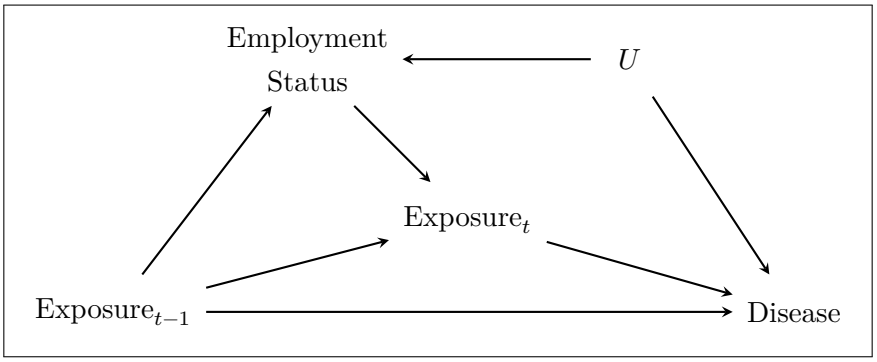
Cancer incidence and HWSE path analysis

GM-UAW Cohort Study

October 20, 2020



This packet summarizes Cox proportional hazard model results relating cumulative exposure to straight, soluble, and synthetic metalworking fluids (MWF) to cancer incidence of 14 types and for all sites combined (includes types not shown here) in the UAW-GM Cohort. The types are colon, rectal, pancreatic, esophageal, stomach, laryngeal, lung & bronchial, breast, prostate, kidney and renal pelvic, bladder, melanoma, leukemia, and non-Hodgkin lymphoma. In addition, path analyses testing for the presence of healthy worker survivor effect ar presented. These include Cox models relating emloyment status to cancer incidence and one Cox model relating cumulative MWF exposure to leaving work. The path analyses largely follow the methods outlined in Garcia et al.[1]

The study population, summarized in Table 1, includes subjects from the UAW-GM Cohort who were still alive at the start of cancer incidence follow-up. Cancer incidence data were abstracted from Michigan Cancer Registry for all plants from years 1985 onward. Cancer incidence data for plants 1 and 2 were supplemented with data from the Surveillance, Epidemiology, and End Results Program (SEER). Follow-up begins three years after hire and no earlier than 1973 for plants 1 and 2 or 1985 for plant 3. Follow-up ends upon reaching the the oldest observed age at death (considered lost to follow-up), death, cancer incidence, or the year 2015, whichever comes first. In the path analyses for employment status and cancer incidence, subjects were also censored upon reaching their 80^{th} birthday.

Table 1: Summary of population characteristics. Follow-up for cancer incidence extends from 1985 through 2015.

	n	p	
Study population size (N)	39 132	100%	
Race			
White	25 119	64%	
Black	6 862	18%	
Unknown	7 151	18%	
Sex			
Male	34 498	88%	
Female	4 634	12%	
Plant[♮]			
Plant 1	11 467	29%	
Plant 2	15 910	41%	
Plant 3	11 755	30%	
Ever exposed to MWFs			
Straight	21 294	54%	
Soluble	34 055	87%	
Synthetic	12 530	32%	
Diagnosed with cancer by end of follow-up	7 894	20%	
	Median	25^{th} %tile	75^{th} %tile
Years of follow-up	39.5	34.3	46.98
Years at work[*]	15.73	7.65	27.06
Year of hire	1965	1951	1973
Age at hire (years)	24	20	31
Year of birth	1937	1921	1948
Year of first cancer diagnosis	1999	1991	2007
Age at first cancer diagnosis (years)	67	59	74
Cumulative exposure[♯] to MWFs ($mg/m^3 \cdot y$)			
Straight	0.69	0.21	2.53
Soluble	4.93	1.93	13.31
Synthetic	0.44	0.15	1.56

[♮] Some individuals worked at several sites; plant indicates the site of longest work record time.

[*] Among those with known date of worker exit.

[♯] Summary statistics calculated for ever-exposed individuals at end of follow-up only. Exposures were lagged 21 years.

Table 2: Adjusted HR estimates for cancer incidence and employment status.

	n	HR	(95% CI)	p
Stomach cancer (142 events)				
Still employed	19	1.00	–	
Not employed	123	1.04	(0.57, 1.90)	0.89
Left work (under 50)	57	0.83	(0.43, 1.57)	0.56
Left work (50 or older)	66	1.41	(0.73, 2.71)	0.31
Left work (under 55)	77	0.96	(0.51, 1.79)	0.90
Left work (55 or older)	46	1.23	(0.63, 2.41)	0.55
Left work (under 60)	97	1.03	(0.56, 1.90)	0.92
Left work (60 or older)	26	1.09	(0.53, 2.24)	0.82
Bladder cancer (296 events)				
Still employed	27	1.00	–	
Not employed	269	0.82	(0.50, 1.34)	0.43
Left work (under 50)	115	0.68	(0.40, 1.14)	0.14
Left work (50 or older)	154	0.98	(0.58, 1.64)	0.93
Left work (under 55)	151	0.71	(0.43, 1.19)	0.20
Left work (55 or older)	118	0.99	(0.58, 1.67)	0.96
Left work (under 60)	198	0.77	(0.46, 1.27)	0.31
Left work (60 or older)	71	0.94	(0.55, 1.62)	0.83
Non-Hodgkin's lymphoma (210 events)				
Still employed	22	1.00	–	
Not employed	188	1.05	(0.60, 1.85)	0.86
Left work (under 50)	104	1.05	(0.59, 1.89)	0.87
Left work (50 or older)	84	1.05	(0.57, 1.94)	0.87
Left work (under 55)	119	0.94	(0.52, 1.69)	0.84
Left work (55 or older)	69	1.34	(0.71, 2.52)	0.36

Left work (under 60)	149	0.98	(0.55, 1.75)	0.95
Left work (60 or older)	39	1.32	(0.68, 2.56)	0.42

Table 3: Adjusted HR estimates for **leaving work**.

Covariate	level	n	HR	(95% CI)	p	
Cumulative straight	0	15241	1.00	–		
	>0 to 0.402	5984	1.13	(1.09, 1.16)	<0.005	$*$
	>0.402 to 2.07	5984	1.04	(1.01, 1.08)	0.02	$*$
	>2.07	5984	1.04	(1.00, 1.07)	0.03	$*$
Cumulative soluble	0 to 0.05	3822	1.00	–		
	>0.05 to 3.86	9576	1.18	(1.14, 1.23)	<0.005	$*$
	>3.86 to 16.1	9897	1.09	(1.05, 1.14)	<0.005	$*$
	>16.1	9898	1.00	(0.96, 1.04)	1.00	
Cumulative synthetic	0	24584	1.00	–		
	>0 to 0.261	2870	0.91	(0.87, 0.95)	<0.005	$*$
	>0.261 to 1.48	2869	0.94	(0.89, 0.98)	0.01	$*$
	>1.48	2870	0.99	(0.95, 1.04)	0.74	
Race	White	27973	1.00	–		
	Black	5220	0.69	(0.67, 0.72)	<0.005	$*$
Plant	1	14028	1.00	–		
	2	11826	0.70	(0.67, 0.73)	<0.005	$*$
	3	7339	0.52	(0.50, 0.54)	<0.005	$*$
Sex	Male	30254	1.00	–		
	Female	2939	1.43	(1.37, 1.49)	<0.005	$*$
P-spline of calendar year ($df = 16.99$)		33193		–	<0.005	$*$
P-spline of year of hire ($df = 16.21$)		33193		–	<0.005	$*$

Table 4: Adjusted HR estimates for incidence of **stomach cancer** ($n = 214$).

Covariate	level	n	HR	(95% CI)	p	
Cumulative straight	0	108	1.00	–		
	>0 to 0.347	36	1.13	(0.72, 1.78)	0.60	
	>0.347 to 3.28	35	0.73	(0.46, 1.14)	0.16	
	>3.28	35	1.54	(1.01, 2.36)	0.05	
Cumulative soluble	0 to 0.05	50	1.00	–		
	>0.05 to 4.02	54	0.64	(0.41, 0.99)	0.04	$*$
	>4.02 to 13.1	55	0.78	(0.50, 1.24)	0.30	
	>13.1	55	0.80	(0.49, 1.30)	0.37	
Cumulative synthetic	0	158	1.00	–		
	>0 to 0.64	28	0.98	(0.59, 1.63)	0.95	
	>0.64	28	1.12	(0.70, 1.80)	0.63	
Race	White	159	1.00	–		
	Black	55	1.70	(1.18, 2.45)	<0.005	$*$
Plant	1	73	1.00	–		
	2	91	1.18	(0.76, 1.84)	0.46	
	3	50	0.78	(0.49, 1.23)	0.28	
Sex	Male	198	1.00	–		
	Female	16	0.49	(0.28, 0.83)	0.01	$*$
P-spline of calendar year ($df = 8.19$)		214		–	0.84	
P-spline of year of hire ($df = 11.35$)		214		–	0.81	

Table 5: Adjusted HR estimates for incidence of **bladder cancer** ($n = 533$).

Covariate	level	n	HR	(95% CI)	p	
Cumulative straight	0	236	1.00	–		
	>0 to 0.388	99	1.32	(1.00, 1.74)	0.05	
	>0.388 to 2.71	99	1.03	(0.78, 1.35)	0.84	
	>2.71	99	1.29	(1.00, 1.67)	0.05	
Cumulative soluble	0 to 0.05	88	1.00	–		
	>0.05 to 3.86	146	0.85	(0.64, 1.13)	0.27	
	>3.86 to 13	149	0.98	(0.73, 1.33)	0.92	
	>13	150	1.15	(0.84, 1.58)	0.39	
Cumulative synthetic	0	393	1.00	–		
	>0 to 0.255	47	0.85	(0.59, 1.21)	0.36	
	>0.255 to 1.28	46	0.89	(0.63, 1.27)	0.54	
	>1.28	47	0.80	(0.57, 1.11)	0.18	
Race	White	479	1.00	–		
	Black	54	0.56	(0.41, 0.76)	<0.005	$*$
Plant	1	144	1.00	–		
	2	186	0.94	(0.70, 1.26)	0.69	
	3	203	1.13	(0.87, 1.47)	0.35	
Sex	Male	510	1.00	–		
	Female	23	0.30	(0.20, 0.47)	<0.005	$*$
P-spline of calendar year ($df = 9.01$)		533		–	0.53	
P-spline of year of hire ($df = 7.93$)		533		–	<0.005	$*$

Table 6: Adjusted HR estimates for incidence of **non-hodgkin's lymphoma** ($n = 393$).

Covariate	level	n	HR	(95% CI)	p	
Cumulative straight	0	172	1.00	–		
	>0 to 0.34	74	1.17	(0.84, 1.61)	0.35	
	>0.34 to 2.19	73	0.90	(0.65, 1.23)	0.51	
	>2.19	74	1.21	(0.90, 1.64)	0.21	
Cumulative soluble	0 to 0.05	54	1.00	–		
	>0.05 to 3.04	111	1.37	(0.96, 1.96)	0.08	
	>3.04 to 11.1	114	1.42	(0.97, 2.07)	0.07	
	>11.1	114	1.64	(1.09, 2.45)	0.02	$*$
Cumulative synthetic	0	273	1.00	–		
	>0 to 0.245	40	0.91	(0.61, 1.37)	0.66	
	>0.245 to 1.46	40	0.99	(0.67, 1.46)	0.95	
	>1.46	40	1.07	(0.74, 1.55)	0.72	
Race	White	347	1.00	–		
	Black	46	0.64	(0.46, 0.90)	0.01	$*$
Plant	1	99	1.00	–		
	2	156	1.10	(0.78, 1.56)	0.60	
	3	138	1.01	(0.73, 1.38)	0.96	
Sex	Male	348	1.00	–		
	Female	45	0.93	(0.66, 1.29)	0.65	
P-spline of calendar year ($df = 10.4$)		393		–	0.02	$*$
P-spline of year of hire ($df = 9$)		393		–	0.41	

Table 7: Adjusted HR estimates for incidence of the indicated outcome, associated with race. Caution: these estimates are simply the conditional estimates from the previous table.

Outcome	level	n	HR	(95% CI)	p	
Stomach cancer	White	159	1.00	–		
	Black	55	1.70	(1.18, 2.45)	< 0.005	$*$
Bladder cancer	White	479	1.00	–		
	Black	54	0.56	(0.41, 0.76)	< 0.005	$*$
Non-Hodgkin's lymphoma	White	347	1.00	–		
	Black	46	0.64	(0.46, 0.90)	0.01	$*$

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1. Garcia E, Picciotto S, Costello S, Bradshaw PT, Eisen EA. Assessment of the healthy worker survivor effect in cancer studies of the united autoworkers-general motors cohort. *Occupational and environmental medicine*. 2017;74(4):294-300.