

# Association between polycyclic aromatic hydrocarbons (PAH) dietary exposure and mortality risk in the E3N cohort

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**Table 1: Baseline characteristics<sup>a</sup> of the study population according to PAH4 dietary intake in the E3N cohort (N=72 513)**

	PAH4 dietary intake (ng/day)				
	All (N=72 513)	Q1 (N=18 128)	Q2 (N=18 128)	Q3 (N=18 129)	Q4 (N=18 128)
Age (years)	52.9 (6.7)	54.2 (7)	53 (6.7)	52.5 (6.6)	52.1 (6.3)
Follow-up duration (years)	16.5 (3.4)	16.5 (3.5)	16.6 (3.4)	16.6 (3.4)	16.5 (3.4)
BMI (kg/m <sup>2</sup> )	22.7 (3.1)	22.5 (3)	22.6 (3)	22.8 (3.1)	23 (3.3)
<18.5	2 641 (3.64)	789 (4.35)	677 (3.73)	588 (3.24)	587 (3.24)
[18.5 – 25[	56 739 (78.25)	14 299 (78.88)	14 405 (79.46)	14 189 (78.27)	13 846 (76.38)
≥25	13 133 (18.11)	3 040 (16.77)	3 046 (16.80)	3 352 (18.49)	3 695 (20.38)
Birth generation					
≤1 930	7 282 (10.04)	2 592 (14.30)	1 759 (9.70)	1 602 (8.84)	1 329 (7.33)
]1 930 – 1 935]	9 989 (13.78)	3 045 (16.80)	2 613 (14.41)	2 268 (12.51)	2 063 (11.38)
]1 935 – 1 940]	14 698 (20.27)	3 770 (20.80)	3 725 (20.55)	3 654 (20.16)	3 549 (19.58)
]1 940 – 1 945]	17 803 (24.55)	4 128 (22.77)	4 405 (24.30)	4 545 (25.07)	4 725 (26.06)
>1 945	22 741 (31.36)	4 593 (25.34)	5 626 (31.03)	6 060 (33.43)	6 462 (35.65)
Education level					
<12 years	8 177 (11.28)	2 368 (13.06)	1 996 (11.01)	1 910 (10.54)	1 903 (10.50)
12 to 14 years	38 376 (52.92)	9 605 (52.98)	9 738 (53.72)	9 608 (53.00)	9 425 (51.99)
>14 years	25 960 (35.80)	6 155 (33.95)	6 394 (35.27)	6 611 (36.47)	6 800 (37.51)
Smoking status					
Never	40 240 (55.49)	10 727 (59.17)	10 161 (56.05)	9 867 (54.43)	9 485 (52.32)
Former	23 121 (31.89)	5 277 (29.11)	5 719 (31.55)	5 953 (32.84)	6 172 (34.05)
Current	9 152 (12.62)	2 124 (11.72)	2 248 (12.40)	2 309 (12.74)	2 471 (13.63)
Physical activity (MET-hours/week)	49.3 (50.5)	48.2 (54.2)	48.1 (50.6)	49.3 (46.3)	51.7 (50.3)
Menopausal status and recent use of MHT					
Premenopausal	37 276 (51.41)	7 976 (44.00)	9 235 (50.94)	9 831 (54.23)	10 234 (56.45)
Menopausal and recent MHT use	10 038 (13.84)	2 590 (14.29)	2 556 (14.10)	2 475 (13.65)	2 417 (13.33)
Menopausal and no recent MHT use	21 651 (29.86)	6 613 (36.48)	5 467 (30.16)	4 925 (27.17)	4 646 (25.63)
Menopausal but we don't know if and when the MHT was used	3 548 (4.89)	949 (5.23)	870 (4.80)	898 (4.95)	831 (4.58)
Energy intake (excluding energy from alcohol and lipids, kcal/day)	1 329 (356.5)	1 085.2 (262.1)	1 279 (291.2)	1 403.1 (327.3)	1 548.5 (363.7)

Alcohol consumption (g ethanol/day)	11.6 (13.9)	8.8 (11.9)	10.7 (12.9)	12.3 (14.1)	14.7 (15.8)
Lipids consumption (g/day)	88.9 (27)	69.1 (18.1)	83.7 (20.1)	94.9 (23.4)	108.1 (28.5)
Adherence to healthy dietary pattern	-0.002 (0.979)	-0.4 (0.8)	-0.2 (0.9)	0.1 (0.9)	0.4 (1.1)
Bread and salty cereal products consumption (g/day)	128.1 (77.9)	96.5 (62.1)	122 (71.6)	136.8 (77.9)	157.2 (85.4)
Fat consumption (g/day)	17.2 (10.8)	12.3 (7.7)	15.7 (8.9)	18.4 (10.5)	22.4 (12.7)
Sea products consumption (g/day)	38.2 (27.4)	25.6 (19)	32.8 (21)	39.6 (24.2)	54.6 (34)
Cakes and sweet cereal products consumption (g/day)	43.7 (37.5)	29.4 (27.1)	40.7 (32.9)	48.3 (38.1)	56.3 (44.3)
Pizza, quiche, crepe consumption (g/day)	20.5 (22)	11.1 (12.2)	17.7 (16.2)	23.5 (21.7)	29.9 (29.4)
Starch food consumption (g/day)	156.8 (86.9)	117.5 (71.9)	150.6 (78.1)	168.7 (84.8)	190.1 (94.4)
Dairy products consumption (g/day)	344 (209.4)	321 (201)	334.5 (203.1)	351.1 (210.8)	369.5 (219.3)
Meat consumption (g/day)	95.8 (47.2)	83.2 (43)	94.4 (45)	100.4 (46.7)	105.3 (50.7)
Charcuterie consumption (g/day)	13.5 (14.5)	7.2 (8.8)	11.7 (11.6)	15.4 (14.2)	19.9 (18.4)
Eggs consumption (g/day)	25 (20.2)	18.4 (16.2)	22.9 (17.5)	27.2 (19.9)	31.7 (24)
Coffee consumption (L/day)	332.6 (282.2)	286.3 (250.3)	323.7 (269)	348 (285.1)	372.3 (313.3)
Vegetables consumption (g/day)	389.6 (178.9)	362.4 (174.2)	381.3 (172.6)	395.6 (176)	419.2 (187.5)
Sandwich, hamburger consumption (g/day)	9.3 (19.6)	4.1 (10.7)	7.9 (15.9)	10.8 (19.8)	14.4 (26.8)
Offal consumption (g/day)	7.3 (11.1)	4.9 (8.2)	6.6 (10.1)	7.8 (11)	9.8 (13.7)
Alcohol consumption (L/day)	134.8 (167.8)	100.4 (142.3)	123 (155.3)	143.3 (169.3)	172.4 (192)
Fruits consumption (g/day)	346.6 (200.5)	330.9 (194.4)	338.7 (195.7)	349 (198.8)	367.8 (210.8)
Soda consumption (L/day)	10.6 (44.9)	7.6 (39.1)	9.6 (42.6)	11.5 (43.8)	13.6 (52.6)
Sugar products consumption (g/day)	31.8 (26.4)	27.6 (24.7)	31.3 (25.5)	33.4 (26.8)	34.7 (28)
Teas consumption (L/day)	187 (280.5)	181.5 (277.6)	178.8 (273.6)	185.6 (279.7)	202 (290.2)
Vinaigrette consumption (g/day)	15.6 (9)	14.1 (8.7)	15 (8.5)	16 (9)	17.2 (9.5)
Water consumption (L/day)	860.5 (547.4)	810.2 (538.6)	839.1 (529)	875 (544.4)	917.9 (570.7)

<sup>a</sup> Mean (std) for continuous variables, N (%) for categorical variables

**Table 2: Hazard ratios (95% CI) estimated by Cox multivariable regression models for the risk of all-cause mortality according to PAH4 dietary intake (ng/day) estimated according to the lower bound scenario in the E3N cohort (N=72 513)**

	N non-cases/ N cases	Model 1 <sup>a</sup> HR (95% CI)	Model 2 <sup>b</sup> HR (95% CI)	Model 3 <sup>c</sup> HR (95% CI)
<b>Continuous PAH4 dietary intake (ng/day)</b>	67 893/4 620	1 (0.97-1.03)	0.99 (0.96-1.02)	1 (0.97-1.04)
p-value		0.907	0.482	0.907
<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>				
Q1 (2.1-49.9)	16 777/1 351	Ref	Ref	Ref
Q2 (49.9-66.1)	16 971/1 157	0.97 (0.89-1.05)	0.96 (0.89-1.04)	0.98 (0.9-1.06)
Q3 (66.1-88.5)	17 045/1 084	0.96 (0.89-1.04)	0.95 (0.88-1.03)	0.97 (0.89-1.06)
Q4 (88.5-535.5)	17 100/1 028	0.96 (0.88-1.04)	0.94 (0.86-1.02)	0.96 (0.87-1.06)
p-trend		0.306	0.129	0.429

<sup>a</sup> **Model 1:** Adjustment on age as time-scale (years)

<sup>b</sup> **Model 2:** M1 + adjustment on BMI (kg/m<sup>2</sup>), birth generation (<=1930, ]1930 – 1935], ]1935 – 1940], ]1940 – 1945], >1945), education level (<12 years, 12 to 14 years, >14 years), smoking status (never smoker, former smoker, current smoker), physical activity (MET-hours/week), menopausal status and recent MHT use (premenopausal, menopausal and recent MHT use, menopausal and no recent MHT use, menopausal but we don't know if and when the MHT was used)

<sup>c</sup> **Model 3:** M2 + adjustment on total energy intake (excluding energy from alcohol and lipids, kcal/day), alcohol consumption (g ethanol/day), lipids consumption (g/day)

**Table 3: Hazard ratios (95% CI) estimated by Cox multivariable regression models of the association between PAH4 dietary intake (ng/day) estimated according to the lower bound scenario with specific-cause mortality risk in the E3N cohort**

		<b>N non-cases/ N cases</b>	<b>Model 3<sup>a</sup> HR (95% CI)</b>
<b>All-cancer (N=72 451)</b>	<b>Continuous PAH4 dietary intake (ng/day)</b>	69 725/2 726	1.02 (0.97-1.06)
	p-value		0.511
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		Ref
	Q1 (2.1-49.9)	17 343/761	
	Q2 (49.9-66.1)	17 417/699	1 (0.9-1.11)
	Q3 (66.1-88.5)	17 486/628	0.93 (0.83-1.04)
	Q4 (88.5-535.5)	17 479/638	0.96 (0.85-1.09)
p-trend		0.445	
<b>Breast cancer (N=72 309)</b>	<b>Continuous PAH4 dietary intake (ng/day)</b>	71 519/790	0.99 (0.91-1.08)
	p-value		0.823
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		Ref
	Q1 (2.1-49.9)	17 856/210	
	Q2 (49.9-66.1)	17 860/214	1.08 (0.89-1.31)
	Q3 (66.1-88.5)	17 890/194	1 (0.81-1.24)
	Q4 (88.5-535.5)	17 913/172	0.89 (0.7-1.13)
p-trend		0.192	
<b>Colorectal cancer (N=72 309)</b>	<b>Continuous PAH4 dietary intake (ng/day)</b>	72 066/243	0.99 (0.85-1.15)
	p-value		0.875
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		Ref
	Q1 (2.1-49.9)	17 997/69	
	Q2 (49.9-66.1)	18 014/60	0.95 (0.67-1.37)
	Q3 (66.1-88.5)	18 027/57	0.94 (0.64-1.38)
	Q4 (88.5-535.5)	18 028/57	0.94 (0.62-1.45)
p-trend		0.816	
<b>Lung/tracheal cancer (N=72 309)</b>	<b>Continuous PAH4 dietary intake (ng/day)</b>	72 032/277	1.15 (1.02-1.29)
	p-value		0.023
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		Ref
	Q1 (2.1-49.9)	17 988/78	
	Q2 (49.9-66.1)	18 016/58	0.81 (0.57-1.15)
	Q3 (66.1-88.5)	18 021/63	0.93 (0.65-1.34)
	Q4 (88.5-535.5)	18 007/78	1.19 (0.82-1.75)
p-trend		0.160	
<b>All cardiovascular disease (N=72 451)</b>	<b>Continuous PAH4 dietary intake (ng/day)</b>	71 867/584	1.03 (0.94-1.14)
	p-value		0.475
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		Ref
	Q1 (2.1-49.9)	17 913/191	
	Q2 (49.9-66.1)	17 976/140	0.92 (0.74-1.16)
	Q3 (66.1-88.5)	17 985/129	0.94 (0.73-1.20)
	Q4 (88.5-535.5)	17 993/124	0.99 (0.75-1.30)
p-trend		0.959	
<b>Stroke and coronary heart disease (N=72 451)</b>	<b>Continuous PAH4 dietary intake (ng/day)</b>	72 164/287	1.00 (0.87-1.15)
	p-value		0.985
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		Ref
	Q1 (2.1-49.9)	18 008/96	
	Q2 (49.9-66.1)	18 049/67	0.91 (0.65-1.25)
Q3 (66.1-88.5)	18 053/61	0.93 (0.66-1.33)	

Q4 (88.5-535.5) 18 054/63 1.08 (0.74-1.59)  
p-trend 0.599

<sup>a</sup> **Model 3:** Adjustment on age as time-scale (years), BMI (kg/m<sup>2</sup>), birth generation (<=1930, ]1930 – 1935], ]1935 – 1940], ]1940 – 1945], >1945), education level (<12 years, 12 to 14 years, >14 years), smoking status (never smoker, former smoker, current smoker), physical activity (MET-hours/week), menopausal status and recent MHT use (premenopausal, menopausal and recent MHT use, menopausal and no recent MHT use, menopausal but we don't know if and when the MHT was used), total energy intake (excluding energy from alcohol and lipids, kcal/day), alcohol consumption (g ethanol/day), lipids consumption (g/day)

**Table 4: Hazard ratios (95% CI) estimated by Cox multivariable regression models for the risk of lung/tracheal cancer mortality according to PAH4 dietary intake (ng/day) estimated according to the lower bound scenario, and stratified on smoking status, in the E3N cohort (N=72 309)**

		N non-cases/ N cases	Model 3 <sup>a</sup> HR (95% CI)
Never smoker (N=40 116)	<b>Continuous PAH4 dietary intake (ng/day)</b>	40 018/98	1.09 (0.87-1.37)
	p-value		0.465
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		
	Q1 (2.1-49.9)	10 660/30	Ref
	Q2 (49.9-66.1)	10 102/22	0.9 (0.51-1.59)
	Q3 (66.1-88.5)	9 813/27	1.24 (0.7-2.22)
	Q4 (88.5-535.5)	9 443/19	1.02 (0.52-2.02)
	p-trend		0.782
Former smoker (N=23 073)	<b>Continuous PAH4 dietary intake (ng/day)</b>	22 998/75	1.14 (0.92-1.42)
	p-value		0.238
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		
	Q1 (6.3-49.9)	5 243/17	Ref
	Q2 (49.9-66.1)	5 692/18	1.01 (0.51-2)
	Q3 (66.1-88.5)	5 933/14	0.74 (0.35-1.59)
	Q4 (88.5-511.6)	6 130/26	1.28 (0.61-2.68)
	p-trend		0.429
Current smoker (N=9 120)	<b>Continuous PAH4 dietary intake (ng/day)</b>	9 016/104	1.21 (1.01-1.44)
	p-value		0.037
	<b>Quartiles of PAH4 dietary intake (min-max, ng/day)</b>		
	Q1 (8.0-49.9)	2 085/31	Ref
	Q2 (49.9-66.1)	2 222/18	0.65 (0.36-1.18)
	Q3 (66.1-88.5)	2 275/22	0.87 (0.48-1.59)
	Q4 (88.5-417.3)	2 434/33	1.35 (0.74-2.47)
	p-trend		0.121

<sup>a</sup> **Model 3:** Adjustment on age as time-scale (years), BMI (kg/m<sup>2</sup>), birth generation (<=1930, ]1930 – 1935], ]1935 – 1940], ]1940 – 1945], >1945), education level (<12 years, 12 to 14 years, >14 years), physical activity (MET-hours/week), menopausal status and recent MHT use (premenopausal, menopausal and recent MHT use, menopausal and no recent MHT use, menopausal but we don't know if and when the MHT was used), total energy intake (excluding energy from alcohol and lipids, kcal/day), alcohol consumption (g ethanol/day), lipids consumption (g/day)