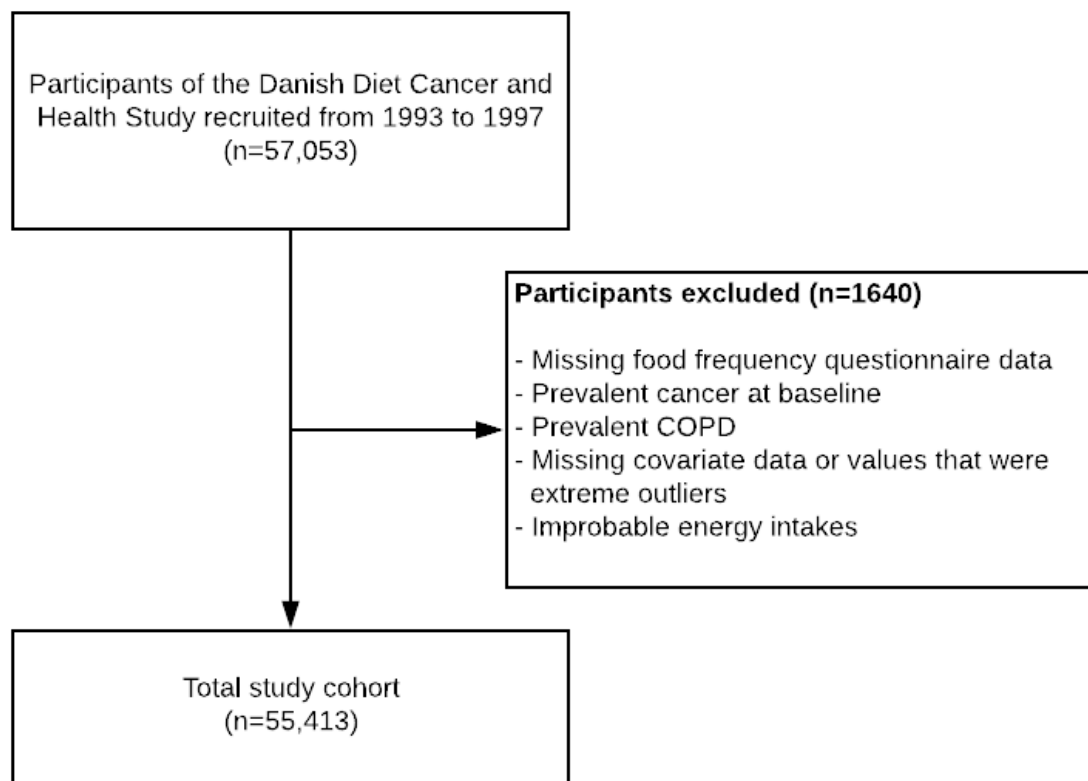


**Flavonoid intakes associate with a lower risk of chronic obstructive pulmonary disease  
in smokers**

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**Online Data Supplement**



**Figure E1.** Participant flow diagram in the Danish Diet, Cancer, and Health study.

## **METHODS**

### Covariates:

Participants completed several questionnaires upon enrolment in the Danish Diet, Cancer and Health study, from which we obtained data on their sex, age, education, smoking habits, alcohol consumption, daily physical activity, and diet. In the present study, participants were defined as “current smokers” at baseline if they reported that they were currently smoking daily, “previous smokers” if they indicated that, at any stage in their life, they smoked daily for at least one year, or “never smokers” if they were neither of the above. Anthropometry was measured during a clinical visit at the study centers. Socio-economic status was represented using each participant’s average annual income over the five years prior to study enrolment (defined as household income after taxation and interest, using the value of the Danish currency in 2015). Prevalent diabetes, chronic kidney disease, ischemic heart disease, and ischemic stroke were determined by self-reported data in combination with ICD-8, ICD-10, and Anatomical Therapeutic Chemical (ATC) Classification codes (Table E1).

**Table E1.** Definitions of prevalent comorbidities at baseline

<b>Prevalent disease</b>	<b>Definition</b>
Ischemic heart disease	Self-reported myocardial infarction, ICD-8 diagnosis [410-414] or ICD-10 diagnosis [I20-I25] prior to enrolment
Ischemic stroke	Self-reported stroke, ICD-8 diagnosis [433-434] or ICD-10 diagnosis [I63] prior to enrolment
Diabetes	Self-reported diabetes or use of insulin and other glucose-lowering medications [ATC; A10A, A10B] prior to enrolment
Chronic kidney disease	ICD-8 diagnosis [580-584] or ICD-10 diagnosis [N02-N08, N11-N12, N14, N18-N19, N26, N158-N160, N162-N164, N168, Q61, E102, E112, E132, E142, I120, M321B] prior to enrolment

ATC; Anatomical Therapeutic Chemical Classification, ICD; International Classification of Diseases [the 8<sup>th</sup> revision (ICD-8) until 1993 and the 10<sup>th</sup> revision (ICD-10) from 1994 to present].

**Table E2. Hazard ratios of chronic obstructive pulmonary disease by quintiles of flavonoid compound intakes**

Flavonoid intake quintiles					
	Q1 n = 11,083	Q2 n = 11,083	Q3 n = 11,082	Q4 n = 11,083	Q5 n = 11,082
<b>Flavonols</b>					
<b>Kaempferol</b>					
No. events	1722	1160	1074	846	755
Intake (mg/d) <sup>1</sup>	1 (0–1)	2 (1–3)	4 (3–8)	18 (8–20)	33 (20–68)
HR (95% CI)					
Model 1	ref.	0.84 (0.81, 0.86)	0.59 (0.55, 0.63)	0.45 (0.42, 0.49)	0.45 (0.42, 0.48)
Model 2	ref.	0.96 (0.94, 0.99)	0.89 (0.83, 0.96)	0.87 (0.81, 0.94)	0.86 (0.79, 0.93)
Model 3	ref.	0.98 (0.95, 1.01)	0.94 (0.88, 1.01)	0.92 (0.86, 1.00)	0.91 (0.84, 0.99)
<b>Quercetin</b>					
No. events	1653	1280	1002	874	748
Intake (mg/d) <sup>1</sup>	12 (0–16)	20 (16–24)	29 (24–37)	46 (37–58)	78 (58–168)
HR (95% CI)					
Model 1	ref.	0.73 (0.70, 0.76)	0.57 (0.54, 0.61)	0.47 (0.44, 0.50)	0.42 (0.39, 0.45)
Model 2	ref.	0.93 (0.89, 0.97)	0.88 (0.83, 0.93)	0.85 (0.79, 0.91)	0.82 (0.75, 0.88)
Model 3	ref.	0.94 (0.90, 0.99)	0.91 (0.85, 0.97)	0.89 (0.83, 0.96)	0.87 (0.80, 0.95)
<b>Flavanol monomers</b>					
<b>Epicatechin</b>					
No. events	1626	1293	1036	847	755
Intake (mg/d) <sup>1</sup>	6 (0–9)	12 (9–15)	19 (15–25)	31 (25–39)	53 (39–155)
HR (95% CI)					
Model 1	ref.	0.71 (0.67, 0.74)	0.54 (0.51, 0.58)	0.45 (0.42, 0.48)	0.41 (0.38, 0.44)
Model 2	ref.	0.93 (0.89, 0.97)	0.87 (0.82, 0.93)	0.82 (0.77, 0.88)	0.79 (0.73, 0.85)
Model 3	ref.	0.94 (0.90, 0.99)	0.90 (0.84, 0.96)	0.86 (0.80, 0.92)	0.83 (0.77, 0.90)
<b>Flavanol oligo+polymers</b>					
<b>Proanthocyanidin dimers</b>					
No. events	1671	1204	1069	833	780
Intake (mg/d) <sup>1</sup>	25 (0–38)	49 (38–62)	78 (62–94)	113 (94–138)	177 (138–510)
HR (95% CI)					
Model 1	ref.	0.69 (0.66, 0.72)	0.53 (0.50, 0.56)	0.47 (0.44, 0.50)	0.43 (0.40, 0.47)
Model 2	ref.	0.94 (0.89, 0.98)	0.88 (0.83, 0.93)	0.82 (0.77, 0.88)	0.76 (0.70, 0.82)
Model 3	ref.	0.95 (0.91, 1.00)	0.90 (0.85, 0.96)	0.85 (0.80, 0.92)	0.80 (0.74, 0.87)
<b>Proanthocyanidin trimers</b>					
No. events	1667	1178	878	992	842
Intake (mg/d) <sup>1</sup>	10 (0–14)	17 (14–20)	23 (20–29)	35 (29–42)	54 (42–320)
HR (95% CI)					
Model 1	ref.	0.65 (0.62, 0.67)	0.53 (0.50, 0.56)	0.51 (0.48, 0.54)	0.52 (0.48, 0.56)
Model 2	ref.	0.91 (0.87, 0.95)	0.87 (0.82, 0.92)	0.83 (0.78, 0.89)	0.79 (0.73, 0.85)
Model 3	ref.	0.92 (0.88, 0.97)	0.88 (0.83, 0.94)	0.85 (0.80, 0.91)	0.80 (0.74, 0.87)
<b>Flavanones</b>					
<b>Hesperidin</b>					
No. events	1451	1069	1009	998	1030
Intake (mg/d) <sup>1</sup>	2 (0–4)	6 (4–9)	12 (9–18)	24 (18–38)	54 (38–449)
HR (95% CI)					
Model 1	ref.	0.79 (0.76, 0.83)	0.66 (0.62, 0.71)	0.64 (0.60, 0.69)	0.70 (0.65, 0.75)
Model 2	ref.	0.96 (0.92, 1.00)	0.93 (0.87, 1.00)	0.93 (0.87, 0.99)	0.95 (0.89, 1.02)
Model 3	ref.	0.96 (0.92, 1.00)	0.93 (0.86, 1.00)	0.93 (0.87, 0.99)	0.95 (0.88, 1.02)
<b>Flavones</b>					
<b>Apigenin</b>					
No. events	1495	1131	1022	920	989
Intake (mg/d) <sup>1</sup>	2 (0–2)	3 (2–4)	5 (4–5)	6 (5–8)	10 (8–46)

HR (95% CI)						
Model 1	ref.	0.73 (0.70, 0.77)	0.61 (0.58, 0.65)	0.56 (0.53, 0.60)	0.57 (0.53, 0.62)	
Model 2	ref.	0.92 (0.88, 0.97)	0.88 (0.83, 0.93)	0.86 (0.80, 0.91)	0.86 (0.80, 0.93)	
Model 3	ref.	0.93 (0.88, 0.98)	0.88 (0.83, 0.94)	0.86 (0.80, 0.92)	0.87 (0.80, 0.95)	
<b>Anthocyanins</b>						
<b>Cyanidin</b>						
No. events	1438	1048	918	940	1213	
Intake (mg/d) <sup>1</sup>	1 (0–1)	1 (1–1)	2 (1–3)	4 (3–8)	17 (8–203)	
HR (95% CI)						
Model 1	ref.	0.70 (0.68, 0.73)	0.56 (0.53, 0.60)	0.56 (0.52, 0.60)	0.77 (0.71, 0.83)	
Model 2	ref.	0.89 (0.86, 0.93)	0.83 (0.78, 0.88)	0.83 (0.78, 0.89)	0.93 (0.86, 1.01)	
Model 3	ref.	0.91 (0.87, 0.95)	0.86 (0.80, 0.91)	0.86 (0.80, 0.92)	0.95 (0.87, 1.03)	
<b>Delphinidin</b>						
No. events	1536	885	1015	923	1198	
Intake (mg/d) <sup>1</sup>	0 (0–1)	1 (1–1)	2 (1–4)	5 (4–8)	18 (8–188)	
HR (95% CI)						
Model 1	ref.	0.70 (0.66, 0.73)	0.59 (0.55, 0.63)	0.61 (0.57, 0.65)	0.86 (0.79, 0.93)	
Model 2	ref.	0.87 (0.83, 0.91)	0.81 (0.75, 0.87)	0.82 (0.76, 0.88)	0.93 (0.86, 1.01)	
Model 3	ref.	0.88 (0.84, 0.93)	0.83 (0.77, 0.89)	0.84 (0.78, 0.90)	0.95 (0.87, 1.03)	
<b>Malvidin</b>						
No. events	1819	1457	613	803	865	
Intake (mg/d) <sup>1</sup>	0 (0–1)	2 (1–6)	6 (6–6)	11 (6–14)	35 (14–114)	
HR (95% CI)						
Model 1	ref.	0.75 (0.72, 0.78)	0.50 (0.47, 0.54)	0.47 (0.44, 0.50)	0.55 (0.51, 0.59)	
Model 2	ref.	0.89 (0.86, 0.93)	0.76 (0.69, 0.83)	0.72 (0.66, 0.79)	0.63 (0.57, 0.70)	
Model 3	ref.	0.91 (0.87, 0.94)	0.78 (0.72, 0.86)	0.76 (0.69, 0.83)	0.67 (0.60, 0.75)	

Hazard ratios (95% CI) for chronic obstructive pulmonary disease during 23 years of follow up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1 adjusted for age and sex; Model 1b adjusted for age, sex, BMI, smoking status, smoking pack-years, physical activity, alcohol intake, education and socio-economic status (income); Model 2 adjusted for all covariates in Model 1b plus energy intake and intakes of fish, red meat, processed meat, wholegrains, refined grains, polyunsaturated fatty acids, monounsaturated fatty acids and saturated fatty acids.

<sup>1</sup>Median; range in parentheses (all such values).

**Table E3. Hazard ratios of chronic obstructive pulmonary disease by quintiles of flavonoid intake in current smokers (n = 19,922)**

		Flavonoid intake quintiles				
		Q1 n = 3985	Q2 n = 3984	Q3 n = 3984	Q4 n = 3984	Q5 n = 3985
<b>Total Flavonoids</b>						
HR (95% CI)						
Model 1	ref.		0.83 (0.79, 0.88)	0.73 (0.67, 0.78)	0.64 (0.59, 0.69)	0.58 (0.53, 0.63)
Model 1b	ref.		0.95 (0.89, 1.01)	0.90 (0.83, 0.97)	0.83 (0.77, 0.90)	0.77 (0.70, 0.84)
Model 2	ref.		0.97 (0.91, 1.03)	0.93 (0.86, 1.01)	0.88 (0.80, 0.96)	0.82 (0.74, 0.90)
<b>Flavonols</b>						
HR (95% CI)						
Model 1	ref.		0.86 (0.81, 0.90)	0.75 (0.70, 0.81)	0.65 (0.61, 0.70)	0.57 (0.52, 0.63)
Model 1b	ref.		0.96 (0.90, 1.01)	0.92 (0.85, 0.99)	0.85 (0.79, 0.93)	0.78 (0.71, 0.86)
Model 2	ref.		0.98 (0.93, 1.05)	0.96 (0.88, 1.05)	0.91 (0.84, 1.00)	0.85 (0.77, 0.94)
<b>Flavanol monomers</b>						
HR (95% CI)						
Model 1	ref.		0.89 (0.86, 0.92)	0.76 (0.7, 0.82)	0.67 (0.62, 0.73)	0.61 (0.56, 0.67)
Model 1b	ref.		0.95 (0.92, 0.99)	0.90 (0.83, 0.97)	0.86 (0.80, 0.94)	0.82 (0.74, 0.90)
Model 2	ref.		0.97 (0.94, 1.01)	0.94 (0.87, 1.02)	0.92 (0.84, 1.00)	0.88 (0.79, 0.96)
<b>Flavanol oligo+polymers</b>						
HR (95% CI)						
Model 1	ref.		0.81 (0.76, 0.86)	0.69 (0.64, 0.74)	0.63 (0.58, 0.68)	0.58 (0.53, 0.63)
Model 1b	ref.		0.93 (0.88, 0.99)	0.87 (0.81, 0.94)	0.81 (0.75, 0.88)	0.75 (0.69, 0.82)
Model 2	ref.		0.95 (0.89, 1.01)	0.90 (0.83, 0.97)	0.85 (0.78, 0.93)	0.79 (0.72, 0.87)
<b>Anthocyanins</b>						
HR (95% CI)						
Model 1	ref.		0.73 (0.69, 0.77)	0.62 (0.57, 0.67)	0.65 (0.60, 0.70)	0.72 (0.67, 0.79)
Model 1b	ref.		0.89 (0.83, 0.94)	0.83 (0.76, 0.91)	0.86 (0.79, 0.93)	0.87 (0.79, 0.95)
Model 2	ref.		0.90 (0.84, 0.95)	0.85 (0.78, 0.93)	0.88 (0.81, 0.96)	0.90 (0.82, 0.99)
<b>Flavanones</b>						
HR (95% CI)						
Model 1	ref.		0.88 (0.84, 0.92)	0.78 (0.71, 0.85)	0.75 (0.69, 0.81)	0.77 (0.71, 0.84)
Model 1b	ref.		0.95 (0.91, 1.00)	0.92 (0.84, 1.00)	0.92 (0.85, 1.00)	0.94 (0.86, 1.03)
Model 2	ref.		0.96 (0.91, 1.01)	0.93 (0.85, 1.01)	0.93 (0.86, 1.01)	0.95 (0.87, 1.04)
<b>Flavones</b>						
HR (95% CI)						
Model 1	ref.		0.83 (0.78, 0.88)	0.74 (0.68, 0.79)	0.68 (0.63, 0.73)	0.68 (0.62, 0.74)
Model 1b	ref.		0.93 (0.88, 0.99)	0.88 (0.82, 0.95)	0.84 (0.78, 0.91)	0.83 (0.76, 0.91)
Model 2	ref.		0.95 (0.89, 1.01)	0.91 (0.84, 0.99)	0.87 (0.80, 0.94)	0.85 (0.77, 0.94)

Hazard ratios (95% CI) for chronic obstructive pulmonary disease during 23 years of follow up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1 adjusted for age and sex; Model 1b adjusted for age, sex, BMI, smoking pack-years, physical activity, alcohol intake, education and socio-economic status (income); Model 2 adjusted for all covariates in Model 1b plus energy intake and intakes of fish, red meat, processed meat, wholegrains, refined grains, polyunsaturated fatty acids, monounsaturated fatty acids and saturated fatty acids.

**Table E4. Hazard ratios of chronic obstructive pulmonary disease by quintiles of flavonoid intake in former smokers (n = 15,862)**

		Flavonoid intake quintiles				
		Q1 n = 3173	Q2 n = 3172	Q3 n = 3172	Q4 n = 3172	Q5 n = 3173
<b>Total Flavonoids</b>						
HR (95% CI)						
Model 1	ref.		0.82 (0.73, 0.92)	0.73 (0.63, 0.84)	0.70 (0.60, 0.82)	0.63 (0.53, 0.74)
Model 1b	ref.		0.94 (0.84, 1.06)	0.92 (0.80, 1.06)	0.92 (0.78, 1.07)	0.82 (0.69, 0.97)
Model 2	ref.		0.96 (0.86, 1.08)	0.96 (0.82, 1.11)	0.96 (0.82, 1.14)	0.88 (0.73, 1.05)
<b>Flavonols</b>						
HR (95% CI)						
Model 1	ref.		0.77 (0.69, 0.85)	0.66 (0.57, 0.77)	0.67 (0.58, 0.78)	0.62 (0.52, 0.73)
Model 1b	ref.		0.87 (0.78, 0.97)	0.82 (0.71, 0.96)	0.89 (0.76, 1.04)	0.82 (0.69, 0.98)
Model 2	ref.		0.90 (0.80, 1.00)	0.87 (0.74, 1.02)	0.95 (0.80, 1.12)	0.89 (0.74, 1.06)
<b>Flavanol monomers</b>						
HR (95% CI)						
Model 1	ref.		0.91 (0.85, 0.96)	0.74 (0.63, 0.88)	0.67 (0.57, 0.78)	0.67 (0.57, 0.79)
Model 1b	ref.		0.97 (0.92, 1.03)	0.91 (0.78, 1.08)	0.89 (0.76, 1.05)	0.86 (0.73, 1.02)
Model 2	ref.		0.98 (0.93, 1.05)	0.95 (0.81, 1.13)	0.94 (0.80, 1.11)	0.91 (0.77, 1.08)
<b>Flavanol oligo+polymers</b>						
HR (95% CI)						
Model 1	ref.		0.77 (0.68, 0.87)	0.71 (0.62, 0.81)	0.70 (0.60, 0.81)	0.63 (0.53, 0.74)
Model 1b	ref.		0.91 (0.81, 1.02)	0.88 (0.77, 1.01)	0.88 (0.75, 1.02)	0.79 (0.67, 0.94)
Model 2	ref.		0.93 (0.82, 1.04)	0.91 (0.79, 1.04)	0.91 (0.77, 1.06)	0.83 (0.69, 1.00)
<b>Anthocyanins</b>						
HR (95% CI)						
Model 1	ref.		0.74 (0.66, 0.83)	0.65 (0.56, 0.76)	0.69 (0.59, 0.79)	0.79 (0.67, 0.93)
Model 1b	ref.		0.91 (0.80, 1.03)	0.87 (0.74, 1.03)	0.89 (0.75, 1.04)	0.94 (0.78, 1.13)
Model 2	ref.		0.92 (0.81, 1.04)	0.89 (0.75, 1.06)	0.91 (0.76, 1.07)	0.97 (0.80, 1.16)
<b>Flavanones</b>						
HR (95% CI)						
Model 1	ref.		0.79 (0.71, 0.88)	0.68 (0.58, 0.8)	0.70 (0.61, 0.81)	0.79 (0.67, 0.93)
Model 1b	ref.		0.88 (0.79, 0.98)	0.82 (0.70, 0.97)	0.88 (0.76, 1.02)	0.99 (0.84, 1.16)
Model 2	ref.		0.88 (0.79, 0.98)	0.82 (0.69, 0.97)	0.88 (0.76, 1.03)	0.99 (0.84, 1.18)
<b>Flavones</b>						
HR (95% CI)						
Model 1	ref.		0.71 (0.63, 0.79)	0.63 (0.55, 0.72)	0.68 (0.59, 0.78)	0.77 (0.66, 0.91)
Model 1b	ref.		0.81 (0.73, 0.90)	0.77 (0.68, 0.88)	0.84 (0.73, 0.97)	0.94 (0.80, 1.10)
Model 2	ref.		0.83 (0.74, 0.93)	0.80 (0.69, 0.93)	0.87 (0.75, 1.03)	0.99 (0.82, 1.19)

Hazard ratios (95% CI) for chronic obstructive pulmonary disease during 23 years of follow up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1 adjusted for age and sex; Model 1b adjusted for age, sex, BMI, smoking pack-years, physical activity, alcohol intake, education and socio-economic status (income); Model 2 adjusted for all covariates in Model 1b plus energy intake and intakes of fish, red meat, processed meat, wholegrains, refined grains, polyunsaturated fatty acids, monounsaturated fatty acids and saturated fatty acids.



**Table E5. Hazard ratios of chronic obstructive pulmonary disease by quintiles of flavonoid compound intakes in current smokers (n = 19,922)**

Flavonoid intake quintiles					
	Q1 n = 3985	Q2 n = 3984	Q3 n = 3984	Q4 n = 3984	Q5 n = 3985
<b>Flavonols</b>					
<b>Kaempferol</b>					
HR (95% CI)					
Model 1	ref.	0.90 (0.87, 0.93)	0.75 (0.69, 0.81)	0.67 (0.61, 0.72)	0.61 (0.56, 0.67)
Model 2	ref.	0.96 (0.93, 1.00)	0.90 (0.83, 0.98)	0.87 (0.80, 0.95)	0.82 (0.74, 0.90)
Model 3	ref.	0.99 (0.95, 1.02)	0.96 (0.88, 1.05)	0.94 (0.86, 1.03)	0.88 (0.80, 0.97)
<b>Quercetin</b>					
HR (95% CI)					
Model 1	ref.	0.86 (0.81, 0.91)	0.76 (0.70, 0.81)	0.65 (0.61, 0.70)	0.58 (0.53, 0.63)
Model 2	ref.	0.95 (0.90, 1.01)	0.91 (0.84, 0.98)	0.85 (0.78, 0.92)	0.78 (0.71, 0.86)
Model 3	ref.	0.98 (0.92, 1.04)	0.95 (0.87, 1.03)	0.90 (0.83, 0.98)	0.84 (0.76, 0.93)
<b>Flavanol monomers</b>					
<b>Epicatechin</b>					
HR (95% CI)					
Model 1	ref.	0.82 (0.77, 0.87)	0.71 (0.66, 0.77)	0.62 (0.58, 0.67)	0.57 (0.52, 0.62)
Model 2	ref.	0.93 (0.88, 0.99)	0.88 (0.81, 0.95)	0.81 (0.75, 0.88)	0.75 (0.69, 0.83)
Model 3	ref.	0.95 (0.89, 1.01)	0.91 (0.84, 0.99)	0.86 (0.78, 0.93)	0.80 (0.73, 0.88)
<b>Flavanol oligo+polymers</b>					
<b>Proanthocyanidin dimers</b>					
HR (95% CI)					
Model 1	ref.	0.82 (0.77, 0.87)	0.70 (0.64, 0.75)	0.62 (0.57, 0.67)	0.57 (0.52, 0.62)
Model 2	ref.	0.94 (0.88, 0.99)	0.88 (0.81, 0.95)	0.81 (0.75, 0.88)	0.73 (0.67, 0.80)
Model 3	ref.	0.96 (0.90, 1.02)	0.91 (0.84, 0.99)	0.85 (0.78, 0.93)	0.78 (0.71, 0.86)
<b>Proanthocyanidin trimers</b>					
HR (95% CI)					
Model 1	ref.	0.77 (0.73, 0.81)	0.66 (0.62, 0.71)	0.62 (0.58, 0.67)	0.60 (0.55, 0.65)
Model 2	ref.	0.90 (0.85, 0.95)	0.85 (0.79, 0.92)	0.83 (0.76, 0.90)	0.77 (0.70, 0.85)
Model 3	ref.	0.92 (0.87, 0.97)	0.88 (0.81, 0.95)	0.86 (0.79, 0.93)	0.79 (0.72, 0.88)
<b>Flavanones</b>					
<b>Hesperidin</b>					
HR (95% CI)					
Model 1	ref.	0.89 (0.85, 0.94)	0.80 (0.73, 0.87)	0.77 (0.71, 0.83)	0.78 (0.72, 0.85)
Model 2	ref.	0.97 (0.92, 1.02)	0.94 (0.86, 1.02)	0.94 (0.87, 1.02)	0.95 (0.87, 1.04)
Model 3	ref.	0.97 (0.92, 1.02)	0.94 (0.87, 1.03)	0.94 (0.87, 1.03)	0.96 (0.87, 1.05)
<b>Flavones</b>					
<b>Apigenin</b>					
HR (95% CI)					
Model 1	ref.	0.86 (0.81, 0.91)	0.76 (0.71, 0.82)	0.70 (0.65, 0.76)	0.68 (0.62, 0.74)
Model 2	ref.	0.94 (0.89, 1.00)	0.90 (0.83, 0.97)	0.86 (0.79, 0.92)	0.83 (0.76, 0.91)
Model 3	ref.	0.96 (0.90, 1.02)	0.92 (0.84, 0.99)	0.88 (0.80, 0.95)	0.86 (0.77, 0.95)
<b>Anthocyanins</b>					
<b>Cyanidin</b>					
HR (95% CI)					
Model 1	ref.	0.80 (0.76, 0.83)	0.68 (0.63, 0.74)	0.68 (0.62, 0.73)	0.85 (0.77, 0.93)
Model 2	ref.	0.89 (0.85, 0.94)	0.83 (0.76, 0.89)	0.82 (0.76, 0.89)	0.92 (0.84, 1.02)
Model 3	ref.	0.92 (0.87, 0.96)	0.86 (0.80, 0.93)	0.86 (0.79, 0.94)	0.95 (0.86, 1.05)
<b>Delphinidin</b>					
HR (95% CI)					
Model 1	ref.	0.78 (0.74, 0.81)	0.64 (0.59, 0.69)	0.65 (0.60, 0.71)	0.84 (0.77, 0.92)
Model 2	ref.	0.88 (0.84, 0.93)	0.80 (0.73, 0.88)	0.81 (0.74, 0.89)	0.91 (0.82, 1.00)

Model 3	ref.	0.90 (0.85, 0.94)	0.82 (0.75, 0.90)	0.83 (0.76, 0.91)	0.93 (0.85, 1.02)
<b>Malvidin</b>					
HR (95% CI)					
Model 1	ref.	0.87 (0.84, 0.89)	0.58 (0.53, 0.63)	0.55 (0.50, 0.59)	0.56 (0.51, 0.61)
Model 2	ref.	0.92 (0.89, 0.95)	0.72 (0.64, 0.80)	0.69 (0.62, 0.77)	0.62 (0.54, 0.70)
Model 3	ref.	0.93 (0.89, 0.96)	0.74 (0.67, 0.83)	0.72 (0.65, 0.80)	0.66 (0.58, 0.75)

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Hazard ratios (95% CI) for chronic obstructive pulmonary disease during 23 years of follow up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1 adjusted for age and sex; Model 1b adjusted for age, sex, BMI, smoking pack-years, physical activity, alcohol intake, education and socio-economic status (income); Model 2 adjusted for all covariates in Model 1b plus energy intake and intakes of fish, red meat, processed meat, wholegrains, refined grains, polyunsaturated fatty acids, monounsaturated fatty acids and saturated fatty acids.

**Table E6. Hazard ratios of chronic obstructive pulmonary disease by quintiles of flavonoid compound intakes in former smokers (n = 15,862)**

Flavonoid intake quintiles					
	Q1 n = 3173	Q2 n = 3172	Q3 n = 3172	Q4 n = 3172	Q5 n = 3173
<b>Flavonols</b>					
<b>Kaempferol</b>					
HR (95% CI)					
Model 1	ref.	0.90 (0.85, 0.95)	0.70 (0.59, 0.82)	0.65 (0.55, 0.76)	0.66 (0.56, 0.78)
Model 2	ref.	0.97 (0.91, 1.02)	0.89 (0.75, 1.05)	0.88 (0.75, 1.03)	0.86 (0.73, 1.01)
Model 3	ref.	0.98 (0.93, 1.03)	0.93 (0.79, 1.11)	0.93 (0.79, 1.10)	0.91 (0.77, 1.07)
<b>Quercetin</b>					
HR (95% CI)					
Model 1	ref.	0.77 (0.69, 0.86)	0.68 (0.59, 0.78)	0.70 (0.60, 0.81)	0.62 (0.53, 0.74)
Model 2	ref.	0.86 (0.78, 0.96)	0.83 (0.72, 0.96)	0.90 (0.77, 1.05)	0.82 (0.69, 0.97)
Model 3	ref.	0.89 (0.79, 0.99)	0.87 (0.75, 1.01)	0.96 (0.82, 1.13)	0.89 (0.74, 1.06)
<b>Flavanol monomers</b>					
<b>Epicatechin</b>					
HR (95% CI)					
Model 1	ref.	0.82 (0.73, 0.93)	0.72 (0.62, 0.84)	0.69 (0.59, 0.8)	0.62 (0.52, 0.73)
Model 2	ref.	0.95 (0.84, 1.06)	0.91 (0.78, 1.06)	0.89 (0.76, 1.03)	0.8 (0.67, 0.95)
Model 3	ref.	0.96 (0.86, 1.08)	0.94 (0.81, 1.1)	0.93 (0.79, 1.09)	0.85 (0.71, 1.02)
<b>Flavanol oligo+polymers</b>					
<b>Proanthocyanidin dimers</b>					
HR (95% CI)					
Model 1	ref.	0.80 (0.71, 0.90)	0.71 (0.62, 0.82)	0.69 (0.59, 0.80)	0.60 (0.51, 0.71)
Model 2	ref.	0.93 (0.83, 1.04)	0.90 (0.79, 1.04)	0.89 (0.76, 1.04)	0.77 (0.64, 0.91)
Model 3	ref.	0.95 (0.84, 1.06)	0.93 (0.81, 1.08)	0.92 (0.79, 1.09)	0.82 (0.68, 0.98)
<b>Proanthocyanidin trimers</b>					
HR (95% CI)					
Model 1	ref.	0.76 (0.69, 0.84)	0.66 (0.59, 0.75)	0.63 (0.55, 0.73)	0.61 (0.52, 0.72)
Model 2	ref.	0.90 (0.81, 0.99)	0.84 (0.74, 0.96)	0.81 (0.69, 0.94)	0.76 (0.64, 0.91)
Model 3	ref.	0.91 (0.82, 1.01)	0.86 (0.75, 0.98)	0.83 (0.70, 0.97)	0.79 (0.65, 0.95)
<b>Flavanones</b>					
<b>Hesperidin</b>					
HR (95% CI)					
Model 1	ref.	0.83 (0.74, 0.92)	0.73 (0.62, 0.85)	0.73 (0.63, 0.84)	0.80 (0.68, 0.94)
Model 2	ref.	0.91 (0.82, 1.01)	0.87 (0.74, 1.02)	0.91 (0.78, 1.05)	0.99 (0.85, 1.17)
Model 3	ref.	0.91 (0.82, 1.01)	0.86 (0.73, 1.02)	0.91 (0.78, 1.06)	1.00 (0.85, 1.19)
<b>Flavones</b>					
<b>Apigenin</b>					
HR (95% CI)					
Model 1	ref.	0.74 (0.66, 0.83)	0.65 (0.57, 0.75)	0.68 (0.59, 0.78)	0.76 (0.65, 0.90)
Model 2	ref.	0.83 (0.74, 0.93)	0.79 (0.69, 0.91)	0.83 (0.72, 0.96)	0.91 (0.78, 1.07)
Model 3	ref.	0.85 (0.75, 0.96)	0.81 (0.70, 0.94)	0.86 (0.73, 1.01)	0.96 (0.80, 1.15)
<b>Anthocyanins</b>					
<b>Cyanidin</b>					
HR (95% CI)					
Model 1	ref.	0.79 (0.72, 0.86)	0.69 (0.59, 0.79)	0.69 (0.59, 0.8)	0.92 (0.77, 1.10)
Model 2	ref.	0.85 (0.78, 0.93)	0.77 (0.67, 0.89)	0.77 (0.67, 0.9)	0.93 (0.77, 1.11)
Model 3	ref.	0.87 (0.79, 0.96)	0.80 (0.69, 0.93)	0.8 (0.68, 0.94)	0.94 (0.78, 1.14)
<b>Delphinidin</b>					
HR (95% CI)					
Model 1	ref.	0.72 (0.64, 0.80)	0.61 (0.52, 0.71)	0.62 (0.53, 0.73)	0.94 (0.78, 1.12)
Model 2	ref.	0.84 (0.75, 0.95)	0.78 (0.65, 0.92)	0.79 (0.66, 0.93)	0.97 (0.81, 1.16)

Model 3	ref.	0.85 (0.76, 0.95)	0.78 (0.66, 0.93)	0.79 (0.67, 0.94)	0.98 (0.82, 1.18)
<b>Malvidin</b>					
HR (95% CI)					
Model 1	ref.	0.67 (0.58, 0.76)	0.66 (0.58, 0.76)	0.58 (0.50, 0.66)	0.57 (0.48, 0.68)
Model 2	ref.	0.81 (0.69, 0.96)	0.81 (0.69, 0.96)	0.73 (0.61, 0.88)	0.60 (0.47, 0.76)
Model 3	ref.	0.83 (0.70, 0.99)	0.83 (0.70, 0.98)	0.76 (0.63, 0.92)	0.63 (0.49, 0.80)

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Hazard ratios (95% CI) for chronic obstructive pulmonary disease during 23 years of follow up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1 adjusted for age and sex; Model 1b adjusted for age, sex, BMI, smoking pack-years, physical activity, alcohol intake, education and socio-economic status (income); Model 2 adjusted for all covariates in Model 1b plus energy intake and intakes of fish, red meat, processed meat, wholegrains, refined grains, polyunsaturated fatty acids, monounsaturated fatty acids and saturated fatty acids.

**Table E7. Hazard ratios of chronic obstructive pulmonary disease by quintiles of flavonoid intake excluding cases within the first 5 years of follow-up**

		Flavonoid intake quintiles				
		Q1 n = 11,083	Q2 n = 11,083	Q3 n = 11,082	Q4 n = 11,083	Q5 n = 11,082
<b>Total Flavonoids</b>						
Model 1	ref.		0.72 (0.68, 0.76)	0.56 (0.52, 0.59)	0.48 (0.44, 0.51)	0.44 (0.40, 0.47)
Model 1b	ref.		0.94 (0.90, 0.99)	0.89 (0.83, 0.95)	0.84 (0.78, 0.91)	0.81 (0.74, 0.88)
Model 2	ref.		0.96 (0.91, 1.01)	0.92 (0.86, 0.99)	0.88 (0.81, 0.95)	0.85 (0.78, 0.93)
<b>Flavonols</b>						
Model 1	ref.		0.74 (0.70, 0.77)	0.58 (0.54, 0.62)	0.46 (0.43, 0.50)	0.43 (0.39, 0.46)
Model 1b	ref.		0.94 (0.89, 0.98)	0.89 (0.83, 0.95)	0.85 (0.79, 0.92)	0.83 (0.76, 0.90)
Model 2	ref.		0.96 (0.91, 1.01)	0.93 (0.87, 1.00)	0.91 (0.84, 0.98)	0.89 (0.82, 0.97)
<b>Flavanol monomers</b>						
Model 1	ref.		0.82 (0.79, 0.84)	0.60 (0.55, 0.65)	0.45 (0.42, 0.49)	0.45 (0.42, 0.49)
Model 1b	ref.		0.96 (0.93, 0.99)	0.90 (0.84, 0.98)	0.87 (0.81, 0.95)	0.87 (0.80, 0.94)
Model 2	ref.		0.98 (0.94, 1.01)	0.94 (0.87, 1.02)	0.92 (0.85, 1.00)	0.92 (0.84, 1.00)
<b>Flavanol oligo+polymers</b>						
Model 1	ref.		0.67 (0.64, 0.71)	0.54 (0.51, 0.58)	0.48 (0.45, 0.51)	0.44 (0.41, 0.48)
Model 1b	ref.		0.93 (0.88, 0.98)	0.87 (0.82, 0.93)	0.82 (0.76, 0.88)	0.78 (0.72, 0.85)
Model 2	ref.		0.94 (0.89, 1.00)	0.90 (0.84, 0.96)	0.85 (0.78, 0.91)	0.81 (0.74, 0.89)
<b>Anthocyanins</b>						
Model 1	ref.		0.65 (0.62, 0.69)	0.55 (0.51, 0.59)	0.61 (0.57, 0.65)	0.73 (0.68, 0.79)
Model 1b	ref.		0.92 (0.87, 0.97)	0.88 (0.82, 0.96)	0.90 (0.83, 0.96)	0.91 (0.84, 0.99)
Model 2	ref.		0.93 (0.87, 0.98)	0.90 (0.83, 0.97)	0.92 (0.85, 0.99)	0.93 (0.86, 1.02)
<b>Flavanones</b>						
Model 1	ref.		0.78 (0.74, 0.82)	0.65 (0.61, 0.71)	0.65 (0.61, 0.70)	0.71 (0.66, 0.76)
Model 1b	ref.		0.94 (0.89, 0.98)	0.90 (0.83, 0.97)	0.92 (0.86, 0.99)	0.96 (0.88, 1.03)
Model 2	ref.		0.94 (0.89, 0.99)	0.90 (0.83, 0.98)	0.92 (0.86, 0.99)	0.96 (0.88, 1.04)
<b>Flavones</b>						
Model 1	ref.		0.71 (0.67, 0.75)	0.60 (0.56, 0.63)	0.56 (0.53, 0.6)	0.59 (0.55, 0.64)
Model 1b	ref.		0.91 (0.87, 0.96)	0.87 (0.82, 0.93)	0.85 (0.8, 0.91)	0.87 (0.80, 0.94)
Model 2	ref.		0.92 (0.87, 0.97)	0.88 (0.82, 0.94)	0.87 (0.8, 0.93)	0.88 (0.81, 0.96)

Hazard ratios (95% CI) for chronic obstructive pulmonary disease between 5 and 23 years of follow up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1 adjusted for age and sex; Model 1b adjusted for age, sex, BMI, smoking status, smoking pack-years, physical activity, alcohol intake, education and socio-economic status (income); Model 2 adjusted for all covariates in Model 1b plus energy intake and fish, red meat, processed meat, wholegrains, refined grains, polyunsaturated fatty acids, monounsaturated fatty acids and saturated fatty acids.