

Supplementary table 1. Characteristics of study participants.

	Controls	%	Cases	%
Age, mean (SD)	63.8 (10.3)		66.1 (12.5)	
Gender				
Male	348	87	73	62
Female	51	13	45	38
Region				
Barcelona/Baleares	197	49	77	65
Valles	135	34	13	11
Elche	67	17	26	22
Missing	-	-	2	2
Smoking status				
Never smoker	141	35	50	42
Ever smoker	257	64	64	55
Missing	1	1	3	3
Diabetes				
No	267	67	91	77
Yes	37	9	27	23
Missing	95	24	-	-

Supplementary table 2. Descriptive of toenail trace element (Al, As, Cd, Cr, Cu, Fe, Pb, Mn, Ni, Se, V, Zn) concentrations, in controls and cases. Concentrations are in µg/g.

Element	Controls						Cases						p-value*
	Median	Mean	S.E.	Min.	Max.	N	Median	Mean	S.E.	Min.	Max.	N	
Aluminum (Al)	11.43	20.53	2.08	0.64	574.62	399	8.30	14.63	1.71	1.35	125.82	118	5.25E-02
Arsenic (As)	0.07	0.09	0.00	0.00	0.75	399	0.07	0.10	0.01	0.00	0.55	118	7.22E-01
Cadmium (Cd)	0.01	0.08	0.02	0.00	9.04	399	0.03	0.10	0.04	0.00	4.53	118	1.22E-06
Chromium (Cr)	0.40	1.11	0.14	0.00	30.74	399	0.43	1.12	0.28	0.01	26.93	118	3.77E-01
Copper (Cu)	3.45	4.08	0.19	1.42	59.15	399	3.48	4.17	0.30	1.24	34.44	118	3.35E-01
Iron (Fe)	13.94	35.46	7.48	2.63	2837.72	399	13.43	35.93	13.90	4.15	1639.73	118	9.29E-01
Lead (Pb)	0.47	1.07	0.13	0.00	30.91	399	0.88	2.71	1.34	0.00	156.81	118	2.07E-07
Manganese (Mn)	0.29	0.67	0.07	0.01	17.41	399	0.22	0.49	0.07	0.04	4.20	118	7.70E-02
Nickel (Ni)	0.39	1.59	0.31	0.00	81.72	399	0.23	0.65	0.28	0.01	33.58	118	3.72E-06
Selenium (Se)	0.60	0.62	0.01	0.06	3.92	399	0.51	0.52	0.01	0.00	0.77	118	2.19E-11
Vanadium (V)	0.02	0.05	0.01	0.00	1.07	397	0.02	0.04	0.01	0.00	0.79	118	9.97E-01
Zinc (Zn)	107.22	128.48	5.14	63.71	990.19	399	110.80	120.33	4.05	35.54	420.80	118	1.19E-01

*The p-value is for the Mann-Whitney U test.

Supplementary table 3. Odds ratios (OR), 95% confidence intervals (L95CI-U95CI), and p-values for the association between toenail trace elements (Al, As, Cd, Cr, Cu, Fe, Pb, Mn, Ni, Se, V, Zn) and pancreatic cancer risk. Estimates are adjusted for age, gender, region and smoking status. Estimates further adjusted for diabetes status are also presented.

	Min. Conc. (µg/g)	Max. Conc. (µg/g)	Controls	%	Cases	%	OR	L95CI	U95CI	p-value	OR†	L95CI†	U95CI†	p-value†
Aluminum (Al)														
Q1		≤ 5.5415	99	25	32	29	1.00				1.00			
Q2	5.5416	11.4329	100	25	37	33	0.92	0.51	1.67	7.94E-01	0.94	0.51	1.73	8.34E-01
Q3	11.4330	21.6806	100	25	26	23	0.88	0.47	1.65	6.89E-01	0.89	0.46	1.71	7.28E-01
Q4	> 21.6806		99	25	16	14	0.58	0.29	1.19	1.37E-01	0.56	0.27	1.18	1.28E-01
Trend*										1.23E-01				1.12E-01
Arsenic (As)														
Q1		≤ 0.0518	100	25	34	30	1.00				1.00			
Q2	0.0519	0.0709	100	25	21	19	0.81	0.42	1.56	5.26E-01	0.88	0.45	1.72	6.98E-01
Q3	0.0710	0.1061	100	25	23	20	1.22	0.63	2.36	5.51E-01	1.12	0.57	2.19	7.45E-01
Q4	> 0.1061		98	25	35	31	2.02	1.08	3.78	2.87E-02	1.97	1.03	3.75	3.94E-02
Trend*										9.01E-03				1.75E-02
Cadmium (Cd)														
Q1		≤ 0.0080	100	25	17	15	1.00				1.00			
Q2	0.0081	0.0134	99	25	11	10	0.87	0.37	2.03	7.45E-01	0.92	0.39	2.20	8.57E-01
Q3	0.0135	0.0291	100	25	27	24	2.04	1.00	4.17	5.14E-02	2.18	1.04	4.55	3.79E-02
Q4	> 0.0291		99	25	59	52	3.58	1.86	6.88	1.29E-04	3.96	2.02	7.78	6.46E-05
Trend*										4.65E-06				3.32E-06
Chromium (Cr)														
Q1		≤ 0.1556	100	25	18	16	1.00				1.00			
Q2	0.1557	0.4022	99	25	37	33	2.02	1.02	3.98	4.37E-02	2.08	1.02	4.26	4.47E-02
Q3	0.4023	0.9282	100	25	31	27	1.94	0.97	3.91	6.25E-02	1.72	0.83	3.56	1.47E-01
Q4	> 0.9282		99	25	27	24	1.37	0.67	2.80	3.82E-01	1.22	0.59	2.56	5.90E-01
Trend*										7.50E-01				4.46E-01
Copper (Cu)														
Q1		≤ 2.8208	100	25	26	23	1.00				1.00			
Q2	2.8209	3.4505	100	25	30	26	1.14	0.60	2.15	6.88E-01	1.09	0.56	2.10	8.01E-01
Q3	3.4506	4.2195	99	25	26	23	1.12	0.58	2.19	7.33E-01	1.01	0.51	2.01	9.76E-01
Q4	> 4.2195		99	25	32	28	1.63	0.85	3.13	1.43E-01	1.43	0.73	2.82	2.94E-01
Trend*										1.35E-01				2.84E-01
Iron (Fe)														
Q1		≤ 8.3408	99	25	15	13	1.00				1.00			
Q2	8.3409	13.9367	100	25	46	40	2.96	1.49	5.88	1.90E-03	2.70	1.34	5.44	5.56E-03
Q3	13.9368	29.4019	100	25	33	29	2.68	1.32	5.47	6.58E-03	2.46	1.18	5.10	1.57E-02
Q4	> 29.4019		99	25	20	18	1.82	0.84	3.97	1.30E-01	1.64	0.74	3.65	2.27E-01
Trend*										9.88E-01				8.12E-01

	Min. Conc. (µg/g)	Max. Conc. (µg/g)	Controls	%	Cases	%	OR	L95CI	U95CI	p-value	OR‡	L95CI‡	U95CI‡	p-value‡
Lead (Pb)														
Q1		≤ 0.2534	99	25	8	7	1.00				1.00			
Q2	0.2535	0.4692	100	25	23	20	2.88	1.19	6.99	1.94E-02	2.86	1.16	7.07	2.24E-02
Q3	0.4693	0.9750	100	25	33	29	4.07	1.72	9.61	1.36E-03	4.06	1.69	9.74	1.74E-03
Q4	> 0.9750		99	25	49	43	6.26	2.71	14.47	1.77E-05	5.59	2.38	13.13	7.90E-05
Trend*										3.21E-05				3.11E-04
Manganese (Mn)														
Q1		≤ 0.1359	99	25	31	27	1.00				1.00			
Q2	0.1360	0.2898	100	25	42	37	1.57	0.87	2.83	1.31E-01	1.38	0.75	2.54	3.05E-01
Q3	0.2899	0.5995	100	25	21	19	0.86	0.44	1.67	6.53E-01	0.72	0.36	1.43	3.49E-01
Q4	> 0.5995		99	25	19	17	0.95	0.47	1.91	8.86E-01	0.86	0.42	1.79	6.91E-01
Trend*										4.27E-01				3.74E-01
Nickel (Ni)														
Q1		≤ 0.1856	100	25	40	35	1.00				1.00			
Q2	0.1857	0.3855	99	25	42	37	1.10	0.63	1.92	7.38E-01	1.14	0.64	2.04	6.62E-01
Q3	0.3856	0.8852	100	25	21	18	0.51	0.27	0.98	4.25E-02	0.50	0.26	0.97	4.17E-02
Q4	> 0.8852		99	25	11	10	0.27	0.12	0.59	9.39E-04	0.29	0.13	0.64	2.17E-03
Trend*										1.92E-04				4.07E-04
Selenium (Se)														
Q1		≤ 0.5198	100	25	59	52	1.00				1.00			
Q2	0.5199	0.5965	100	25	30	27	0.57	0.32	1.01	5.45E-02	0.58	0.32	1.05	7.03E-02
Q3	0.5966	0.6829	99	25	19	17	0.25	0.13	0.50	5.72E-05	0.24	0.12	0.48	5.44E-05
Q4	> 0.6829		99	25	5	4	0.05	0.02	0.15	2.14E-08	0.06	0.02	0.16	5.30E-08
Trend*										8.30E-11				2.61E-10
Vanadium (V)														
Q1		≤ 0.0102	99	25	20	18	1.00				1.00			
Q2	0.0103	0.0231	99	25	41	37	1.93	1.02	3.65	4.37E-02	1.89	0.97	3.66	6.00E-02
Q3	0.0232	0.0445	99	25	27	25	1.34	0.68	2.64	3.98E-01	1.20	0.60	2.40	6.04E-01
Q4	> 0.0445		99	25	22	20	1.25	0.61	2.55	5.44E-01	1.14	0.54	2.41	7.37E-01
Trend*										7.89E-01				6.06E-01
Zinc (Zn)														
Q1		≤ 93.3371	100	25	20	18	1.00				1.00			
Q2	93.3372	107.2220	100	25	32	28	1.60	0.82	3.12	1.67E-01	1.85	0.93	3.70	8.01E-02
Q3	107.2221	125.8899	100	25	32	28	1.27	0.65	2.50	4.85E-01	1.44	0.72	2.90	3.03E-01
Q4	> 125.8899		98	25	29	26	1.02	0.51	2.03	9.58E-01	1.05	0.52	2.12	9.00E-01
Trend*										5.86E-01				5.56E-01

*Tests for linear trend were carried out by including the median of each quartile of the toenail trace element concentration as a continuous variable in the logistic regression model.

‡Estimates are further adjusted for diabetes status. Ninety-five controls had no information regarding their diabetes status.

Supplementary table 4. Odds ratios (OR), 95% confidence intervals (L95CI-U95CI), and p-values for the association between toenail trace elements (Al, As, Cd, Cr, Cu, Fe, Pb, Mn, Ni, Se, V, Zn) and pancreatic cancer risk. Estimates are adjusted for age, gender, region and pack-years. Estimates adjusted for duration of cigarette smoking are also presented.

	Min. Conc. (µg/g)	Max. Conc. (µg/g)	Controls	%	Cases	%	OR	L95CI	U95CI	p-value	OR‡	L95CI‡	U95CI‡	p-value‡
Aluminum (Al)														
Q1		≤ 5.5415	62	24	32	29	1.00				1.00			
Q2	5.5416	11.4329	65	26	37	33	0.90	0.44	1.84	7.68E-01	0.89	0.43	1.81	7.41E-01
Q3	11.4330	21.6806	59	23	26	23	1.02	0.49	2.16	9.51E-01	1.01	0.48	2.12	9.89E-01
Q4	> 21.6806		68	27	16	14	0.44	0.19	1.04	6.11E-02	0.43	0.18	1.01	5.40E-02
Trend*										5.56E-02				4.96E-02
Arsenic (As)														
Q1		≤ 0.0518	59	23	34	30	1.00				1.00			
Q2	0.0519	0.0709	67	26	21	19	0.69	0.31	1.52	3.61E-01	0.75	0.34	1.65	4.83E-01
Q3	0.0710	0.1061	67	26	23	20	0.84	0.39	1.83	6.62E-01	0.87	0.40	1.88	7.15E-01
Q4	> 0.1061		61	24	35	31	1.75	0.82	3.75	1.51E-01	1.78	0.83	3.82	1.37E-01
Trend*										5.04E-02				5.27E-02
Cadmium (Cd)														
Q1		≤ 0.0080	65	26	17	15	1.00				1.00			
Q2	0.0081	0.0134	71	28	11	10	0.60	0.23	1.53	2.80E-01	0.56	0.22	1.45	2.35E-01
Q3	0.0135	0.0291	62	24	27	24	1.49	0.65	3.39	3.46E-01	1.32	0.58	3.00	5.03E-01
Q4	> 0.0291		56	22	59	52	3.11	1.46	6.61	3.24E-03	2.77	1.30	5.88	8.13E-03
Trend*										4.71E-05				1.17E-04
Chromium (Cr)														
Q1		≤ 0.1556	67	26	18	16	1.00				1.00			
Q2	0.1557	0.4022	58	23	37	33	1.81	0.81	4.06	1.49E-01	1.77	0.79	3.97	1.65E-01
Q3	0.4023	0.9282	71	28	31	27	1.42	0.64	3.16	3.85E-01	1.42	0.64	3.16	3.91E-01
Q4	> 0.9282		58	23	27	24	1.39	0.61	3.14	4.32E-01	1.39	0.61	3.16	4.28E-01
Trend*										9.10E-01				8.83E-01
Copper (Cu)														
Q1		≤ 2.8208	69	27	26	23	1.00				1.00			
Q2	2.8209	3.4505	67	26	30	26	1.36	0.64	2.91	4.20E-01	1.37	0.64	2.92	4.16E-01
Q3	3.4506	4.2195	59	23	26	23	1.31	0.59	2.90	5.00E-01	1.30	0.59	2.87	5.15E-01
Q4	> 4.2195		59	23	32	28	1.58	0.73	3.41	2.43E-01	1.56	0.72	3.39	2.55E-01
Trend*										2.89E-01				3.05E-01
Iron (Fe)														
Q1		≤ 8.3408	62	24	15	13	1.00				1.00			
Q2	8.3409	13.9367	73	29	46	40	2.06	0.94	4.55	7.27E-02	2.01	0.91	4.43	8.40E-02
Q3	13.9368	29.4019	61	24	33	29	2.17	0.96	4.89	6.32E-02	2.08	0.92	4.70	7.78E-02
Q4	> 29.4019		58	23	20	18	1.20	0.49	2.97	6.88E-01	1.18	0.48	2.92	7.16E-01
Trend*										5.35E-01				5.37E-01

	Min. Conc. (µg/g)	Max. Conc. (µg/g)	Controls	%	Cases	%	OR	L95CI	U95CI	p-value	OR‡	L95CI‡	U95CI‡	p-value‡
Lead (Pb)														
Q1		≤ 0.2534	68	27	8	7	1.00				1.00			
Q2	0.2535	0.4692	65	26	23	20	2.61	0.98	6.97	5.59E-02	2.56	0.96	6.79	5.94E-02
Q3	0.4693	0.9750	59	23	33	29	3.63	1.38	9.58	9.22E-03	3.49	1.33	9.16	1.12E-02
Q4	> 0.9750		62	24	49	43	4.31	1.69	10.95	2.17E-03	4.12	1.62	10.45	2.91E-03
Trend*										8.69E-03				1.18E-02
Manganese (Mn)														
Q1		≤ 0.1359	63	25	31	27	1.00				1.00			
Q2	0.1360	0.2898	68	27	42	37	1.51	0.75	3.05	2.53E-01	1.48	0.73	3.01	2.75E-01
Q3	0.2899	0.5995	68	27	21	19	0.73	0.33	1.62	4.43E-01	0.65	0.29	1.45	2.98E-01
Q4	> 0.5995		55	22	19	17	0.79	0.34	1.84	5.88E-01	0.77	0.33	1.79	5.38E-01
Trend*										2.59E-01				2.43E-01
Nickel (Ni)														
Q1		≤ 0.1856	71	28	40	35	1.00				1.00			
Q2	0.1857	0.3855	60	24	42	37	1.21	0.63	2.33	5.63E-01	1.23	0.64	2.35	5.36E-01
Q3	0.3856	0.8852	64	25	21	18	0.45	0.20	0.98	4.52E-02	0.46	0.21	1.01	5.43E-02
Q4	> 0.8852		59	23	11	10	0.23	0.09	0.60	2.61E-03	0.26	0.10	0.67	5.20E-03
Trend*										5.27E-04				1.17E-03
Selenium (Se)														
Q1		≤ 0.5198	71	28	59	52	1.00				1.00			
Q2	0.5199	0.5965	70	28	30	27	0.61	0.31	1.17	1.36E-01	0.55	0.28	1.07	7.96E-02
Q3	0.5966	0.6829	63	25	19	17	0.22	0.10	0.51	4.27E-04	0.17	0.07	0.41	7.89E-05
Q4	> 0.6829		50	20	5	4	0.06	0.02	0.23	1.94E-05	0.05	0.01	0.20	1.08E-05
Trend*										2.25E-07				7.38E-08
Vanadium (V)														
Q1		≤ 0.0102	66	26	20	18	1.00				1.00			
Q2	0.0103	0.0231	64	25	41	37	1.54	0.73	3.23	2.53E-01	1.51	0.72	3.18	2.73E-01
Q3	0.0232	0.0445	62	25	27	25	1.11	0.51	2.44	7.89E-01	1.09	0.49	2.39	8.36E-01
Q4	> 0.0445		61	24	22	20	0.95	0.42	2.16	9.05E-01	0.91	0.40	2.07	8.15E-01
Trend*										5.13E-01				4.44E-01
Zinc (Zn)														
Q1		≤ 93.3371	64	25	20	18	1.00				1.00			
Q2	93.3372	107.2220	71	28	32	28	1.42	0.66	3.04	3.66E-01	1.42	0.66	3.05	3.63E-01
Q3	107.2221	125.8899	59	23	32	28	1.21	0.55	2.66	6.41E-01	1.20	0.54	2.66	6.48E-01
Q4	> 125.8899		60	24	29	26	0.94	0.41	2.12	8.75E-01	0.89	0.39	2.03	7.84E-01
Trend*										5.96E-01				5.06E-01

*Tests for linear trend were carried out by including the median of each quartile of the toenail trace element concentration as a continuous variable in the logistic regression model.

||One hundred forty five controls had no information on pack-years and duration of cigarette smoking.

‡Estimates are adjusted for duration of cigarette smoking.

	Min. Conc. (µg/g)	Max. Conc. (µg/g)	Controls	%	Cases	%	OR	L95CI	U95CI	p-value
Lead (Pb)										
Q1		≤ 0.2534	97	25	8	7	1.00			
Q2	0.2535	0.4692	100	25	22	20	2.60	1.06	6.38	3.70E-02
Q3	0.4693	0.9750	99	25	32	30	3.89	1.63	9.26	2.14E-03
Q4	> 0.9750		97	25	46	43	5.87	2.52	13.69	4.14E-05
Trend*										5.76E-05
Manganese (Mn)										
Q1		≤ 0.1359	97	25	30	28	1.00			
Q2	0.1360	0.2898	98	25	41	38	1.51	0.82	2.76	1.82E-01
Q3	0.2899	0.5995	99	25	20	19	0.75	0.38	1.47	4.00E-01
Q4	> 0.5995		99	25	17	16	0.78	0.38	1.61	5.05E-01
Trend*										1.98E-01
Nickel (Ni)										
Q1		≤ 0.1856	100	25	39	36	1.00			
Q2	0.1857	0.3855	98	25	42	39	1.13	0.64	1.99	6.76E-01
Q3	0.3856	0.8852	96	24	18	17	0.46	0.23	0.90	2.35E-02
Q4	> 0.8852		99	25	10	9	0.25	0.11	0.55	6.75E-04
Trend*										1.15E-04
Selenium (Se)										
Q1		≤ 0.5198	98	25	58	54	1.00			
Q2	0.5199	0.5965	99	25	27	25	0.56	0.31	1.02	5.69E-02
Q3	0.5966	0.6829	99	25	18	17	0.27	0.14	0.53	1.45E-04
Q4	> 0.6829		97	25	5	5	0.06	0.02	0.17	1.10E-07
Trend*										9.06E-10
Vanadium (V)										
Q1		≤ 0.0102	96	25	20	19	1.00			
Q2	0.0103	0.0231	99	25	39	37	1.75	0.91	3.36	9.43E-02
Q3	0.0232	0.0445	97	25	25	24	1.16	0.58	2.33	6.73E-01
Q4	> 0.0445		99	25	21	20	1.03	0.50	2.14	9.31E-01
Trend*										4.72E-01
Zinc (Zn)										
Q1		≤ 93.3371	99	25	20	19	1.00			
Q2	93.3372	107.2220	99	25	30	28	1.39	0.70	2.75	3.42E-01
Q3	107.2221	125.8899	98	25	30	28	1.16	0.58	2.32	6.68E-01
Q4	> 125.8899		97	25	28	26	1.00	0.50	2.02	9.90E-01
Trend*										6.93E-01

*Tests for linear trend were carried out by including the median of each quartile of the toenail trace element concentration as a continuous variable in the logistic regression model.

||Five controls and four cases had no information on education.

Supplementary table 6. Odds ratios (OR), 95% confidence intervals (L95CI-U95CI), and p-values for the association between toenail concentrations of As, Cd, Pb, Ni, and Se) and pancreatic cancer risk. Estimates are adjusted for age, gender, region, smoking status, and significant trace elements (arsenic, cadmium, lead, nickel, and selenium).

	Min. Conc. (µg/g)	Max. Conc. (µg/g)	Controls %	Cases %	OR	L95CI	U95CI	p-value
Arsenic (As)								
Q1		≤ 0.0518	100	25	34	30	1.00	
Q2	0.0519	0.0709	100	25	21	19	1.29	0.59 2.83 5.27E-01
Q3	0.0710	0.1061	100	25	23	20	1.56	0.68 3.56 2.93E-01
Q4	> 0.1061		98	25	35	31	1.72	0.77 3.86 1.85E-01
Trend*								2.01E-01
Cadmium (Cd)								
Q1		≤ 0.0080	100	25	17	15	1.00	
Q2	0.0081	0.0134	99	25	11	10	0.50	0.19 1.35 1.73E-01
Q3	0.0135	0.0291	100	25	27	24	0.96	0.41 2.28 9.30E-01
Q4	> 0.0291		99	25	59	52	2.71	1.21 6.06 1.49E-02
Trend*								1.64E-04
Lead (Pb)								
Q1		≤ 0.2534	99	25	8	7	1.00	
Q2	0.2535	0.4692	100	25	23	20	3.05	1.12 8.34 2.95E-02
Q3	0.4693	0.9750	100	25	33	29	5.28	1.90 14.69 1.42E-03
Q4	> 0.9750		99	25	49	43	6.38	2.26 18.02 4.61E-04
Trend*								4.56E-03
Nickel (Ni)								
Q1		≤ 0.1856	100	25	40	35	1.00	
Q2	0.1857	0.3855	99	25	42	37	0.79	0.40 1.55 4.91E-01
Q3	0.3856	0.8852	100	25	21	18	0.29	0.13 0.65 2.35E-03
Q4	> 0.8852		99	25	11	10	0.15	0.06 0.39 1.06E-04
Trend*								3.54E-05
Selenium (Se)								
Q1		≤ 0.5198	100	25	59	52	1.00	
Q2	0.5199	0.5965	100	25	30	27	0.73	0.38 1.40 3.37E-01
Q3	0.5966	0.6829	99	25	19	17	0.23	0.11 0.51 2.34E-04
Q4	> 0.6829		99	25	5	4	0.04	0.01 0.12 5.65E-08
Trend*								2.30E-10

*Tests for linear trend were carried out by including the median of each quartile of the toenail trace element concentration as a continuous variable in the logistic regression model.