

## **SUPPLEMENTARY MATERIALS**

### **Supplementary Methods**

#### **Collection and Storage of Plasma Samples**

Blood samples were collected from 18 225 males in HPFS from 1993 to 1995, 32 826 females in NHS from 1989 to 1990, 14 916 males in PHS I from 1982 to 1984, 93 676 females in WHI from 1993 to 1998, and 28 345 females in WHS from 1992 to 1995. In HPFS, NHS, PHS I, and WHS, blood samples were collected by participants, mailed overnight on cold-packs, and then spun to collect plasma (delayed processing); in WHI, whole blood was collected at the first screening visit and separately immediately into plasma. All plasma samples have been stored in well-monitored freezers.

**Supplementary Table 1.** Characteristics at blood collection among patients with pancreatic cancer from 5 prospective cohorts with prediagnostic blood samples<sup>a</sup>

Characteristic	HPFS	NHS	PHS I	WHI	WHS	Overall
No. of patients	76	101	70	208	37	492
Age at blood collection, mean (SD), y	65.6 (7.8)	60.5 (6.7)	57.0 (8.7)	67.0 (7.3)	59.1 (8.9)	63.4 (8.5)
Age at diagnosis, mean (SD), y	72.7 (8.4)	70.7 (7.0)	71.9 (9.5)	71.9 (7.5)	63.4 (9.1)	71.1 (8.3)
Female sex, No (%)	0 (0)	101 (100)	0 (0)	208 (100)	37 (100)	346 (70.3)
Race/ethnicity, No (%)						
White	71 (93.4)	100 (99.0)	51 (72.9)	178 (85.6)	35 (94.6)	435 (88.4)
Black	1 (1.3)	1 (1.0)	1 (1.4)	14 (6.7)	1 (2.7)	18 (3.7)
Other	1 (1.3)	0 (0)	0 (0)	14 (6.7)	0 (0)	15 (3.0)
Missing	3 (3.9)	0 (0)	18 (25.7)	2 (1.0)	1 (2.7)	24 (4.9)
Body mass index, mean (SD), kg/m <sup>2</sup>	25.7 (3.3)	25.6 (5.0)	25.8 (2.9)	27.4 (5.9)	26.4 (5.3)	26.4 (5.0)
Physical activity, mean (SD), MET-h/wk	36.9 (38.5)	15.4 (17.8)	12.0 (11.3)	13.0 (13.2)	17.4 (21.6)	17.4 (22.1)
Tobacco use, No (%)						
Never	26 (34.2)	40 (39.6)	29 (41.4)	96 (46.2)	13 (35.1)	204 (41.5)
Past	42 (55.3)	41 (40.6)	28 (40.0)	92 (44.2)	17 (45.9)	220 (44.7)
Current	8 (10.5)	20 (19.8)	13 (18.6)	17 (8.2)	7 (18.9)	65 (13.2)
Missing	0 (0)	0 (0)	0 (0)	3 (1.4)	0 (0)	3 (0.6)
Alcohol ( $\geq 1$ drink/day), No (%)	32 (42.1)	24 (23.8)	23 (32.9)	36 (17.3)	7 (18.9)	122 (24.8)
History of diabetes, No (%)	3 (3.9)	5 (5.0)	3 (4.3)	15 (7.2)	3 (8.1)	29 (5.9)
Fasting status at blood collection, No (%)						
<8 h	23 (30.3)	22 (21.8)	47 (67.1)	0 (0)	15 (40.5)	107 (21.7)
$\geq 8$ h	47 (61.8)	72 (71.3)	21 (30.0)	208 (100)	19 (51.4)	367 (74.6)
Missing	6 (7.9)	7 (6.9)	2 (2.9)	0 (0)	3 (8.1)	18 (3.7)
Time from blood collection to diagnosis, median (range), y	6.5 (0.5 to 14.2)	10.6 (1.2 to 19.1)	16.4 (1.4 to 24.5)	5.2 (0.1 to 12.1)	4.2 (0.4 to 11.3)	6.7 (0.1 to 24.5)
Diagnosis period, No (%)						
1984-1989	0 (0)	0 (0)	9 (12.9)	0 (0)	0 (0)	9 (1.8)
1990-1994	2 (2.6)	13 (12.9)	12 (17.1)	0 (0)	7 (18.9)	34 (6.9)
1995-1999	33 (43.4)	30 (29.7)	19 (27.1)	81 (38.9)	23 (62.2)	186 (37.8)
2000-2004	25 (32.9)	43 (42.6)	24 (34.3)	102 (49.0)	7 (18.9)	201 (40.9)
2005-2009	16 (21.1)	15 (14.9)	6 (8.6)	25 (12.0)	0 (0)	62 (12.6)
Cancer stage, No (%)						
Localized	11 (14.5)	19 (18.8)	14 (20.0)	13 (6.3)	8 (21.6)	65 (13.2)
Locally advanced	11 (14.5)	12 (11.9)	13 (18.6)	77 (37.0)	7 (18.9)	120 (24.4)
Metastatic	33 (43.4)	44 (43.6)	31 (44.3)	91 (43.8)	20 (54.1)	219 (44.5)
Unknown	21 (27.6)	26 (25.7)	12 (17.1)	27 (13.0)	2 (5.4)	88 (17.9)
Median overall survival by stage, mo						
Localized	14	21	14.5	25	11.5	17
Locally advanced	10	9	9	12	10	10
Metastatic	4	3	3	4	4.5	3
Unknown	4	6.5	7	5	3	6

<sup>a</sup> HPFS = Health Professionals Follow-Up Study; MET = metabolic equivalent; NHS = Nurses' Health Study; PHS = Physicians' Health Study; SD = standard deviation; WHI = Women's Health Initiative; WHS = Women's Health Study.

**Supplementary Table 2.** Spearman’s rank correlation coefficients between prediagnostic plasma inflammatory biomarkers and covariates among patients with pancreatic cancer from 5 prospective cohorts<sup>a</sup>

Variable	Inflammatory biomarker score <sup>b</sup>	CRP	IL-6	TNF- $\alpha$ R2	Age	BMI
Inflammatory biomarker score <sup>b</sup>	1	0.70 <sup>c</sup>	0.73 <sup>c</sup>	0.60 <sup>c</sup>	0.18 <sup>c</sup>	0.35 <sup>c</sup>
CRP		1	0.50 <sup>c</sup>	0.23 <sup>c</sup>	-0.005	0.34 <sup>c</sup>
IL-6			1	0.34 <sup>c</sup>	0.14 <sup>c</sup>	0.30 <sup>c</sup>
TNF- $\alpha$ R2				1	0.30 <sup>c</sup>	0.17 <sup>c</sup>
Age					1	-0.06
BMI						1

<sup>a</sup> Adjusted for cohort (Health Professionals Follow-Up Study, Nurses’ Health Study, Physicians’ Health Study I, Women’s Health Initiative, Women’s Health Study; also adjusted for sex) and fasting time at blood collection in hours (<4, 4 to <8, 8 to <12,  $\geq$ 12, missing). BMI = body mass index; CRP = C-reactive protein; IL-6 = interleukin-6; TNF- $\alpha$ R2 = tumor necrosis factor- $\alpha$  receptor 2.

<sup>b</sup> Calculated by summing the number of inflammatory biomarkers (C-reactive protein, interleukin-6, and tumor necrosis factor- $\alpha$  receptor 2) with levels above the study population medians.

<sup>c</sup>  $P < .05$ .

**Supplementary Table 3.** Multivariable hazard ratios and 95% confidence intervals for death among patients with pancreatic cancer from 5 prospective cohorts by prediagnostic inflammatory biomarker score, stratified by covariates<sup>a</sup>

Stratification covariate	Patients/ deaths	Inflammatory biomarker score <sup>b</sup>				<i>P</i> <sub>interaction</sub> <sup>c</sup>
		0	1	2	3	
Sex						.56
Female	339/315	(Referent)	1.16 (0.79 to 1.70)	1.18 (0.81 to 1.71)	1.54 (1.06 to 2.25)	
Male	145/143	(Referent)	0.80 (0.49 to 1.29)	1.03 (0.57 to 1.89)	1.89 (0.87 to 4.11)	
Body mass index						.41
<25.0 kg/m <sup>2</sup>	211/199	(Referent)	1.15 (0.79 to 1.69)	0.95 (0.57 to 1.60)	1.56 (0.93 to 2.61)	
≥25.0 kg/m <sup>2</sup>	273/259	(Referent)	1.14 (0.72 to 1.81)	1.45 (0.95 to 2.22)	1.87 (1.19 to 2.93)	
Tobacco use						.80
Never	202/186	(Referent)	0.88 (0.57 to 1.37)	1.32 (0.83 to 2.09)	1.60 (0.97 to 2.65)	
Past	216/206	(Referent)	1.55 (0.97 to 2.48)	1.25 (0.78 to 2.02)	2.01 (1.20 to 3.34)	
Current	63/63	(Referent)	0.47 (0.14 to 1.59)	1.17 (0.37 to 3.66)	0.95 (0.33 to 2.70)	
Time from blood collection to diagnosis						.89
<10 y	347/328	(Referent)	1.14 (0.79 to 1.63)	1.22 (0.86 to 1.74)	1.53 (1.07 to 2.19)	
≥10 y	137/130	(Referent)	0.94 (0.56 to 1.58)	1.37 (0.75 to 2.48)	2.40 (1.11 to 5.19)	
Cancer stage						.69
Localized	64/60	(Referent)	2.52 (0.98 to 6.51)	4.33 (1.14 to 16.44)	2.52 (0.78 to 8.12)	
Locally advanced	120/106	(Referent)	1.35 (0.61 to 3.00)	1.59 (0.68 to 3.69)	2.04 (0.88 to 4.75)	
Metastatic	217/214	(Referent)	0.92 (0.60 to 1.39)	1.22 (0.79 to 1.88)	1.80 (1.11 to 2.92)	

<sup>a</sup> Hazard ratios from Cox proportional hazards regression adjusted for age at diagnosis (continuous), cohort (Health Professionals Follow-Up Study, Nurses' Health Study, Physicians' Health Study I, Women's Health Initiative, Women's Health Study; also adjusted for sex), race/ethnicity (white, black, other, missing), smoking status (never, past, current, missing), month of blood collection (2-month intervals), fasting time at blood collection in hours (<4, 4 to <8, 8 to <12, ≥12, missing), diagnosis period (1984-1999, 2000-2009), and cancer stage (localized, locally advanced, metastatic, unknown), excluding the stratification covariate.

<sup>b</sup> Calculated by summing the number of inflammatory biomarkers (C-reactive protein, interleukin-6, and tumor necrosis factor- $\alpha$  receptor 2) with levels above the study population medians.

<sup>c</sup> Test for interaction performed by entering cross-product terms of the score and the stratification variable in Cox proportional hazards regression, evaluated by the likelihood ratio test.

**Supplementary Table 4.** Characteristics at diagnosis among patients with pancreatic cancer from 2 prospective cohorts with prediagnostic diet information<sup>a</sup>

Characteristic	HPFS	NHS	Overall
No. of patients	480	673	1153
Age at diagnosis, mean (SD), y	73.5 (9.3)	72.3 (8.0)	72.8 (8.6)
Female sex, No (%)	0 (0)	673 (100)	673 (58.4)
Race/ethnicity, No (%)			
White	439 (91.5)	654 (97.2)	1093 (94.8)
Black	7 (1.5)	9 (1.3)	16 (1.4)
Other	12 (2.5)	10 (1.5)	22 (1.9)
Missing	22 (4.6)	0 (0)	22 (1.9)
Body mass index, mean (SD), kg/m <sup>2</sup>	25.5 (3.3)	26.5 (5.5)	26.1 (4.7)
Physical activity, mean (SD), MET-h/wk	31.2 (36.2)	16.0 (20.6)	22.3 (29.1)
Tobacco use, No (%)			
Never	148 (30.8)	280 (41.6)	428 (37.1)
Past	233 (48.5)	293 (43.5)	526 (45.6)
Current	39 (8.1)	88 (13.1)	127 (11.0)
Missing	60 (12.5)	12 (1.8)	72 (6.2)
Alcohol ( $\geq 1$ drink/day), No (%)	166 (34.6)	122 (18.1)	288 (25.0)
Diabetes status, No (%)			
No or unreported	382 (79.6)	524 (77.9)	906 (78.6)
Short-term diabetes ( $\leq 4$ y)	23 (4.8)	47 (7.0)	70 (6.1)
Long-term diabetes ( $> 4$ y)	75 (15.6)	102 (15.2)	177 (15.4)
Diagnosis period, No (%)			
1986-1989	38 (7.9)	30 (4.5)	68 (5.9)
1990-1994	73 (15.2)	62 (9.2)	135 (11.7)
1995-1999	98 (20.4)	108 (16.0)	206 (17.9)
2000-2004	99 (20.6)	180 (26.7)	279 (24.2)
2005-2009	99 (20.6)	193 (28.7)	292 (25.3)
2010-2014	73 (15.2)	100 (14.9)	173 (15.0)
Cancer stage, No (%)			
Localized	72 (15.0)	88 (13.1)	160 (13.9)
Locally advanced	62 (12.9)	67 (10.0)	129 (11.2)
Metastatic	222 (46.3)	330 (49.0)	552 (47.9)
Unknown	124 (25.8)	188 (27.9)	312 (27.1)
Median overall survival by stage, mo			
Localized	18	19	19
Locally advanced	7	11	8
Metastatic	3	3	3
Unknown	5	7	6

<sup>a</sup> HPFS = Health Professionals Follow-Up Study; MET = metabolic equivalent; NHS = Nurses' Health Study; SD = standard deviation.

**Supplementary Table 5.** Multivariable hazard ratios and 95% confidence intervals for death among patients with pancreatic cancer from 2 prospective cohorts by quartile of the empirical dietary inflammatory pattern score in the prediagnostic period, stratified by covariates<sup>a</sup>

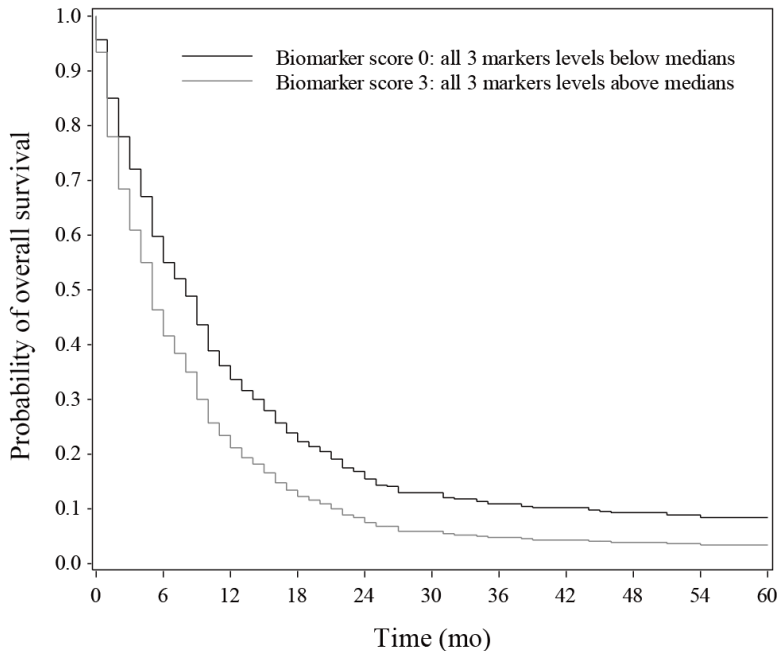
Stratification covariate	Patients/ deaths	Quartile of the empirical dietary inflammatory pattern score				<i>P</i> <sub>interaction</sub>
		1	2	3	4	
Sex						.28
Female	673/655	(Referent)	1.13 (0.90 to 1.41)	0.98 (0.78 to 1.23)	1.58 (1.25 to 2.00)	
Male	480/463	(Referent)	1.07 (0.81 to 1.41)	1.01 (0.78 to 1.32)	1.10 (0.84 to 1.43)	
Body mass index						.95
<25.0 kg/m <sup>2</sup>	530/513	(Referent)	1.10 (0.87 to 1.40)	0.93 (0.73 to 1.20)	1.39 (1.07 to 1.80)	
≥25.0 kg/m <sup>2</sup>	623/605	(Referent)	1.12 (0.87 to 1.43)	1.07 (0.84 to 1.35)	1.38 (1.08 to 1.76)	
Tobacco use						.65
Never	428/411	(Referent)	1.02 (0.76 to 1.38)	0.95 (0.71 to 1.27)	1.41 (1.05 to 1.91)	
Past	526/512	(Referent)	1.19 (0.93 to 1.53)	1.01 (0.79 to 1.28)	1.28 (0.99 to 1.65)	
Current	127/126	(Referent)	0.62 (0.36 to 1.06)	0.47 (0.26 to 0.85)	0.99 (0.59 to 1.65)	
Cancer stage						.40
Localized	160/144	(Referent)	0.84 (0.51 to 1.38)	0.88 (0.53 to 1.45)	1.12 (0.71 to 1.77)	
Locally advanced	129/123	(Referent)	0.94 (0.54 to 1.63)	0.66 (0.39 to 1.11)	0.96 (0.57 to 1.64)	
Metastatic	552/549	(Referent)	1.05 (0.82 to 1.34)	1.06 (0.84 to 1.35)	1.44 (1.12 to 1.86)	

<sup>a</sup> Hazard ratios from Cox proportional hazards regression adjusted for age at diagnosis (continuous), cohort (Health Professionals Follow-Up Study, Nurses' Health Study; also adjusted for sex), race/ethnicity (white, black, other, missing), smoking status (never, past, current, missing), diagnosis period (1986-1999, 2000-2014), cancer stage (localized, locally advanced, metastatic, unknown), and total energy intake (continuous), excluding the stratification covariate.

<sup>b</sup> Test for interaction performed by entering cross-product terms of the quartile of the score as an ordinal variable and the stratification variable in Cox proportional hazards regression, evaluated by the likelihood ratio test.

**Supplementary Figure 1.** Overall survival curves by (A) prediagnostic inflammatory biomarker score among patients with pancreatic cancer from 5 prospective cohorts and by (B) empirical dietary inflammatory pattern (EDIP) score among patients from 2 prospective cohorts, adjusted for variables that were included in the primary model. The inflammatory biomarker score was calculated by summing the number of inflammatory biomarkers (C-reactive protein, interleukin-6, and tumor necrosis factor- $\alpha$  receptor 2) with levels above the study population medians.

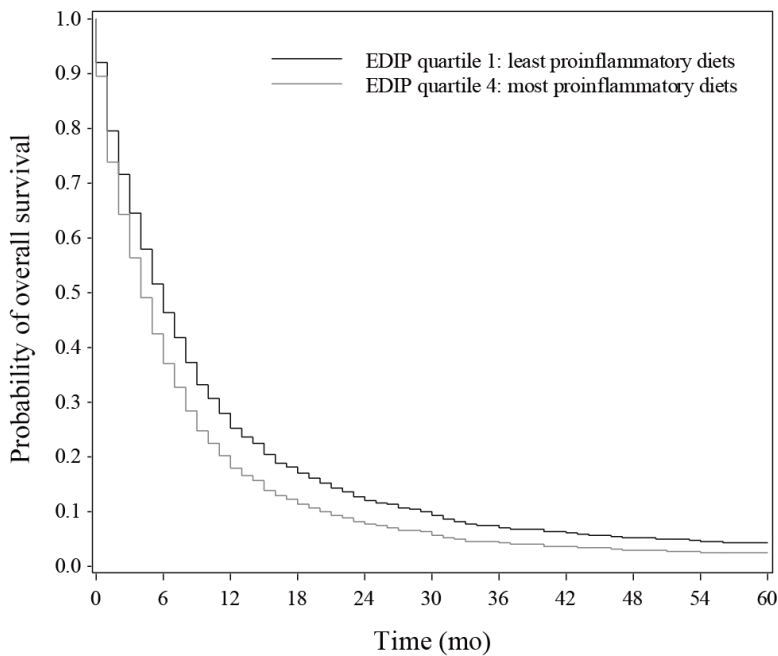
A



Number at Risk  
 Biomarker score 0  
 Biomarker score 3

	111	68	36	25	18	17	14	13	10	9	9
	115	53	29	14	10	6	4	4	4	4	2

B



Number at Risk  
 EDIP quartile 1  
 EDIP quartile 4

	288	135	80	50	35	26	18	17	13	11	10
	288	126	57	31	18	13	8	6	5	4	4