DOI: 10.1289/EHP13380

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Supplemental Material

Lung Cancer Risks Associated with Occupational Exposure to Pairs of Five Lung Carcinogens: Results from a Pooled Analysis of Case-Control Studies (SYNERGY)

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Table S1. Pairwise interactions between five occupational lung carcinogens (asbestos, chromium-VI, nickel, PAH, and silica) in relation to lung cancer risk overall and for major lung cancer subtypes in male workers in SYNERGY pooled analyses

Combinations of occupational exposures		Lu	ung cancer	Aden	ocarcinoma	Squamous cell cancers		Small cell lung cancer		
MEN	Controls N=16451	Cases N=13605	OR (95% CI)	Cases N=3325	OR (95% CI)	Cases N=5828	OR (95% CI)	Cases N=2200	OR (95% CI)	
Asbestos & chromium-VI										
Never exposed to both	8122	5121	1 [Reference]	1416	1 [Reference]	1991	1 [Reference]	817	1 [Reference]	
Never exposed to asbestos and ever exposed to chromium-VI	1527	1526	1.34 (1.22, 1.46)	332	1.12 (0.96, 1.29)	692	1.54 (1.36, 1.72)	254	1.43 (1.19, 1.67)	
Ever exposed to asbestos and never exposed to chromium-VI	4509	4353	1.32 (1.24, 1.40)	1013	1.17 (1.06, 1.28)	1954	1.45 (1.33, 1.57)	682	1.26 (1.11, 1.41)	
Ever exposed to both	2293	2605	1.47 (1.35, 1.58)	564	1.26 (1.11, 1.41)	1191	1.62 (1.46, 1.78)	447	1.54 (1.32, 1.75)	
p-value multiplicative interaction			0.002		0.63		<0.001		0.16	
RERI			-0.19(-0.36, -0.03)		-0.04 (-0.26, 0.18)		-0.37 (-0.61, -0.14)		-0.15 (-0.46, 0.16)	
Asbestos & nickel										
Never exposed to both	8507	5576	1 [Reference]	1523	1 [Reference]	2191	1 [Reference]	901	1 [Reference]	
Never exposed to asbestos and ever exposed to nickel	1142	1071	1.24 (1.12, 1.37)	225	1.01 (0.84, 1.17)	492	1.41 (1.22, 1.59)	170	1.31 (1.06, 1.56)	
Ever exposed to asbestos and never exposed to nickel	4804	4813	1.32 (1.24, 1.4)	1099	1.15 (1.04, 1.26)	2156	1.43 (1.31, 1.54)	789	1.29 (1.15, 1.44)	
Ever exposed to both	1998	2145	1.38 (1.27, 1.49)	478	1.23 (1.08, 1.38)	989	1.50 (1.34, 1.65)	340	1.34 (1.14, 1.54)	
p-value multiplicative interaction			0.01		0.56		<0.001		0.06	
RERI			-0.18 (-0.35, -0.01)		0.08 (-0.15, 0.3)		-0.34 (-0.57, -0.1)		-0.26 (-0.58, 0.06)	
Asbestos & PAH										
Never exposed to both	8343	5537	1 [Reference]	1477	1 [Reference]	2201	1 [Reference]	893	1 [Reference]	
Never exposed to asbestos and ever exposed to PAH	1306	1110	1.06 (0.95, 1.16)	271	0.99 (0.84, 1.14)	482	1.12 (0.98, 1.27)	178	1.19 (0.97, 1.41)	
Ever exposed to asbestos and never exposed to PAH	4031	4047	1.30 (1.21, 1.38)	952	1.19 (1.08, 1.31)	1803	1.37 (1.25, 1.48)	666	1.29 (1.14, 1.44)	
Ever exposed to both	2771	2911	1.31 (1.22, 1.41)	625	1.14 (1.01, 1.27)	1342	1.45 (1.31, 1.58)	463	1.30 (1.13, 1.48)	
p-value multiplicative interaction			0.49		0.70		0.48		0.17	
RERI			-0.04 (-0.19, 0.1)		-0.05 (-0.25, 0.16)		-0.04 (-0.24, 0.16)		-0.18 (-0.46, 0.11)	

Asbestos & silica									
Never exposed to both	7971	5050	1 [Reference]	1383	1 [Reference]	1972	1 [Reference]	789	1 [Reference]
Never exposed to asbestos and ever exposed to silica	1678	1597	1.35 (1.23, 1.47)	365	1.20 (1.03, 1.37)	711	1.48 (1.31, 1.65)	282	1.44 (1.21, 1.67)
Ever exposed to asbestos and never exposed to silica	4340	3906	1.27 (1.19, 1.35)	982	1.20 (1.08, 1.31)	1665	1.33 (1.21, 1.44)	602	1.23 (1.08, 1.38)
Ever exposed to both	2462	3052	1.57 (1.45, 1.69)	595	1.26 (1.11, 1.41)	1480	1.80 (1.63, 1.97)	527	1.61 (1.39, 1.83)
p-value multiplicative interaction			0.14		0.16		0.24		0.40
RERI			-0.05 (-0.21, 0.11)		-0.14 (-0.36, 0.08)		-0.01 (-0.23, 0.21)		-0.06 (-0.35, 0.24)
Chromium-VI & PAH									
Never exposed to both	10794	7785	1 [Reference]	2028	1 [Reference]	3207	1 [Reference]	1231	1 [Reference]
Never exposed to chromium-VI and ever exposed to PAH	1837	1689	1.09 (1.00, 1.18)	401	1.01 (0.88, 1.14)	738	1.16 (1.03, 1.28)	268	1.12 (0.94, 1.29)
Ever exposed to chromium-VI and never exposed to PAH	1580	1799	1.35 (1.23, 1.46)	401	1.20 (1.04, 1.35)	797	1.44 (1.29, 1.59)	328	1.45 (1.24, 1.67)
Ever exposed to both	2240	2332	1.23 (1.13, 1.32)	495	1.08 (0.95, 1.21)	1086	1.33 (1.21, 1.46)	373	1.32 (1.14, 1.5)
p-value multiplicative interaction			0.01		0.30		0.01		0.09
RERI			-0.21 (-0.37, -0.05)		-0.12 (-0.35, 0.1)		-0.27 (-0.48, -0.05)		-0.25 (-0.55, 0.06)
Chromium-VI & silica									
Never exposed to both	10081	6932	1 [Reference]	1908	1 [Reference]	2732	1 [Reference]	1083	1 [Reference]
Never exposed to chromium-VI and ever exposed to silica	2550	2542	1.28 (1.19, 1.38)	521	1.05 (0.93, 1.17)	1213	1.44 (1.3, 1.57)	416	1.28 (1.1, 1.45)
Ever exposed to chromium-VI and never exposed to silica	2230	2024	1.17 (1.08, 1.27)	457	1.02 (0.90, 1.14)	905	1.27 (1.14, 1.39)	308	1.19 (1.01, 1.36)
Ever exposed to both	1590	2107	1.55 (1.42, 1.68)	439	1.31 (1.14, 1.48)	978	1.75 (1.57, 1.93)	393	1.74 (1.49, 2.00)
p-value multiplicative interaction			0.67		0.05		0.64		0.23
RERI			0.09 (-0.07, 0.26)		0.24 (0.02, 0.46)		0.05 (-0.18, 0.28)		0.28 (-0.03, 0.59)
Nickel & PAH									
Never exposed to both	11383	8551	1 [Reference]	2188	1 [Reference]	3546	1 [Reference]	1397	1 [Reference]
Never exposed to nickel and ever exposed to PAH	1928	1838	1.10 (1.01, 1.19)	434	1.02 (0.89, 1.14)	801	1.15 (1.04, 1.27)	293	1.10 (0.94, 1.26)
Ever exposed to nickel and never exposed to PAH	991	1033	1.26 (1.13, 1.39)	241	1.17 (0.98, 1.36)	458	1.31 (1.14, 1.49)	162	1.17 (0.94, 1.39)

Ever exposed to both	2149	2183	1.17 (1.08, 1.26)	462	1.05 (0.92, 1.17)	1023	1.26 (1.14, 1.38)	348	1.22 (1.05, 1.39)
p-value multiplicative interaction			0.02		0.27		0.05		0.72
RERI			-0.19 (-0.36, -0.01)		-0.14 (-0.39, 0.11)		-0.20 (-0.43, 0.03)		-0.04 (-0.35, 0.26)
Nickel & silica									
Never exposed to both	10107	6972	1 [Reference]	1917	1 [Reference]	2749	1 [Reference]	1086	1 [Reference]
Never exposed to nickel and ever exposed to silica	3204	3417	1.34 (1.25, 1.43)	705	1.10 (0.98, 1.21)	1598	1.5 (1.37, 1.63)	604	1.43 (1.26, 1.6)
Ever exposed to nickel and never exposed to silica	2204	1984	1.17 (1.07, 1.26)	448	1.01 (0.89, 1.14)	888	1.26 (1.13, 1.38)	305	1.20 (1.02, 1.37)
Ever exposed to both	936	1232	1.55 (1.39, 1.71)	255	1.34 (1.12, 1.56)	593	1.75 (1.53, 1.97)	205	1.61 (1.32, 1.91)
p-value multiplicative interaction			0.97		0.09		0.37		0.65
RERI			0.05 (-0.14, 0.24)		0.23 (-0.02, 0.48)		-0.01 (-0.27, 0.25)		-0.01 (-0.36, 0.34)
PAH & silica									
Never exposed to both	9468	6455	1 [Reference]	1772	1 [Reference]	2546	1 [Reference]	1012	1 [Reference]
Never exposed to PAH and ever exposed to silica	2906	3129	1.36 (1.26, 1.45)	657	1.13 (1.00, 1.25)	1458	1.53 (1.39, 1.67)	547	1.44 (1.26, 1.62)
Ever exposed to PAH and never exposed to silica	2843	2501	1.11 (1.03, 1.19)	593	0.99 (0.88, 1.10)	1091	1.21 (1.09, 1.32)	379	1.16 (1.00, 1.31)
Ever exposed to both	1234	1520	1.44 (1.30, 1.57)	303	1.19 (1.02, 1.37)	733	1.64 (1.45, 1.83)	262	1.54 (1.28, 1.8)
p-value multiplicative interaction			0.46		0.49		0.14		0.50
RERI			-0.03 (-0.19, 0.14)		0.08 (-0.14, 0.3)		-0.1 (-0.33, 0.13)		-0.05 (-0.37,0.26)

ORs were adjusted for study centre, age group (category), smoking pack-years (current and former smokers: <10, 10-19, and \geq 20 pack-years, never-smokers) and time since quitting smoking (current smokers; former smokers: <7, 8–15, 16–25, and \geq 26 years; never-smokers).

Table S2. Pairwise interactions between five occupational lung carcinogens (asbestos, chromium VI, nickel, PAH, and silica) in relation to lung cancer risk overall and for major lung cancer subtypes in female workers in SYNERGY pooled analyses

	Lu	ing cancer	Ade	nocarcinoma	Squar	mous cell cancers	Small cell lung cancer		
Controls N=4514	Cases N=3296	OR (95% CI)	Cases N=1427	OR (95% CI)	Cases N=675	OR (95% CI)	Cases N=530	OR (95% CI)	
3915	2726	1 [Reference]	1216	1 [Reference]	539	1 [Reference]	416	1 [Reference]	
89	88	1.15 (0.75, 1.54)	33	1.08 (0.60,1.55)	19	1.11 (0.45, 1.77)	20	1.96 (0.73,3.2)	
453	411	1.11 (0.93, 1.3)	156	0.99 (0.78, 1.2)	100	1.26 (0.90, 1.61)	77	1.37 (0.92,1.82)	
57	71	1.32 (0.79,1.85)	22	0.93 (0.43, 1.43)	17	1.10 (0.39, 1.82)	17	2.99 (0.94,5.03)	
		0.89		0.71		0.61		0.84	
		0.06 (-0.61,0.74)		-0.14 (-0.85, 0.57)		-0.26 (-1.27, 0.75)		0.65 (-1.72,3.01)	
3923	2730	1 [Reference]	1218	1 [Reference]	539	1 [Reference]	418	1 [Reference]	
81	84	1.26 (0.81, 1.71)	31	1.18 (0.64, 1.72)	19	1.25 (0.5,2.01)	18	2.10 (0.71,3.48)	
460	415	1.11 (0.93, 1.3)	159	1.00 (0.79, 1.21)	99	1.24(0.89,1.59)	79	1.42 (0.96,1.89)	
50	67	1.38 (0.8,1.96)	19	0.91(0.39,1.43)	18	1.26 (0.43, 2.08)	15	2.56 (0.71,4.41)	
		0.95		0.50		0.65		0.76	
		0.01 (-0.74, 0.75)		-0.27 (-1.03, 0.5)		-0.24 (-1.38, 0.91)		0.04(-2.26,2.34)	
8343	5537	1 [Reference]	1477	1 [Reference]	2201	1 [Reference]	893	1 [Reference]	
478	446	1.19 (1.0, 1.38)	176	1.09 (0.86, 1.31)	105	1.61 (1.17, 2.05)	92	1.75 (1.21, 2.30)	
352	310	1.10 (0.90, 1.31)	126	1.03 (0.78, 1.27)	66	1.15 (0.77, 1.54)	60	1.51 (0.96, 2.07)	
158	172	1.31 (0.97, 1.65)	52	0.92 (0.6, 1.25)	51	1.71 (1.02, 2.39)	34	2.00 (1.03, 2.98)	
		0.98		0.41		0.76		0.40	
		0.02 (-0.41, 0.44)		-0.19 (-0.63, 0.26)		-0.06 (-0.9, 0.78)		-0.26 (-1.44, 0.92)	
3719	2617	1 [Reference]	1167	1 [Reference]	517	1 [Reference]	397	1 [Reference]	
285			82	1.06 (0.77, 1.35)	41	-	39	1.27 (0.69, 1.85)	
447			151	0.92 (0.72, 1.13)	98	1.15 (0.82, 1.48)	73	1.26 (0.84, 1.68)	
63	77	1.57 (0.97, 2.16)	27	1.46 (0.75, 2.17)	19	1.91 (0.70, 3.12)	21	4.32 (1.35, 7.29)	
		0.13		0.19		0.24		0.02	
+	1	0.46 (-0.18, 1.1)	}	0.47 (-0.30, 1.24)	 	0.72 (-0.55, 1.99)	1	2.79 (-0.19, 5.76)	
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Chromium-VI & PAH									
Never exposed to both	3830	2630	1 [Reference]	1176	1 [Reference]	512	1 [Reference]	393	1 [Reference]
Never exposed to chromium-VI and ever exposed to PAH	538	507	1.20 (1.02, 1.39)	196	1.08 (0.87, 1.29)	127	1.65 (1.23,2.07)	100	1.57 (1.11, 2.04)
Ever exposed to chromium-VI and never exposed to PAH	48	48	1.19 (0.65, 1.73)	23	1.37 (0.63,2.12)	7	0.71(0.07,1.35)	11	1.85 (0.35,3.35)
Ever exposed to both	98	111	1.25 (0.85,1.65)	32	0.86 (0.48, 1.24)	29	1.36 (0.67, 2.06)	26	2.77 (1.19, 4.36)
p-value multiplicative interaction			0.64		0.13		0.78		0.93
RERI			-0.14 (-0.83,0.54)		-0.60 (-1.45, 0.25)		0.00 (-1.00, 1.00)		0.35 (-1.82, 2.53)
Chromium-VI & silica									
Never exposed to both	4053	2894	1 [Reference]	1273	1 [Reference]	582	1 [Reference]	449	1 [Reference]
Never exposed to chromium-VI and ever exposed to silica	315	243	1.13 (0.90, 1.36)	99	1.18 (0.88,1.49)	57	1.32 (0.84,1.79)	44	1.29 (0.72,1.86)
Ever exposed to chromium-VI and never exposed to silica	113	128	1.22 (0.86,1.58)	45	1.08 (0.66, 1.49)	33	1.24 (0.65,1.84)	21	1.53 (0.65, 2.42)
Ever exposed to both	33	31	1.17 (0.52, 1.83)	10	0.86 (0.2, 1.53)	3	0.48 (-0.13, 1.09)	16	5.80 (1.10, 10.51)
p-value multiplicative interaction			0.62		0.38		0.06		0.05
RERI			-0.18 (-0.95,0.59)		-0.40 (-1.22, 0.43)		-1.09 (-2.06, -0.11)		3.98 (-0.76,8.72)
Nickel & PAH									
Never exposed to both	3845	2638	1 [Reference]	1181	1 [Reference]	512	1 [Reference]	396	1 [Reference]
Never exposed to nickel and ever exposed to PAH	538		1.21 (1.03, 1.39)	196	1.09(0.88,1.3)	126	1.66 (1.24,2.07)	101	1.59 (1.12, 2.07)
Ever exposed to nickel and never exposed to PAH	33	40	1.57 (0.75,2.38)	18	1.76(0.67,2.85)	7	1.05 (0.04,2.06)	8	1.84 (0.10, 3.57)
Ever exposed to hicker and never exposed to FAIT	98	111	1.24 (0.85,1.64)	32	0.86 (0.48,1.24)	30	1.40 (0.69,2.1)	25	2.56 (1.09, 4.02)
p-value multiplicative interaction	36	111	0.18	32	0.86 (0.48,1.24)	30	0.70	23	0.81
RERI			-0.53 (-1.45, 0.39)		-0.98 (-2.15, 0.18)		-0.31 (-1.58, 0.96)		0.12 (-2.16,2.40)
Nickel & silica									
Never exposed to both	4055	2896	1 [Reference]	1275	1 [Reference]	582	1 [Reference]	449	1 [Reference]
Never exposed to nickel and ever exposed to silica	328	249	1.11 (0.89, 1.33)	102	1.16 (0.86, 1.45)	56	1.24 (0.79, 1.69)	48	1.41 (0.8, 2.01)
Ever exposed to nickel and never exposed to silica	111	126	1.25 (0.87,1.62)	43	1.08(0.66,1.50)	33	1.29 (0.67, 1.91)	21	1.61 (0.67, 2.55)
Ever exposed to both	20	25	1.59 (0.52, 2.66)	7	1.05 (0.06, 2.04)	4	0.88 (-0.23, 1.99)	12	5.86 (0.26, 11.45)
p-value multiplicative interaction			0.72		0.74		0.39		0.11
RERI			0.23(-0.91,1.37)		-0.19 (-1.29, 0.92)		-0.65 (-1.98, 0.68)		3.84 (-1.81, 9.48)
PAH & silica									
Never exposed to both	3587	2480	1 [Reference]	1113	1 [Reference]	480	1 [Reference]	368	1 [Reference]
			_ []		_ []	, ,,,	_ [300	_ [
Never exposed to PAH and ever exposed to silica		198	1.03 (0.80 1.25)	86	1.10 (0.80 1.4)	39	1.04 (0.62 1 47)	36	1.19 (0.63 1.76)
Never exposed to PAH and ever exposed to silica Ever exposed to PAH and never exposed to silica	291 579		1.03 (0.80, 1.25) 1.15 (0.98, 1.33)	86 205	1.10 (0.80, 1.4) 1.02 (0.82, 1.21)	39 135	1.04 (0.62, 1.47) 1.53 (1.15, 1.91)	36 102	1.19 (0.63, 1.76) 1.48 (1.05, 1.91)

p-value multiplicative interaction		0.09	0.48	0.30	0.01
RERI		0.58 (-0.14, 1.30)	0.27 (-0.52, 1.06)	0.82 (-0.75, 2.39)	3.45 (0.10, 6.8)

ORs were adjusted for study centre, age group (category), smoking pack-years (current and former smokers: <10, 10-19, and \geq 20 pack-years, never-smokers) and time since quitting smoking (current smokers; former smokers: <7, 8–15, 16–25, and \geq 26 years; never-smokers).

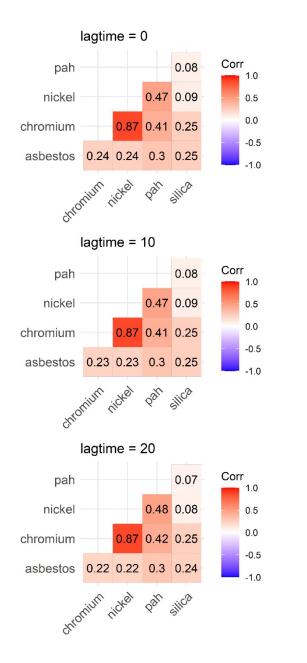
Table S3. Risk of lung cancer (OR), relative excess risk due to interaction (RERI), and test for multiplicative interaction (P-value) associated with single and pairwise combinations of occupational exposure to asbestos, chromium VI, nickel, PAH, and silica in male workers in SYNERGY by smoking status (never, former, and current cigarette smokers)

Combinations of occupational exposures in men	Never Sm	okers		Former S	mokers		Current Smokers*			
	Control s N=4437	Cases N=49 0	OR (95% CI)	Control s N=7328	Cases N=478 7	OR (95% CI)	Control s N=4686	Cases N=832 8	OR (95% CI)	
Asbestos & chromium-VI										
Never exposed to both	2517	240		3502	1857		2103	3024		
Ever exposed to asbestos and never exposed to chromium-VI	1075	134	1.38 (1.06, 1.7)	2038	1533	1.38 (1.25, 1.51)	1396	2686	1.25 (1.14, 1.37)	
Never exposed to asbestos and ever exposed to chromium-VI	374	45	1.34 (0.88, 1.8)	691	508	1.29 (1.11, 1.46)	462	973	1.39 (1.20, 1.57)	
Ever exposed to both	471	71	1.81 (1.28, 2.34)	1097	889	1.46 (1.29, 1.63)	725	1645	1.42 (1.26, 1.58)	
p-value multiplicative interaction			0.92			0.04			0.02	
RERI			0.09 (-0.60,0.77)			-0.20 (-0.45, 0.04)			-0.22 (-0.45, 0.02)	
Asbestos & nickel										
Never exposed to both	2611	258		3686	2007		2210	3311		
Ever exposed to asbestos and never exposed to nickel	1124	144	1.37 (1.06, 1.67)	2181	1684	1.39 (1.26, 1.51)	1499	2985	1.24 (1.13, 1.35)	
Never exposed to asbestos and ever exposed to nickel	280	27	1.08 (0.62, 1.53)	507	358	1.27 (1.07, 1.47)	355	686	1.24 (1.06, 1.43)	
Ever exposed to both	422	61	1.68 (1.16, 2.20)	954	738	1.39 (1.22, 1.55)	622	1346	1.32 (1.17, 1.48)	
p-value multiplicative interaction			0.63			0.02			0.11	
RERI			0.23 (-0.45, 0.91)			-0.27 (-0.53,0.00)			-0.16 (-0.40,0.08)	
Asbestos & PAH				1						
Never exposed to both	2598	250		3596	1996		2149	3291		
Ever exposed to asbestos and never exposed to PAH	949	129	1.48 (1.13, 1.82)	1828	1423	1.36 (1.22, 1.49)	1254	2495	1.21 (1.09, 1.32)	
Never exposed to asbestos and ever exposed to PAH	293	35	1.25 (0.77, 1.72)	597	369	1.02 (0.86, 1.17)	416	706	1.05 (0.90, 1.19)	
Ever exposed to both	597	76	1.47 (1.06, 1.89)	1307	999	1.33 (1.18, 1.47)	867	1836	1.26 (1.13, 1.40)	
p-value multiplicative interaction			0.37			0.68			1.00	
RERI			-0.25 (-0.91, 0.40)			-0.05 (-0.27, 0.17)			0.01 (-0.19, 0.21)	
Asbestos & silica										
Never exposed to both	2412	229		3414	1750		2145	3071		
Ever exposed to asbestos and never exposed to silica	1053	129	1.41 (1.08, 1.74)	1938	1327	1.31 (1.18, 1.44)	1349	2450	1.21 (1.10, 1.32)	
Never exposed to asbestos and ever exposed to silica	479	56	1.34 (0.91, 1.76)	779	615	1.34 (1.16, 1.51)	420	926	1.38 (1.19, 1.56)	
Ever exposed to both	493	76	1.77 (1.25, 2.29)	1197	1095	1.64 (1.45, 1.82)	772	1881	1.46 (1.30, 1.62)	

p-value multiplicative interaction			0.79			0.44			0.14
RERI			0.03 (-0.62, 0.67)			-0.01 (-0.26,			-0.13 (-0.36,
						0.23)			0.11)
Chromium-VI & PAH									
Never exposed to both	3182	323		4702	2810		2910	4652	
Ever exposed to chromium-VI and never exposed to PAH	365	56	1.57 (1.08,2.05)	722	609	1.32 (1.15, 1.49)	493	1134	1.34 (1.17, 1.50)
Never exposed to chromium-VI and ever exposed to PAH	410	51	1.23 (0.84,1.62)	838	580	1.09 (0.95,1.23)	589	1058	1.06 (0.94,1.18)
Ever exposed to both	480	60	1.37 (0.96,1.78)	1066	788	1.18 (1.04, 1.31)	694	1484	1.25 (1.11, 1.38)
p-value multiplicative interaction			0.19			0.05			0.17
RERI			-0.42 (-1.13, 0.28)			-0.23 (-0.47, 0.01)			-0.15 (-0.38, 0.08)
Chromium-VI & silica									
Never exposed to both	2946	295		4335	2404		2800	4233	1073
Ever exposed to chromium-VI and never exposed to silica	519	63	1.35 (0.96, 1.75)	1017	673	1.14 (1.01, 1.28)	694	1288	1.18 (1.05, 1.31)
Never exposed to chromium-VI and ever exposed to silica	646	79	1.30 (0.94,1.66)	1205	986	1.31 (1.17, 1.45)	699	1477	1.23 (1.10, 1.37)
Ever exposed to both	326	53	1.73 (1.17, 2.29)	771	724	1.51 (1.33, 1.70)	493	1330	1.55 (1.36, 1.74)
p-value multiplicative interaction			0.95			0.92			0.50
RERI			0.08 (-0.63, 0.78)			0.06 (-0.18, 0.3)			0.14 (-0.1, 0.38)
Nickel & PAH									
Never exposed to both	3305	347		4988	3071		3090	5133	
Ever exposed to nickel and never exposed to PAH	242	32	1.35 (0.82, 1.88)	436	348	1.30 (1.09, 1.51)	313	653	1.21 (1.03, 1.39)
Never exposed to nickel and ever exposed to PAH	430	55	1.22 (0.85,1.60)	879	620	1.09 (0.96, 1.22)	619	1163	1.07 (0.95,1.19)
Ever exposed to both	460	56	1.30 (0.90, 1.70)	1025	748	1.14 (1.01, 1.27)	664	1379	1.18 (1.05, 1.31)
p-value multiplicative interaction			0.40			0.06			0.35
RERI			-0.27 (-1.00, 0.46)			-0.25 (-0.51, 0.02)			-0.11(-0.35,0.13)
Nickel & silica									
Never exposed to both	2949	297		4347	2421		2811	4254	
Ever exposed to nickel and never exposed to silica	516	61	1.31 (0.92, 1.7)	1005	656	1.13 (0.99, 1.26)	683	1267	1.18 (1.05, 1.31)
Never exposed to nickel and ever exposed to silica	786	105	1.40 (1.05, 1.74)	1520	1270	1.32 (1.19, 1.46)	898	2042	1.33 (1.2, 1.46)
Ever exposed to both	186	27	1.62 (0.92, 2.33)	456	440	1.60 (1.35, 1.84)	294	765	1.48 (1.26, 1.71)
p-value multiplicative interaction			0.67			0.50			0.59
RERI			-0.08 (-0.90, 0.74)			0.15 (-0.13, 0.43)			-0.02 (-0.29, 0.24)
PAH & silica					1				

Never exposed to both	2815	278		4056	2253		2597	3924	
Ever exposed to PAH and never exposed to silica	650	80	1.34 (0.98,1.7)	1296	824	1.05 (0.94, 1.17)	897	1597	1.12 (1.01, 1.23)
Never exposed to PAH and ever exposed to silica	732	101	1.48 (1.10, 1.86)	1368	1166	1.33 (1.19, 1.47)	806	1862	1.35 (1.21, 1.49)
Ever exposed to both	240	31	1.41 (0.84,1.98)	608	544	1.47 (1.27, 1.68)	386	945	1.38 (1.19, 1.57)
p-value multiplicative interaction			0.19			0.58			0.33
RERI			-0.41 (-1.13,			0.09 (-0.15, 0.34)			-0.09 (-0.32,
			0.31)						0.15)

All models were adjusted for study centre and age group (category). For current smokers, models were also adjusted for smoking pack-years (log[cPY+1]). For former smokers, models were also adjusted for smoking pack-years and time since quitting smoking (<7, 8–15, 16–25, and \ge 26 years).



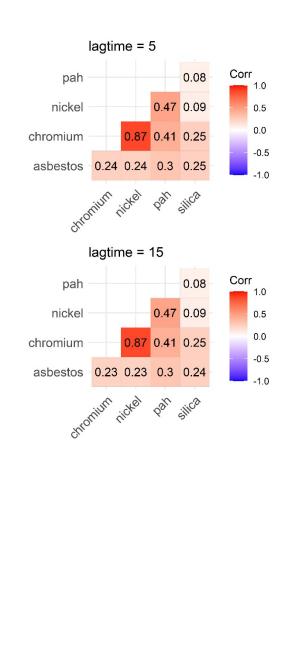


Figure S1. Heatmaps of Cramer's V statistics (Corr) between the never/ever occupational exposures by lag time in years