### **Supplementary Data**

Title of the manuscript: "Residential proximity to industrial pollution sources and colorectal cancer risk: a multicase-control study (MCC-Spain)".

This document is available as supplementary data for inclusion as online documentation. It includes:

- a) Appendix A, showing the description of the risk gradient analysis (assessment of the existence of radial effects near industrial facilities).
- b) Table S1, showing the list of industrial groups, together with their E-PRTR categories, and number of installations by industrial group and province.
- c) Table S2, showing the sensitivity analysis with the characteristics of included and excluded colorectal cancer cases.
- d) Table S3, showing the odds ratios of colorectal cancer by industrial distance and industrial group.
- e) Table S4, showing the odds ratios of colorectal cancer by industrial distance and industrial group, for the sensitivity analysis with only individuals living in their current residence for ≥10 years (longterm residents).
- f) Table S5, showing the specific pollutants that can be released by the facilities to both air and water, according to the industrial groups.
- g) Table S6, showing amounts (in kg) of carcinogens (IARC classification) and other toxic substances released by the facilities in the study area in 2009, grouped by industrial sector.
- h) Table S7, showing the odds ratios of colorectal cancer for ever-decreasing radiuses within a 30-kilometer area surrounding each industrial installation, both overall and by industrial group, for the sensitivity analysis with only individuals living in their current residence for ≥10 years (long-term residents).
- i) Figure S1, showing a flow chart displaying the selection process of colorectal cancer cases and controls.
- j) Figure S2, showing the box-and-whisker plots with the years of commencement of operations of the 134 industries studied, according to the industrial group.

- k) Figure S3, showing the odds ratios of colorectal cancer by groups of carcinogenic and other toxic substances with statistically significant results and a number of cases and controls ≥10, for the sensitivity analysis with only individuals living in their current residence for ≥10 years (long-term residents).
- Figure S4, showing the odds ratios of colorectal cancer by specific pollutant with statistically significant results and a number of cases and controls ≥10, for the sensitivity analysis with only individuals living in their current residence for ≥10 years (long-term residents).

Supplementary Data, Appendix A.

#### Analysis 5 (assessment of the existence of radial effects near industrial facilities)

The risk gradient analysis near industrial installations was confined to an area of 30 km surrounding each installation, and the ORs were estimated using mixed multiple unconditional logistic regression models, as follows:

a) All industries as a whole (all sectors): for each subject i, a new variable "minimum distance<sub>i</sub>" was defined as:

$$minimum \ distance_i = \ min\{industrial \ distance_{ij}\}_j$$

$$i=1, ..., 3505$$
 subjects,  $j=1, ..., 134$  facilities

where *industrial distance<sub>ij</sub>* is the distance between subject *i* and facility *j*. This new explanatory variable was categorized in concentric rings (0-1, 1-1.5, 1.5-2, 2-2.5, 2.5-3, and 3-30 km as reference). This was included in the models as both a categorical and a continuous variable, thereby making it possible for: the effect of the respective distances to be estimated by the former; the existence of radial effects to be ascertained by the latter (rise in OR with increasing proximity to an installation); and, by applying the likelihood ratio test, the statistical significance of such minimum distance-related effects to be computed.

b) By industrial group: for each subject i and industrial group k, 22 new variables "minimum distance\_industrial group<sub>ik</sub>" were calculated as:

minimum distance\_industrial group<sub>ik</sub> =  $min\{industrial \ group \ distance_{ij}\}_i$ 

*i*=1, ..., 3505 subjects, *k*=1, ..., 22 industrial groups, *j*=1, ..., no. of facilities of industrial group *k*, where *industrial group distance<sub>ij</sub>* is the distance between subject *i* and facility *j* belonging to industrial group *k*. These new explanatory variables were categorized in concentric rings (0-1, 1-1.5, 1.5-2, 2-2.5, 2.5-3, and 3-30 km as reference). These were included in the models as categorical and continuous variables, and subjects that had some industry other than the group analyzed at  $\leq$ 3 km were excluded.

Supplementary Data, Table S1: list of industrial groups, together with their E-PRTR categories, and number of installations by industrial group and province.

						Prov	inces						
Industrial group	E-PRTR category	Asturias	Barcelona	Cantabria	Granada	Gipuzkoa	Huelva	Leon	Madrid	Murcia	Navarre	Valencia	TOTAL
Combustion installations	1.c	1	1	0	1	1	2	1	0	0	0	0	7
Production and processing of metals	2.a, 2.b, 2.c.i, 2.c.ii, 2.d, 2.e	1	3	4	0	2	1	0	0	0	2	0	13
Galvanization	2.c.iii	2	0	0	0	0	0	0	0	1	0	0	3
Surface treatment of metals and plastic	2.f	2	10	6	1	2	0	0	1	0	4	1	27
Mining industry	3.a, 3.b	0	0	0	0	0	0	1	0	0	0	0	1
Cement and lime	3.c, 3.d	1	0	0	0	1	0	1	0	0	0	0	3
Glass and mineral fibers	3.e, 3.f	0	3	0	0	0	0	1	0	0	0	0	4
Ceramic	3.g	1	0	1	4	0	2	0	0	0	0	0	8
Organic chemical industry	4.a	0	9	0	1	0	0	0	0	0	1	0	11
Inorganic chemical industry	4.b	0	1	0	0	0	1	0	0	0	0	0	2
Fertilizers	4.c	0	0	0	0	0	1	0	0	0	0	0	1
Biocides	4.d	0	0	0	0	0	0	0	0	1	0	0	1
Pharmaceutical products	4.e	0	2	0	0	0	0	1	1	0	0	0	4
Explosives and pyrotechnics	4.f	0	0	0	0	0	1	0	0	2	0	0	3
Hazardous waste	5.a, 5.b	0	1	4	0	0	1	0	0	0	0	0	6
Non-hazardous waste	5.c, 5.d	0	0	1	0	1	0	0	0	0	0	0	2
Disposal or recycling of animal waste	5.e	0	1	0	0	0	0	0	0	0	0	1	2
Urban waste-water treatment plants	5.f, 5.g	0	1	1	1	0	1	1	0	0	0	2	7
Paper and wood production	6.a, 6.b, 6.c	0	1	0	0	0	1	0	0	0	1	0	3
Food and beverage sector	8.a, 8.b, 8.c	0	4	0	1	0	0	3	1	2	2	3	16
Surface treatment using organic solvents	9.c	0	1	0	0	2	0	0	0	2	2	1	8
Ship building	9.e	1	0	1	0	0	0	0	0	0	0	0	2
TOTAL		9	38	18	9	9	11	9	3	8	12	8	134

Supplementary Data, Table S2: sensitivity analysis with the characteristics of included and excluded

colorectal cancer cases.

	n (%) or	mean (SD)	_
Characteristic		Excluded cases (n=1583)	<i>p</i> -value <sup>a</sup>
Age, mean (SD)	67.2 (10.0)	66.9 (11.1)	0.858
Sex, n (%)			
Men	352 (63.2)	1013 (64.0)	
Women	205 (36.8)	570 (36.0)	0.775
Province, n (%)			
Asturias	62 (11.1)	15 (0.9)	
Barcelona	130 (23.3)	566 (35.8)	
Cantabria	18 (3.2)	133 (8.4)	
Gipuzkoa	9 (1.6)	110 (6.9)	
Granada	44 (7.9)	120 (7.6)	
Huelva	32 (5.8)	39 (2.5)	
Leon	199 (35.7)	191 (12.1)	
Madrid	27 (4.9)	205 (12.9)	
Murcia	10 (1.8)	24 (1.5)	
Navarre	14 (2.5)	111 (7.0)	
Valencia	12 (2.2)	69 (4.4)	< 0.001
Body mass index $(kg/m^2)$ , mean (SD)	27.6 (4.6)	27.4 (4.5)	0.495
Family history of colorectal cancer, n (%)			
None	442 (79.4)	1237 (78.1)	
Second degree only	20 (3.6)	58 (3.7)	
1 first degree	81 (14.5)	223 (14.1)	
>1 first degree	14 (2.5)	41 (2.6)	
Missing	_	24 (1.5)	0.997
Tobacco smoking, n (%)			
Never	210 (37.7)	668 (42.2)	
Former smoker	251 (45.1)	599 (37.9)	
Current smoker	96 (17.2)	303 (19.1)	
Missing	-	13 (0.8)	0.017
Educational level, n (%)			
Less than primary school	159 (28.5)	529 (33.4)	
Primary school completed	215 (38.6)	591 (37.3)	
Secondary school	124 (22.3)	302 (19.1)	
University graduate	59 (10.6)	161 (10.2)	0.146
Physical activity in leisure time (MET), mean (SD)	155.4 (272.1)	135.84 (250.4)	0.109
Total energy intake (kcal/day), mean (SD)	1980.8 (605.6)	2023.0 (647.4)	0.232
Alcohol consumption (g/day), mean (SD)	22.8 (32.8)	24.5 (34.9)	0.719
Vegetable intake (g/day), mean (SD)	173.5 (111.8)	175.6 (107.5)	0.391
Red/processed meat intake (g/day), mean (SD)	71.9 (43.7)	75.2 (49.7)	0.303
Living in their current residence for $\geq 10$ years, n (%)	451 (81.0)	1340 (84.6)	0.051

<sup>a</sup>Two-sided Chi-square test (with Yates's correction for continuity), and Mann-Whitney U-test (with continuity correction) test where appropriate.

## Supplementary Data, Table S3: odds ratios of colorectal cancer by industrial distance and industrial group.

		Individuals residir	ng at ≤1 km				Individuals residing	g at ≤1.5 km				Individuals residi	ng at ≤2 km				Individuals residir	ng at ≤2.5 k	m			Individuals resid	ing at ≤3 kn	n	
Industrial group (no. industries)	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95% CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>
Reference	1215 167	1.00	-	-	-	1215 167	1.00	-	-	-	1215 167	1.00	-	-	-	1215 167	1.00	-	-	-	1215 167	1.00	-	-	-
All sectors (134)	295 86	2.03 (1.44-2.87)	-	-		560 157	1.96 (1.47-2.61)				1015 235	1.51 (1.16-1.96)	-		-	1354 325	1.39 (1.09-1.77)				1733 390	1.26 (1.00-1.59)			-
Combustion installations (6)	11 2	0.20 (0.04-0.97)	0.045	0.113	0.373	24 4	0.24 (0.08-0.73)	0.012	0.028	0.095	36 5	0.23 (0.08-0.61)	0.004	0.010	0.034	89 11	0.31 (0.16-0.62)	0.001	0.003	0.011	252 20	0.29 (0.17-0.49)	< 0.001	< 0.001	< 0.001
Production and processing of metals (13)	138 17	1.41 (0.78-2.56)	0.259	0.486	1.000	168 19	1.43 (0.80-2.55)	0.224	0.299	1.000	225 31	1.91 (1.15-3.17)	0.012	0.023	0.081	453 58	2.28 (1.45-3.57)	< 0.001	$<\!0.001$	< 0.001	515 76	2.66 (1.77-4.00)	< 0.001	$<\!0.001$	< 0.001
Galvanization (3)	16 3	0.86 (0.23-3.20)	0.816	0.981	1.000	34 8	0.80 (0.33-1.94)	0.627	0.711	1.000	68 24	1.09 (0.57-2.09)	0.787	0.935	1.000	106 40	1.11 (0.61-2.03)	0.729	0.880	1.000	133 51	1.11 (0.58-2.13)	0.747	0.822	1.000
Surface treatment of metals and plastic (27)	48 29	5.45 (3.13-9.50)	< 0.001	< 0.001	< 0.001	224 56	2.65 (1.79-3.92)	< 0.001	$<\!0.001$	< 0.001	487 82	2.10 (1.47-3.01)	< 0.001	$<\!0.001$	< 0.001	642 96	1.55 (1.11-2.18)	0.011	0.023	0.084	968 145	1.48 (1.08-2.02)	0.014	0.028	0.103
Mining industry (1)	23 4	0.25 (0.08-0.79)	0.017	0.064	0.212	26 4	0.21 (0.07-0.65)	0.007	0.020	0.068	26 4	0.21 (0.07-0.65)	0.007	0.015	0.052	26 4	0.21 (0.07-0.65)	0.007	0.016	0.060	26 4	0.21 (0.07-0.65)	0.007	0.017	0.063
Cement and lime (3)	17 3	0.23 (0.06-0.83)	0.025	0.075	0.249	28 4	0.20 (0.07-0.60)	0.004	0.014	0.047	31 4	0.19 (0.06-0.58)	0.003	0.008	0.029	49 4	0.19 (0.06-0.55)	0.003	0.008	0.029	84 7	0.31 (0.13-0.74)	0.008	0.018	0.065
Glass and mineral fibers (4)	5 2	2.41 (0.45-13.05)	0.307	0.512	1.000	41 11	1.81 (0.87-3.79)	0.113	0.192	0.661	46 26	4.24 (2.39-7.54)	< 0.001	$<\!0.001$	< 0.001	149 59	3.24 (2.12-4.96)	< 0.001	$<\!0.001$	$<\!0.001$	271 74	2.06 (1.39-3.07)	< 0.001	$<\!0.001$	< 0.001
Ceramic (8)	14 2	1.33 (0.25-7.07)	0.734	0.981	1.000	22 7	2.48 (0.89-6.89)	0.082	0.155	0.533	83 11	1.29 (0.59-2.80)	0.523	0.710	1.000	107 14	1.18 (0.59-2.35)	0.639	0.839	1.000	119 19	1.35 (0.73-2.50)	0.343	0.503	1.000
Organic chemical industry (11)	17 24	11.54 (5.69-23.40)	< 0.001	$<\!0.001$	< 0.001	95 66	5.78 (3.75-8.91)	< 0.001	$<\!0.001$	< 0.001	219 82	3.57 (2.33-5.47)	< 0.001	$<\!0.001$	< 0.001	347 115	4.70 (3.12-7.08)	< 0.001	$<\!0.001$	$<\!0.001$	436 133	4.80 (3.20-7.20)	< 0.001	$<\!0.001$	< 0.001
Inorganic chemical industry (2)	0 2	inf (0-inf)	0.844	0.981	1.000	6 20	34.68 (12.81-93.92)	< 0.001	$<\!0.001$	< 0.001	36 43	10.77 (6.29-18.44)	< 0.001	$<\!0.001$	< 0.001	80 60	6.56 (4.21-10.24)	< 0.001	$<\!0.001$	$<\!0.001$	92 69	6.74 (4.38-10.36)	< 0.001	$<\!0.001$	< 0.001
Fertilizers (1)	0 0	-	-	-	-	0 0	-	-	-	-	0 0	-	-	-	-	0 0	-	-	-	-	15 2	0.53 (0.11-2.61)	0.435	0.563	1.000
Biocides (1)	0 0	-	-	-	-	0 0	-	-	-	-	0 0	-	-	-	-	6 2	1.30 (0.21-8.15)	0.779	0.880	1.000	10 4	1.49 (0.33-6.71)	0.603	0.698	1.000
Pharmaceutical products (4)	17 6	0.97 (0.35-2.67)	0.956	0.981	1.000	86 21	1.42 (0.81-2.46)	0.218	0.299	1.000	191 49	1.39 (0.93-2.09)	0.108	0.187	0.662	321 98	1.34 (0.97-1.84)	0.073	0.128	0.466	457 141	1.28 (0.96-1.70)	0.097	0.178	0.656
Explosives and pyrotechnics (3)	0 0	-	-	-	-	0 0	-	-	-	-	3 0	0 (0-inf)	0.937	0.971	1.000	11 2	0.64 (0.12-3.57)	0.610	0.839	1.000	15 2	0.47 (0.09-2.45)	0.370	0.509	1.000
Hazardous waste (6)	26 2	0.90 (0.18-4.51)	0.902	0.981	1.000	90 8	0.97 (0.40-2.35)	0.954	0.954	1.000	129 14	1.02 (0.50-2.09)	0.966	0.971	1.000	279 26	0.57 (0.26-1.27)	0.172	0.258	0.941	320 33	0.69 (0.36-1.32)	0.259	0.407	1.000
Non-hazardous waste (2)	0 0	-	-	-	-	2 1	4.67 (0.38-57.40)	0.229	0.299	1.000	2 1	4.67 (0.38-57.40)	0.229	0.335	1.000	25 5	4.19 (1.38-12.76)	0.012	0.023	0.084	84 8	1.76 (0.71-4.40)	0.224	0.379	1.000
Disposal or recycling of animal waste (2)	0 0	-	-	-	-	0 0	-	-	-	-	0 0	-	-	-	-	11 0	0 (0-inf)	0.915	0.961	1.000	66 9	1.27 (0.55-2.93)	0.572	0.698	1.000
Urban waste-water treatment plants (7)	0 0	-	-	-	-	1 1	1.38 (0.08-24.24)	0.827	0.879	1.000	29 5	0.50 (0.18-1.38)	0.178	0.282	1.000	188 44	0.72 (0.46-1.13)	0.152	0.246	0.895	337 87	0.99 (0.68-1.44)	0.955	0.955	1.000
Paper and wood production (3)	0 0	-	-	-	-	0 0	-	-	-	-	2 0	0 (0-inf)	0.971	0.971	1.000	9 0	0 (0-inf)	0.976	0.976	1.000	103 2	0.10 (0.02-0.41)	0.001	0.003	0.010
Food and beverage sector (16)	12 15	3.47 (1.47-8.16)	0.004	0.020	0.066	36 34	5.38 (3.03-9.56)	$<\!0.001$	< 0.001	< 0.001	121 53	4.93 (3.05-7.96)	< 0.001	$<\!0.001$	$<\!0.001$	187 73	5.89 (3.82-9.09)	$<\!0.001$	$<\!0.001$	< 0.001	390 111	3.34 (2.38-4.68)	< 0.001	$<\!0.001$	< 0.001
Surface treatment using organic solvents (8)	46 4	2.39 (0.67-8.51)	0.179	0.384	1.000	57 7	3.76 (1.32-10.73)	0.013	0.028	0.095	117 24	4.28 (2.31-7.93)	< 0.001	$<\!0.001$	< 0.001	237 68	6.62 (4.22-10.36)	< 0.001	$<\!0.001$	$<\!0.001$	302 88	6.16 (4.06-9.36)	< 0.001	$<\!0.001$	< 0.001
Ship building (2)	15 0	0 (0-inf)	0.981	0.981	1.000	27 5	0.55 (0.19-1.61)	0.275	0.334	1.000	54 18	1.15 (0.58-2.31)	0.689	0.873	1.000	190 48	0.93 (0.61-1.67)	0.796	0.880	1.000	190 48	0.93 (0.51-1.67)	0.796	0.834	1.000

<sup>a</sup>Number of cases.

<sup>b</sup>Number of controls.

<sup>c</sup>ORs were estimated from various mixed multiple logistic regression models (an independent model for each industrial distance), that included age, sex, body mass index 1-year before the interview, family history of colorectal cancer, tobacco smoking, educational level, physical activity, total energy intake, alcohol consumption, vegetable intake, and province of residence (as a random effect).

<sup>d</sup>*p*-value associated with hypothesis test for the mixed multiple logistic regression model.

<sup>e</sup>p-value adjusted by Benjamini & Hochberg's method.

<sup>f</sup>*p*-value adjusted by Benjamini & Yekutieli's method.

Supplementary Data, Table S4: odds ratios of colorectal cancer by industrial distance and industrial group, for the sensitivity analysis with only individuals living in

their current residence for  $\geq 10$  years (long-term residents).

	Individuals residing at ≤1 km						Individuals res	iding at ≤1.5 k	m			Individuals resid	ling at ≤2 kn	n			Individuals residu	ng at ≤2.5 k	m		Individuals residing at ≤3 km				
Industrial group (no. industries)	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> C	a <sup>b</sup> OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95%CI)°	$p^{d}$	p-BH <sup>e</sup>	p-BY <sup>f</sup>	Co <sup>a</sup> Ca <sup>b</sup>	OR (95% CI) <sup>c</sup>	$p^{d}$	p-BH <sup>e</sup>	p-BY
Reference	999 136	1.00	-	-	-	999 13	6 1.00	-	-	-	999 136	1.00	-	-	-	999 136	1.00	-	-	-	999 136	1.00	-	-	
All sectors (134)	239 75	2.26 (1.54-3.30)			-	466 12	1.91 (1.38-2.62)	-	-		852 193	1.51 (1.13-2.02)	-		-	1130 262	1.35 (1.03-1.77)		-	-	1464 315	1.20 (0.92-1.56)		-	
Combustion installations (6)	9 2	0.21 (0.04-1.06)	0.059	0.148	0.489	20	4 0.29 (0.09-0.91)	0.034	0.083	0.284	27 5	0.28 (0.10-0.79)	0.016	0.038	0.135	75 11	0.39 (0.19-0.78)	0.008	0.021	0.077	226 19	0.32 (0.19-0.55)	< 0.001	< 0.001	< 0.00
Production and processing of metals (13)	115 14	1.31 (0.68-2.52)	0.421	0.702	1.000	135 1	6 1.42 (0.76-2.66)	0.276	0.387	1.000	183 23	1.57 (0.89-2.78)	0.118	0.224	0.795	372 47	2.17 (1.31-3.58)	0.003	0.011	0.038	422 62	2.67 (1.69-4.22)	< 0.001	< 0.001	< 0.00
Galvanization (3)	13 3	1.35 (0.35-5.26)	0.669	0.981	1.000	29	6 0.83 (0.30-2.29)	0.717	0.762	1.000	54 14	0.90 (0.41-1.98)	0.792	0.885	1.000	81 27	1.19 (0.58-2.41)	0.637	0.787	1.000	104 33	0.98 (0.46-2.08)	0.954	0.962	1.00
Surface treatment of metals and plastic (27)	44 27	5.70 (3.16-10.28)	< 0.001	$<\!0.001$	< 0.001	192 4	7 2.53 (1.64-3.89)	< 0.001	$<\!0.001$	< 0.001	408 71	2.16 (1.46-3.20)	< 0.001	$<\!0.001$	< 0.001	533 80	1.53 (1.05-2.23)	0.028	0.059	0.214	815 116	1.40 (0.99-1.98)	0.060	0.120	0.44
Mining industry (1)	18 4	0.32 (0.10-1.03)	0.057	0.148	0.489	21	4 0.25 (0.08-0.80)	0.020	0.057	0.195	21 4	0.25 (0.08-0.80)	0.020	0.042	0.150	21 4	0.25 (0.08-0.80)	0.020	0.047	0.170	21 4	0.25 (0.08-0.80)	0.020	0.044	0.16
Cement and lime (3)	14 3	0.26 (0.07-0.99)	0.049	0.148	0.489	23	4 0.24 (0.08-0.75)	0.014	0.048	0.164	26 4	0.23 (0.07-0.71)	0.011	0.030	0.106	42 4	0.22 (0.07-0.68)	0.008	0.021	0.077	75 6	0.31 (0.12-0.79)	0.014	0.034	0.12
Glass and mineral fibers (4)	4 2	2.98 (0.51-17.29)	0.224	0.480	1.000	35	9 1.61 (0.71-3.62)	0.252	0.387	1.000	39 20	3.49 (1.83-6.65)	< 0.001	$<\!0.001$	< 0.001	134 52	3.20 (2.01-5.10)	< 0.001	< 0.001	< 0.001	248 65	2.08 (1.33-3.24)	0.001	0.003	0.01
Ceramic (8)	9 0	0 (0-inf)	0.907	0.981	1.000	14	4 1.85 (0.51-6.74)	0.351	0.426	1.000	61 8	1.19 (0.50-2.88)	0.693	0.844	1.000	78 11	1.27 (0.59-2.75)	0.541	0.710	1.000	88 15	1.46 (0.74-2.91)	0.277	0.435	1.00
Organic chemical industry (11)	16 23	12.51 (5.99-26.11)	< 0.001	$<\!0.001$	< 0.001	88 4	5.64 (3.53-9.01)	< 0.001	$<\!0.001$	< 0.001	209 73	3.73 (2.33-5.97)	< 0.001	$<\!0.001$	< 0.001	323 98	4.59 (2.91-7.23)	< 0.001	$<\!0.001$	$<\!0.001$	400 109	4.21 (2.69-6.58)	< 0.001	< 0.001	< 0.00
Inorganic chemical industry (2)	0 2	inf (0-inf)	0.981	0.981	1.000	5 1	5 29.31 (9.68-88.7	) <0.001	$<\!0.001$	< 0.001	26 38	13.17 (7.15-24.24)	< 0.001	$<\!0.001$	< 0.001	66 53	7.16 (4.39-11.67)	< 0.001	< 0.001	< 0.001	77 61	7.16 (4.48-11.45)	< 0.001	< 0.001	< 0.00
Fertilizers (1)	0 0	-	-	-	-	0	0 -	-	-	-	0 0	-	-	-	-	0 0	-	-	-	-	9 2	0.73 (0.14-3.85)	0.715	0.851	1.00
Biocides (1)	0 0	-	-	-	-	0	0 -	-	-	-	0 0	-	-	-	-	4 2	2.09 (0.27-16.06)	0.480	0.672	1.000	5 3	2.49 (0.40-15.67)	0.330	0.484	1.00
Pharmaceutical products (4)	12 5	1.14 (0.37-3.54)	0.817	0.981	1.000	72 1	7 1.39 (0.75-2.56)	0.296	0.387	1.000	157 40	1.36 (0.87-2.13)	0.180	0.285	1.000	266 81	1.28 (0.90-1.82)	0.163	0.285	1.000	386 119	1.26 (0.92-1.73)	0.149	0.252	0.93
Explosives and pyrotechnics (3)	0 0	-	-	-	-	0	0 -	-	-	-	2 0	0 (0-inf)	0.947	0.986	1.000	8 2	0.86 (0.14-5.36)	0.875	0.935	1.000	11 2	0.61 (0.11-3.45)	0.579	0.749	1.00
Hazardous waste (6)	14 1	1.07 (0.13-9.09)	0.954	0.981	1.000	59	7 1.35 (0.51-3.52)	0.545	0.618	1.000	91 12	1.16 (0.53-2.54)	0.711	0.844	1.000	214 23	0.67 (0.29-1.57)	0.358	0.537	1.000	250 29	0.72 (0.36-1.45)	0.361	0.496	1.00
Non-hazardous waste (2)	0 0	-	-	-	-	1	1 8.58 (0.46-161.90	0.152	0.274	0.941	1 1	8.58 (0.46-161.90)	0.152	0.263	0.931	18 4	3.89 (1.10-13.74)	0.035	0.067	0.244	60 7	2.13 (0.78-5.82)	0.139	0.252	0.93
Disposal or recycling of animal waste (2)	0 0	-	-	-	-	0	0 -	-	-	-	0 0	-	-	-	-	11 0	0 (0-inf)	0.890	0.935	1.000	58 8	1.14 (0.47-2.79)	0.774	0.851	1.00
Urban waste-water treatment plants (7)	0 0	-	-	-	-	1	1 1.32 (0.07-23.52	0.851	0.851	1.000	27 5	0.55 (0.20-1.58)	0.268	0.392	1.000	163 38	0.72 (0.44-1.18)	0.197	0.318	1.000	289 74	0.99 (0.65-1.50)	0.962	0.962	1.00
Paper and wood production (3)	0 0	-	-	-	-	0	0 -	-	-	-	1 0	0 (0-inf)	0.986	0.986	1.000	6 0	0 (0-inf)	0.973	0.973	1.000	97 2	0.11 (0.03-0.44)	0.002	0.006	0.02
Food and beverage sector (16)	9 12	3.92 (1.48-10.41)	0.006	0.030	0.100	29 2	. 5.98 (3.12-11.44	< 0.001	$<\!0.001$	< 0.001	105 45	5.83 (3.38-10.06)	< 0.001	$<\!0.001$	< 0.001	157 62	7.12 (4.35-11.66)	< 0.001	$<\!0.001$	$<\!0.001$	335 97	3.54 (2.44-5.14)	< 0.001	< 0.001	< 0.00
Surface treatment using organic solvents (8)	42 3	1.99 (0.46-8.56)	0.354	0.664	1.000	53	5 2.86 (0.84-9.73)	0.092	0.196	0.672	108 19	4.07 (2.02-8.22)	< 0.001	$<\!0.001$	< 0.001	214 55	6.19 (3.78-10.15)	< 0.001	$<\!0.001$	$<\!0.001$	267 73	6.07 (3.81-9.66)	< 0.001	< 0.001	< 0.00
Ship building (2)	14 0	0 (0-inf)	0.974	0.981	1.000	26	3 0.39 (0.11-1.45)	0.161	0.274	0.941	46 13	1.24 (0.55-2.76)	0.604	0.820	1.000	149 33	0.89 (0.45-1.76)	0.742	0.866	1.000	149 33	0.89 (0.45-1.76)	0.742	0.851	1.00
<sup>a</sup> Number of cases.																									

<sup>b</sup>Number of controls.

<sup>c</sup>ORs were estimated from various mixed multiple logistic regression models (an independent model for each industrial distance), that included age, sex, body mass index 1-year before the interview, family history of colorectal cancer, tobacco smoking, educational level, physical activity, total energy intake, alcohol consumption, vegetable intake, and province of residence (as a random effect).

<sup>d</sup>*p*-value associated with hypothesis test for the mixed multiple logistic regression model.

<sup>d</sup>*p*-value associated with hypothesis test for the mixed multiple logistic regression model.

<sup>e</sup>p-value adjusted by Benjamini & Hochberg's method.

<sup>f</sup>*p*-value adjusted by Benjamini & Yekutieli's method.

Supplementary Data, Table S5: specific pollutants that can be released by the facilities to both air and water, by industrial group, according to the E-PRTR categories.

	Pollutants released	1 by industrial groups
Industrial group	Air	Water
Combustion installations	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dioxins+furans, trichloroethylene, benzene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dioxins+furans, PAHs <sup>b</sup> , toluene, fluoranthene, benzo(g,h,i)perylene
Production and processing of metals	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, hexachlorobenzene, lindane, dioxins+furans, polychlorinated biphenyls, anthracene, benzene, naphthalene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, pentachlorophenol, anthracene, nonylphenol and nonylphenol ethoxylates, naphthalene, organotin compounds, PAHs <sup>b</sup> , octylphenols and octylphenol ethoxylates, fluoranthene, benzo(g,h,i)perylene, benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene, indeno(1,2,3-cd)pyrene
Galvanization	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, nickel and compounds, lead and compounds, zinc and compounds, dioxins+furans, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, nickel and compounds, lead and compounds, zinc and compounds, PAHs <sup>b</sup>
Surface treatment of metals and plastic	NMVOC <sup>a</sup> , cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, benzene, dichloromethane, 1,2,3,4,5,6-hexachlorocyclohexane, tetrachloroethylene, trichloroethylene, di-(2-ethyl hexyl) phthalate, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, anthracene, naphthalene, organotin compounds, di-(2-ethyl hexyl) phthalate, PAHs <sup>b</sup> , fluoranthene, trichloromethane, toluene, benzo(b)fluoranthene, ethyl benzene, xylenes
Mining industry	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, NMVOC <sup>a</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Arsenic and compounds, cadmium and compounds, copper and compounds, nickel and compounds, lead and compounds, zinc and compounds
Cement and lime	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dioxins+furans, polychlorinated biphenyls, anthracene, benzene, naphthalene, di-(2- ethyl hexyl) phthalate, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , thallium, antimony, cobalt, manganese, vanadium	Copper and compounds, zinc and compounds
Glass and mineral fibers	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dioxins+furans, polychlorinated biphenyls, benzene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, benzene, ethyl benzene, toluene, xylenes, octylphenols and octylphenol ethoxylates
Ceramic	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, benzene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , thallium, antimony, cobalt, manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, trichloromethane, naphthalene
Organic chemical industry	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, 1,2-dichloroethane, dichloromethane, dioxins+furans, tetrachloroethylene, tetrachloromethane, trichloromethane, vinyl chloride, anthracene, benzene, ethylene oxide, naphthalene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , antimony, cobalt, manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, aldrin, atrazine, chlordane, chlorfenvinphos, chlorpyrifos, DDT, 1,2-dichloroethane, dichloromethane, dieldrin, endosulfan, endrin, hexachlorobenzene, hexachlorobutadiene, 1,2,3,4,5,6-hexachlorocyclohexane, mirex, dioxins+furans, simazine, tetrachloroethylene, trichlorobenzenes, trichloroethylene, trichloromethane, vinyl chloride, anthracene, benzene, brominated diphenylethers, nonylphenol and nonylphenol ethoxylates, ethyl benzene, naphthalene, organotin compounds, di-(2-ethyl hexyl) phthalate, PAHs <sup>b</sup> , toluene, tributyltin and compounds, xylenes, octylphenols and octylphenol ethoxylates, fluoranthene, isodrin, benzo(b)fluoranthene, indeno(g,h,i)perylene
Inorganic chemical industry	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dichloromethane, dioxins+furans, tetrachloromethane, trichloromethane, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , antimony	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, hexachlorobenzene, dioxins+furans, trichloromethane, organotin compounds, PAHs <sup>b</sup> , fluoranthene
Fertilizers	NMVOC <sup>a</sup> , zinc and compounds, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , cobalt	
Biocides	NMVOC <sup>a</sup> , dichloromethane, PM <sub>10</sub> <sup>c</sup>	Copper and compounds, zinc and compounds, ethyl benzene, xylenes
Pharmaceutical products	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and	Chromium and compounds, copper and compounds, mercury and compounds, lead and compounds, zinc and compounds, 1,2-dichloroethane, dichloromethane, tetrachloroethylene, tetrachloromethane,

	Pollutants release	d by industrial groups
Industrial group	Air	Water
	compounds, 1,2-dichloroethane, dichloromethane, tetrachloromethane, trichloromethane, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , thallium, antimony, cobalt, manganese, vanadium	trichloroethylene, trichloromethane, benzene, ethyl benzene, toluene, xylenes, naphthalene, PAHs <sup>b</sup> , fluoranthene, benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene
Explosives and pyrotechnics	NMVOC <sup>a</sup> , lead and compounds, PM <sub>10</sub> <sup>c</sup>	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds
Hazardous waste	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, hexachlorobenzene, dioxins+furans, tetrachloroethylene, trichloroethylene, benzene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , thallium, antimony, cobalt, manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dichloromethane, benzene, polychlorinated biphenyls, tetrachloroethylene, trichloroethylene, trichloroethylene, ethyl benzene, naphthalene, organotin compounds, PAHs <sup>b</sup> , toluene, xylenes
Non-hazardous waste	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, dioxins+furans, dichloromethane, tetrachloroethylene, tetrachloromethane, trichloroethylene, vinyl chloride, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , antimony, cobalt, manganese, vanadium	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, alachlor, aldrin, atrazine, chlordane, chlorfenvinphos, chlorpyrifos, DDT, 1,2-dichloroethane, dichloromethane, dieldrin, diuron, endosulfan, endrin, heptachlor, hexachlorobenzene, hexachlorobutadiene, 1,2,3,4,5,6-hexachlorocyclohexane, lindane, mirex, dioxins+furans, pentachlorobenzene, pentachlorophenol, polychlorinated biphenyls, simazine, tetrachloroethylene, trichlorobenzenes, trichloroethylene, trichloromethane, vinyl chloride, anthracene, benzene, brominated diphenylethers, nonylphenol and nonylphenol ethoxylates, ethyl benzene, isoproturon, naphthalene, organotin compounds, di-(2-ethyl hexyl) phthalate, PAHs <sup>b</sup> , toluene, tributyltin and compounds, triphenyltin and compounds, xylenes, octylphenols and octylphenol ethoxylates, flouranthene, isodrin, hexabromobiphenyl
Disposal or recycling of animal waste	NMVOC <sup>a</sup> , PAHs <sup>b</sup> , dioxins+furans, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Zinc and compounds, dioxins+furans
Urban waste-water treatment plants	NMVOC <sup>a</sup> , cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, dioxins+furans, PM <sub>10</sub> <sup>c</sup>	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, atrazine, 1,2-dichloroethane, diuron, lindane, pentachlorophenol, simazine, tetrachloroethylene, tetrachloromethane, trichloromethane, anthracene, benzene, nonylphenol and nonylphenol ethoxylates, ethyl benzene, isoproturon, naphthalene, organotin compounds, di-(2-ethyl hexyl) phthalate, PAHs <sup>b</sup> , toluene, tributyltin and compounds, xylenes, octylphenols and octylphenol ethoxylates, fluoranthene, benzo(g,h,i)perylene, benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene, indeno(1,2,3-cd)pyrene
Paper and wood production	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, di-(2-ethyl hexyl) phthalate, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, tetrachloroethylene, trichlorobenzenes, trichloroethylene, trichloromethane, organotin compounds, di-(2-ethyl hexyl) phthalate, PAHs <sup>b</sup> , toluene
Food and beverage sector	NMVOC <sup>a</sup> , arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, dioxins+furans, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, naphthalene, PAHs <sup>b</sup> , toluene, fluoranthene, benzo(g,h,i)perylene, benzo(a)pyrene, benzo(b)fluoranthene
Surface treatment using organic solvents	NMVOC <sup>a</sup> , chromium and compounds, copper and compounds, nickel and compounds, lead and compounds, zinc and compounds, dichloromethane, naphthalene, PAHs <sup>b</sup> , PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup>	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, 1,2-dichloroethane, trichloroethylene, trichloromethane, organotin compounds, toluene, naphthalene, PAHs <sup>b</sup>
Ship building	NMVOC <sup>a</sup> , cadmium and compounds, chromium and compounds, copper and compounds, nickel and compounds, lead and compounds, zinc and compounds, PM <sub>10</sub> <sup>c</sup> , TSP <sup>d</sup> , antimony, cobalt, manganese	Arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, mercury and compounds, nickel and compounds, lead and compounds, zinc and compounds, organotin compounds, PAHs <sup>b</sup>
<sup>a</sup> Non-methane volatile organic compounds.		

<sup>a</sup>Non-methane volatile organic compounds. <sup>b</sup>Polycyclic aromatic hydrocarbons. <sup>p</sup>Articulate matter with a diameter between 2.5 and 10 μm. <sup>d</sup>Total suspended particulate matter.

Supplementary Data, Table S6: amounts (in kg) of carcinogens (IARC classification) and other toxic substances released by the facilities in the study area in 2009,

grouped by industrial sector.

	IARC groups <sup>a</sup>						Groups of toxic substances <sup>b</sup>										
Industrial group	Group 1		Group 2B	Metals	Pesticides	PACs	Non-HPCs	Plasticizers	POPs	VOCs	Solvents	Other					
Combustion installations	1,718,883	805	173	6294	0	321	0	3	173	470,346	600	1,716,080					
Production and processing of metals	3,265,670	16,748	8	126,640	33	4291	0.1	0	4280	706,345	177,408	3,078,955					
Galvanization	17,225	111	6	4117	3	0.04	0	0	0.04	10,040	80	17,004					
Surface treatment of metals and plastic	55,593	4685	206	6786	87	6	0	200	87	1,133,477	4610	52,310					
Mining industry	1,490,970	6	0	796	0	0.0003	0	0	0.0003	2444	0.03	1,490,818					
Cement and lime	1,029,713	670	1,203	3130	0	2090	0	417	1273	701,026	11,697	1,016,121					
Glass and mineral fibers	330,813	1122	3	2548	0	0.0005	0	0	0.0005	2,491,041	422	329,743					
Ceramic	947,261	147	10	1788	6	3	0	0	3	107,659	1280	945,038					
Organic chemical industry	132,575	888	10,275	985	83	18,399	52	2	31	2,802,712	11,131	75,743					
Inorganic chemical industry	113,591	112	19	1549	0	0.0002	0	0	0.0002	6306	23	113,513					
Fertilizers	124,324	0.01	61	0.04	0	0.0001	0	0	0.0001	186	61	124,324					
Biocides	1118	81	0.2	7	0	0	0	0	0	6945	81	1118					
Pharmaceutical products	3129	313,251	91,873	834	0.02	0.01	0	0	0.01	4,202,038	405,237	2993					
Explosives and pyrotechnics	530	10	0.1	167	0.01	0.003	0	0	0.02	15,353	164	239					
Hazardous waste	23,245	139	2	1035	0.8	149	0	0	150	8811	13	22,704					
Non-hazardous waste	35,747	966	2	844	45	1.2	0.9	2	44	172,698	1111	34,926					
Disposal or recycling of animal waste	141,489	20	0	274	0	0.8	0	0	0.8	11,403	0.3	141,287					
Urban waste-water treatment plants	11,879	1840	281	34,626	161	62	347	178	60	128,541	555	3502					
Paper and wood production	331,563	110	0	3242	0.5	0.4	0	0	0.9	853,178	4495	326,456					
Food and beverage sector	89,801	6	3	868	2	1.5	0	0	1.4	542,625	52	89,528					
Surface treatment using organic solvents	86,403	185	203	885	0.01	224	0	0	24	10,398,598	1819	86,224					
Ship building	2	0	0	0	0	2	0	0	2	209	0	0					
TOTAL	9,951,524	341,901	104,328	197,415	421	25,552	400	802	6131	24,771,982	620,838	9,668,628					

<sup>a</sup>IARC carcinogenic classification: Group 1: carcinogenic to humans (arsenic and compounds, cadmium and compounds, nickel and compounds, lindane, dioxins+furans, pentachlorophenol, polychlorinated biphenyls, trichloroethylene, vinyl chloride, benzene, ethylene oxide, polycyclic aromatic hydrocarbons (PAHs), particulate matter (PM<sub>10</sub>), total suspended particulate matter, and benzo(a)pyrene); Group 2A: probably carcinogenic to humans (lead and compounds, aldrin, DDT, dichloromethane, dieldrin, tetrachloroethylene, and hexabromobiphenyl); Group 2B: possibly carcinogenic to humans (chlordane, 1,2-dichloroethane, heptachlor, hexachlorobenzene, 1,2,3,4,5,6-hexachlorocyclohexane, mirex, tetrachloromethane, 1,1,2,2-tetrachloroethane, ethyl benzene, naphthalene, di-(2-ethyl hexyl) phthalate, cobalt and compounds, benzo(b)fluoranthene, and indeno(1,2,3-cd)pyrene).

<sup>b</sup>Metals (arsenic and compounds, cadmium and compounds, chromium and compounds, copper and compounds, nickel and compounds, lead and compounds, zinc and compounds, organotin compounds, tributyltin and compounds, triphenyltin and compounds, triphenyltin, and isodrin); PACs: polycyclic aromatic chemicals (anthracene, ethylene oxide, naphthalene, PAHs, fluoranthene, benzo(g,h.i)perylene, benzo(a)pyrene, benzo(b)fluoranthene, and indeno(1,2,3-cd)pyrene); Non-HPCs: non-halogenated phenolic chemicals (nonylphenol ethoxylates, and octylphenol ethoxylates); Plasticizers (di-(2-ethyl hexyl) phthalate, and C<sub>10-13</sub>-chloroalkanes); POPs: persistent organic pollutants (aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, 1,2,3,4,5,6-hexachlorocyclohexane, lindane, mirex, dioxins+furans, pentachlorobenzene, polychlorinated biphenyls, benzo(a)pyrene, benzo(b)fluoranthene, weaklorobenzene, indane, mirex, dioxins+furans, pentachlorobenzene, polychlorinated biphenyls, benzo(a)pyrene, benzo(k)fluoranthene; VOCs: volatile organic compounds (non-methane volatile organic compounds, 1,2-dichloroethane, dichloromethane, hexachlorobenzenes, 1,1,1-trichloroethylene, trichloroethylene, trichl

Supplementary Data, Table S7: odds ratios of colorectal cancer for ever-decreasing radiuses within a 30-kilometer area surrounding each industrial installation, both

overall and by industrial group, for the sensitivity analysis with only individuals living in their current residence for  $\geq 10$  years (long-term residents).

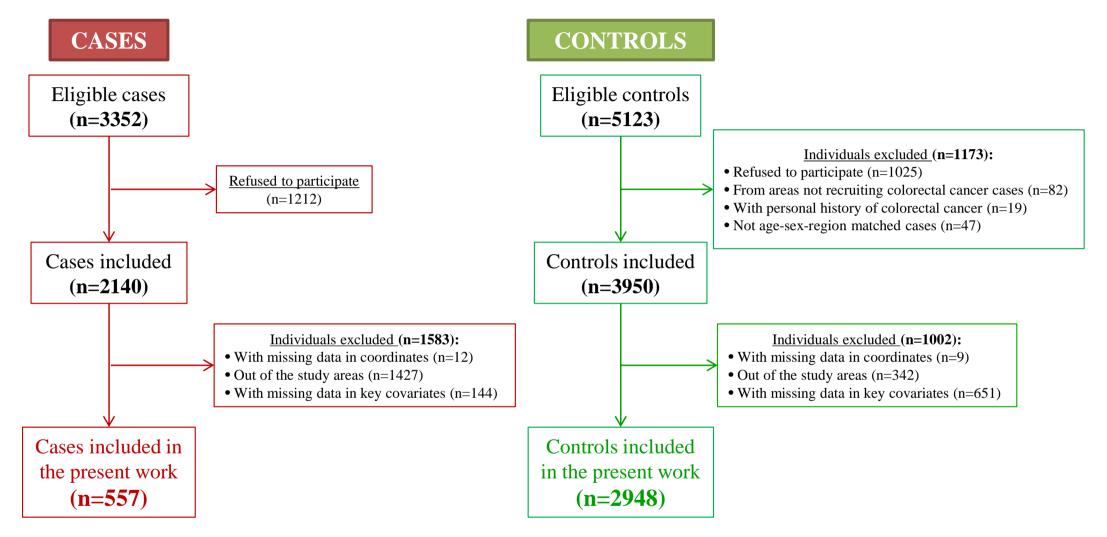
									Categorical variable	s								Continuous variab	
			[0-1 km)			[1-1.5 km)			[1.5-2 km)			[2-2.5 km)			[2.5-3 km)	Refer [3-30			
Industrial group	$\mathrm{Co}^{\mathrm{a}}$	$Ca^{b}$	OR (95%CI)	Co <sup>a</sup>	$Ca^b$	OR (95%CI)	Co <sup>a</sup>	$Ca^b$	OR (95%CI)	Co <sup>a</sup>	$\operatorname{Ca}^{\mathrm{b}}$	OR (95%CI)	$\mathrm{Co}^{\mathrm{a}}$	$\operatorname{Ca}^{\mathrm{b}}$	OR (95%CI)	Co <sup>a</sup>	Ca <sup>b</sup>	OR	p-trend
All sectors	239	75	2.28 (1.56-3.33)	227	53	1.55 (1.03-2.32)	386	65	0.95 (0.64-1.41)	278	69	1.05 (0.73-1.51)	334	53	0.77 (0.52-1.14)	996	135	1.16	< 0.001
Combustion installations	9	2	0.25 (0.05-1.30)	11	2	0.26 (0.05-1.40)	7	1	0.17 (0.02-1.78)	48	6	0.48 (0.18-1.32)	151	8	0.36 (0.16-0.85)	496	95	0.69	0.002
Production and processing of metals	115	14	1.73 (0.81-3.71)	20	2	4.56 (0.84-24.91)	48	7	3.04 (1.05-8.77)	189	24	2.94 (1.41-6.13)	50	15	4.06 (1.87-8.82)	435	41	1.12	0.102
Galvanization	13	3	0.74 (0.13-4.33)	16	3	0.34 (0.06-1.81)	25	8	0.64 (0.20-2.07)	27	13	0.88 (0.30-2.59)	23	6	0.66 (0.19-2.35)	25	12	0.88	0.346
Surface treatment of metals and plastic	44	27	7.13 (3.72-13.65)	148	20	1.73 (0.95-3.15)	216	24	1.63 (0.90-2.97)	125	9	0.63 (0.28-1.40)	282	36	1.35 (0.79-2.33)	872	54	1.31	< 0.001
Mining industry	18	4	0.32 (0.08-1.19)	3	0	0 (0-inf)	0	0	-	0	0	-	0	0	-	75	52	0.76	0.039
Cement and lime	14	3	0.20 (0.05-0.90)	9	1	0.11 (0.01-1.07)	3	0	0 (0-inf)	16	0	0 (0-inf)	33	2	1.59 (0.26-9.76)	251	66	0.68	0.005
Glass and mineral fibers	4	2	5.73 (0.91-35.98)	31	7	2.76 (0.97-7.80)	4	11	35.76 (9.18-139.31)	95	32	4.97 (2.44-10.09)	114	13	1.61 (0.70-3.67)	310	71	1.56	< 0.001
Ceramic	9	0	0 (0-inf)	5	4	1.23 (0.25-6.06)	47	4	0.09 (0.02-0.39)	17	3	0.24 (0.05-1.14)	10	4	0.51 (0.12-2.20)	50	26	0.71	0.050
Organic chemical industry	16	23	14.05 (6.09-32.42)	72	35	4.60 (2.29-9.27)	121	15	1.25 (0.51-3.06)	114	25	2.79 (1.34-5.82)	77	11	1.70 (0.75-3.84)	242	21	1.55	< 0.001
Inorganic chemical industry	0	2	inf (0-inf)	5	13	22.34 (6.51-76.64)	21	23	8.43 (3.79-18.78)	40	15	3.06 (1.35-6.92)	11	8	6.50 (1.77-23.88)	241	25	2.10	< 0.001
Fertilizers	0	0	-	0	0	-	0	0	-	0	0	-	9	2	0.50 (0.03-8.09)	18	9	0.50	0.622
Biocides	0	0	-	0	0	-	0	0	-	4	2	$NE^{c}$	1	1	$NE^{c}$	1	0	NE <sup>c</sup>	NE <sup>c</sup>
Pharmaceutical products	12	5	1.42 (0.44-4.59)	60	12	1.87 (0.90-3.85)	85	23	1.44 (0.77-2.69)	109	41	1.33 (0.81-2.16)	120	38	1.46 (0.88-2.44)	737	89	1.13	0.060
Explosives and pyrotechnics	0	0	-	0	0	-	2	0	0 (0-inf)	7	2	1.01 (0.01-81.22)	4	0	0 (0-inf)	10	7	0.50	0.396
Hazardous waste	14	1	0.64 (0.06-6.63)	45	6	0.83 (0.22-3.08)	32	5	0.87 (0.24-3.24)	123	11	0.60 (0.19-1.91)	36	6	0.86 (0.29-2.56)	244	25	0.97	0.831
Non-hazardous waste	0	0	-	1	1	76.36 (1.04-5632.56)	0	0	-	17	3	21.71 (1.19-396.41)	42	3	14.15 (0.87-230.64)	155	2	3.18	0.018
Disposal or recycling of animal waste	0	0	-	0	0	-	0	0	-	11	0	0 (0-inf)	47	8	2.99 (1.12-8.00)	247	17	1.73	0.188
Urban waste-water treatment plants	0	0	-	1	1	1.76 (0.09-34.00)	26	4	0.57 (0.17-1.89)	136	33	1.08 (0.60-1.93)	126	36	1.67 (0.92-3.03)	360	84	0.98	0.855
Paper and wood production	0	0	-	0	0	-	1	0	0 (0-inf)	5	0	0 (0-inf)	91	2	0.09 (0.02-0.50)	255	28	0.09	0.006
Food and beverage sector	9	12	4.18 (1.50-11.60)	20	16	10.95 (4.39-27.33)	76	17	7.39 (3.11-17.56)	52	17	8.81 (3.97-19.54)	178	35	1.80 (1.05-3.06)	795	106	1.63	< 0.001
Surface treatment using organic solvents	42	3	4.33 (0.80-23.49)	11	2	14.97 (2.36-94.93)	55	14	12.44 (4.56-33.91)	106	36	9.93 (4.83-20.39)	53	18	7.73 (3.22-18.54)	415	21	2.13	< 0.001
Ship building	14	0	0 (0-inf)	12	3	0.37 (0.07-1.97)	20	10	0.99 (0.29-3.39)	56	8	0.31 (0.10-0.94)	47	12	0.89 (0.29-2.75)	27	12	0.74	0.045

<sup>a</sup>Number of controls.

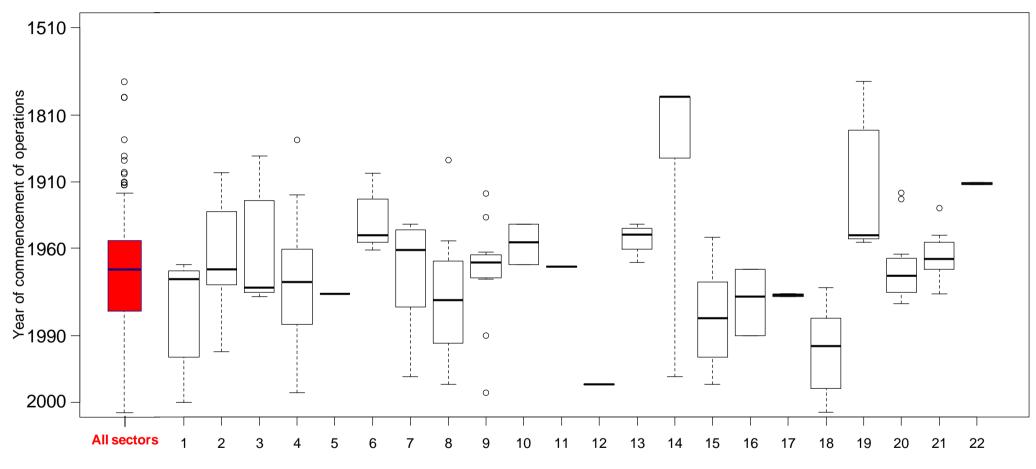
<sup>b</sup>Number of cases.

°Not estimated: risk could not be estimated.

Supplementary Data, Figure S1: flow chart displaying the selection process of colorectal cancer cases and controls.



Supplementary Data, Figure S2: box-and-whisker plots with the years of commencement of operations of the 134 industries studied, according to the industrial group. Y-axis is plotted in logarithmic scale.



# 134 installations

#### Categories of industrial groups\*

\*1=Combustion installations. 2=Production and processing of metals. 3=Galvanization. 4=Surface treatment of metals and plastic. 5=Mining industry. 6=Cement and lime. 7=Glass and mineral fibers. 8=Ceramic. 9=Organic chemical industry. 10=Inorganic chemical industry. 11=Fertilizers. 12=Biocides. 13=Pharmaceutical products. 14=Explosives and pyrotechnics. 15=Hazardous waste. 16=Non-hazardous waste. 17=Disposal or recycling of animal waste. 18=Urban waste-water treatment plants. 19=Paper and wood production. 20=Food and beverage sector. 21=Surface treatment using organic solvents. 22=Ship building.

Supplementary Data, Figure S3: odds ratios of colorectal cancer by groups of carcinogenic and other toxic substances with statistically significant results and a number of cases and controls  $\geq 10$ , for the sensitivity analysis with only individuals living in their current residence for  $\geq 10$  years (long-term residents). X-axis is plotted in logarithmic scale.

	Distance: 1 km	Distance: 1.5 km	Distance: 2 km	Distance: 2.5 km	Distance: 3 km
GROUPS OF POLLUTANTS IARC groups (no. industries) Group 1 (99) Group 2A (50) Group 2B (20)	Co   Ca   OR (95% Cl)     238   74   2.22 (1.52 - 3.25)     121   20   0.90 (0.51 - 1.61)     59   9	Co   Ca   OR (95%CI)     444   122   1.93 (1.40 - 2.67)     237   50   1.45 (0.94 - 2.23)     144   39   1.65 (1.03 - 2.63)	Co   Ca   OR (95%CI)     796   177   1.45 (1.08 - 1.96)   ■     491   95   1.51 (1.03 - 2.21)   ■     305   77   1.83 (1.22 - 2.73)   ■	Co   Ca   OR (95% CI)     796   177   1.45 (1.08 - 1.96)     491   95   1.51 (1.03 - 2.21)     305   77   1.83 (1.22 - 2.73)	Co   Ca   OR (95%CI)     1348   302   1.23 (0.95 - 1.61)     904   171   1.45 (1.06 - 1.99)     519   110   1.45 (1.02 - 2.05)
Groups of toxic substances (no. industrie Metais (83) Pesticides (6) PACs (26) Non-HPCs (3) POPs (36) VOCs (67) Solvents (26) Other (77)	229   62   2.06 (1.38 · 3.06)     48   14   2.86 (1.44 · 5.70)     17   8     0   0     96   19     132   21     1.18 (0.65 · 2.13)     65   5     205   68     0.7   1.0     0.7   1.0     0.7   1.0	436 112 1.94 (1.39 - 2.70)   136 41 3.42 (2.10 - 5.57)   67 32 1.67 (0.98 - 2.84)   4 10 241 54 1.55   241 54 1.55 (1.03 - 2.34)   300 70 1.74 (1.19 - 2.56)   342 108 2.17 (1.55 - 3.04)   0.5 1.0 2.0 4.0 60.80	786 166 1.43 (1.06 - 1.95)   184 44 2.39 (15.0 - 3.80)   194 69 1.83 (1.17 - 2.85)   41 38 9.25 (5.24 - 16.33)   402 74 1.05 (0.71 - 1.56)   649 135 1.53 (1.10 - 2.12)   375 53 0.65 (0.54 - 1.33)   618 154 1.59 (1.17 - 2.16)	786 166 1.43 (1.06 - 1.95)   184 44 2.39 (1.50 - 3.80)   194 69 1.83 (1.17 - 2.85)   41 38 9.25 (5.24 - 16.33)   402 74 1.05 (0.77 - 1.56)   649 135 1.53 (1.10 - 2.12)   375 53 0.65 (0.54 - 1.33)   618 154 1.59 (1.17 - 2.16)   0.6 1.0 5.0 10.0 20.0	1327 289 1.23 (0.94 - 1.60)   371 61 1.28 (0.84 - 1.95)   818 145 1.27 (0.91 - 1.77)   146 68 6.31 (3.97 - 10.04)   927 146 0.96 (0.69 - 1.33)   1221 252 1.26 (0.96 - 1.67)   762 129 1.34 (0.96 - 1.87)   1227 266 1.23 (0.94 - 1.61)

Supplementary Data, Figure S4: odds ratios of colorectal cancer by specific pollutant with statistically significant results and a number of cases and controls  $\geq 10$ ,

for the sensitivity analysis with only individuals living in their current residence for  $\geq 10$  years (long-term residents). X-axis is plotted in logarithmic scale.

