UAW-GM Cohort Study

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

November 13, 2019

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	1.52	0.70	(0.17, 13.26)	
> 0.3	mg/m^3·years	14	1.13	0.91	(0.14, 8.92)	
Trend				0.94		
Lung cancer (1378 cases)						
0	mg/m^3·years	660				
> 0 to 0.3	mg/m^3·years	240	1.18	0.44	(0.77, 1.80)	
> 0.3 to 1.4	mg/m^3·years	239	1.02	0.92	(0.67, 1.55)	
> 1.4	mg/m^3·years	239	0.96	0.84	(0.64, 1.43)	
Trend				0.57		
Esophageal cancer (127 cases)						
0	mg/m^3·years	57				
> 0 to 0.5	mg/m^3·years	24	2.65	0.05	(1.00, 7.03)	*
> 0.5 to 2.2	mg/m^3·years	23	3.50	0.01	(1.37, 8.97)	*
> 2.2	mg/m^3·years	23	3.06	0.01	(1.26, 7.44)	*
Trend				0.59		
Stomach cancer (159 cases)						
0	mg/m^3·years	90				
> 0 to 0.3	mg/m^3·years	23	1.27	0.69	(0.39, 4.06)	
> 0.3 to 2.6	mg/m^3·years	23	0.94	0.92	(0.30, 2.98)	
> 2.6	mg/m^3·years	23	1.82	0.27	(0.62, 5.33)	

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				0.06		·
Colon cancer (288 cases)						
0	mg/m^3·years	137				
> 0 to 0.3	mg/m^3·years	51	0.38	0.12	(0.11, 1.28)	
> 0.3 to 2.4	mg/m^3·years	50	0.30	0.05	(0.09, 1.00)	*
> 2.4	mg/m^3·years	50	0.41	0.14	(0.13, 1.32)	
Trend				0.63		
Rectal cancer (61 cases)						
0	mg/m^3·years	32				
> 0 to 0.6	mg/m^3·years	15	1.08	0.94	(0.13, 9.10)	
> 0.6	mg/m^3·years	14	0.86	0.89	(0.11, 6.76)	
Trend				0.29		
Bladder cancer (96 cases)						
0	mg/m^3·years	41				
> 0 to 0.5	mg/m^3·years	27	2.45	0.13	(0.78, 7.68)	
> 0.5	mg/m^3·years	28	1.26	0.67	(0.43, 3.68)	
Trend				0.85		
Liver cancer (84 cases)						
0	mg/m^3·years	31				
> 0 to 0.9	mg/m^3·years	26	0.61	0.64	(0.08, 4.88)	
> 0.9	mg/m^3·years	27	0.91	0.93	(0.12, 6.95)	
Trend				0.84		
Pancreatic cancer (245 cases)						
0	mg/m^3·years	118				
> 0 to 0.2	mg/m^3·years	43	1.33	0.57	(0.50, 3.55)	
> 0.2 to 0.8	mg/m^3·years	42	1.25	0.66	(0.47, 3.31)	
> 0.8	mg/m^3·years	42	0.66	0.39	(0.26, 1.68)	
Trend				0.21		
Skin cancer (52 cases)						
0	mg/m^3·years	24				
> 0 to 0.9	mg/m^3·years	14	1.15	0.90	(0.13, 9.85)	
> 0.9	mg/m^3·years	14	1.32	0.80	(0.16, 10.73)	
Trend				0.30		
Prostate cancer (287 cases)						
0	mg/m^3·years	94				
> 0 to 0.3	mg/m^3·years	65	1.38	0.46	(0.59, 3.20)	
> 0.3 to 1.5	mg/m^3·years	64	1.17	0.71	(0.50, 2.73)	
> 1.5	mg/m^3·years	64	1.02	0.97	(0.46, 2.27)	
Trend				0.61		
Brain and nervous system cancers (93 cases)						
0	mg/m^3·years	51				
> 0 to 0.9	mg/m^3·years	21	0.50	0.51	(0.06, 3.99)	
> 0.9	mg/m^3·years	21	0.72	0.75	(0.10, 5.48)	
Trend				0.83		
Leukemia (149 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	68			
> 0 to 0.3	mg/m^3·years	27	1.66	0.39	(0.52, 5.29)
> 0.3 to 1.7	mg/m^3·years	27	1.38	0.58	(0.44, 4.29)
> 1.7	mg/m^3·years	27	1.30	0.63	(0.44, 3.83)
Trend				0.89	
Breast cancer (69 cases)					
0	mg/m^3·years	46			
> 0 to 0.7	mg/m^3·years	11	1.24	0.79	(0.24, 6.40)
> 0.7	mg/m^3·years	12	2.40	0.26	(0.53, 10.92)
Trend				0.11	

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	mg/m^3·years	27				
> 0 to 7.2	mg/m^3·years	23	0.81	0.59	(0.37, 1.75)	
> 7.2	mg/m^3·years	22	1.22	0.65	(0.52, 2.84)	
Trend				0.33		
Lung cancer (1861 cases)						
0	mg/m^3·years	660				
> 0 to 2.7	mg/m^3·years	401	1.06	0.49	(0.90, 1.24)	
> 2.7 to 9	mg/m^3·years	400	1.08	0.40	(0.91, 1.28)	
> 9	mg/m^3·years	400	1.14	0.15	(0.95, 1.37)	
Trend				0.15		
Esophageal cancer (168 cases)						
0	mg/m^3·years	57				
> 0 to 3	mg/m^3·years	35	1.06	0.83	(0.62, 1.82)	
> 3 to 10.2	mg/m^3·years	38	1.31	0.35	(0.74, 2.33)	
> 10.2	mg/m^3·years	38	1.69	0.10	(0.91, 3.16)	·
Trend				0.09		·
Stomach cancer (189 cases)						
0	mg/m^3·years	90				
> 0 to 4.2	mg/m^3·years	33	0.48	0.01	(0.28, 0.84)	*
> 4.2 to 11	mg/m^3·years	33	0.84	0.56	(0.47, 1.50)	
> 11	mg/m^3·years	33	0.78	0.42	(0.42, 1.44)	
Trend				0.99		
Colon cancer (403 cases)						
0	mg/m^3·years	137				
> 0 to 2.8	mg/m^3·years	89	0.94	0.73	(0.68, 1.31)	
> 2.8 to 11.4	mg/m^3·years	88	0.72	0.07	(0.51, 1.03)	·

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	
> 11.4	mg/m^3·years	89	0.88	0.51	(0.61, 1.28)	
Trend				0.93		
Rectal cancer (82 cases)						
0	mg/m^3·years	32				
> 0 to 5.8	mg/m^3·years	23	0.96	0.91	(0.47, 1.95)	
> 5.8	mg/m^3·years	27	1.34	0.45	(0.63, 2.86)	
Trend				0.07		·
Bladder cancer (134 cases)						
0	mg/m^3·years	41				
> 0 to 3	mg/m^3·years	31	0.97	0.92	(0.56, 1.69)	
> 3 to 8	mg/m^3·years	30	1.15	0.63	(0.65, 2.04)	
> 8	mg/m^3·years	32	0.87	0.65	(0.48, 1.58)	
Trend				0.28		
Liver cancer (122 cases)						
0	mg/m^3·years	31				
> 0 to 1.7	mg/m^3·years	30	1.90	0.04	(1.04, 3.47)	*
> 1.7 to 6	mg/m^3·years	30	1.61	0.13	(0.87, 3.01)	
> 6	mg/m^3·years	31	1.14	0.70	(0.59, 2.22)	
Trend				0.57		
Pancreatic cancer (309 cases)						
0	mg/m^3·years	118				
> 0 to 2.8	mg/m^3·years	64	0.56	0.00	(0.38, 0.83)	*
> 2.8 to 8.2	mg/m^3·years	63	0.65	0.04	(0.43, 0.98)	*
> 8.2	mg/m^3·years	64	0.62	0.03	(0.40, 0.95)	*
Trend				0.69		
Skin cancer (68 cases)						
0	mg/m^3·years	24				
> 0 to 4.3	mg/m^3·years	22	1.74	0.18	(0.77, 3.92)	
> 4.3	mg/m^3·years	22	1.73	0.24	(0.69, 4.32)	
Trend				0.66		
Prostate cancer (411 cases)						
0	mg/m^3·years	94				
> 0 to 3.7	mg/m^3·years	106	1.00	0.98	(0.72, 1.40)	
> 3.7 to 11.6	mg/m^3·years	105	1.00	0.99	(0.70, 1.41)	
> 11.6	mg/m^3·years	106	0.94	0.73	(0.65, 1.35)	
Trend				0.00		*
Brain and nervous system cancers (127 cases)						
0	mg/m^3·years	51				
> 0 to 2.5	mg/m^3·years	26	1.45	0.24	(0.78, 2.66)	
> 2.5 to 7.9	mg/m^3·years	25	1.77	0.09	(0.92, 3.39)	·
> 7.9	mg/m^3·years	25	1.65	0.16	(0.82, 3.32)	
Trend				0.62		
Leukemia (196 cases)						
0	mg/m^3·years	68				
> 0 to 2.3	mg/m^3·years	43	1.34	0.25	(0.81, 2.23)	

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.

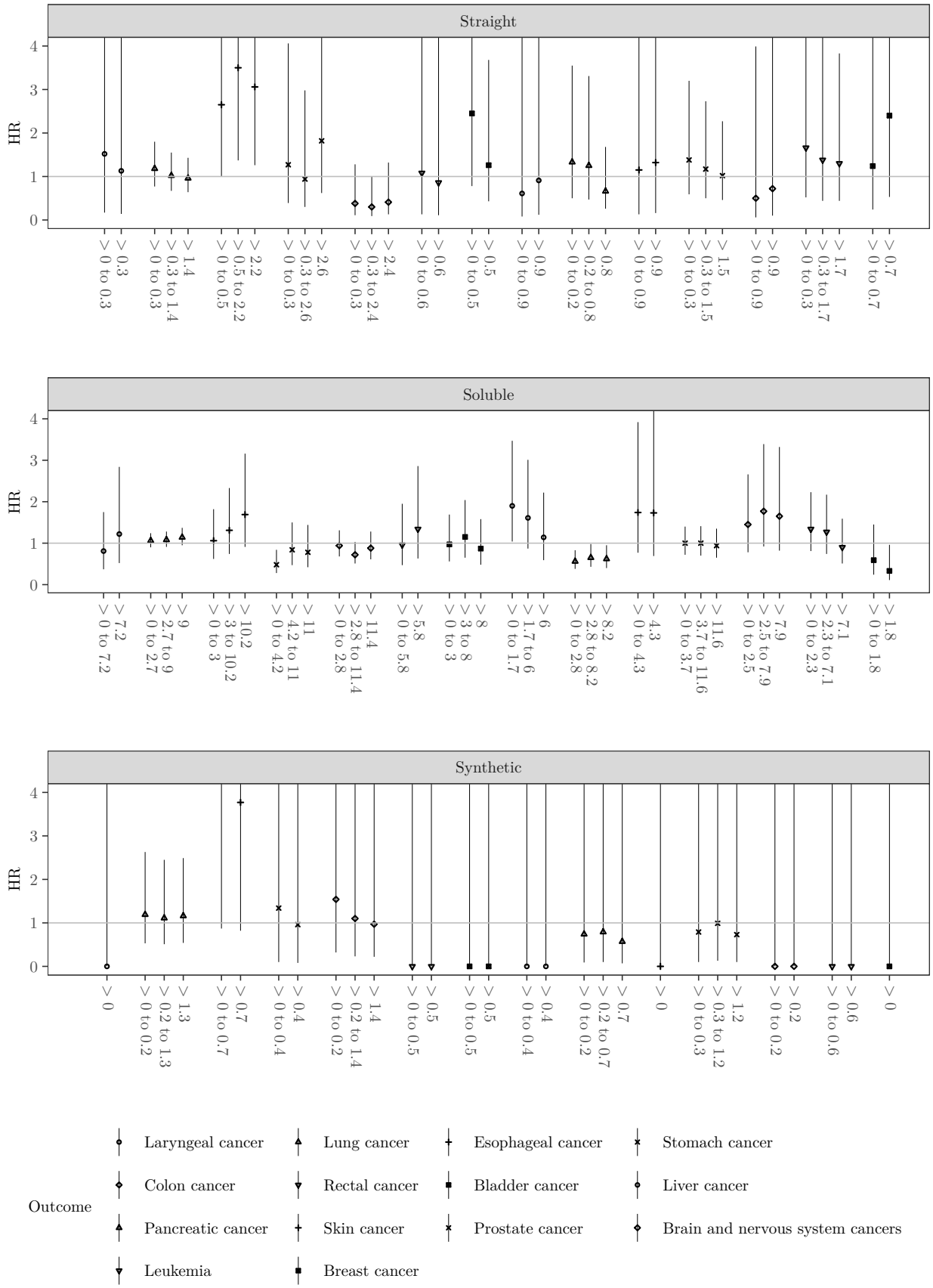
		Number of cases	HR	p	95% CI	
> 2.3 to 7.1	mg/m^3·years	42	1.27	0.39	(0.74, 2.17)	
> 7.1	mg/m^3·years	43	0.90	0.72	(0.51, 1.59)	
Trend				0.29		
Breast cancer (74 cases)						
0	mg/m^3·years	46				
> 0 to 1.8	mg/m^3·years	15	0.59	0.25	(0.24, 1.45)	
> 1.8	mg/m^3·years	13	0.33	0.04	(0.11, 0.96)	*
Trend				0.40		

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 (1039 cases)						
0	mg/m^3·years	660				
> 0 to 0.2	mg/m^3·years	127	1.19	0.67	(0.53, 2.63)	
> 0.2 to 1.3	mg/m^3·years	126	1.11	0.79	(0.51, 2.45)	
> 1.3	mg/m^3·years	126	1.16	0.71	(0.54, 2.49)	
Trend				0.65		
Esophageal cancer (92 cases)						
0	mg/m^3·years	57				
> 0 to 0.7	mg/m^3·years	18	4.52	0.07	(0.87, 23.55)	·
> 0.7	mg/m^3·years	17	3.77	0.09	(0.82, 17.43)	·
Trend				0.79		
Stomach cancer (112 cases)						
0	mg/m^3·years	84				
> 0 to 0.4	mg/m^3·years	15	1.34	0.82	(0.10, 17.23)	
> 0.4	mg/m^3·years	13	0.96	0.98	(0.08, 11.07)	
Trend				0.61		
Colon cancer (204 cases)						
0	mg/m^3·years	137				
> 0 to 0.2	mg/m^3·years	23	1.54	0.59	(0.32, 7.39)	
> 0.2 to 1.4	mg/m^3·years	22	1.10	0.90	(0.23, 5.17)	
> 1.4	mg/m^3·years	22	0.97	0.96	(0.22, 4.26)	
Trend				0.53		
Rectal cancer (49 cases)						
0	mg/m^3·years	32				
> 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)	

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 (57 cases)					
0	mg/m^3·years	31			
> 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	0.74	0.78	(0.09, 6.18)
> 0.2 to 0.7	mg/m^3·years	22	0.79	0.83	(0.10, 6.52)
> 0.7	mg/m^3·years	22	0.57	0.60	(0.07, 4.45)
Trend				0.23	
Skin cancer (37 cases)					
0	mg/m^3·years	24			
> 0	mg/m^3·years	13	0.00	0.99	(0.00, Inf)
Prostate cancer (196 cases)					
0	mg/m^3·years	94			
> 0 to 0.3	mg/m^3·years	34	0.79	0.82	(0.10, 6.40)
> 0.3 to 1.2	mg/m^3·years	34	0.99	0.99	(0.13, 7.88)
> 1.2	mg/m^3·years	34	0.73	0.77	(0.10, 5.60)
Trend				0.30	
Brain and nervous system cancers (79 cases)					
0	mg/m^3·years	51			
> 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 (104 cases)					
0	mg/m^3·years	62			
> 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 (56 cases)					
0	mg/m^3·years	46			
> 0	mg/m^3·years	10	0.00	0.99	(0.00, Inf)


Straight
Soluble
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Outcome
Laryngeal cancer
Lung cancer
Esophageal cancer
Stomach cancer
Colon cancer
Rectal cancer
Bladder cancer
Liver cancer
Pancreatic cancer
Skin cancer
Prostate cancer
Brain and nervous system cancers
Leukemia
Breast cancer