

**Ischaemic Heart Disease mortality and occupational radiation exposure in a nested matched case-control study of British nuclear fuel cycle workers: investigation of confounding by lifestyle, physiological traits and occupational exposures**

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## **ONLINE SUPPLEMENTARY MATERIALS**

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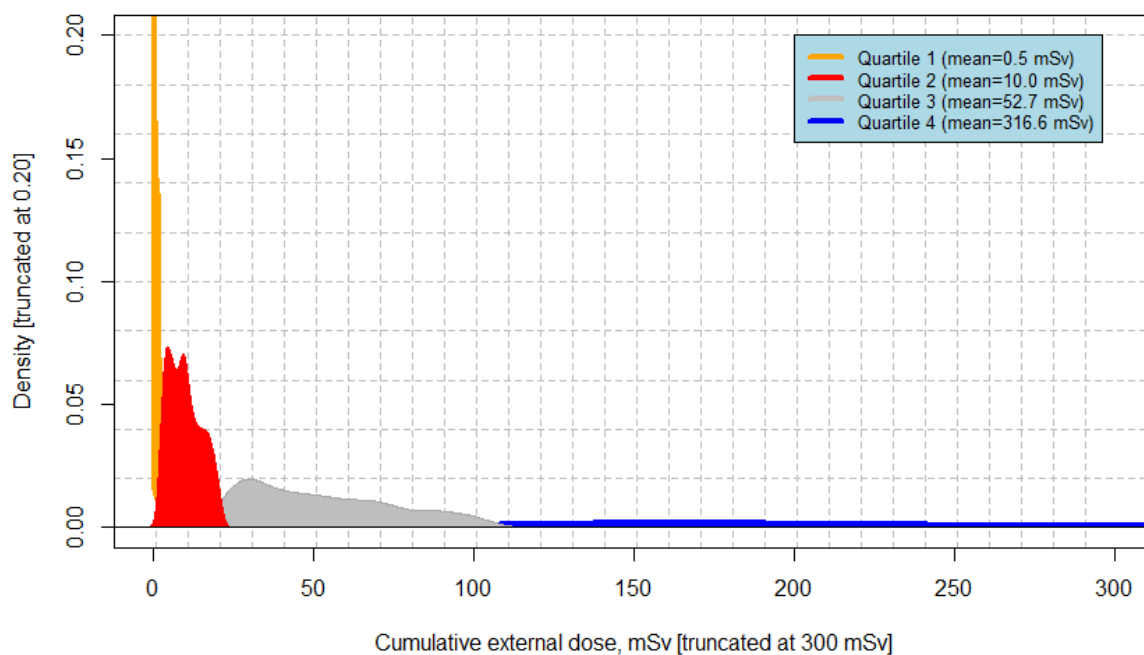
**Table S1.** Bivariate associations between population factors included in the study and IHD mortality

Population factor	N cases	N controls	Odds Ratio	95% Confidence Interval	p-value
Site					
Sellafield	651	651		*	
Springfields	569	569			
Cumulative unlagged external radiation dose, mSv (arithmetic mean)					
<2.6 (0.48)	306	301	1.00		
2.6-21.4 (9.99)	304	307	0.97	0.77-1.22	0.79
21.4-102.8 (52.68)	305	321	0.94	0.75-1.18	0.59
102.8-1655.8 (316.63)	305	291	1.04	0.81-1.34	0.74
Log-linear trend (per 100 mSv)			0.99	0.94-1.05	0.72
Cumulative unlagged internal radiation dose, mSv (arithmetic mean)					
0.01-2.89	187	218	1.00		
2.89-52.28	187	224	0.98	0.73-1.31	0.90
52.28-5,057.27	188	185	1.38	0.98-1.96	0.07
unmonitored	658	593	1.41	1.09-1.81	0.01
Age of death (or censoring) (years, in quartiles)					
27.1-56.0	307	315	1.00		
56.1-63.1	309	302	4.99	1.09-22.80	0.04
63.2-68.5	301	297	5.12	0.96-27.22	0.06
68.6-77.0	303	306	3.41	0.48-24.33	0.22
Monitored for internal radiation					
no	658	593	1.00		
yes	562	627	0.80	0.68-0.94	0.01
Employment duration in years (censored)	11.1 (0.1-41.6)	10.8 (0.1-40.5)	1.00	0.99-1.01	0.45
Age at start of employment, years. Mean (range)	36.2 (15.9-51.0)	36.5 (15.8-50.9)	1.21	1.09-1.35	0.00
Decade of employment start					
<1949	41	39	1.00		
1950-1959	809	817	0.90	0.49-1.68	0.75
1960-1969	258	257	1.89	0.57-5.77	0.32
>1970	112	107	10.86	0.97-121.4	0.05
Socio-economic status <sup>1</sup>					
1-2 (highest)	15	22	1.00		
3	473	508	1.33	0.68-2.58	0.40
4	647	608	1.54	0.79-2.99	0.20
5 (lowest)	43	31	2.05	0.92-4.56	0.08
missing	42	51	1.17	0.53-2.57	0.69
Longest-held job					

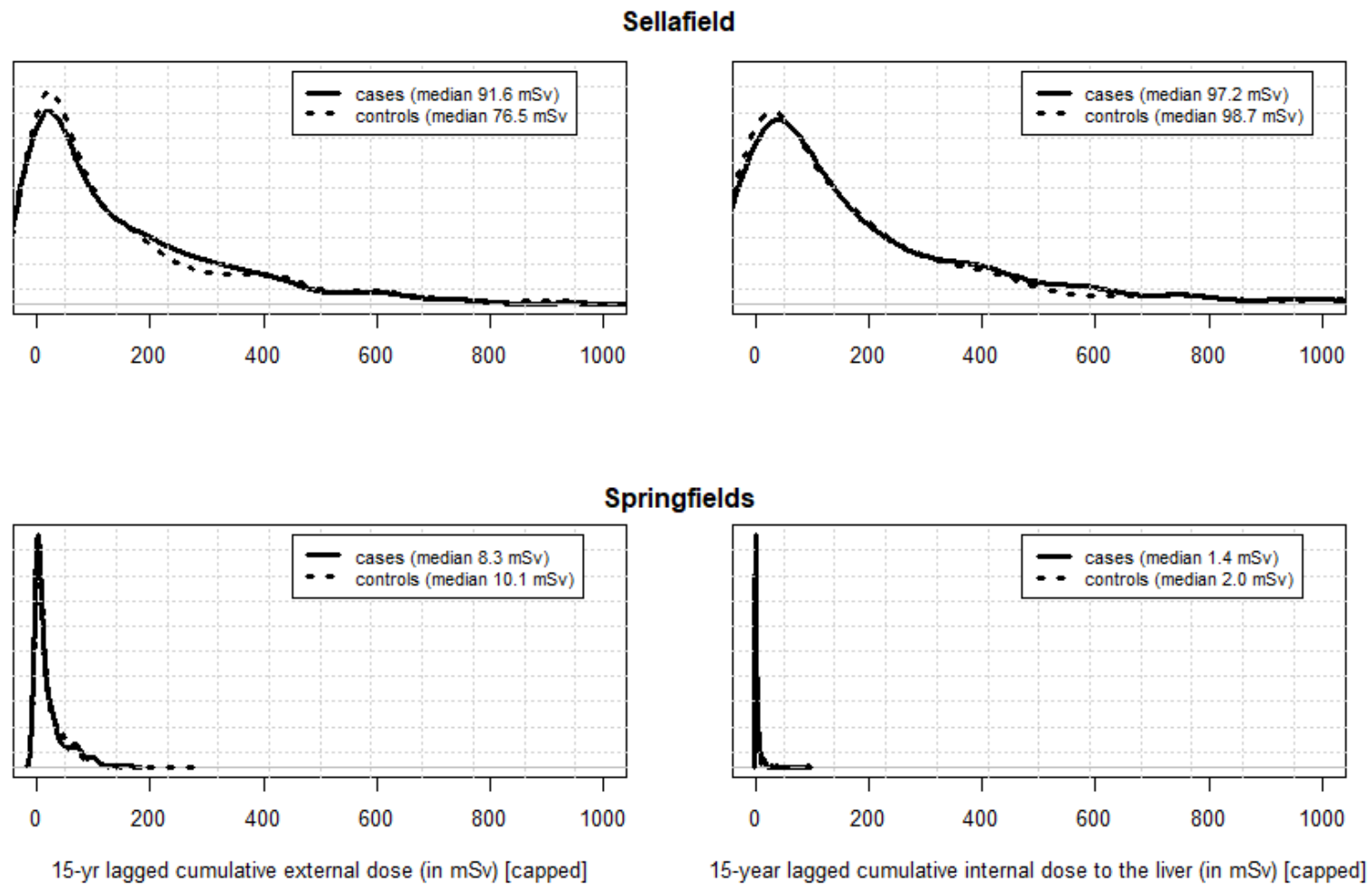
Process worker	625	639	1.00		
Other worker	554	531	1.07	0.90-1.28	0.42
missing	41	50	0.83	0.54-1.29	0.42
Body Mass Index					
<18.5	28	29	1.05	0.61-1.78	0.87
18.5-24.9	762	815	1.00		
25.0-29.9	344	304	1.22	1.01-1.46	0.04
30+	50	42	1.29	0.85-1.97	0.23
missing	36	30	1.27	0.76-2.14	0.36
Pre-employment diastolic blood pressure (mmHg)					
<70	26	24	1.00		
70-85	486	586	0.76	0.43-1.36	0.36
86-99	444	414	1.04	0.58-1.86	0.90
100+	198	137	1.45	0.79-2.68	0.23
missing	66	59	1.08	0.55-2.10	0.83
Pre-employment systolic blood pressure (mmHg)					
<120	66	101	1.00		
120-138	453	525	1.32	0.94-1.84	0.10
138-159	450	389	1.81	1.29-2.55	0.01
160+	185	146	2.04	1.39-3.01	0.00
missing	66	59	1.76	1.08-2.87	0.02
Pre-employment smoking status					
Current smoker	207	285	1.00		
Non/ex-smoker	667	567	1.62	1.31-2.01	0.00
missing	346	368	1.29	1.01-1.66	0.04
Shift-work					
Ever	453	447	1.00		
Never	688	688	0.98	0.83-1.17	0.85
Missing	79	85	0.87	0.57-1.33	0.52
Cumulative NIL <sub>85</sub> exposure (dB(A)-years)					
<85.0	445	471	1.00		
85.0-94.8	257	255	1.07	0.85-1.35	0.56
94.9-99.7	270	239	1.21	0.97-1.51	0.10
99.8+	243	249	1.03	0.82-1.29	0.80
missing	5	6	0.89	0.27-2.95	0.85

\*: matching is performed on site and there is no cross-over between sites

<sup>1</sup> Based on longest-held job



**Figure S1.** Density plots of cumulative unlagged external doses (mSv) in the four dose quartiles (note that in the figure, but not in the categorization itself, these overlap because of how densities are plotted).



**Figure S2.** Density plots of cumulative 15-year lagged dose distributions for external and internal radiation exposures by nuclear site. Industrial non-radiation workers are included.

**Table S2.** Associations between cumulative radiation dose from external sources and IHD mortality using different external dose lags

External Dose Lag (years)	Cumulative external radiation dose (mSv)	Odds Ratio <sup>1</sup>	95% Confidence Interval	p-value
0 (Table 2, Model 5)	<2.6	1.00	(ref)	
	2.6-21.4	1.17	0.91-1.51	0.22
	21.4-102.8	1.20	0.92-1.56	0.17
	102.8-1655.8	1.42	1.04-1.95	0.03
	log-linear trend (per 100 mSv)	1.02	0.96-1.08	0.54
5	<3.1	1.00	(ref)	
	3.1-24.3	1.14	0.88-1.46	0.32
	24.3-101.4	1.23	0.95-1.61	0.12
	101.4-1,621.4	1.37	1.00-1.86	0.05
	log-linear trend (per 100 mSv)	1.03	0.96-1.09	0.42
10	<2.9	1.00	(ref)	
	2.9-25.1	1.17	0.91-1.51	0.21
	25.1-106.4	1.13	0.87-1.46	0.36
	106.4-1,514.9	1.47	1.08-2.00	0.02
	log-linear trend (per 100 mSv)	1.04	0.97-1.11	0.26
15 (Table 3, Model 5)	<1.9	1.00	(ref)	
	1.9-25.1	0.97	0.76-1.26	0.84
	25.1-108.8	1.03	0.79-1.34	0.85
	108.8-1,290.7	1.35	0.99-1.84	0.05
	log-linear trend (per 100 mSv)	1.05	0.98-1.12	0.17

<sup>1</sup> adjusted for age at death (or censoring), monitored for internal radiation, age at start of employment at either site, decade of start of employment, socio-economic status, and longest-held job. Industrial non-radiation workers included in reference groups.

**Table S3.** Subgroup analysis by nuclear site for all industrial workers and radiation worker pairs separately (results refer to Manuscript Figure 2)

		<b>Sellafield (651 pairs)</b>			<b>Springfields (569 pairs)</b>		
<b>Cumulative external dose, mSv</b>		all industrial workers (all case-control pairs in the study)					
	<b>Dose category<sup>1</sup></b>	<b>OR<sup>2</sup></b>	<b>95% CI</b>	<b>Dose category<sup>1</sup></b>	<b>OR<sup>2</sup></b>	<b>95%CI</b>	
<b>no dose lag</b>	0-11.48	1.00	(ref)	0-0.77	1.00	(ref)	
	11.48-69.07	1.02	0.73-1.42	0.77-7.13	1.05	0.70-1.57	
	69.07-237.84	1.10	0.77-1.58	7.13-26.70	1.21	0.79-1.86	
	>237.84	1.07	0.73-1.58	26.70-188.76	1.39	0.87-2.19	
<b>15-year dose lag</b>	0-12.40	1.00	(ref)	0-0.22	1.00	(ref)	
	12.40-91.56	1.11	0.81-1.52	0.22-8.29	1.00	0.67-1.49	
	91.56-238.98	1.37	0.93-2.00	8.29-29.75	1.24	0.79-1.92	
	>238.98	1.32	0.90-1.93	>29.75	1.49	0.93-2.39	
<b>Radiation workers (pairs monitored for external radiation)<sup>3</sup></b>							
		<b>Sellafield (385 pairs)</b>		<b>Springfields (330 pairs)</b>			
	<b>Dose category<sup>1</sup></b>	<b>OR<sup>4</sup></b>	<b>95% CI</b>	<b>Dose category<sup>1</sup></b>	<b>OR<sup>4</sup></b>	<b>95%CI</b>	
<b>no dose lag</b>	0.1-27.8	1.00	(ref)	0.1-3.1	1.00	(ref)	
	27.8-112.0	1.15	0.75-1.76	3.1-10.6	1.69	1.02-2.78	
	112.0-286.7	1.90	1.15-3.13	10.6-37.3	1.86	1.10-3.16	
	286.7-1,111.2	1.83	1.10-3.04	37.3-188.8	2.30	1.30-4.08	
<b>15-year dose lag</b>	0.1-39.8	1.00	(ref)	0.1-3.1	1.00	(ref)	
	39.8-129.5	1.12	0.73-1.72	3.1-10.6	1.18	0.73-1.88	
	129.5-294.8	1.61	0.99-2.60	10.6-37.3	1.65	0.97-2.81	
	>294.8	1.71	1.07-2.73	>37.3	1.71	1.00-2.92	

<sup>1</sup>: Cumulative dose categories based on nuclear-site specific quartiles of distribution in cases (note that therefore, results differ from Manuscript Table 4)

<sup>2</sup>: adjusted for age at death (or censoring), monitored for internal radiation exposure, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Non-radiation industrial workers are included in the reference groups.

<sup>3</sup>: Case-control pairs with complete occupational history only (uncensored pairs)

<sup>4</sup>: adjusted for age at death (or censoring), monitored for internal radiation exposure, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status.

**Table S4.** Subgroup analyses using truncated cumulative external and internal doses by nuclear site

<b>Pairs with unlagged cumulative external radiation dose &lt;= 350 mSv<sup>1</sup></b>							
		<b>Whole sample (1,025 pairs)</b>		<b>Sellafield (456 pairs)</b>		<b>Springfields (569 pairs)</b>	
		<b>OR<sup>2</sup></b>	<b>95%CI</b>	<b>OR<sup>2</sup></b>	<b>95%CI</b>	<b>OR<sup>2</sup></b>	<b>95%CI</b>
Cumulative external radiation dose (mSv)	0-1.7	1.00	(ref)	1.00	(ref)	1.00	(ref)
	1.7-14.5	1.20	0.91-1.58	1.20	0.72-2.00	1.26	0.88-1.80
	14.5-61.1	1.35	1.01-1.81	1.21	0.78-1.88	1.58	1.03-2.38
	>61.1	1.28	0.93-1.76	1.20	0.77-1.88	1.23	0.74-2.03
	Log-linear (per 100 mSv)	1.16	1.00-1.35	1.11	0.93-1.33	1.20	0.80-1.80
		<b>OR<sup>4</sup></b>	<b>95%CI</b>	<b>OR<sup>4</sup></b>	<b>95%CI</b>	<b>OR<sup>4</sup></b>	<b>95%CI</b>
Cumulative internal radiation dose (mSv)	0.01-2.0	1.00	(ref)	1.00	(ref)	1.00	(ref)
	2.0-16.9	0.82	0.58-1.17	1.57	0.56-4.40	0.71	0.48-1.06
	16.9-5,057	1.52	1.02-2.26	2.15	0.91-5.05	1.14	0.53-2.45
	Not monitored	1.61	1.19-2.18	2.06	0.90-4.72	1.66	1.16-2.37
<b>Pairs with 15-year lagged cumulative external radiation dose &lt;= 267 mSv<sup>3</sup></b>							
		<b>Whole sample (977 pairs)</b>		<b>Sellafield (408 pairs)</b>		<b>Springfields (569 pairs)</b>	
		<b>OR<sup>2</sup></b>	<b>95%CI</b>	<b>OR<sup>2</sup></b>	<b>95%CI</b>	<b>OR<sup>2</sup></b>	<b>95%CI</b>
Cumulative external radiation dose (mSv)	<0.6	1.00	(ref)	1.00	(ref)	1.00	(ref)
	0.6-15.3	0.79	0.59-1.05	0.97	0.56-1.68	0.73	0.51-1.05
	15.3-61.6	1.01	0.75-1.37	0.94	0.59-1.51	0.99	0.65-1.51
	>61.6	1.07	0.78-1.47	0.96	0.62-1.49	1.33	0.79-2.24
	Log-linear (per 100 mSv)	1.15	0.95-1.40	1.09	0.87-1.38	1.31	0.82-2.07
		<b>OR<sup>4</sup></b>	<b>95%CI</b>	<b>OR<sup>4</sup></b>	<b>95%CI</b>	<b>OR<sup>4</sup></b>	<b>95%CI</b>
Cumulative internal radiation dose (mSv)	0.0-0.8	1.00	(ref)	1.00	(ref)	1.00	(ref)
	0.8-6.8	0.58	0.39-0.86	0.63	0.16-2.51	0.52	0.33-0.80
	6.8-3,642	0.75	0.48-1.16	1.39	0.51-3.85	0.30	0.15-0.60
	Not monitored	1.39	1.00-1.93	1.61	0.63-4.08	1.63	1.10-2.40

<sup>1</sup>: maximum cumulative unlagged external radiation dose at the Springfields nuclear site in this study

<sup>2</sup>: adjusted for age at death (or censoring), monitored for internal radiation, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Industrial non-radiation workers included in reference groups.

<sup>3</sup>: maximum 15-year lagged cumulative external radiation dose at the Springfields nuclear site in this study

<sup>4</sup>: adjusted for age at death (or censoring), cumulative external radiation dose, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Not monitored groups include non-radiation workers.



**Table S5.** Analyses of industrial radiation worker (cumulative external radiation dose >0 mSv) pairs only, including subgroup analyses for radiation worker pairs monitored for external exposure only and radiation worker pairs monitored for both external and internal exposure.

		Pairs of Radiation Workers (715 pairs)		Pairs of Radiation Workers both monitored for external radiation only (152 pairs)		Pairs of Radiation Workers both monitored for external and internal radiation (229 pairs)			
<b>No dose lag<sup>1</sup></b>									
		<b>OR<sup>2</sup></b>	<b>95%CI</b>		<b>OR<sup>2</sup></b>	<b>95%CI</b>		<b>OR<sup>2</sup></b>	<b>95%CI</b>
<b>Cumulative external radiation dose (mSv)</b>	<8.9	1.00	(ref)	<5.9	1.00	(ref)	<10.6	1.00	(ref)
	8.9-34.2	1.40	1.02-1.91	5.9-23.2	2.04	0.91-4.53	10.6-46.6	1.23	0.72-2.10
	34.2-144.8	1.58	1.11-2.23	23.8-136.4	2.02	0.85-4.80	46.6-141.2	1.40	0.78-2.51
	>144.8	2.50	1.61-3.89	>136.4	1.05	3.04-36.5	>151.2	2.16	1.00-4.66
	log-linear (per 100 mSv)	1.09	1.01-1.17	log-linear (per 100 mSv)	1.56	1.17-2.07	log-linear (per 100 mSv)	1.09	0.93-1.27
		<b>OR<sup>3</sup></b>	<b>95%CI</b>		<b>OR<sup>3</sup></b>	<b>95%CI</b>		<b>OR<sup>3</sup></b>	<b>95%CI</b>
<b>Cumulative internal radiation dose (mSv)</b>	0.01-3.6	1.00	(ref)				0.01-2.55	1	(ref)
	3.6-82.3	1.01	0.68-1.49		N/A		2.55-29.0	0.74	0.41-1.33
	>82.3	1.30	0.82-2.05				>29.0	1.35	0.54-3.35
	Not monitored	1.40	1.00-1.96						
<b>15-year lagged dose<sup>1</sup></b>									
		<b>OR<sup>2</sup></b>	<b>95%CI</b>		<b>OR<sup>2</sup></b>	<b>95%CI</b>		<b>OR<sup>2</sup></b>	<b>95%CI</b>
<b>Cumulative external radiation dose (mSv)</b>	<10.6	1.00	(ref)	<8.6	1.00	(ref)	<13.4	1.00	(ref)
	10.6-44.4	0.99	0.71-1.38	8.6-30.1	1.28	0.60-2.73	13.4-45.5	1.20	0.67-2.15
	44.4-155.8	1.10	0.78-1.55	30.1-117.6	1.32	0.60-2.92	45.5-125.5	1.31	0.72-2.39
	>155.8	1.54	1.01-2.35	>117.6	1.87	0.77-4.56	>125.5	1.57	0.69-3.57
	log-linear (per 100 mSv)	1.05	0.97-1.14	log-linear (per 100 mSv)	1.10	0.87-1.38	log-linear (per 100 mSv)	1.04	0.89-1.21
		<b>OR<sup>3</sup></b>	<b>95%CI</b>		<b>OR<sup>3</sup></b>	<b>95%CI</b>		<b>OR<sup>3</sup></b>	<b>95%CI</b>
<b>Cumulative internal radiation dose (mSv)</b>	0.0-1.7	1.00	(ref)				0.01-1.45	1.00	(ref)
	1.7-30.7	0.63	0.43-0.94		N/A		1.45-13.3	0.48	0.27-0.84

<b>radiation dose (mSv)</b>	>30.7	1.00	0.62-1.63	>13.3	0.74	0.32-1.68
	Not monitored	1.18	0.82-1.69-			

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<sup>1</sup>: cumulative exposure quartiles (tertiles for cumulative internal dose) based on subgroup specific distribution of exposure in cases.

<sup>2</sup>: adjusted for age at death (or censoring), monitored for internal radiation, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status, and longest-held job.

<sup>3</sup>: adjusted for age at death (or censoring), cumulative external radiation dose, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status, and longest-held job

**Table S6.** Subgroup analyses of industrial worker case-control pairs by employment duration

<b>unlagged</b>		<b>Pairs employed &gt;5 years (461 pairs)</b>		<b>Pairs employed ≤ 5 years (242 pairs)</b>	
		<b>OR<sup>1</sup></b>	<b>95%CI</b>	<b>OR<sup>1</sup></b>	<b>95%CI</b>
<b>Cumulative external radiation dose (mSv)</b>	<2.6	1.00	(ref)	1.00	(ref)
	2.6-21.4	1.15	0.66-1.99	0.80	0.48-1.34
	21.4-102.8	1.28	0.76-2.16	0.97	0.51-1.82
	>102.8	1.26	0.70-2.28	0.36	0.06-2.06
	Log-linear (per 100 mSv)	0.97	0.88-1.06	0.60	0.24-1.53
<b>Cumulative internal radiation dose (mSv)</b>	0.01-2.89	1.00	(ref)	1.00	(ref)
	2.89-52.28	0.73	0.43-1.23	1.06	0.44-2.57
	>52.28	1.05	0.58-1.89	2.66	0.87-8.12
	Not monitored	1.45	0.90-2.34	1.90	1.00-3.58
<b>15-year lagged</b>		<b>OR<sup>1</sup></b>	<b>95%CI</b>	<b>OR<sup>1</sup></b>	<b>95%CI</b>
<b>Cumulative external radiation dose (mSv)</b>	<1.9	1.00	(ref)	1.00	(ref)
	1.9-25.1	0.87	0.53-1.43	1.06	0.62-1.79
	25.1-108.8	0.83	0.50-1.38	1.15	0.60-2.20
	>108.8	0.83	0.47-1.47	1.13	0.52-2.47
	Log-linear (per 100 mSv)	0.91	0.82-1.01	1.06	0.76-1.49
<b>Cumulative internal radiation dose (mSv)</b>	0.0-1.5	1.00	(ref)	1.00	(ref)
	1.5-33.0	0.39	0.22-0.70	1.27	0.51-3.19
	>33.0	0.65	0.33-1.27	2.18	0.65-7.33
	Not monitored	1.18	0.70-1.97	2.27	1.11-4.62

<sup>1</sup>: adjusted for age at death (or censoring), monitored for internal radiation, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Industrial non-radiation workers included in reference groups.

<sup>2</sup>: adjusted for age at death (or censoring), cumulative external radiation dose, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Not monitored groups include non-radiation workers.

**Table S7.** Subgroup analyses of industrial workers case-control pairs by longest-held occupation

No dose lag		Pairs of Process workers (271 pairs)		Pairs of Other workers (406 pairs)	
		<b>OR<sup>1</sup></b>	<b>95%CI</b>	<b>OR<sup>1</sup></b>	<b>95%CI</b>
<b>Cumulative external radiation dose (mSv)</b>	<2.6	1.00	(ref)	1.00	(ref)
	2.6-21.4	1.34	0.77-2.34	1.44	0.92-2.26
	21.4-102.8	1.31	0.73-2.34	1.37	0.86-2.17
	>102.8	0.89	0.43-1.85	1.63	0.95-2.79
	Log-Linear (per 100 mSv)	0.92	0.81-1.06	1.09	0.97-1.23
<b>Cumulative internal radiation dose (mSv)</b>	0.01-2.89	<b>OR<sup>2</sup></b> 1.00	<b>95%CI</b> (ref)	<b>OR<sup>2</sup></b> 1.00	<b>95%CI</b> (ref)
	2.89-52.28	1.05	0.60-1.81	1.16	0.57-2.38
	>52.28	0.86	0.35-2.08	1.17	0.60-2.31
	Not monitored	1.62	0.89-2.92	1.24	0.72-2.12
<b>15-year lagged dose</b>		<b>OR<sup>1</sup></b>	<b>95%CI</b>	<b>OR<sup>1</sup></b>	<b>95%CI</b>
<b>Cumulative external radiation dose (mSv)</b>	<1.9	1.00	(ref)	1.00	(ref)
	1.9-25.1	1.05	0.60-1.83	1.05	0.68-1.63
	25.1-108.8	0.98	0.53-1.81	1.32	0.83-2.10
	>108.8	0.42	0.18-0.96	1.96	1.19-3.24
	Log-Linear (per 100 mSv)	0.86	0.73-1.02	1.17	1.04-1.32
<b>Cumulative internal radiation dose (mSv)</b>	0.0-1.5	<b>OR<sup>2</sup></b> 1.00	<b>95%CI</b> (ref)	<b>OR<sup>2</sup></b> 1.00	<b>95%CI</b> (ref)
	1.5-33.0	0.60	0.33-1.09	0.57	0.26-1.28
	>33.0	0.60	0.22-1.66	0.99	0.49-1.99
	Not monitored	1.52	0.82-2.81	1.31	0.76-2.24

<sup>1</sup>: adjusted for age at death (or censoring), monitored for internal radiation, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Industrial non-radiation workers included in reference groups.

<sup>2</sup>: adjusted for age at death (or censoring), cumulative external radiation dose, decade of start of employment on site, age at start of employment, process worker (yes/no), socio-economic status. Not monitored groups include non-radiation workers.