Supplementary Data

Title of the manuscript: "Ovarian cancer mortality and industrial pollution."

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.

b) Table S1, showing the list of industrial groups with E-PRTR categories used and number of installations.

c) Table S2, showing observed and expected cases, and the relative risk of dying from ovarian cancer in towns for ever-decreasing radiuses within a 50-kilometer area surrounding each complex, by industrial group (risk gradient analysis, with categorical and continuous variables).

d) Figure S1, showing the geographic distribution of Spanish installations, according to the industrial group.

e) Figure S2, showing the box-and-whisker plots with the years of commencement of operations of the 1970 pre-1993 installations in Spain, according to the industrial group.

Supplementary Data, Appendix A.

Risk gradient analysis

The risk gradient analysis in the vicinity of installations was confined to an area of 50 km surrounding each installation, and the RRs were estimated using mixed Poisson regression models, as follows:

a) *All industries as a whole (all sectors)*: for each town, we calculated a new variable, "*minimum distance$_i$*", defined as:

$$\text{minimum distance}_i = min\{\text{industrial distance}_{ij}\}_j$$

i=1, …, 8098 towns, j=1, …, 1970 facilities

where *industrial distance$_{ij}$* is the distance between town i and facility j. This new explanatory variable was categorized in concentric rings (0-2, 2-3, 3-4, 4-5; and 5-50 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 RR 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 town and industrial group, we calculated 27 new variables, "*minimum distance_industrial group$_{ik}$*", defined as:

$$\text{minimum distance\_industrial group}_{ik} = min\{\text{industrial group distance}_{ij}\}_j$$

i=1, …, 8098 towns, k=1, …, 27 industrial groups, j=1, …, no. of facilities of industrial group k,

where *industrial group distance$_{ij}$* is the distance between town i and facility j belonging to industrial group k. These new explanatory variables were categorized in concentric rings (0-2, 2-3, 3-4, 4-5; and 5-50 as reference). These were included in the models as categorical and continuous variables, and towns that had some industry other than the group analyzed within a radius of 5 km of the municipal centroid were excluded.

Supplementary Data, Table S1.

Industrial group	E-PRTR category	No. of facilities
Combustion installations	1.c	64
Refineries and coke ovens	1.a, 1.d	13
Production and processing of metals	2.a, 2.b, 2.c.i, 2.c.ii, 2.d, 2.e	141
Galvanization	2.c.iii	30
Surface treatment of metals and plastic	2.f	225
Mining industry	3.a, 3.b	92
Cement and lime	3.c, 3.d	60
Glass and mineral fibers	3.e, 3.f	39
Ceramic	3.g	326
Organic chemical industry	4.a	121
Inorganic chemical industry	4.b	62
Fertilizers	4.c	21
Biocides	4.d	10
Pharmaceutical products	4.e	45
Explosives and pyrotechnics	4.f	53
Hazardous waste	5.a, 5.b	40
Non-hazardous waste	5.c, 5.d	66
Disposal or recycling of animal waste	5.e	31
Urban waste-water treatment plants	5.f, 5.g	58
Paper and wood production	6.a, 6.b, 6.c	76
Pre-treatment or dyeing of textiles	9.a	22
Tanning of hides and skins	9.b	2
Food and beverage sector	8.a, 8.b, 8.c	282
Aquiculture	7.b	4
Surface treatment using organic solvents	9.c	76
Production of carbon or electro-graphite	9.d	2
Ship building	9.e	9
TOTAL		1970

Supplementary Data, Table S2.

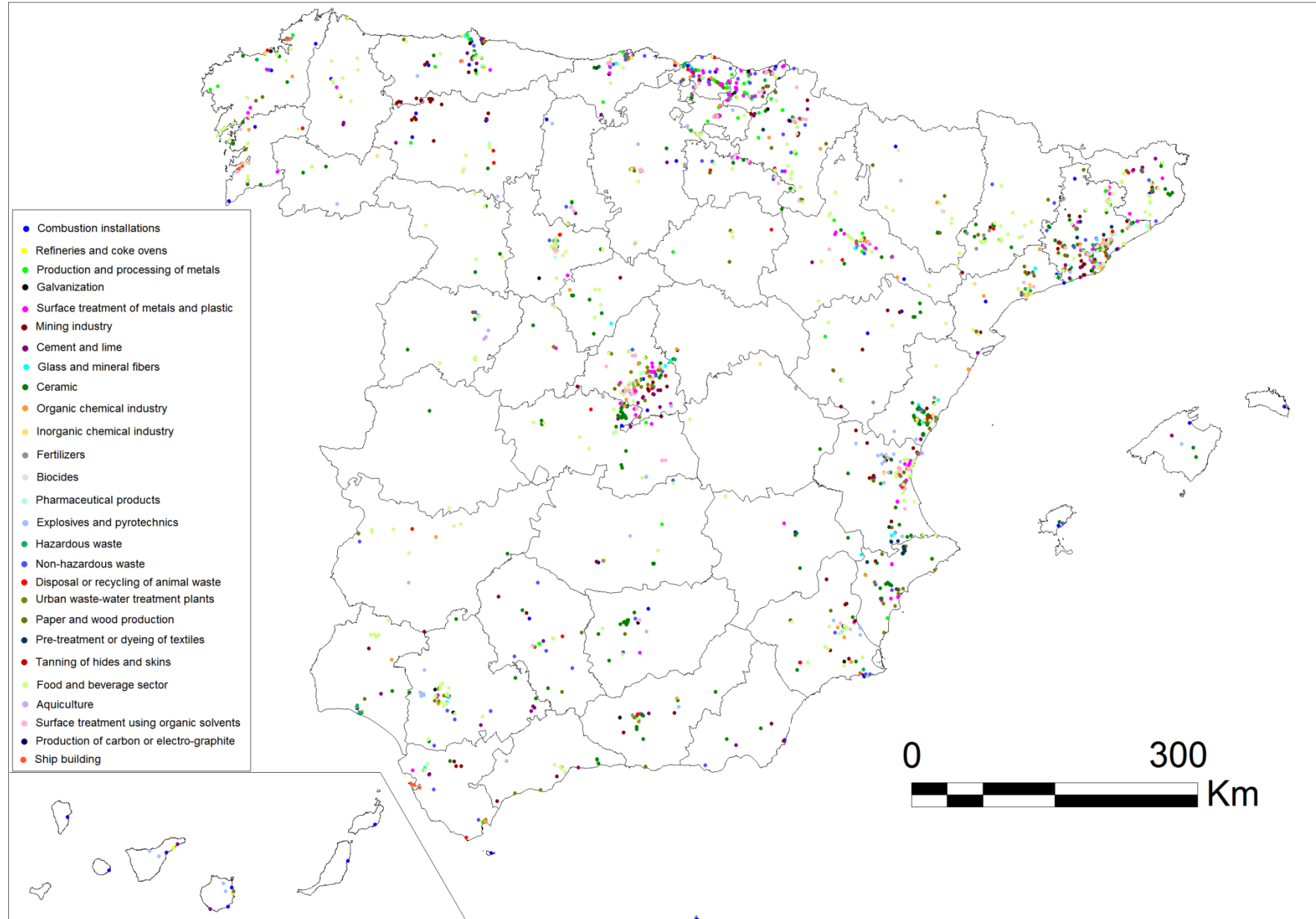| | Categorical variables | | | | | | | | | | | | | | | | | | | Continuous variables | |
| | [0-2 km] | | | | (2-3 km) | | | | (3-4 km) | | | | (4-5 km) | | | | (5-50 km)[a] | | | |
Industrial group	Obs[b]	Exp[c]	RR[d]	95%CI[e]	Obs[b]	Exp[c]	RR[d]	95%CI[e]	Obs[b]	Exp[c]	RR[d]	95%CI[e]	Obs[b]	Exp[c]	RR[d]	95%CI[e]	Obs[b]	Exp[c]	RR[d]	p trend
All sectors	4587	4514.2	1.06	1.01-1.12	3869	3642.0	1.09	1.03-1.15	1768	1736.6	1.06	0.99-1.13	2141	2185.8	1.04	0.97-1.11	5535	5801.9	1.02	0.0128
Combustion installations	221	236.6	0.93	0.80-1.08	105	89.6	1.12	0.91-1.37	594	608.8	0.95	0.86-1.06	452	403.3	1.06	0.94-1.20	2892	2986.4	0.99	0.4403
Refineries and coke ovens	145	115.0	1.24	1.01-1.52	10	4.9	2.17	1.14-4.11	231	199.3	1.10	0.90-1.35	355	306.4	1.14	0.97-1.34	735	734.8	1.06	0.0320
Production and processing of metals	616	630.3	1.03	0.92-1.17	580	587.3	1.04	0.92-1.17	615	613.6	1.07	0.94-1.20	934	860.9	1.08	0.97-1.22	1913	2011.7	1.00	0.8468
Galvanization	218	197.5	1.32	1.10-1.58	268	303.1	0.95	0.79-1.14	196	205.6	1.10	0.88-1.36	78	78.0	1.13	0.88-1.45	1141	1257.7	1.04	0.0505
Surface treatment of metals and plastic	1386	1402.5	1.03	0.94-1.12	1825	1751.0	1.05	0.97-1.14	554	574.0	0.99	0.89-1.10	1136	994.5	1.14	1.04-1.26	2424	2527.8	1.00	0.8143
Mining industry	43	31.3	1.39	1.03-1.89	66	80.4	0.85	0.66-1.09	69	62.6	1.13	0.89-1.44	139	152.8	0.94	0.78-1.12	2507	2603.2	1.02	0.5578
Cement and lime	68	83.2	0.88	0.69-1.13	223	240.6	0.93	0.80-1.09	295	339.9	0.89	0.78-1.01	213	201.5	1.06	0.91-1.24	2858	2961.4	0.97	0.0856
Glass and mineral fibers	296	276.1	1.23	1.05-1.42	311	309.1	1.10	0.96-1.27	201	223.6	1.02	0.86-1.20	358	286.8	1.36	1.19-1.56	1214	1242.8	1.03	0.0680
Ceramic	499	483.2	1.06	0.96-1.17	353	323.1	1.09	0.97-1.22	299	267.3	1.16	1.02-1.31	832	827.6	1.02	0.93-1.11	4325	4550.9	1.02	0.0522
Organic chemical industry	453	459.1	1.03	0.91-1.16	534	557.8	0.99	0.88-1.11	575	499.2	1.19	1.06-1.34	1915	1934.9	1.04	0.94-1.15	2267	2348.7	1.00	0.8660
Inorganic chemical industry	203	193.1	1.07	0.91-1.25	1098	1053.9	1.05	0.95-1.16	220	196.9	1.15	0.99-1.34	233	223.8	1.07	0.92-1.24	1825	1886.4	1.02	0.2962
Fertilizers	160	127.1	1.33	1.09-1.64	21	18.2	1.19	0.77-1.86	225	217.4	1.11	0.93-1.33	144	123.5	1.22	0.99-1.50	849	893.5	1.07	0.0124
Biocides	29	32.8	0.82	0.54-1.24	120	131.3	0.89	0.65-1.20	34	32.6	0.98	0.67-1.45	13	15.4	0.78	0.42-1.43	289	293.8	0.96	0.3620
Pharmaceutical products	258	272.5	1.04	0.88-1.22	450	405.9	1.04	1.00-1.36	296	309.2	1.05	0.89-1.24	216	194.9	1.20	1.01-1.44	947	972.3	1.01	0.6009
Explosives and pyrotechnics	90	111.1	0.85	0.68-1.07	114	109.0	1.04	0.84-1.27	508	442.9	1.11	0.96-1.29	218	230.2	0.92	0.77-1.08	2345	2368.1	0.99	0.7260
Hazardous waste	152	133.4	1.30	1.07-1.58	187	192.5	1.12	0.93-1.35	420	433.5	1.07	0.92-1.24	641	583.4	1.21	1.05-1.39	910	955.6	1.03	0.1084
Non-hazardous waste	104	113.7	0.86	0.69-1.08	347	329.5	1.02	0.88-1.17	126	111.7	1.13	0.94-1.37	492	488.4	0.97	0.84-1.11	2179	2288.7	1.00	0.8252
Disposal or recycling of animal waste	78	62.7	1.24	0.98-1.56	163	176.5	0.92	0.77-1.09	256	226.2	1.12	0.97-1.29	791	703.7	1.05	0.93-1.18	1691	1740.8	1.02	0.3938
Urban waste-water treatment plants	166	156.6	1.11	0.94-1.31	524	484.5	1.13	1.10-1.26	414	404.2	1.09	0.97-1.23	3688	3677.1	1.06	0.97-1.16	1951	2066.3	1.03	0.0312
Paper and wood production	511	505.0	1.01	0.90-1.13	260	225.6	1.18	1.03-1.36	755	658.0	1.14	1.03-1.27	334	315.5	1.10	0.97-1.25	2146	2297.9	1.01	0.3969
Pre-treatment or dyeing of textiles	92	90.9	1.10	0.86-1.41	27	28.4	0.97	0.65-1.46	9	7.5	1.14	0.58-2.23	20	34.5	0.63	0.40-1.00	474	499.3	1.02	0.4489
Tanning of hides and skins	21	19.2	2.13	0.90-5.07	4	3.3	1.97	0.43-9.08	4	1.2	5.39	1.30-22.33	1	1.2	1.79	0.21-15.37	62	67.2	1.24	0.0311
Food and beverage sector	845	824.0	1.06	0.98-1.15	1884	1850.0	1.02	0.95-1.10	1193	1103.4	1.11	1.03-1.20	1449	1310.6	1.13	1.05-1.22	4026	4242.7	1.01	0.4075
Aquiculture	2	2.7	1.46	0.30-7.05	0	0.7	0	0-inf	0	0	-	--	4	1.7	4.88	1.52-15.67	77	96.3	1.08	0.6632
Surface treatment using organic solvents	353	425.1	0.86	0.75-0.99	403	390.3	1.07	0.93-1.22	618	620.3	1.03	0.91-1.16	813	719.7	1.15	1.02-1.29	1554	1681.8	0.97	0.0404
Production of carbon or electro-graphite	0	0	-	--	1	0.3	4.40	0.58-33.40	1	0.9	1.69	0.22-13.00	156	128.6	1.84	1.07-3.16	118	142.6	1.68	0.0085
Ship building	305	304.5	1.01	0.81-1.26	144	141.0	0.99	0.74-1.32	27	31.9	0.86	0.56-1.32	14	18.8	0.75	0.43-1.29	468	491.8	1.01	0.7823

[a]Reference group.
[b]Observed deaths.
[c]Expected deaths.
[d]RRs adjusted for population size, percentage of illiteracy, farmers and unemployed persons, average persons per household, and mean income
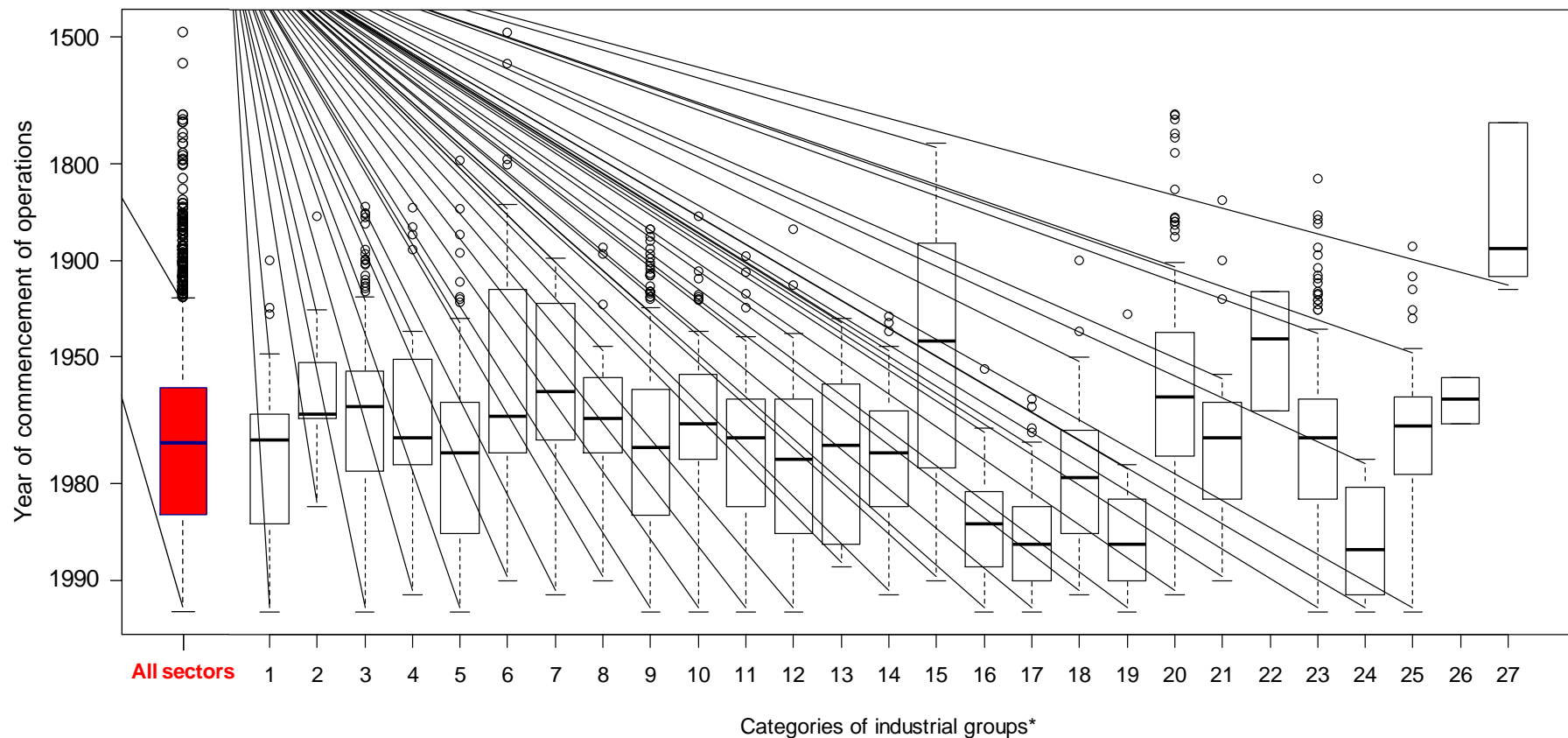[e]95% confidence interval.

Supplementary Data, Figure S1.

Legend:
- Combustion installations
- Refineries and coke ovens
- Production and processing of metals
- Galvanization
- Surface treatment of metals and plastic
- Mining industry
- Cement and lime
- Glass and mineral fibers
- Ceramic
- Organic chemical industry
- Inorganic chemical industry
- Fertilizers
- Biocides
- Pharmaceutical products
- Explosives and pyrotechnics
- Hazardous waste
- Non-hazardous waste
- Disposal or recycling of animal waste
- Urban waste-water treatment plants
- Paper and wood production
- Pre-treatment or dyeing of textiles
- Tanning of hides and skins
- Food and beverage sector
- Aquiculture
- Surface treatment using organic solvents
- Production of carbon or electro-graphite
- Ship building

0   300 Km

Supplementary Data, Figure S2.

1970 pre-1993 installations

*1=Combustion installations. 2=Refineries and coke ovens. 3=Production and processing of metals. 4=Galvanization. 5=Surface treatment of metals and plastic. 6=Mining industry. 7=Cement and lime. 8=Glass and mineral fibers. 9=Ceramic. 10=Organic chemical industry. 11=Inorganic chemical industry. 12=Fertilizers. 13=Biocides. 14=Pharmaceutical products. 15=Explosives and pyrotechnics. 16=Hazardous waste. 17=Non-hazardous waste. 18=Disposal or recycling of animal waste. 19=Urban waste-water treatment plants. 20=Paper and wood production. 21=Pre-treatment or dyeing of textiles. 22=Tanning of hides and skins. 23=Food and beverage sector. 24=Aquiculture. 25=Surface treatment using organic solvents. 26=Production of carbon or electro-graphite. 27=Ship building.