 to 0.9	mg/m^3·years	14	0.89	0.92	(0.11, 7.54)	
> 0.9	mg/m^3·years	14	1.02	0.98	(0.13, 8.32)	
Trend				0.65		
Prostate cancer (288 cases)						
0	mg/m^3·years	95				
> 0 to 0.3	mg/m^3·years	65	1.50	0.28	(0.72, 3.10)	
> 0.3 to 1.5	mg/m^3·years	64	1.27	0.52	(0.61, 2.66)	
> 1.5	mg/m^3·years	64	1.10	0.79	(0.55, 2.20)	
Trend				0.73		
Brain and nervous system cancers (94 cases)						
0	mg/m^3·years	52				
> 0 to 0.9	mg/m^3·years	21	0.33	0.30	(0.04, 2.64)	
> 0.9	mg/m^3·years	21	0.49	0.48	(0.06, 3.69)	
Trend				0.70		
Leukemia (150 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	p	95% CI	
0	mg/m^3·years	69				
> 0 to 0.3	mg/m^3·years	27	1.87	0.21	(0.70, 4.96)	
> 0.3 to 1.7	mg/m^3·years	27	1.51	0.41	(0.57, 4.04)	
> 1.7	mg/m^3·years	27	1.41	0.47	(0.56, 3.56)	
Trend				0.87		
Breast cancer (70 cases)						
0	mg/m^3·years	47				
> 0 to 0.7	mg/m^3·years	11	1.15	0.84	(0.30, 4.41)	
> 0.7	mg/m^3·years	12	2.33	0.21	(0.63, 8.63)	
Trend				0.07		·

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	27				
> 0.1 to 7.2	mg/m^3·years	23	0.87	0.73	(0.41, 1.86)	
> 7.2	mg/m^3·years	22	1.29	0.54	(0.56, 2.97)	
Trend				0.21		
Lung cancer (1861 cases)						
0 to 0.055	mg/m^3·years	685				
> 0.1 to 2.9	mg/m^3·years	392	1.01	0.87	(0.87, 1.18)	
> 2.9 to 9.3	mg/m^3·years	392	1.06	0.52	(0.89, 1.25)	
> 9.3	mg/m^3·years	392	1.12	0.23	(0.93, 1.34)	
Trend				0.10		·
Esophageal cancer (168 cases)						
0 to 0.055	mg/m^3·years	57				
> 0.1 to 3	mg/m^3·years	35	1.18	0.54	(0.69, 2.01)	
> 3 to 10.2	mg/m^3·years	38	1.40	0.24	(0.80, 2.47)	
> 10.2	mg/m^3·years	38	1.81	0.06	(0.98, 3.37)	·
Trend				0.10		
Stomach cancer (189 cases)						
0 to 0.055	mg/m^3·years	90				
> 0.1 to 4.2	mg/m^3·years	33	0.55	0.03	(0.32, 0.95)	*
> 4.2 to 11	mg/m^3·years	33	0.93	0.80	(0.53, 1.64)	
> 11	mg/m^3·years	33	0.86	0.63	(0.47, 1.58)	
Trend				0.92		
Colon cancer (403 cases)						
0 to 0.055	mg/m^3·years	141				
> 0.1 to 2.9	mg/m^3·years	88	0.96	0.80	(0.70, 1.32)	
> 2.9 to 11.5	mg/m^3·years	87	0.72	0.07	(0.51, 1.02)	·

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	
> 11.5	mg/m^3·years	87	0.87	0.45	(0.60, 1.25)	
Trend				0.86		
Rectal cancer (82 cases)						
0 to 0.055	mg/m^3·years	35				
> 0.1 to 6.5	mg/m^3·years	21	0.69	0.31	(0.34, 1.41)	
> 6.5	mg/m^3·years	26	1.15	0.72	(0.54, 2.45)	
Trend				0.48		
Bladder cancer (134 cases)						
0 to 0.055	mg/m^3·years	41				
> 0.1 to 3	mg/m^3·years	31	1.07	0.82	(0.62, 1.85)	
> 3 to 8	mg/m^3·years	30	1.22	0.49	(0.69, 2.15)	
> 8	mg/m^3·years	32	0.92	0.78	(0.51, 1.66)	
Trend				0.32		
Liver cancer (122 cases)						
0 to 0.055	mg/m^3·years	34				
> 0.1 to 1.9	mg/m^3·years	29	1.57	0.13	(0.87, 2.84)	
> 1.9 to 6.5	mg/m^3·years	29	1.43	0.25	(0.78, 2.64)	
> 6.5	mg/m^3·years	30	1.05	0.89	(0.54, 2.02)	
Trend				0.50		
Pancreatic cancer (309 cases)						
0 to 0.055	mg/m^3·years	118				
> 0.1 to 2.8	mg/m^3·years	64	0.66	0.03	(0.45, 0.97)	*
> 2.8 to 8.2	mg/m^3·years	63	0.73	0.12	(0.48, 1.09)	
> 8.2	mg/m^3·years	64	0.69	0.09	(0.45, 1.06)	·
Trend				0.66		
Skin cancer (68 cases)						
0 to 0.055	mg/m^3·years	25				
> 0.1 to 4.4	mg/m^3·years	22	1.67	0.20	(0.76, 3.70)	
> 4.4	mg/m^3·years	21	1.51	0.37	(0.61, 3.72)	
Trend				0.81		
Prostate cancer (411 cases)						
0 to 0.055	mg/m^3·years	98				
> 0.1 to 3.9	mg/m^3·years	105	0.97	0.87	(0.70, 1.35)	
> 3.9 to 11.9	mg/m^3·years	104	0.98	0.90	(0.69, 1.38)	
> 11.9	mg/m^3·years	104	0.92	0.66	(0.64, 1.32)	
Trend				0.06		·
Brain and nervous system cancers (127 cases)						
0 to 0.055	mg/m^3·years	52				
> 0.1 to 2.5	mg/m^3·years	25	1.48	0.20	(0.81, 2.71)	
> 2.5 to 7.9	mg/m^3·years	25	1.79	0.08	(0.94, 3.40)	·
> 7.9	mg/m^3·years	25	1.68	0.14	(0.84, 3.36)	
Trend				0.61		
Leukemia (196 cases)						
0 to 0.055	mg/m^3·years	71				
> 0.1 to 2.5	mg/m^3·years	42	1.27	0.35	(0.77, 2.08)	

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	
> 2.5 to 7.3	mg/m^3·years	41	1.19	0.52	(0.70, 2.02)	
> 7.3	mg/m^3·years	42	0.84	0.55	(0.48, 1.47)	
Trend				0.20		
Breast cancer (74 cases)						
0 to 0.055	mg/m^3·years	48				
> 0.1 to 2	mg/m^3·years	14	0.63	0.27	(0.27, 1.44)	
> 2	mg/m^3·years	12	0.34	0.04	(0.13, 0.94)	*
Trend				0.38		

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 (42 cases)					
0	mg/m^3·years	27			
> 0	mg/m^3·years	15	0.00	0.99	(0.00, Inf)
Lung cancer (1053 cases)					
0	mg/m^3·years	674			
> 0 to 0.2	mg/m^3·years	127	1.24	0.49	(0.67, 2.32)
> 0.2 to 1.3	mg/m^3·years	126	1.18	0.60	(0.64, 2.19)
> 1.3	mg/m^3·years	126	1.22	0.52	(0.67, 2.21)
Trend				0.66	
Esophageal cancer (92 cases)					
0	mg/m^3·years	57			
> 0 to 0.7	mg/m^3·years	18	2.97	0.20	(0.56, 15.65)
> 0.7	mg/m^3·years	17	2.58	0.24	(0.53, 12.62)
Trend				0.78	
Stomach cancer (112 cases)					
0	mg/m^3·years	84			
> 0 to 0.4	mg/m^3·years	15	0.55	0.67	(0.04, 8.06)
> 0.4	mg/m^3·years	13	0.42	0.52	(0.03, 5.89)
Trend				0.52	
Colon cancer (207 cases)					
0	mg/m^3·years	140			
> 0 to 0.2	mg/m^3·years	23	0.84	0.82	(0.17, 4.06)
> 0.2 to 1.4	mg/m^3·years	22	0.61	0.54	(0.12, 2.97)
> 1.4	mg/m^3·years	22	0.54	0.43	(0.11, 2.52)
Trend				0.34	
Rectal cancer (50 cases)					
0	mg/m^3·years	33			
> 0 to 0.5	mg/m^3·years	8	0.00	0.99	(0.00, Inf)
> 0.5	mg/m^3·years	9	0.00	0.99	(0.00, Inf)

Clean referent group, messy exposure groups; exposure lagged 30 years; soluble referent at 0.055 mg/m^3·y

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
Trend				0.66	
Bladder cancer (68 cases)					
0	mg/m^3·years	41			
> 0 to 0.5	mg/m^3·years	14	0.00	0.99	(0.00, Inf)
> 0.5	mg/m^3·years	13	0.00	0.99	(0.00, Inf)
Trend				0.66	
Liver cancer (59 cases)					
0	mg/m^3·years	33			
> 0 to 0.4	mg/m^3·years	13	0.00	0.99	(0.00, Inf)
> 0.4	mg/m^3·years	13	0.00	0.99	(0.00, Inf)
Trend				0.66	
Pancreatic cancer (184 cases)					
0	mg/m^3·years	118			
> 0 to 0.2	mg/m^3·years	22	0.36	0.35	(0.04, 3.11)
> 0.2 to 0.7	mg/m^3·years	22	0.38	0.38	(0.04, 3.35)
> 0.7	mg/m^3·years	22	0.28	0.24	(0.03, 2.36)
Trend				0.55	
Skin cancer (38 cases)					
0	mg/m^3·years	25			
> 0	mg/m^3·years	13	0.00	0.99	(0.00, Inf)
Prostate cancer (197 cases)					
0	mg/m^3·years	95			
> 0 to 0.3	mg/m^3·years	34	1.37	0.65	(0.35, 5.30)
> 0.3 to 1.2	mg/m^3·years	34	1.69	0.44	(0.44, 6.50)
> 1.2	mg/m^3·years	34	1.24	0.75	(0.33, 4.57)
Trend				0.80	
Brain and nervous system cancers (80 cases)					
0	mg/m^3·years	52			
> 0 to 0.2	mg/m^3·years	14	0.00	0.99	(0.00, Inf)
> 0.2	mg/m^3·years	14	0.00	0.99	(0.00, Inf)
Trend				0.67	
Leukemia (105 cases)					
0	mg/m^3·years	63			
> 0 to 0.6	mg/m^3·years	21	0.00	0.99	(0.00, Inf)
> 0.6	mg/m^3·years	21	0.00	0.99	(0.00, Inf)
Trend				0.66	
Breast cancer (57 cases)					
0	mg/m^3·years	47			
> 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 0.055 mg/m^3·y