Web Extra

Title: Cancer mortality after low dose exposure to ionizing radiation: a cohort study of workers in France, the United Kingdom, and the United States (INWORKS)

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Supplementary table A. Outcome categories and associated codes in revisions 6-10 of the ICD.

Outcome category	ICD-6	ICD-7	ICD-8	ICD-9	ICD-10
Solid cancer	140-199	140-199	140-199	140-199, except 176.5 (Kaposi's sarcoma of lymph nodes)	C00-C80, C97 except C46.3 (Kaposi's sarcoma of lymph nodes)

Exclusion of lung cancer, defined as:

Outcome category	ICD-6	ICD-7	ICD-8	ICD-9	ICD-10
Lung/ trachea/ bronchus	162-163	162.0-162.1, 162.8, 163 (pleura excluded)	162	162	C33-C34

Exclusion of smoking-related cancers, defined as:

Outcome category	ICD-6	ICD-7	ICD-8	ICD-9	ICD-10
Buccal cavity & pharynx	140-148	140-148	140-149	140-149	C00-C14
Oesophagus	150	150	150	150	C15
Stomach	151	151	151	151	C16
Colon (excl. small intestine)	153	153	153	153	C18
Rectum	154	154	154	154.0,154.1, 154.8	C19-C20
Liver	155	155.0	155.0,155.1	155	C22
Gallbladder		155.1	156	156	C23, C24
Pancreas	157	157	157	157	C25
Nasal cavity		160	160	160	C30, C31
Larynx	161	161	161	161	C32
Lung/ trachea/ bronchus	as above				
Cervix uteri		171	180	180	C53
Ovary	175	175	183	183	C56, C57.0-C57.4, C57.8
Bladder	181	181	188,189.9	188,189.3-189.9	C67
Kidney	180	180	189.0-189.2	189.0-189.2	C64-C66

Exclusion of cancer of the lung, liver and bone, defined as:

Outcome category	ICD-6	ICD-7	ICD-8	ICD-9	ICD-10
Lung/ trachea/ bronchus	as above				
Liver/ gallbladder/ biliary passages	155-156	155-156	155-156,197.8	155-156	C22-C24
Bone	196	196	170	170	C40, C41

Exclusion of cancer of the lung and pleura, defined as:

Outcome category	ICD-6	ICD-7	ICD-8	ICD-9	ICD-10
Lung/ trachea/ bronchus	as above				
Pleura	*	162.2	163.0	163	C38.4; C45.0 (mesothelioma)

*cannot be separated

Analysis of chronic obstructive pulmonary disease, defined as:

Outcome category	ICD-6	ICD-7	ICD-8	ICD-9	ICD-10
chronic obstructive pulmonary disease	501-502, 527.1	501-502, 527.1	490-492	490-492,496	J40-J43, J44

Supplementary table B. Estimates of excess relative rate (ERR) per Gy for death due to specific cancer categories in INWORKS. 5-, 10-, 15-, and 20-year exposure lag assumptions.

Lag assumption	Deaths	ERR per Gy[†]	90% CI	LRT	*p*
5 year					
All cancer	31,009	0.47	0.25 to 0.70	13.04	<0.001
Solid cancer	28,089	0.46	0.23 to 0.70	11.45	0.001
Solid cancer other than lung	19,823	0.43	0.16 to 0.71	7.08	0.008
10 year					
All cancer	31,009	0.53	0.30 to 0.77	15.29	<0.001
Solid cancer	28,089	0.52	0.27 to 0.77	13.28	<0.001
Solid cancer other than lung	19,823	0.46	0.18 to 0.76	7.75	0.005
15 year					
All cancer	31,009	0.57	0.33 to 0.84	16.02	<0.001
Solid cancer	28,089	0.55	0.29 to 0.82	13.44	<0.001
Solid cancer other than lung	19,823	0.51	0.21 to 0.82	8.23	0.004
20 year					
All cancer	31,009	0.58	0.32 to 0.87	13.93	<0.001
Solid cancer	28,089	0.54	0.26 to 0.83	10.84	0.001
Solid cancer other than lung	19,823	0.46	0.14 to 0.80	5.95	0.02

p is the p-value for the reported likelihood ratio test (LRT) statistic and is evaluated under a Chi-square distribution with 1 degree of freedom.

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

Supplementary table C. Estimates of excess relative rate (ERR) per Gy for death due to solid cancer in INWORKS. Analyses on restricted dose ranges.

Restricted dose range	Deaths	ERR per Gy[†]	90% CI	LRT	*p*
No restriction	28,089	0.52	0.27 to 0.77	13.28	<0.001
<400 mGy	27,960	0.63	0.34 to 0.92	13.49	<0.001
<200 mGy	27,429	0.97	0.55 to 1.39	15.69	<0.001
<100 mGy	26,283	1.12	0.45 to 1.80	7.82	0.005
<50 mGy	24,518	1.38	0.20 to 2.60	3.74	0.05
<20 mGy	21,293	1.30	-1.33 to 4.06	0.66	0.42

10 year lag assumption.

P is the p-value for the reported likelihood ratio test (LRT) statistic, and is evaluated under a Chi-square distribution with 1 degree of freedom.

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

Supplementary table D. Estimates of excess relative rate (ERR) per Gy for death due to specific outcome categories in INWORKS. Analyses restricted by year of hire.

Restricted by year of hire	Deaths	ERR per Gy[†]	90% CI	LRT	*p*
Hired 1958+ [238,639 workers; 7.87 million person-years]					
All cancer	16,361	1.12	0.68 to 1.60	19.93	<0.001
Solid cancer	14,868	1.22	0.74 to 1.72	20.84	<0.001
Solid cancer other than lung	10,692	1.20	0.65 to 1.78	15.12	<0.001
COPD	1,657	-0.50	-1.53 to 0.53[*f*]	0.56	0.45
Hired 1965+ [189,386 workers; 5.89 million person-years]					
All cancer	8,918	1.23	0.49 to 2.04	8.14	0.004
Solid cancer	8,119	1.44	0.65 to 2.32	9.79	0.002
Solid cancer other than lung	5,842	1.38	0.47 to 2.39	6.78	0.009
COPD	837	0.24	-2.05 to 2.53[*f*]	0.03	0.86

10 year lag assumption.

COPD, Chronic obstructive pulmonary disease.

[*f*] Wald-type confidence interval

p is the p-value for the reported likelihood ratio test (LRT) statistic and is evaluated under a Chi-square distribution with 1 degree of freedom.

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

Supplementary table E. Estimates of excess relative rate (ERR) per Gy for death due to solid cancer within strata of internal monitoring status. 10-year lag assumption.

		Deaths	ERR per Gy[†]	90% CI
Internal monitoring status[†]				
	Flag 1	23,410	0.82	0.46 to 1.22
	Flag 2	4,679	0.21	-0.11 to 0.56

[†]Workers were grouped into two categories. Flag 1: Not flagged for incorporated radionuclides or internal monitoring. Flag 2: flagged for incorporated radionuclides or internal monitoring.

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

Supplementary table F. Estimates of excess relative rate (ERR) per Gy for death due to solid cancer within strata of neutron monitoring status. 10-year lag assumption.

		Deaths	ERR per Gy[†]	90% CI
Neutron monitoring status[†]				
	Flag 1	24,213	0.55	0.23 to 0.90
	Flag 2	2,468	0.49	0.12 to 0.93
	Flag 3	1,408	0.36	-0.51 to 1.43

[†]Workers were grouped into three categories. Flag 1: No positive recorded neutron dose. Flag 2: Positive recorded neutron dose not exceeding 10% of the total equivalent dose for external radiation. Flag 3: Recorded neutron dose exceeding 10% of the total equivalent dose for external radiation.

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

Supplementary table G. Estimates of excess relative rate (ERR) per Gy for death due to specific cancer categories in INWORKS.

Previous INWORKS analysis [308,297 workers; 8.2 million person-years]			
	Deaths	ERR per Gy[†]	90% CI
All cancer	19,748	0.51	0.23 to 0.82
Solid cancer	17,957	0.47	0.18 to 0.79
Solid cancer excluding lung	12,155	0.46	0.11 to 0.85
Current INWORKS analysis [309,932 workers; 10.7 million person-years]			
	Deaths	ERR per Gy[†]	90% CI
All cancer	31,009	0.53	0.30 to 0.77
Solid cancer	28,089	0.52	0.27 to 0.77
Solid cancer excluding lung	19,823	0.46	0.18 to 0.76

10 year lag assumption.
CI: confidence interval.

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

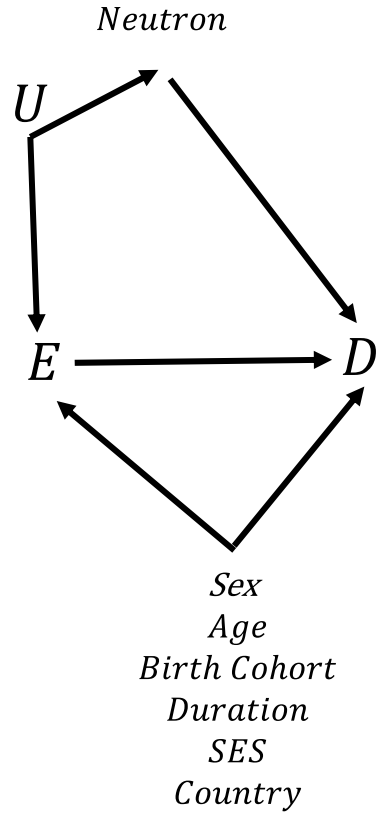
Supplementary table H. Analysis using recorded external doses rather than adjusted estimates of colon dose. Estimates of excess relative rate (ERR) per Gy[†] for death due to cancer, solid cancer and solid cancer other than lung in INWORKS.

	ERR per Gy[†]	90% CI	LRT	*p*
Recorded photon dose, 10-year lag				
All cancer	0.38	0.22 to 0.55	15.24	<0.001
Solid cancer	0.37	0.19 to 0.55	13.02	<0.001
Solid cancer other than lung	0.33	0.13 to 0.55	7.59	0.006

p is the p-value for the reported likelihood ratio test (LRT) statistic and is evaluated under a Chi-square distribution with 1 degree of freedom

[†]strata: country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring status.

Supplementary figure A. Directed acyclic graph used to inform covariate adjustment in the relationship between occupational dose due to photon exposure (E) and solid cancer (D).



Neutron monitoring status should be adjusted for because neutron exposure may cause cancer and because photon exposure and neutron monitoring may be associated due to a common cause, U (e.g., employment area and task assignment). Sex should be adjusted for because male and female workers have different baseline cancer rates and tend to differ in occupational radiation exposure (e.g., due to gender segregation in employment and task assignment). Age, birth cohort, and duration of employment or radiation work should be adjusted for because these are related to baseline cancer rates and to cumulative occupational radiation exposure (e.g., due to changes and accrual over time of exposure). Socioeconomic status (SES) should be adjusted for because white-collar and blue-collar workers have different baseline cancer rates and tend to differ in occupational radiation exposure (e.g., due to employment and task assignment). Country should be adjusted for because countries have different baseline cancer rates and differ in occupational radiation exposure.

Supplementary figure B. Relative rate of mortality due to solid cancer other than lung by categories of cumulative colon dose, lagged 10 years in INWORKS. Grey lines indicate 90% confidence intervals, and the dashed line depicts the fitted linear model for the change in the excess relative rate of mortality due to solid cancer other than lung with dose.