

## Cancer incidence and HWSE path analysis

### GM-UAW Cohort Study

March 9, 2021

This packet summarizes Cox proportional hazard model results relating cumulative exposure to straight, soluble, and synthetic metalworking fluids (MWF), lagged 21 years, to cancer incidence of 14 types and for all sites combined (includes types not shown here) in the UAW-GM Cohort.

- Colon cancer
- Rectal cancer
- Pancreatic cancer
- Esophageal cancer
- Stomach cancer
- Laryngeal cancer
- Lung and bronchial cancers
- Breast cancer
- Prostate cancer
- Kidney and renal pelvic cancers
- Bladder cancer
- Melanoma
- Leukemia
- Non-Hodgkin lymphoma

In addition, path analyses for evidence of the healthy worker survivor effect are presented. These include Cox models relating employment status to cancer incidence and one Cox model relating cumulative MWF exposure to leaving work. In these models, metalworking fluid was lagged 1 year only. The path analyses largely follow the methods outlined in Garcia et al.<sup>1</sup>

The study population, summarized in Table 1, included 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).

In all analyses, follow-up began three years after hire and no earlier than 1973 for plants 1 and 2 or 1985 for plant 3; follow-up ended upon experiencing the outcome of interest, attaining the oldest observed age at death (considered lost to follow-up), dying, or reaching the year 2015, whichever came first. In path analyses involving employment status, subjects were censored on December 31, 1994 (end of employment records) if they did not leave work before then. Missing race was handled by multiple imputation ( $M = 50$ ).<sup>2</sup>

Table 1: Summary of population characteristics. In plants 1 and 2, follow-up for cancer incidence extends from 1973 through 2015. In plant 3, follow-up starts in 1985.

	<i>n</i>	<i>p</i>	
Study population size ( <i>N</i> )	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 <sup>‡</sup>			
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 <sup>th</sup> %tile	75 <sup>th</sup> %tile
Years of follow-up	39.5	34.3	46.98
Years at work*	15.73	7.65	27.06
Year of hire	1965	1952	1973
Age at hire (years)	24	20	31
Year of birth	1937	1921	1949
Year of first cancer diagnosis	1999	1991	2007
Age at first cancer diagnosis (years)	67	59	74
Cumulative exposure <sup>#</sup> to MWFs (mg/m <sup>3</sup> ·y)			
Straight	0.69	0.21	2.53
Soluble	4.93	1.93	13.31
Synthetic	0.44	0.15	1.56

<sup>‡</sup> Some individuals worked at several sites; plant indicates the site of longest work record time.

\* Among those with known date of worker exit.

<sup>#</sup> Summary statistics calculated for ever-exposed individuals at end of follow-up only. Exposures were lagged 21 years.

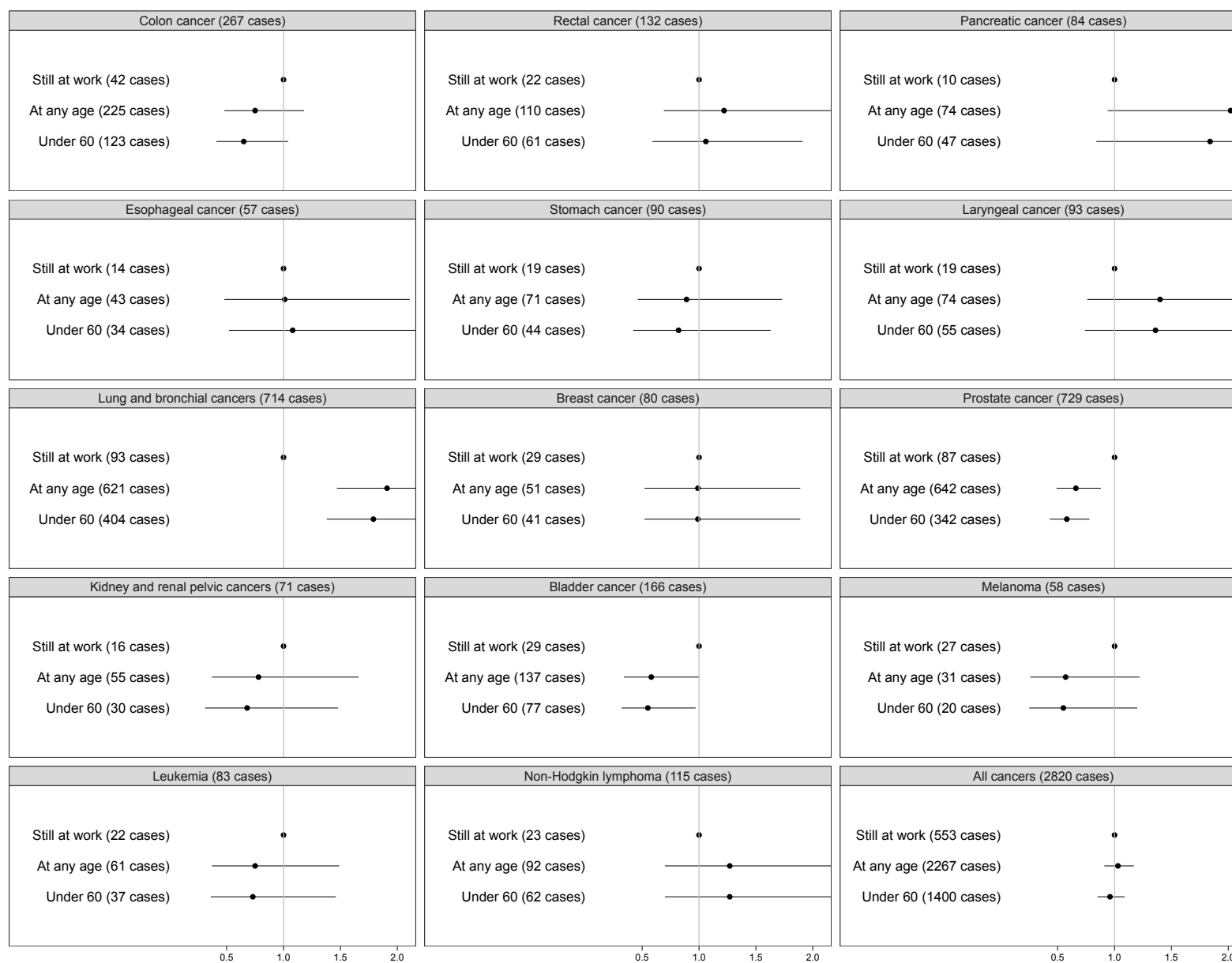
Figure 4: Adjusted hazard ratios for cancer incidence associated with leaving work in the **UAW-GM Cohort** (HWSE Condition 2).

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

	<i>n</i>	HR	(95% CI)	<i>p</i>	
Colon cancer (267 events)					
Still employed	42	1.00	—		
Not employed	225	0.75	(0.48, 1.18)	0.22	
Left work (under 50)	75	0.56	(0.34, 0.93)	0.02	*
Left work (50 or older)	150	0.98	(0.60, 1.59)	0.93	
Left work (under 55)	90	0.59	(0.37, 0.96)	0.03	*
Left work (55 or older)	135	1.10	(0.67, 1.82)	0.70	
Left work (under 60)	123	0.65	(0.41, 1.04)	0.07	
Left work (60 or older)	102	1.18	(0.70, 1.97)	0.54	
Rectal cancer (132 events)					
Still employed	22	1.00	—		
Not employed	110	1.22	(0.69, 2.16)	0.50	
Left work (under 50)	38	0.91	(0.49, 1.71)	0.78	
Left work (50 or older)	72	1.80	(0.95, 3.44)	0.07	
Left work (under 55)	47	0.99	(0.54, 1.81)	0.97	
Left work (55 or older)	63	1.99	(1.02, 3.91)	0.04	*
Left work (under 60)	61	1.06	(0.59, 1.91)	0.85	
Left work (60 or older)	49	2.28	(1.13, 4.62)	0.02	*
Pancreatic cancer (84 events)					
Still employed	10	1.00	—		
Not employed	74	2.02	(0.94, 4.35)	0.07	
Left work (under 50)	25	1.35	(0.59, 3.11)	0.48	
Left work (50 or older)	49	3.23	(1.40, 7.43)	0.01	*
Left work (under 55)	30	1.46	(0.65, 3.28)	0.37	
Left work (55 or older)	44	4.13	(1.72, 9.95)	< 0.005	*

Cancer incidence (including SEER data)

Left work (under 60)	47	1.84	(0.84, 4.01)	0.13	
Left work (60 or older)	27	3.04	(1.23, 7.52)	0.02	*
Esophageal cancer (57 events)					
Still employed	14	1.00	—		
Not employed	43	1.01	(0.48, 2.11)	0.98	
Left work (under 50)	20	0.97	(0.44, 2.15)	0.94	
Left work (50 or older)	23	1.06	(0.46, 2.44)	0.89	
Left work (under 55)	25	1.01	(0.47, 2.16)	0.99	
Left work (55 or older)	18	1.01	(0.42, 2.48)	0.98	
Left work (under 60)	34	1.08	(0.52, 2.27)	0.83	
Left work (60 or older)	9	0.64	(0.22, 1.81)	0.40	
Stomach cancer (90 events)					
Still employed	19	1.00	—		
Not employed	71	0.89	(0.46, 1.73)	0.73	
Left work (under 50)	28	0.73	(0.36, 1.50)	0.39	
Left work (50 or older)	43	1.18	(0.56, 2.50)	0.66	
Left work (under 55)	34	0.78	(0.39, 1.56)	0.47	
Left work (55 or older)	37	1.24	(0.57, 2.70)	0.59	
Left work (under 60)	44	0.82	(0.42, 1.63)	0.58	
Left work (60 or older)	27	1.27	(0.56, 2.90)	0.57	
Laryngeal cancer (93 events)					
Still employed	19	1.00	—		
Not employed	74	1.40	(0.76, 2.58)	0.28	
Left work (under 50)	26	0.89	(0.45, 1.77)	0.74	
Left work (50 or older)	48	2.49	(1.25, 4.94)	0.01	*
Left work (under 55)	35	1.06	(0.56, 2.02)	0.86	
Left work (55 or older)	39	3.06	(1.44, 6.47)	< 0.005	*

Cancer incidence (including SEER data)

Left work (under 60)	55	1.36	(0.74, 2.52)	0.33	
Left work (60 or older)	19	1.70	(0.74, 3.91)	0.21	
Lung and bronchial cancers (714 events)					
Still employed	93	1.00	—		
Not employed	621	1.91	(1.47, 2.48)	< 0.005	*
Left work (under 50)	236	1.47	(1.11, 1.94)	0.01	*
Left work (50 or older)	385	2.76	(2.08, 3.68)	< 0.005	*
Left work (under 55)	304	1.65	(1.26, 2.15)	< 0.005	*
Left work (55 or older)	317	2.87	(2.13, 3.87)	< 0.005	*
Left work (under 60)	404	1.79	(1.38, 2.33)	< 0.005	*
Left work (60 or older)	217	2.66	(1.94, 3.64)	< 0.005	*
Breast cancer (80 events)					
Still employed	29	1.00	—		
Not employed	51	0.99	(0.52, 1.89)	0.99	
Left work (under 50)	27	0.98	(0.50, 1.93)	0.95	
Left work (50 or older)	24	1.02	(0.47, 2.21)	0.95	
Left work (under 55)	32	0.96	(0.49, 1.85)	0.89	
Left work (55 or older)	19	1.16	(0.51, 2.65)	0.72	
Left work (under 60)	41	0.99	(0.52, 1.89)	0.97	
Left work (60 or older)	10	1.07	(0.41, 2.76)	0.89	
Prostate cancer (729 events)					
Still employed	87	1.00	—		
Not employed	642	0.66	(0.49, 0.88)	< 0.005	*
Left work (under 50)	202	0.53	(0.39, 0.73)	< 0.005	*
Left work (50 or older)	440	0.74	(0.55, 1.00)	0.05	
Left work (under 55)	244	0.54	(0.40, 0.73)	< 0.005	*
Left work (55 or older)	398	0.81	(0.60, 1.10)	0.18	

Cancer incidence (including SEER data)

Left work (under 60)	342	0.58	(0.43, 0.78)	< 0.005	*
Left work (60 or older)	300	0.86	(0.63, 1.19)	0.37	
Kidney and renal pelvic cancers (71 events)					
Still employed	16	1.00	—		
Not employed	55	0.78	(0.37, 1.66)	0.52	
Left work (under 50)	15	0.49	(0.21, 1.15)	0.10	
Left work (50 or older)	40	1.37	(0.58, 3.22)	0.47	
Left work (under 55)	20	0.57	(0.25, 1.30)	0.18	
Left work (55 or older)	35	1.49	(0.61, 3.63)	0.39	
Left work (under 60)	30	0.68	(0.31, 1.48)	0.34	
Left work (60 or older)	25	1.31	(0.53, 3.28)	0.56	
Bladder cancer (166 events)					
Still employed	29	1.00	—		
Not employed	137	0.58	(0.34, 1.00)	0.05	
Left work (under 50)	38	0.41	(0.22, 0.76)	< 0.005	*
Left work (50 or older)	99	0.72	(0.40, 1.28)	0.27	
Left work (under 55)	52	0.48	(0.27, 0.87)	0.02	*
Left work (55 or older)	85	0.71	(0.39, 1.28)	0.26	
Left work (under 60)	77	0.55	(0.32, 0.97)	0.04	*
Left work (60 or older)	60	0.64	(0.35, 1.19)	0.16	
Melanoma (58 events)					
Still employed	27	1.00	—		
Not employed	31	0.57	(0.26, 1.22)	0.15	
Left work (under 50)	14	0.53	(0.23, 1.17)	0.12	
Left work (50 or older)	17	0.72	(0.27, 1.97)	0.53	
Left work (under 55)	17	0.55	(0.25, 1.21)	0.14	
Left work (55 or older)	14	0.65	(0.23, 1.86)	0.42	

Cancer incidence (including SEER data)

Left work (under 60)	20	0.55	(0.25, 1.20)	0.13	
Left work (60 or older)	11	0.73	(0.24, 2.19)	0.57	
Leukemia (83 events)					
Still employed	22	1.00	—		
Not employed	61	0.75	(0.37, 1.49)	0.41	
Left work (under 50)	23	0.66	(0.32, 1.39)	0.27	
Left work (50 or older)	38	0.94	(0.42, 2.13)	0.89	
Left work (under 55)	30	0.72	(0.36, 1.47)	0.37	
Left work (55 or older)	31	0.84	(0.36, 1.95)	0.68	
Left work (under 60)	37	0.73	(0.36, 1.46)	0.37	
Left work (60 or older)	24	0.91	(0.38, 2.21)	0.84	
Non-Hodgkin lymphoma (115 events)					
Still employed	23	1.00	—		
Not employed	92	1.27	(0.70, 2.31)	0.43	
Left work (under 50)	44	1.36	(0.73, 2.52)	0.33	
Left work (50 or older)	48	1.13	(0.58, 2.23)	0.72	
Left work (under 55)	48	1.24	(0.67, 2.28)	0.49	
Left work (55 or older)	44	1.38	(0.68, 2.79)	0.37	
Left work (under 60)	62	1.27	(0.70, 2.31)	0.44	
Left work (60 or older)	30	1.31	(0.61, 2.79)	0.49	
All cancers (2820 events)					
Still employed	553	1.00	—		
Not employed	2267	1.03	(0.91, 1.17)	0.60	
Left work (under 50)	839	0.83	(0.73, 0.95)	0.01	*
Left work (50 or older)	1428	1.37	(1.20, 1.57)	< 0.005	*
Left work (under 55)	1043	0.89	(0.78, 1.01)	0.07	
Left work (55 or older)	1224	1.48	(1.28, 1.70)	< 0.005	*



Cancer incidence (including SEER data)

Left work (under 60)	1400	0.96	(0.85, 1.09)	0.53	
Left work (60 or older)	867	1.45	(1.25, 1.68)	< 0.005	*

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