

Supplementary Information 3: Detailed results of spline models

On the non-linearity of radon-induced lung cancer

Environmental Science and Pollution Research

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1 Spline models (Δ AIC-weighted)

1.1 Odds ratio (OR) estimate: Δ AIC-weighted

Overall lung cancer

S3-Table 1 Odds ration estimates for overall LC (after model averaging): Δ BGIC($c=1$, $r=0.5$) and AIC-weighted

	Δ BGIC($c=1$, $r=0.5$)-weighted			Δ AIC-weighted			both weighting-schemes	
	OR	95%-CI	p-value	OR	95%-CI	p-value	betw./total var.	# models
10 Bq/m ³	1.68	0.88-2.70	0.1097	1.66	0.90-2.59	0.0977	0%	44
20 Bq/m ³	1.42	1.03-1.80	0.0314	1.41	1.03-1.78	0.0285	1%	44
25 Bq/m ³	1.31	1.00-1.60	0.0453	1.31	1.01-1.59	0.0385	1%	44
30 Bq/m ³	1.22	0.98-1.43	0.0694	1.22	0.99-1.42	0.0582	1%	44
40 Bq/m ³	1.09	0.96-1.20	0.1426	1.09	0.97-1.20	0.1333	2%	44
50 Bq/m ³	1.05	0.98-1.10	0.1230	1.05	0.98-1.10	0.1307	3%	44
55 Bq/m ³	1.01	0.99-1.03	0.2251	1.01	0.99-1.02	0.2406	4%	44
64 Bq/m ³	1.00	reference		1.00	reference	.		44
75 Bq/m ³	1.10	1.03-1.14	0.0012	1.10	1.04-1.14	0.0010	6%	44
80 Bq/m ³	1.14	1.06-1.20	0.0002	1.14	1.07-1.20	0.0001	5%	44
100 Bq/m ³	1.34	1.20-1.46	<.0001	1.34	1.20-1.45	<.0001	5%	44
150 Bq/m ³	1.65	1.48-1.78	<.0001	1.65	1.48-1.78	<.0001	1%	44
164 Bq/m ³	1.70	1.52-1.85	<.0001	1.70	1.52-1.85	<.0001	1%	44
200 Bq/m ³	1.94	1.54-2.31	<.0001	1.93	1.53-2.28	<.0001	1%	44
250 Bq/m ³	2.35	1.17-3.92	0.0160	2.34	1.24-3.72	0.0083	1%	44

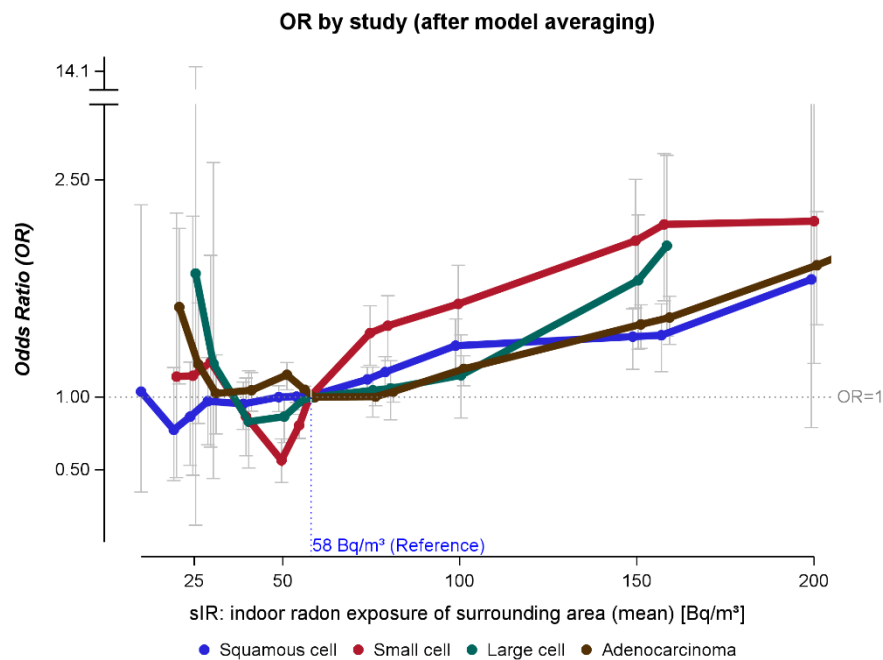
sIR: mean spatial indoor radon exposure in the surrounding area; OR: averaged odds ratios (reference class: 64 Bq/m³ - median observer sIR in controls); AIC Akaike information criterion; BGIC(c,r) Bayesian-type generalized information criteria; avg. by Rubin's equation with model weights derived from Δ AIC); all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years); 95%-CI 95% confidence interval; betw./total var.: Percentage of between point estimate variance on the total variance; # model: number of models that were averaged

S3-Table 2 Odds ration estimates (after model averaging): Δ AIC-weighted by histology

sIR	SqCLC		SCLC		LCLC		AdenoLC	
	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
10 Bq/m ³	1.03	0.34-2.32						
20 Bq/m ³	0.77	0.42-1.20	1.14	0.44-2.27			1.62	1.09-2.16
25 Bq/m ³	0.86	0.53-1.24	1.14	0.46-2.24	1.85	0.11-14.1	1.22	0.81-1.64
30 Bq/m ³	0.97	0.67-1.27	1.24	0.65-1.97	1.23	0.44-2.61	1.02	0.74-1.29
40 Bq/m ³	0.95	0.77-1.10	0.86	0.59-1.13	0.83	0.51-1.18	1.04	0.90-1.17
50 Bq/m ³	1.00	0.90-1.08	0.56	0.40-0.71	0.86	0.68-1.02	1.15	1.05-1.23
55 Bq/m ³	1.00	0.96-1.03	0.80	0.71-0.88	0.97	0.91-1.02	1.05	1.01-1.07
58 Bq/m ³ (reference)	1.00	reference	1.00	reference	1.00	reference	1.00	reference
75 Bq/m ³	1.12	1.01-1.20	1.44	1.22-1.63	1.04	0.86-1.20	1.00	0.94-1.05
80 Bq/m ³	1.17	1.04	1.27	1.49	1.25	1.69	1.06	0.84-1.25
100 Bq/m ³	1.35	1.13-1.54	1.64	1.33-1.91	1.15	0.85-1.42	1.19	1.07-1.28
150 Bq/m ³	1.41	1.19-1.60	2.07	1.61-2.50	1.80	1.32-2.25	1.50	1.33-1.63
158 Bq/m ³ (ref.+100)	1.42	1.17-1.64	2.19	1.66-2.68	2.04	1.42-2.67	1.54	1.36-1.69
200 Bq/m ³	1.81	0.79-3.32	2.21	1.23-3.40			1.90	1.49-2.27
250 Bq/m ³							2.40	1.13-4.14

sIR: mean spatial indoor radon exposure in the surrounding area; OR: averaged odds ratios (reference class: 58 Bq/m³ - LRE lowest risk exposure; avg. by Rubin's equation with model weights derived from Δ AIC); all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years); 95%-CI 95% confidence interval; LCLC: large cell lung cancer; SCLC: small cell lung cancer; SqCLC: squamous cell lung cancer, AdenoLC: lung adenocarcinoma

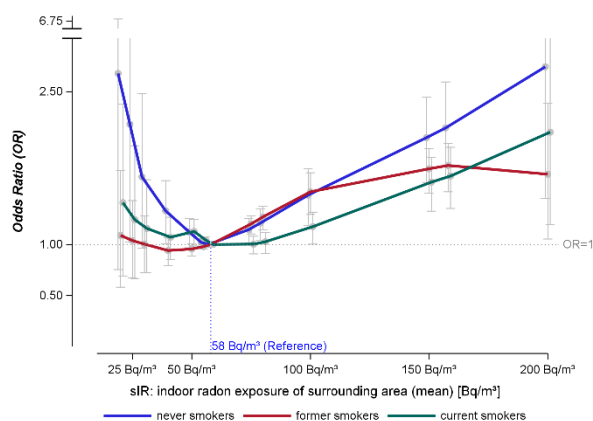
Subgroups by histology

S3-Figure 1 Odds ratio estimates (after model averaging): Δ AIC-weighted by histologyS3-Table 3 Odds ratio estimates (after model averaging): Δ AIC-weighted by smoking

sIR	never smokers		former smokers		current smokers	
	OR	95%-CI	OR	95%-CI	OR	95%-CI
20 Bq/m ³	2.67	0.75-6.76	1.08	0.58-1.72	1.40	0.69-2.37
25 Bq/m ³	2.17	1.02-3.77	1.04	0.67-1.43	1.24	0.66-1.96
30 Bq/m ³	1.66	0.96-2.47	1.00	0.72-1.27	1.15	0.72-1.63
40 Bq/m ³	1.32	1.00-1.62	0.94	0.79-1.06	1.07	0.85-1.26
50 Bq/m ³	1.12	0.96-1.25	0.95	0.88-1.00	1.12	0.98-1.24
55 Bq/m ³	1.02	0.97-1.05	0.98	0.95-0.99	1.04	0.99-1.07
58 Bq/m ³ (reference)	1.00	reference	1.00	reference	1.00	reference
75 Bq/m ³	1.14	1.01-1.25	1.20	1.10-1.28	1.00	0.90-1.08
80 Bq/m ³	1.20	1.04-1.35	1.27	1.14-1.37	1.02	0.91-1.12
100 Bq/m ³	1.48	1.18-1.74	1.51	1.29-1.70	1.17	1.00-1.31
150 Bq/m ³	2.04	1.60-2.44	1.74	1.50-1.93	1.61	1.32-1.85
158 Bq/m ³ (ref.+100)	2.14	1.65-2.59	1.77	1.51-1.99	1.67	1.35-1.95
200 Bq/m ³	2.74	1.45-4.36	1.68	1.05-2.38	2.10	1.19-3.18

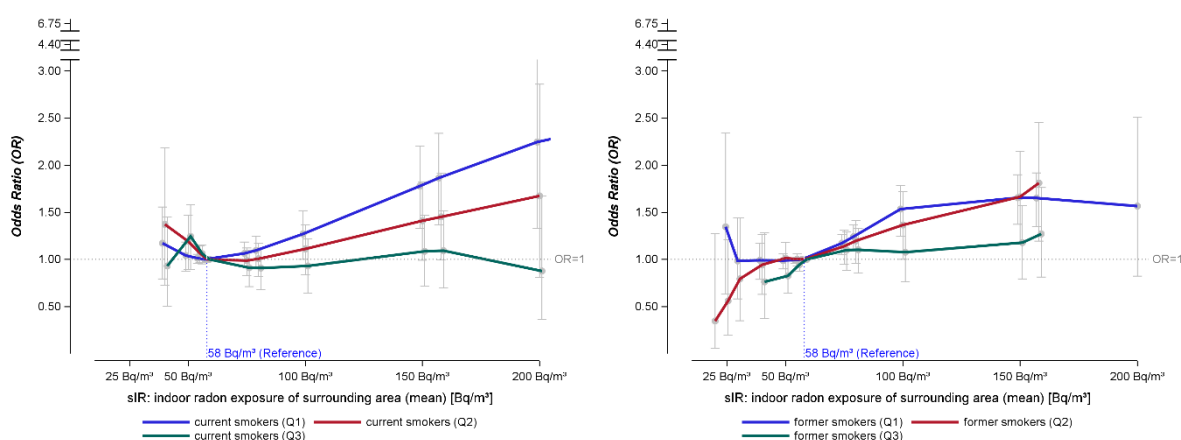
sIR: mean spatial indoor radon exposure in the surrounding area; OR: averaged odds ratios (reference class: 58 Bq/m³ - LRE lowest risk exposure; avg. by Rubin's equation with model weights derived from Δ AIC); all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years); 95%-CI 95% confidence interval

Subgroups by smoking

S3-Figure 2 Odds ration estimates (after model averaging): Δ AIC-weighted by smoking groupS3-Table 4 Odds ration estimates (after model averaging): Δ AIC-weighted by smoking group and amount

sIR	current smokers (Q1)		current smokers (Q2)		current smokers (Q3)		former smokers (Q1)		former smokers (Q2)		former smokers (Q3)	
	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
20 Bq/m ³										0.05-1.27		
25 Bq/m ³							1.34	0.63-2.34	0.55	0.19-1.20		
30 Bq/m ³							0.98	0.58-1.44	0.79	0.35-1.44		
40 Bq/m ³	1.17	0.79-1.55	1.37	0.72-2.18	0.93	0.50-1.45	0.99	0.78-1.17	0.94	0.62-1.26	0.76	0.37-1.28
50 Bq/m ³	1.04	0.87-1.18	1.19	0.89-1.46	1.24	0.89-1.58	0.99	0.90-1.06	1.01	0.82-1.18	0.82	0.64-0.99
55 Bq/m ³	1.01	0.95-1.05	1.06	0.96-1.14	1.06	0.95-1.15	0.99	0.96-1.01	1.00	0.93-1.06	0.94	0.87-1.00
58 Bq/m ³ (reference)	1.00	reference	1.00	reference	1.00	reference	1.00	reference	1.00	reference	1.00	reference
75 Bq/m ³	1.06	0.91-1.18	0.98	0.82-1.12	0.91	0.71-1.09	1.17	1.05-1.26	1.14	0.94-1.30	1.09	0.88-1.28
80 Bq/m ³	1.09	0.92-1.24	1.00	0.81-1.17	0.90	0.68-1.12	1.24	1.09-1.36	1.19	0.95-1.41	1.10	0.85-1.33
100 Bq/m ³	1.27	1.00-1.51	1.11	0.83-1.37	0.93	0.64-1.21	1.53	1.24-1.78	1.36	1.00-1.71	1.07	0.76-1.38
150 Bq/m ³	1.78	1.32-2.20	1.40	0.99-1.82	1.08	0.72-1.47	1.65	1.37-1.90	1.66	1.17-2.14	1.17	0.79-1.57
158 Bq/m ³ (ref.+100)	1.86	1.36-2.33	1.45	0.99-1.91	1.09	0.69-1.51	1.65	1.34-1.92	1.80	1.19-2.45	1.27	0.81-1.76
200 Bq/m ³	2.24	1.32-3.30	1.67	0.80-2.85	0.87	0.36-1.67	1.56	0.82-2.50				

sIR: mean spatial indoor radon exposure in the surrounding area; Q1 lowest, Q2 middle and Q3 largest pack years thirds;
 OR: averaged odds ratios (reference class: 58 Bq/m³ -LRE lowest risk exposure; avg. by Rubin's equation with model weights derived from Δ AIC); all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years); 95%-CI 95% confidence interval

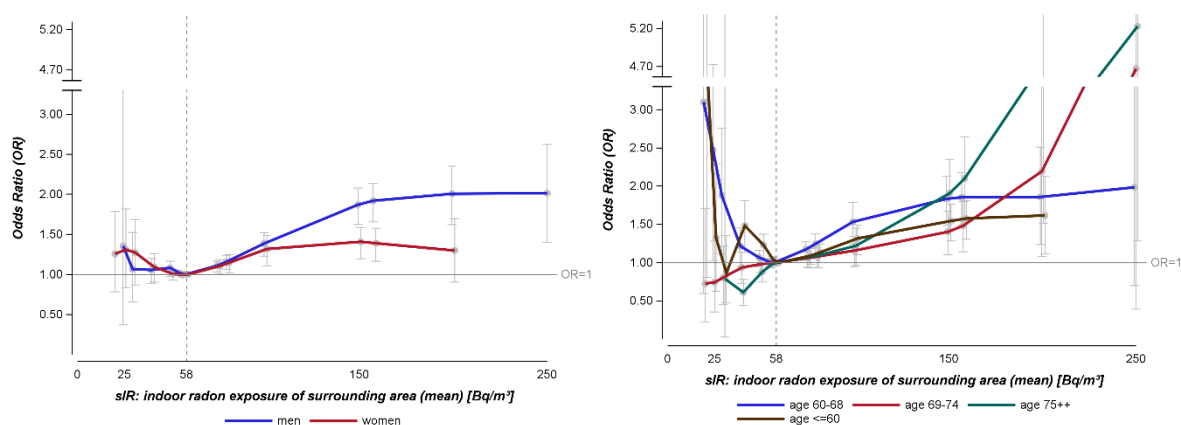
S3-Figure 3 Odds ration estimates (after model averaging): Δ AIC-weighted by smoking group and amount

Subgroups by sex and age

S3-Table 5 Odds ration estimates (after model averaging): Δ AIC-weighted by sex and age

sIR	age ≤ 60		age 60-68		age 69-74		age 75++		men		women	
	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
20 Bq/m ³	3.68	0.80-11.2	3.10	0.59-10.4	0.72	0.22-1.71					1.25	0.78-1.78
25 Bq/m ³	1.32	0.62-2.29	2.47	1.02-4.72	0.74	0.35-1.28			1.35	0.37-3.49	1.31	0.83-1.82
30 Bq/m ³	0.86	0.47-1.35	1.87	1.10-2.76	0.80	0.45-1.22	0.78	0.02-10.5	1.06	0.65-1.52	1.27	0.86-1.68
40 Bq/m ³	1.48	1.13-1.80	1.21	0.95-1.45	0.93	0.72-1.13	0.61	0.43-0.78	1.05	0.88-1.19	1.09	0.90-1.26
50 Bq/m ³	1.22	1.05-1.37	1.06	0.94-1.16	0.98	0.87-1.06	0.87	0.74-0.98	1.08	0.97-1.16	1.00	0.92-1.06
55 Bq/m ³	1.04	0.99-1.08	1.01	0.97-1.04	0.99	0.95-1.02	0.97	0.92-1.00	1.01	0.98-1.04	0.99	0.96-1.01
58 Bq/m ³ (reference)	1.00	reference	1.00	reference	1.00	reference	1.00	reference	1.00	reference	1.00	reference
75 Bq/m ³	1.08	0.97-1.17	1.17	1.04-1.27	1.05	0.94-1.15	1.07	0.93-1.18	1.10	1.03-1.16	1.10	1.00-1.18
80 Bq/m ³	1.13	1.00-1.24	1.24	1.08-1.37	1.07	0.93-1.19	1.09	0.92-1.23	1.15	1.06-1.23	1.14	1.02-1.25
100 Bq/m ³	1.31	1.10-1.49	1.53	1.24-1.78	1.15	0.94-1.34	1.22	0.96-1.44	1.38	1.22-1.51	1.31	1.10-1.49
150 Bq/m ³	1.54	1.28-1.76	1.83	1.49-2.13	1.40	1.10-1.67	1.90	1.43-2.34	1.87	1.62-2.07	1.40	1.19-1.58
158 Bq/m ³ (ref.+100)	1.57	1.30-1.81	1.85	1.49-2.17	1.48	1.14-1.79	2.10	1.53-2.64	1.92	1.65-2.13	1.38	1.16-1.57
200 Bq/m ³	1.61	1.10-2.13	1.86	1.23-2.51	2.19	1.07-3.69	3.63	1.51-6.90	2.00	1.61-2.35	1.30	0.90-1.69
250 Bq/m ³			1.98	0.69-4.27	4.67	0.39-28.5	5.22	1.28-14.6			1.40	0.2-6.2

sIR: mean spatial indoor radon exposure in the surrounding area; OR: averaged odds ratios (reference class: 58 Bq/m³ - LRE lowest risk exposure; avg. by Rubin's equation with model weights derived from Δ AIC); all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years); 95%-CI 95% confidence interval

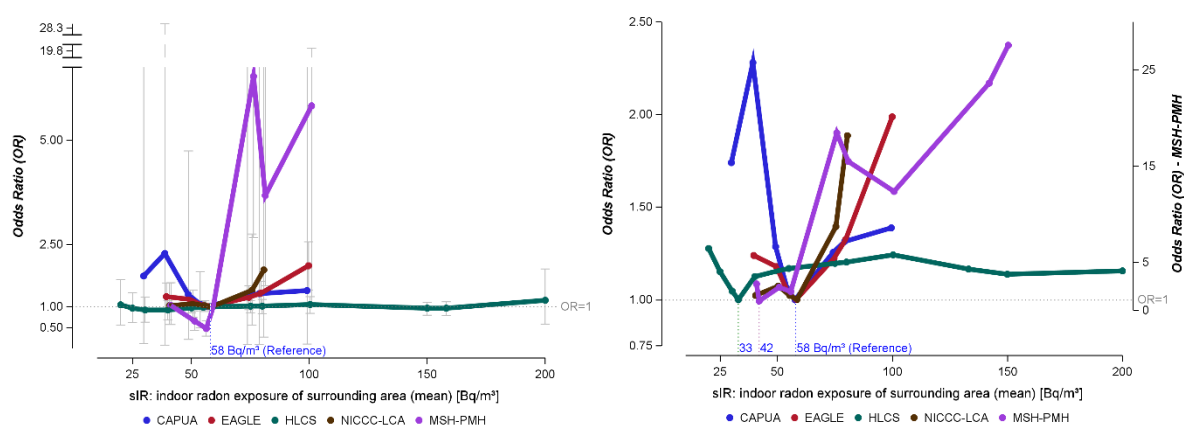
S3-Figure 4 Odds ration estimates (after model averaging): Δ AIC-weighted by sex and age

Subgroups by study site

S3-Table 6 Odds ration estimates (after model averaging): Δ AIC-weighted by study site

sIR	CAPUA		EAGLE		HSPH		NICCC-LCA		MSH-PMH	
	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
20 Bq/m ³					1.04	0.55-1.65				
25 Bq/m ³					0.96	0.62-1.33				
30 Bq/m ³	1.73	0.11-12.8			0.92	0.62-1.22				
40 Bq/m ³	2.28	0.07-28.3	1.23	0.90-1.56	0.91	0.68-1.14	1.02	0.56-1.57	1.02	0.57-1.58
50 Bq/m ³	1.28	0.21-4.73	1.17	0.92-1.40	0.96	0.85-1.06	1.07	0.75-1.39	0.65	0.42-0.89
55 Bq/m ³	1.06	0.49-1.84	1.03	0.93-1.11	0.98	0.94-1.02	1.02	0.88-1.13	0.47	0.29-0.66
58 Bq/m ³ (reference)	1.00	reference	1.00	reference	1.00	reference	1.00	reference	1.00	reference
75 Bq/m ³	1.25	0.08-8.82	1.22	0.92-1.49	1.01	0.85-1.14	1.39	0.55-2.73	6.53	2.65-12.6
80 Bq/m ³	1.31	0.09-9.10	1.32	1.01-1.61	1.01	0.83-1.17	1.88	0.26-7.86	3.67	1.49-7.08
100 Bq/m ³	1.38	0.10-9.20	1.98	1.40-2.56	1.05	0.83-1.24			5.82	1.09-19.8
150 Bq/m ³					0.96	0.79-1.10				
158 Bq/m ³ (ref.+100)					0.96	0.79-1.12				
200 Bq/m ³					1.15	0.58-1.90				

sIR: mean spatial indoor radon exposure in the surrounding area; OR: averaged odds ratios (reference class: 58 Bq/m³ - LRE lowest risk exposure; avg. by Rubin's equation with model weights derived from Δ AIC); all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years); 95%-CI 95% confidence interval;

S3-Figure 5 Odds ration estimates (after model averaging): Δ AIC-weighted by participating study

sIR: mean spatial indoor radon exposure in the surrounding area; all ORs are adjusted for sex, age, smoking (type: never, former and current smoker; age start smoking; time since stop smoking; pack years) and averaged by Rubin's equation with model weights derived from Δ AIC; left panel: OR with reference class: 58 Bq/m³; right panel: OR with study specific reference class: 33, 42 or 58 Bq/m³ - OR for MSH-PMH scaled differently.

1.2 Lowest risk exposure level (LRE): Δ AIC-weightedS3-Table 7 lowest risk exposure (LRE): overall LC and subgroups (Δ AIC-weighted)

		no. fitted splines	non-hormesis splines	hormesis splines	mean LRE [Bq/m ³]	95%-CI	range
total sample		44	2	42 95%	57.6	56.1-59.2	38.0-64.0
sex	men	44	9	35 80%	42.4	38.4-46.3	29.0-60.0
	women	44	9	35 80%	54.5	52.1-56.8	18.0-61.0
age	Q1: ≤ 60 years	44	4	40 91%	36.0	32.1-39.9	28.0-75.0
	Q2: 60-68 years	44	3	41 93%	56.9	55.6-58.2	42.0-62.0
	Q3: 69-74 years	44	30	14 32%	26.3	25.5-27.0	24.0-28.0
	Q4: ≥ 75 years	44	19	25 57%	37.4	35.9-39.0	32.0-43.0
never smoker		44	1	43 98%	57.1	54.7-59.5	35.0-70.0
former smoker	Q1: < 38 py	44	4	40 91%	43.4	39.9-47.0	28.0-58.0
	Q2: 38-59 py	44	41	3 7%	21.2	20.0-22.3	21.0-22.0
	Q3: > 59 py	43	10	33 77%	42.7	41.3-44.1	37.0-48.0
current smoker	Q1: < 38 py	42	23	19 45%	46.6	40.3-52.9	33.0-62.0
	Q2: 38-59 py	42	25	17 40%	52.7	44.6-60.7	34.0-75.0
	Q3: > 59 py	43	26	17 40%	66.3	53.7-78.9	37.0-100.0
participating study	MSH-PMH	28	10	18 64%	42.7	42.4-43.1	42.0-55.0
	NICCC-LCA	28	5	23 82%	50.0	45.9-54.1	37.0-66.0
	CAPUA	32	22	10 31%	54.8	52.4-57.2	50.0-61.0
	EAGLE	32	2	30 94%	57.0	55.8-58.3	40.0-60.0
	HLCS	44	28	16 36%	35.5	34.0-37.1	31.0-43.0
histology	SqCLC	44	22	22 50%	29.8	24.0-35.6	16.0-50.0
	SCLC	44	8	36 82%	47.4	46.0-48.9	24.0-50.0
	LCLC	44	8	36 82%	41.7	40.5-42.8	36.0-50.0
	AdenoLC	44	1	43 98%	40.0	35.7-44.3	28.0-75.0

LRE: lowest risk exposure level [Bq/m³]; no. models: number of spline models a LRE could be determined between 10 and 125 Bq/m³; 95% confidence intervals; range: minimum to maximum; Q1-Q4: quartiles; py pack years; age: Q1-Q4: quartiles; smoking: Q1-Q3: thirds (Q1: ≤ 38 py, Q2: 38-59 py, Q3: > 59 py); LCLC: large cell lung cancer; SCLC: small cell lung cancer; SqCLC: squamous cell lung cancer, AdenoLC: lung adenocarcinoma

2 Spline models (Δ BIC-weighted)

2.1 Odds ratio (OR) estimate: Δ BIC-weighted

S3-Table 8 Odds ratio estimates for overall LC (after model averaging): Δ BIC-weighted

	ΔBIC-weighted				
	OR	95%	p-value	betw./total var.	# models
10 Bq/m³	1.38	0.99-1.76	0.0547	4%	44
20 Bq/m³	1.26	1.00-1.50	0.0485	4%	44
25 Bq/m³	1.21	0.99-1.40	0.0501	5%	44
30 Bq/m³	1.16	0.99-1.30	0.0578	5%	44
40 Bq/m³	1.06	0.97-1.14	0.1446	4%	44
50 Bq/m³	1.00	0.97-1.03	0.5604	7%	44
55 Bq/m³	0.99	0.98-1.00	0.8462	10%	44
58 Bq/m³	1.00	reference			44
75 Bq/m³	1.07	1.03-1.11	0.0002	6%	44
80 Bq/m³	1.11	1.06-1.15	<.0001	5%	44
100 Bq/m³	1.27	1.17-1.35	<.0001	6%	44
150 Bq/m³	1.61	1.46-1.73	<.0001	1%	44
164 Bq/m³	1.67	1.50-1.80	<.0001	1%	44
200 Bq/m³	1.89	1.58-2.15	<.0001	2%	44
250 Bq/m³	2.33	1.76-2.87	<.0001	3%	44

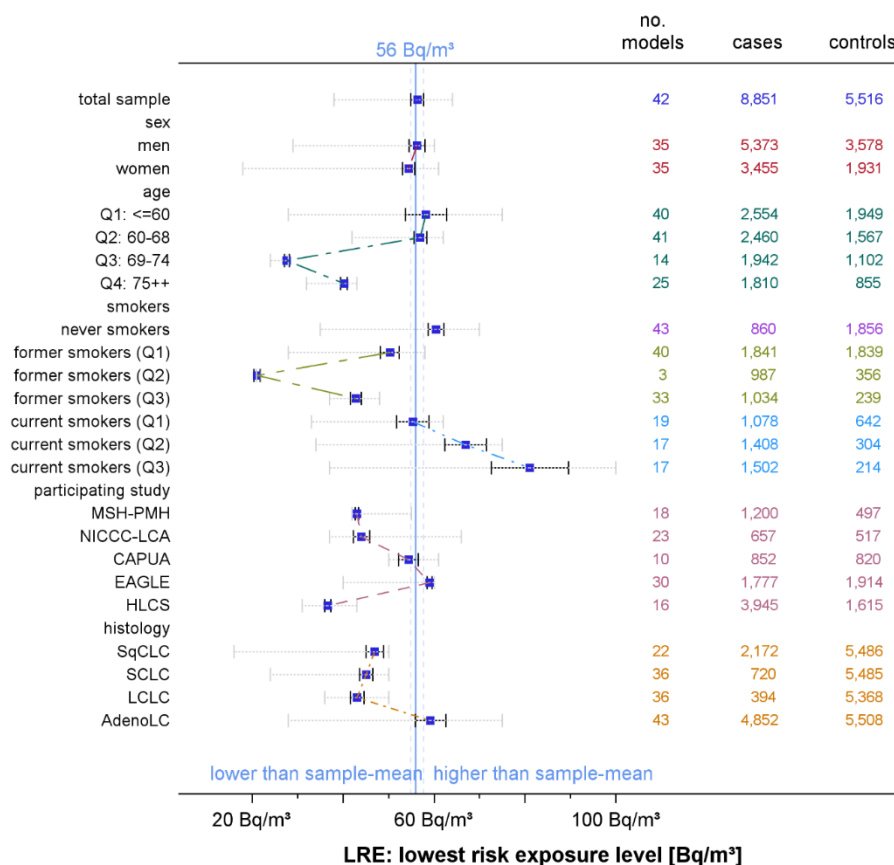
Reference class: 58 Bq/m³ (median observer sIR); averaged OR odds ratio (by Rubin's equation, model weights derived from AIC or BIC), 95%-CI 95% confidence interval; betw./total var. Percentage of between point estimate variance on the total variance; # model Number of models that were averaged

2.2 Lowest risk exposure level (LRE): Δ BIC-weighted

S3-Table 9 Lowest risk exposure level (LRE): overall LC and subgroups (Δ BIC-weighted)

		no. models	mean LRE [Bq/m ³]	95%-CI	range
total sample		42	56.3	54.9-57.7	38.0-64.0
sex	men	35	56.3	54.5-58.1	29.0-60.0
	women	35	54.4	53.0-55.8	18.0-61.0
age	Q1: ≤60 years	40	58.2	53.7-62.8	28.0-75.0
	Q2: 60-68 years	41	57.0	55.6-58.4	42.0-62.0
	Q3: 69-74 years	14	27.6	27.1-28.2	24.0-28.0
	Q4: ≥75 years	25	40.2	39.5-40.9	32.0-43.0
never smoker		43	60.5	58.7-62.2	35.0-70.0
former smoker	Q1: <38 py	40	50.3	48.2-52.3	28.0-58.0
	Q2: 38-59 py	3	21.1	20.4-21.7	21.0-22.0
	Q3: >59 py	33	42.8	41.6-44.1	37.0-48.0
current smoker	Q1: <38 py	19	55.3	51.8-58.8	33.0-62.0
	Q2: 38-59 py	17	66.9	62.3-71.5	34.0-75.0
	Q3: >59 py	17	81.1	72.6-89.6	37.0-100.0
study site	MSH-PMH	18	43.1	42.7-43.4	42.0-55.0
	NICCC-LCA	23	44.1	42.3-45.8	37.0-66.0
	CAPUA	10	54.4	52.2-56.6	50.0-61.0
	EAGLE	30	59.0	58.5-59.5	40.0-60.0
	HSPH	16	36.6	36.0-37.3	31.0-43.0
histology	SqCLC	22	47.0	45.1-48.9	16.0-50.0
	SCLC	36	45.1	43.7-46.6	24.0-50.0
	LCLC	36	43.1	41.6-44.6	36.0-50.0
	AdenoLC	43	59.2	55.8-62.6	28.0-75.0

LRE: lowest risk exposure level [Bq/m³]; no. models: number of spline models a LRE could be determined between 10 and 125 Bq/m³; 95% confidence intervals; range: minimum to maximum; age Q1-Q4: quartiles; smoking Q1-Q3: thirds; py pack years; LCLC: large cell lung cancer; SCLC: small cell lung cancer; SqCLC: squamous cell lung cancer, AdenoLC: lung adenocarcinoma

S3-Figure 6 Lowest risk exposure level (LRE): overall LC and subgroups (Δ BIC-weighted)

LRE: lowest risk exposure level [Bq/m³]; no. models: number of spline models a LRE could be determined between 10 and 125 Bq/m³; 95% confidence intervals; range: minimum to maximum; age Q1-Q4: quartiles; smoking Q1-Q3: thirds by pack years; LCLC: large cell lung cancer; SCLC: small cell lung cancer; SqCLC: squamous cell lung cancer, AdenoLC: lung adenocarcinoma