

Supplementary material

Agricultural crop density in the municipalities of France and the incidence of childhood leukemia: an ecological study

Summary of tables and figures

Table S 1 Minimum detectable SIR, based on the expected number of cases in the municipalities of the highest quartile of crop density, ensuring a power of 80%, for a one-sided test at the 5 % level ...	2
Table S 2 Percentiles of the distribution of the UAA/total area ratio in the municipalities of France for specific types of crop, over 3 periods (based on the 1988, 2000 and 2010 agricultural censuses).....	3
Figure S 3 Density of agriculture (all crops) in the municipalities of France – Agricultural census 2000	4
Figure S 4 Density of the specific crops studied in the municipalities of France – Agricultural census 2000.....	5
Table S 5 Spearman coefficient of correlation between the specific crop densities	6
Table S 6 Spearman coefficient of correlation between the crop densities at the different agricultural censuses	7
Table S 7 Association between the incidence of childhood leukemia and non-permanent crop density ¹ in the French municipalities, 1990- 2014.....	8
Table S 8 Association between the incidence of childhood leukemia and specific crop density ¹ in the French municipalities, 1990-2014	11
Table S 9 Distribution of the deprivation index and UV radiation status in the French pediatric population by category of crop density	14
Table S 10 Association between viticulture density and the incidence of AL stratified on the level of residential exposure to UV radiation (>105.5 J/cm ² vs. ≤ 105.5 J/cm ²)	15
Table S 11 Association between the incidence of childhood leukemia and viticulture density in semi-quartiles in the French municipalities, 1990-2014.....	16
Table S 12 The ten most common crops grown in France and the USA in 2000 ¹	17

Table S 1 Minimum detectable SIR, based on the expected number of cases in the municipalities of the highest quartile of crop density, ensuring a power of 80%, for a one-sided test at the 5 % level

Type of crop	AL (11,487 cases)		ALL (9,488 cases)		AML (1,803 cases)	
	E	min SIR	E	min SIR	E	min SIR
Total agricultural area	2,000	1.06	1,700	1.06	320	1.14
Cereals	1,500	1.07	1,200	1.07	220	1.17
Oilseeds	400	1.13	320	1.14	60	1.35
Viticulture	200	1.18	160	1.21	30	1.51
Industrial crops						
Legumes: beans, peas, protein crops	100	1.26	80	1.30	15	1.75
Arboriculture	75	1.31	60	1.35	10	1.94
Fresh vegetables, strawberries, melons						
Potatoes	60	1.35	50	1.38	10	1.94

E: approximate number of expected cases in the municipalities of the highest quartile of crop density

AL: all acute leukemia

ALL: acute lymphoblastic leukemia

AML: acute myeloid leukemia

Table S 2 Percentiles of the distribution of the UAA/total area ratio in the municipalities of France for specific types of crop, over 3 periods (based on the 1988, 2000 and 2010 agricultural censuses)

Crop ¹	P5	P25	P50	P75	P95	P99
Total UAA	0	2.8	23.8	52.6	87.6	120.2
Straw cereals	0	0	3.6	13.5	36.9	57.9
Corn	0	0	0.1	3.2	14.4	25.2
Viticulture	0	0	0	0	10.2	35.2
Arboriculture	0	0	0	0.1	2.3	10.8
Oilseeds	0	0	0	2.1	11.1	21.5
Potatoes	0	0	0	0	1.8	8.8
Fresh vegetables, strawberries, melons	0	0	0	0.3	3.0	9.3
Legumes: beans, peas, protein crops	0	0	0	0.3	3.7	9.2
Industrial crops	0	0	0	0.1	6.6	15.9

¹ Distribution weighted by the pediatric population in the municipalities

UAA: utilized agricultural area, in hectares

P5, P25, P50, P75, P95, P99: 5th, 25th, 50th, 75th, 95th and 99th percentiles of the UAA/total area ratio, respectively.

Some values of the 99th percentile are greater than 100 because the UAA is reported for the municipality of the farm. Some land may be in an adjacent municipality and the total UAA reported may be greater than the area of the municipality of the farm.

Figure S 3 Density of agriculture (all crops) in the municipalities of France – Agricultural census 2000

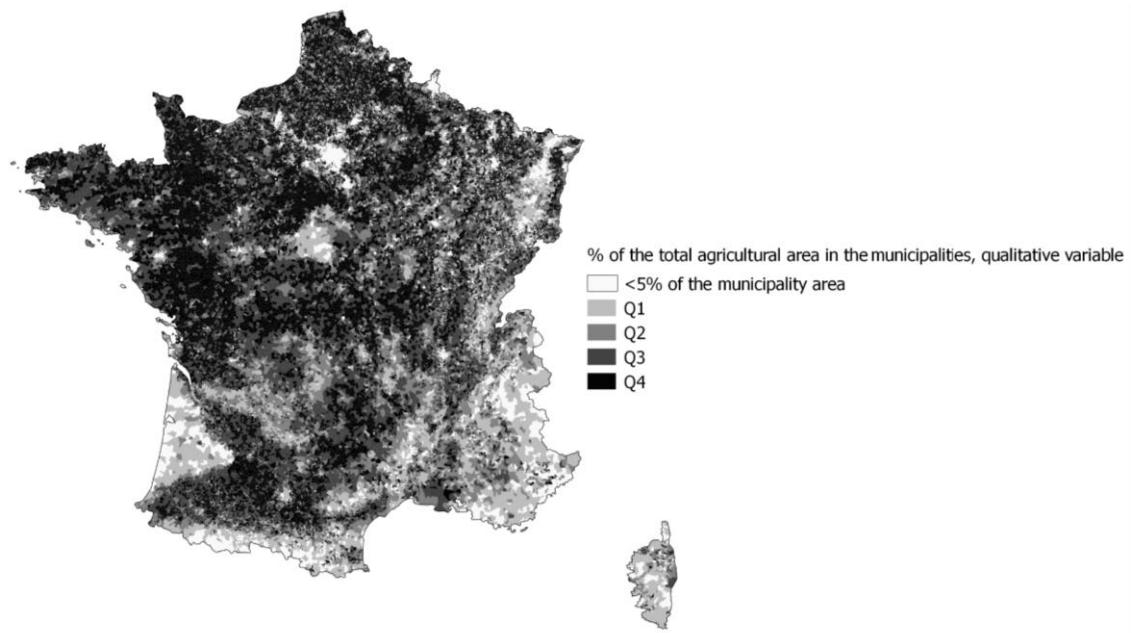


Figure S 4 Density of the specific crops studied in the municipalities of France – Agricultural census 2000

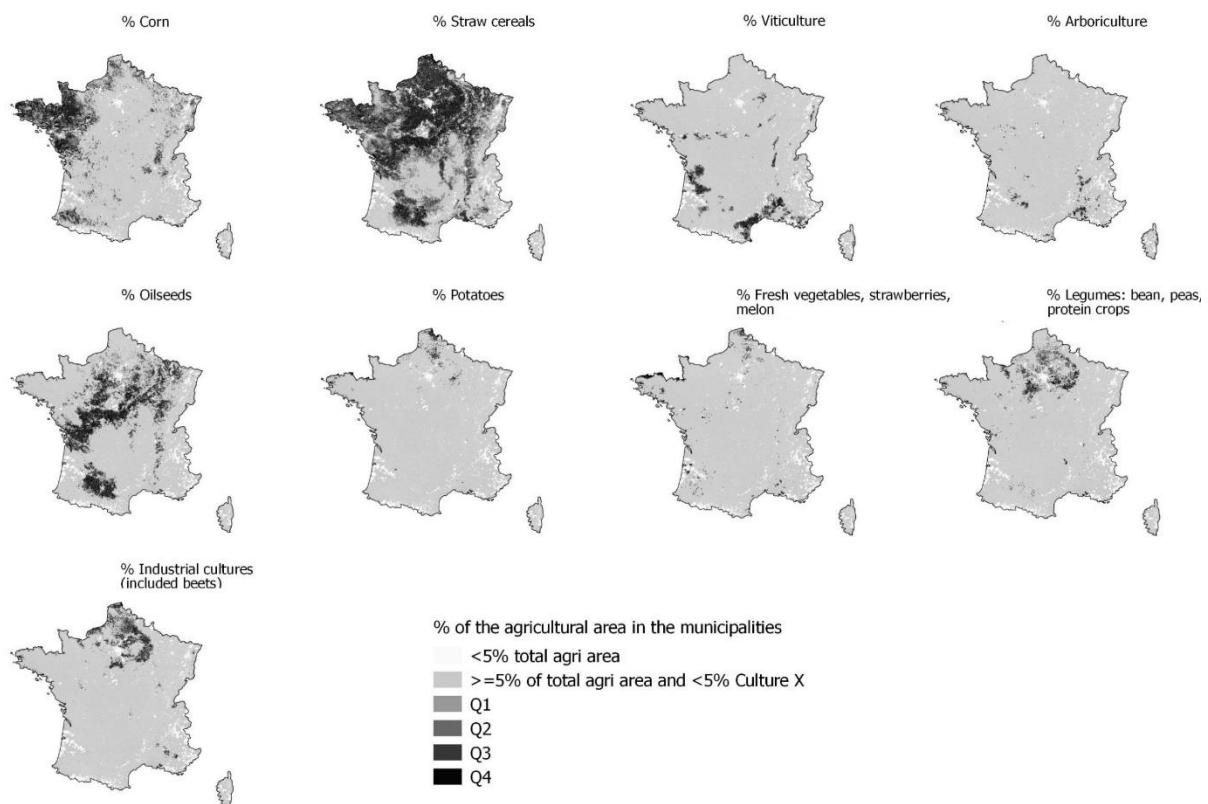


Table S 5 Spearman correlation coefficient between the specific crop densities

Spearman coefficient	Corn	Straw cereals	Vineyards	Arboriculture	Oilseeds	Potatoes	Fresh vegetables	Legumes	Industrial crops
Corn	1.00	0.23 <.0001	-0.06 <.0001	0.02 <.0001	-0.06 <.0001	0.10 <.0001	0.11 <.0001	-0.04 <.0001	-0.01 0.2
Straw cereals		1.00 <.0001	-0.11 <.0001	-0.04 <.0001	0.64	0.52 <.0001	0.33 <.0001	0.66	0.66
Vineyards			1.00 <.0001	0.22 <.0001	-0.09 <.0001	0.05 <.0001	0.15 <.0001	-0.004 0.66	0.03 0.0001
Arboriculture				1.00 <.0001	0.01 0.15	0.10 <.0001	0.20 0.2607	0.05 <.0001	0.02 0.0065
Oilseeds					1.00 1.00	0.08 <.0001	0.01 0.60	0.26 0.47	0.06 0.66
Potatoes						1.00 1.00	0.60 <.0001	0.47 0.26	0.66 0.44
Fresh vegetables							1.00 1.00	0.26 0.57	<.0001 0.57
Legumes								1.00 1.00	<.0001 0.0001
Industrial crops									1.00

In grey: p-value of the Spearman coefficient; in bold: high correlation cited in the publication

Table S 6 Spearman correlation coefficient between the crop densities at the different agricultural censuses (1988,2000,2010)

	Straw cereals		Corn		Viticulture		Arboriculture		Potatoes		Fresh vegetables		Legumes		Industrial crops	
	1988	2000	1988	2000	1988	2000	1988	2000	1988	2000	1988	2000	1988	2000	1988	2000
1988	1	-	1	-	1	-	1	-	1	-	1	-	1	-	1	-
2000	0.94	1	0.87	1	0.88	1	0.64	1	0.55	1	0.68	1	0.71	1	0.81	1
2010	0.90	0.95	0.70	0.71	0.77	0.83	0.56	0.67	0.44	0.60	0.57	0.70	0.65	0.69	0.71	0.78

All p-values were <0.001

Table S 7 Association between the incidence of childhood leukemia and non-permanent crop density¹ in the French municipalities, 1990- 2014

	Average density ²	Number of units ³	PY/year	Acute leukemia					Acute lymphoblastic leukemia					Acute myeloid leukemia					
				O	E	SIR	CI	P ⁴	O	E	SIR	CI	P ⁴	O	E	SIR	CI	P ⁴	
Corn																			
% UAA[0-5[0.0	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03		2,708	2,752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15		
% UAA>=5 & % corn <5	1.1	69,507	6,009,743	6,100	6,034.6	1.01	0.99-1.04		5,060	4,980.7	1.02	0.99-1.04		934	952.8	0.98	0.92-1.05		
[5-7.1[6.0	7,857	524,760	522	527.2	0.99	0.91-1.08		438	436.7	1.00	0.91-1.10		76	81.4	0.93	0.75-1.17		
[7.1-10.2[8.5	7,553	524,739	580	528.0	1.10	1.01-1.19		480	437.4	1.10	1.00-1.20		85	81.5	1.04	0.84-1.29		
[10.2-14.9[12.3	7,345	524,716	462	529.0	0.87	0.80-0.96		388	438.5	0.88	0.80-0.98		67	81.1	0.83	0.65-1.05		
>=14.9	22.4	8,193	524,735	508	532.0	0.95	0.88-1.04		414	442.4	0.94	0.85-1.03		85	80.0	1.06	0.86-1.31		
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0				
Test of heterogeneity								0.01						0.02			0.36		
Test of departure from log-linearity								0.01						0.02			0.26		
SIRR for Δx=10%															0.98	0.9-1.08	0.65		
Straw cereals																			
% UAA[0-5[0.1	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03		2,708	2,752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15		
% UAA>=5 & % cer <5	1.9	31,433	2,973,517	3,007	2,993.7	1.00	0.97-1.04		2,487	2,472.0	1.01	0.97-1.05		451	470.8	0.96	0.87-1.05		
[5-9.1[6.9	12,870	1,283,521	1,264	1,287.8	0.98	0.93-1.04		1,035	1,063.4	0.97	0.92-1.03		209	202.6	1.03	0.90-1.18		
[9.1-14.9[11.8	13,552	1,284,078	1,317	1,289.2	1.02	0.97-1.08		1,130	1,065.1	1.06	1.00-1.12		172	202.2	0.85	0.73-0.99		
[14.9-24.8[19.3	16,071	1,283,726	1,313	1,290.2	1.02	0.96-1.07		1,080	1,067.2	1.01	0.95-1.07		216	201.0	1.07	0.94-1.23		
>=24.8	39.2	26,529	1,283,851	1,271	1,289.9	0.99	0.93-1.04		1,048	1,067.8	0.98	0.92-1.04		199	200.1	0.99	0.87-1.14		
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0				
Test of heterogeneity								0.86						0.31			0.13		
Test of departure from log-linearity								0.75						0.20			0.07		
SIRR for Δx=10%								1.00	0.98-1.01	0.47				1.00	0.98-1.02	0.48	1.00	0.96-1.03	0.43
Oilseeds																			
% UAA[0-5[0.0	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03		2,708	2,752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15		
% UAA>=5 & % olea <5	1.0	71,295	6,540,248	6,540	6,575.7	0.99	0.97-1.02		5,394	5,431.7	0.99	0.97-1.02		1,026	1,032.4	0.99	0.93-1.06		
[5-6.6[5.8	5,486	391,662	406	392.6	1.03	0.94-1.14		360	324.6	1.11	1.00-1.23		38	61.4	0.62	0.45-0.85		
[6.6-9.1[7.8	6,308	392,566	405	394.5	1.03	0.93-1.13		344	326.4	1.05	0.95-1.17		56	61.3	0.91	0.70-1.19		
[9.1-13.4[11.0	7,338	392,143	423	393.4	1.08	0.98-1.18		355	325.7	1.09	0.98-1.21		60	60.9	0.99	0.77-1.27		
>=13.4	20.1	10,028	392,074	398	394.6	1.01	0.91-1.11		327	327.0	1.00	0.90-1.11		67	60.7	1.10	0.87-1.40		
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0				
Test of heterogeneity								0.66						0.15			0.02		
Test of departure from log-linearity								0.75						0.21			0.01		

SIRR for $\Delta x=10\%^5$				1.03 0.98-1.07 0.13					1.04 0.99-1.09 0.07								
Potatoes																	
% UAA[0-5[0.0	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03		2,708	2,752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15
% UAA>=5 & % pot. <5	0.2	97,509	7,871,148	7,929	7,912.8	1.00	0.98-1.02		6,588	6,538.7	1.01	0.98-1.03		1,201	1,239.6	0.97	0.92-1.03
[5-6.4[5.6	685	58,907	67	58.9	1.14	0.90-1.44		57	48.7	1.17	0.90-1.52		9	9.2	0.98	0.51-1.88
[6.4-8.5[7.4	669	59,826	69	60.1	1.15	0.91-1.45		53	49.6	1.07	0.82-1.40		15	9.4	1.60	0.96-2.65
[8.5-12.1[10.3	726	59,549	55	59.7	0.92	0.71-1.20		40	49.4	0.81	0.59-1.10		14	9.2	1.52	0.90-2.57
>=12.1	18.0	866	59,262	52	59.4	0.88	0.67-1.15		42	49.1	0.86	0.63-1.16		8	9.3	0.86	0.43-1.72
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0		
Test of heterogeneity								0.57						0.34			0.15
Test of departure from log-linearity																	0.12
SIRR for $\Delta x=10\%^5$								0.98	0.87-1.1	0.65				0.94	0.83-1.07	0.82	
Fresh vegetables, strawberries, melon																	
% UAA[0-5[0.1	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03		2,708	2,752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15
% UAA>=5 & % veg. <5	0.4	97,799	7,804,527	7,871	7,846.7	1.00	0.98-1.03		6,540	6,484.7	1.01	0.98-1.03		1,195	1,228.7	0.97	0.92-1.03
[5-6.1[5.5	598	75,555	77	76.0	1.01	0.81-1.27		61	62.8	0.97	0.76-1.25		13	11.9	1.09	0.63-1.88
[6.1-7.8[6.9	665	76,543	67	76.2	0.88	0.69-1.12		56	62.9	0.89	0.69-1.16		11	12.1	0.91	0.50-1.64
[7.8-11.5[9.4	692	73,514	75	73.4	1.02	0.81-1.28		57	60.6	0.94	0.73-1.22		14	11.6	1.20	0.71-2.03
>=11.5	19.9	701	78,554	82	78.4	1.05	0.84-1.30		66	64.7	1.02	0.8-1.30		14	12.4	1.13	0.67-1.91
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0		
Test of heterogeneity								0.90						0.81			0.63
Test of departure from log-linearity																	0.53
SIRR for $\Delta x=10\%^5$								1.01	0.92-1.11	0.43				0.99	0.88-1.1	0.60	
Legumes: beans, peas, protein crops																	
% UAA[0-5[0.0	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03		2,708	2,752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15
% UAA>=5 & % leg <5	0.5	92,124	7,727,146	7,760	7,769.7	1.00	0.98-1.02		6,448	6,420.8	1.00	0.98-1.03		1,176	1,216.7	0.97	0.91-1.02
[5-5.9[5.4	1,715	95,314	113	95.3	1.19	0.99-1.43		94	78.7	1.19	0.98-1.46		18	15.0	1.20	0.75-1.90
[5.9-7.3[6.6	1,914	95,476	95	95.5	0.99	0.81-1.22		76	78.9	0.96	0.77-1.21		15	15.1	0.99	0.6-1.65
[7.3-9.8[8.4	2,157	95,907	97	95.9	1.01	0.83-1.23		74	79.2	0.93	0.74-1.17		20	15.1	1.33	0.86-2.06
>=9.8	13.8	2,545	94,850	107	94.3	1.13	0.94-1.37		88	77.9	1.13	0.92-1.39		18	14.9	1.21	0.76-1.92
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0		
Test of heterogeneity								0.43						0.38			0.34
Test of departure from log-linearity																	0.36
SIRR for $\Delta x=10\%^5$								1.09	0.98-1.22	0.06				1.07	0.95-1.21	0.13	

Industrial crops																			
% UAA[0-5[0.0	6,081	3,241,048	3,315	3,336.2	0.99	0.96-1.03	2,708	2,752.4	0.98	0.95-1.02	556	526.3	1.06	0.97-1.15				
% UAA>=5 & % ind. Cult. <5	0.4	88,760	7,389,609	7,454	7,429.6	1.00	0.98-1.03	6,194	6,139.2	1.01	0.98-1.03	1,128	1,164.1	0.97	0.91-1.03				
[5-7[5.9	2,426	180,230	187	180.7	1.03	0.90-1.19	152	149.4	1.02	0.87-1.19	32	28.2	1.13	0.8-1.60				
[7-9.4[8.1	2,457	177,254	170	178.2	0.95	0.82-1.11	138	147.5	0.94	0.79-1.11	30	27.7	1.08	0.76-1.55				
[9.4-13.6[11.1	3,012	181,874	176	182.2	0.97	0.83-1.12	140	150.5	0.93	0.79-1.10	30	28.6	1.05	0.73-1.50				
>=13.6	19.5	3,800	179,726	185	180.0	1.03	0.89-1.19	156	148.9	1.05	0.90-1.23	27	28.1	0.96	0.66-1.40				
Total		106,536	11,349,740	11,487	11,487.0			9,488	9,488.0			1,803	1,803.0						
Test of heterogeneity							0.95					0.71							0.61
Test of departure from log-linearity								0.88				0.56							0.47
SIRR for $\Delta x=10\%$ ⁵						1.00	0.94-1.06	0.49			1.00	0.93-1.07	0.48			1.01	0.87-1.18	0.44	

O: Observed number of cases; E: expected number of cases under the hypothesis of a homogeneous incidence rate by period, for each age x sex category throughout mainland France; SIR:

Standardized Incidence Ratio = O/E; CI: 95% Confidence Interval; UAA: total utilized agricultural area

¹ The crop density in a municipality is defined as the ratio of the area used for the crop over the total area of this municipality (based on national agricultural census data);

² Average crop density weighted by the pediatric population at risk living in the municipalities of the category;

³ Number of statistical units, defined as "municipalities x period" in each category;

⁴ p-value of the tests (chi-square test of heterogeneity between categories of agricultural density, departure from log-linearity test, one-sided test of the regression coefficient in the semi-quantitative model (H_0 : slope = 0 vs H_1 : slope >0);

⁵ SIRR (for $\Delta x=10\%$) = Relative Standardized Incidence Ratio with 95% confidence limits: Multiplicative variation of the SIR for a 10% increase in the crop density derived from of a log-linear Poisson regression model adjusted to the observations (the outcome is the observed number of cases by municipality x period; the offset is the expected number of cases; and the independent covariate is the crop density).

Table S 8 Association between the incidence of childhood leukemia and specific crop density¹ in the French municipalities, 1990-2014

	Average density ²	Number of units ³	PY/year	Acute leukemia					Acute lymphoblastic leukemia					Acute myeloid leukemia						
				O	E	SIR	CI	P ⁴	O	E	SIR	CI	P ⁴	O	E	SIR	CI	P ⁴		
Durum wheat																				
% UAA[0-5[0.0	6081	3241048.1	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15			
% UAA >=5 et % wheat <5	0.2	96484	7739153.0	7779	7777.7	1.00	0.98-1.02		6450	6426.5	1.00	0.98-1.03		1186	1219.4	0.97	0.92-1.03			
[5-6.6[5.8	812	92405.7	104	93.1	1.12	0.92-1.35		85	77.1	1.10	0.89-1.36		19	14.3	1.33	0.85-2.08			
[6.6-9.2[7.8	869	93112.0	87	93.8	0.93	0.75-1.14		78	77.6	1.00	0.80-1.25		9	14.5	0.62	0.32-1.19			
[9.2-13.5[11.2	812	92007.3	108	92.7	1.16	0.96-1.41		89	76.7	1.16	0.94-1.43		18	14.4	1.25	0.79-1.99			
>=13.5	22.9	1478	92014.1	94	93.4	1.01	0.82-1.23		78	77.6	1.01	0.81-1.26		15	14.2	1.06	0.64-1.75			
Total		106,536	11,349,740	11,487	11,487.0			0.51	9,488	9,488.0				1,803	1,803.0			0.20		
Test of heterogeneity																				
Test of departure from log-linearity								0.45												
SIRR for Δx=10% ⁵						1.03	0.96-1.11	0.23						1.04	0.96-1.12	0.20		0.13		
Common wheat																				
% UAA [0-5[0.1	6081	3241048.1	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15			
% UAA>=5 et % wheat <5	1.4	44998	4115429.5	4190	4137.9	1.01	0.98-1.04		3470	3417.2	1.02	0.98-1.05		637	650.4	0.98	0.91-1.06			
[5-8.2[6.5	9922	998306.1	960	1003.2	0.96	0.90-1.02		801	828.8	0.97	0.90-1.04		146	157.4	0.93	0.79-1.09			
[8.2-12.8[10.4	11305	998426.5	1033	1002.5	1.03	0.97-1.10		875	828.6	1.06	0.99-1.13		146	156.9	0.93	0.79-1.09			
[12.8-21.1[16.5	14075	998250.9	973	1004.3	0.97	0.91-1.03		793	830.9	0.95	0.89-1.02		164	156.2	1.05	0.90-1.22			
>=21.1	32.4	20155	998279.2	1016	1002.9	1.01	0.95-1.08		841	830.0	1.01	0.95-1.08		154	155.8	0.99	0.84-1.16			
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0			0.56		
Test of heterogeneity								0.45												
Test of departure from log-linearity								0.31							1.00	0.98-1.02	0.46		0.43	
SIRR for Δx=10% ⁵						1.00	0.98-1.02	0.50										0.99	0.94-1.04	0.63
Barley																				
% UAA [0-5[0.0	6081	3241048	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15			
% UAA>=5 et % barley <5	1.3	73216	6842637	6874	6885.6	1.00	0.97-1.02		5690	5689.3	1.00	0.97-1.03		1057	1078.9	0.98	0.92-1.04			
[5-6.1[5.5	4975	313810	330	313.4	1.05	0.95-1.17		283	258.8	1.09	0.97-1.23		39	49.4	0.79	0.58-1.08			
[6.1-7.8[6.9	5682	319232	327	319.5	1.02	0.92-1.14		280	264.2	1.06	0.94-1.19		46	49.9	0.92	0.69-1.23			
[7.8-11[9.1	7036	316585	320	316.1	1.01	0.91-1.13		259	261.5	0.99	0.88-1.12		58	49.4	1.17	0.91-1.52			
>=11	16.4	9546	316428	321	316.2	1.02	0.91-1.13		268	261.7	1.02	0.91-1.15		47	49.2	0.96	0.72-1.27			
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0			0.28		
Test of heterogeneity								0.93												
Test of departure from log-linearity								0.94								0.58		0.20		

SIRR for $\Delta x=10\%$ ⁵				1.02 0.96-1.08 0.23					1.04 0.97-1.10 0.14					0.96 0.82-1.12 0.70				
Rapeseed																		
% UAA[0-5[0.0	6081	3241048.1	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15	
% UAA>=5 and % rape <5	0.8	82517	7216104.5	7235	7250.4	1.00	0.98-1.02		5983	5989.2	1.00	0.97-1.02		1123	1138.6	0.99	0.93-1.05	
[5-6.3[5.6	3745	224328.9	251	225.4	1.11	0.98-1.26		223	186.5	1.20	1.05-1.36		23	35.0	0.66	0.44-0.99	
[6.3-8.2[7.2	4135	221947.9	223	223.5	1.00	0.87-1.14		191	185.3	1.03	0.89-1.19		29	34.3	0.84	0.59-1.21	
[8.2-11.4[9.6	4296	223159.2	236	225.4	1.05	0.92-1.19		197	186.8	1.05	0.92-1.21		34	34.6	0.98	0.70-1.38	
>=11.4	16.9	5762	223151.7	227	226.1	1.00	0.88-1.14		186	187.8	0.99	0.86-1.14		38	34.2	1.11	0.81-1.53	
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0			
Test of heterogeneity							0.63							0.15				0.16
Test of departure from log-linearity							0.59							0.14				0.11
SIRR for $\Delta x=10\%$ ⁵							1.03	0.96-1.10	0.21					1.04	0.97-1.12	0.13		0.96 0.81-1.14 0.70
Sunflower																		
% UAA [0-5[0.0	6081	3241048.1	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15	
% UAA>=5 and % sunflower <5	0.4	90306	7602139.9	7659	7644.8	1.00	0.98-1.02		6347	6317.4	1.00	0.98-1.03		1173	1197.4	0.98	0.93-1.04	
[5-6.2[5.6	1867	126643.2	127	126.5	1.00	0.84-1.19		112	104.4	1.07	0.89-1.29		13	20.0	0.65	0.38-1.12	
[6.2-8.2[7.1	2184	126601.5	122	126.5	0.96	0.81-1.15		102	104.5	0.98	0.80-1.18		19	19.8	0.96	0.61-1.50	
[8.2-12.1[10.0	2654	126736.6	138	126.3	1.09	0.92-1.29		115	104.4	1.10	0.92-1.32		20	19.8	1.01	0.65-1.56	
>=12.1	18.0	3444	126571.00	126	126.7	0.99	0.84-1.18		104	104.8	0.99	0.82-1.20		22	19.8	1.11	0.73-1.69	
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0			
Test of heterogeneity							0.93							0.78				0.39
Test of departure from log-linearity							0.87							0.71				0.27
SIRR for $\Delta x=10\%$ ⁵							1.01	0.94-1.10	0.37					1.03	0.94-1.12	0.28		0.99 0.80-1.21 0.55
Industrial beets																		
% UAA[0-5[0.0	6081	3241048.1	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02		556	526.3	1.06	0.97-1.15	
% UAA >=5 et % beets <5	0.3	90878	7523936	7613	7564.9	1.01	0.98-1.03		6323	6251.2	1.01	0.99-1.04		1155	1185.0	0.97	0.92-1.03	
[5-6.8[5.9	2079	146073	150	146.2	1.03	0.87-1.20		122	120.9	1.01	0.84-1.20		25	22.8	1.10	0.74-1.62	
[6.8-8.9[7.8	1948	146180	131	146.6	0.89	0.75-1.06		106	121.2	0.87	0.72-1.06		21	22.9	0.92	0.60-1.40	
[8.9-12.8[10.5	2500	146328	138	146.4	0.94	0.80-1.11		113	121.0	0.93	0.78-1.12		22	23.0	0.96	0.63-1.45	
>=12.8	18.3	3050	146175	140	146.6	0.95	0.81-1.13		116	121.2	0.96	0.80-1.15		24	23.0	1.05	0.70-1.56	
Total		106,536	11,349,740	11,487	11,487.0				9,488	9,488.0				1,803	1,803.0			
Test of heterogeneity							0.69							0.51				0.72
Test of departure from log-linearity							0.76							0.55				0.58
SIRR for $\Delta x=10\%$ ⁵							0.96	0.89-1.03	0.86					0.96	0.88-1.04	0.87		1.00 0.83-1.20 0.49

O: Observed number of cases; E: expected number of cases under the hypothesis of a homogeneous incidence rate by period, for each age x sex category throughout mainland France; SIR: Standardized Incidence Ratio = O/E; CI: 95% Confidence Interval; UAA: total utilized agricultural area

¹ The crop density in a municipality is defined as the ratio of the area used for the crop over the total area of this municipality (based on national agricultural census data);

² Average crop density weighted by the pediatric population at risk living in the municipalities of the category;

³ Number of statistical units, defined as "municipalities x period" in each category;

⁴ p-value of the tests (chi-square test of heterogeneity between categories of agricultural density, departure from log-linearity test, one-sided test of the regression coefficient in the semi-quantitative model (H_0 : slope = 0 vs H_1 : slope >0);

⁵ SIRR (for $\Delta x = 10\%$) = Relative Standardized Incidence Ratio with 95% confidence limits: Multiplicative variation of the SIR for a 10% increase in the crop density derived from a log-linear Poisson regression model adjusted to the observations (the outcome is the observed number of cases by municipality x period; the offset is the expected number of cases; and the independent covariate is the crop density).

Table S 9 Distribution of the deprivation index and UV radiation status in the French pediatric population by category of crop density

	Most deprived municipalities		Municipalities with UV radiation >105.5 J/cm ²	
	PA/year	%	PA/year	%
Straw cereals				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % cer <5	517487.0	17.4	1455493.0	48.9
[5-9.1[300585.0	23.4	444856.1	34.7
[9.1-14.9[320896.1	25.0	333373.5	26.0
[14.9-24.8[353980.5	27.6	256969.6	20.0
>=24.8	353297.1	27.5	136365.5	10.6
Corn				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % corn <5	1272950.2	21.2	2198577.8	36.6
[5-7.1[149315.4	28.5	114766.7	21.9
[7.1-10.2[150970.9	28.8	98996.1	18.9
[10.2-14.9[146798.0	28.0	99715.4	19.0
>=14.9	126211.4	24.1	115001.6	21.9
Viticulture				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % vit. <5	1707905.4	23.3	2041305.2	27.8
[5-9.9[39209.1	20.2	137764.4	71.0
[9.9-15.9[33470.6	17.3	145684.4	75.2
[15.9-25[25650.6	13.3	145634.6	75.4
>=25	40010.0	20.6	156669.0	80.7
Arboriculture				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % arb. <5	1777372.9	22.7	2412025.7	30.8
[5-6.4[12077.6	17.0	48804.5	68.6
[6.4-9.3[15411.2	22.2	48382.2	69.8
[9.3-13.2[17066.0	24.3	56935.0	81.2
>=13.2	24318.2	34.6	60910.4	86.8
Oilseeds				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % olea <5	1514913.8	23.2	2192019.7	33.5
[5-6.6[77987.9	19.9	101637.8	26.0
[6.6-9.1[92724.8	23.6	103636.5	26.4
[9.1-13.4[79183.0	20.2	109703.1	28.0
>=13.4	81436.4	20.8	120060.5	30.6
Potatoes				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % pot. <5	1765442.5	22.4	2622374.2	33.3
[5-6.4[23759.9	40.3	1614.6	2.7
[6.4-8.5[19055.7	31.9	1328.4	2.2
[8.5-12.1[19028.5	32.0	616.0	1.0
>=12.1	18959.3	32.0	1124.5	1.9
Fresh vegetables, strawberries, melons				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % veg. <5	1778602.9	22.8	2534296.1	32.5
[5-6.1[21667.3	28.7	25244.5	33.4
[6.1-7.8[19375.2	25.3	28038.1	36.6
[7.8-11.5[13890.6	18.9	20345.1	27.7
>=11.5	12709.7	16.2	19133.8	24.4
Legumes: beans, peas, protein crops				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % leg <5	1761376.3	22.8	2599196.6	33.6
[5-5.9[23182.8	24.3	8251.5	8.7
[5.9-7.3[22352.0	23.4	6409.8	6.7
[7.3-9.8[21562.6	22.5	7135.4	7.4
>=9.8	17772.2	18.7	6064.3	6.4
Industrial crops				
% UAA [0-5[406220.0	12.5	766710.6	23.7
% UAA>=5 & % ind. Crops <5	1587623.0	21.5	2615982.1	35.4
[5-7[62035.9	34.4	5540.3	3.1
[7-9.4[64491.1	36.4	2638.9	1.5
[9.4-13.6[68822.5	37.8	1993.9	1.1
>=13.6	63273.3	35.2	902.4	0.5

Table S 10 Association between viticulture density and the incidence of AL stratified on the level of residential exposure to UV radiation ($>105.5 \text{ J/cm}^2$ vs. $\leq 105.5 \text{ J/cm}^2$)

UV	Crop density ¹	Average Viticulture Density	Number of units ³	PY/year	Acute lymphoblastic leukemia				
					O	E	SIR	CI	P ⁴
$\leq 105.5 \text{ J/cm}^2$	% UAA [0-5[0.0	3576	2474337.5	1981	2049.4	0.97	0.93-1.01	
	% UAA $\geq 5\%$ & % Viticulture < 5 %	0.1	65878	5292247.1	4340	4281.2	1.01	0.98-1.04	
	[5-9.9[7.1	664	56137.4	45	45.3	0.99	0.74-1.33	
	[9.9-15.9[12.0	410	48170.9	38	39.2	0.97	0.70-1.33	
	[15.9-25[19.2	405	47606.3	45	38.4	1.17	0.88-1.57	
	≥ 25	45.7	497	37472.8	35	30.5	1.15	0.82-1.60	
	Total		71430	7955972	6484	6484.0			0.43
	Test of heterogeneity								
	Test of departure from log-linearity								0.45
	SIRR for $\Delta x=10\%$ ⁵						1.04	0.97-1.10	0.14
$> 105.5 \text{ J/cm}^2$	% UAA [0-5[0.2	2505	766710.6	727	686.5	1.06	0.98-1.14	
	% UAA $\geq 5\%$ & % Viticulture < 5 %	0.6	26609	2041305.2	1756	1802.4	0.97	0.93-1.02	
	[5-9.9[7.3	1423	137764.4	123	120.6	1.02	0.86-1.22	
	[9.9-15.9[12.7	1155	145684.4	111	128.5	0.86	0.72-1.04	
	[15.9-25[19.8	1172	145634.6	134	128.4	1.04	0.88-1.24	
	≥ 25	42.5	2242	156669	153	137.6	1.11	0.95-1.30	
	Total		35106	3393768.2	3004	3004.0			0.16
	Test of heterogeneity								
	Test of departure from log-linearity								0.14
	SIRR for $\Delta x=10\%$ ⁵						1.02	0.98-1.06	0.16

O: Observed number of cases; E: expected number of cases under the hypothesis of a homogeneous incidence rate by period, for each age x sex category throughout mainland France; SIR:

Standardized Incidence Ratio = O/E; CI: 95% Confidence Interval; UAA: total utilized agricultural area

¹ The crop density in a municipality is defined as the ratio of the area used for the crop over the total area of this municipality (based on national agricultural census data);

² Average crop density weighted by the pediatric population at risk living in the municipalities of the category;

³ Number of statistical units, defined as "municipalities x period" in each category;

⁴ p-value of the tests (chi-square test of heterogeneity between categories of agricultural density, departure from log-linearity test, one-sided test of the regression coefficient in the semi-quantitative model (H_0 : slope = 0 vs H_1 : slope >0);

⁵ SIRR (for $\Delta x=10\%$) = Relative Standardized Incidence Ratio with 95% confidence limits: Multiplicative variation of the SIR for a 10% increase in the crop density derived from a log-linear Poisson regression model adjusted to the observations (the outcome is the observed number of cases by municipality x period; the offset is the expected number of cases; and the independent covariate is the crop density).

Table S 11 Association between the incidence of childhood leukemia and viticulture density in semi-quartiles in the French municipalities, 1990-2014

Viticulture density ¹	Density average ²	Number of units ³	PY/year	Acute leukemia					Acute lymphoblastic leukemia				
				O	E	SIR	CI	P ⁴	O	E	SIR	CI	P ⁴
Viticulture /semi-quartiles													
% UAA [0-5[0.1	6081	3241048.1	3315	3336.2	0.99	0.96-1.03		2708	2752.4	0.98	0.95-1.02	
% UAA ≥ 5% and % Viticulture <5 %	0.2	92487	7333552.3	7365	7373.6	1.00	0.98-1.02		6096	6093.5	1.00	0.98-1.03	
[5-7.1[6.1	1051	96997.3	99	96.6	1.02	0.84-1.25		85	79.8	1.07	0.86-1.32	
[7.1-9.9[8.4	1036	96904.5	99	96.9	1.02	0.84-1.24		83	80.1	1.04	0.84-1.29	
[9.9-12.4[11.0	697	97469.4	89	98.4	0.90	0.73-1.11		70	81.5	0.86	0.68-1.09	
[12.4-15.9[14.0	868	96386.0	90	96.7	0.93	0.76-1.14		79	79.9	0.99	0.79-1.23	
[15.9-19.3[17.3	669	96731.2	101	97.4	1.04	0.85-1.26		89	80.3	1.11	0.90-1.36	
[19.3-25.0[22.0	908	96509.8	103	96.6	1.07	0.88-1.29		90	79.8	1.13	0.92-1.39	
[25-38.1[31.0	1270	97238.2	106	97.3	1.09	0.90-1.32		88	80.5	1.09	0.89-1.35	
≥ 38.1	55.2	1469	96903.6	120	97.2	1.24	1.03-1.48		100	80.3	1.25	1.02-1.52	
Total		106536	11349740	11487	11487			0.54	9488	9488			0.33
Test of heterogeneity													
Test of departure from log-linearity							0.07					0.14	
Estimated SIRR for Δx=10% ⁵						1.03	1.00-1.06	0.01			1.04	1.01-1.07	0.005

O: Observed number of cases; E: expected number of cases under the hypothesis of a homogeneous incidence rate by period, for each age x sex category throughout mainland France; SIR:

Standardized Incidence Ratio = O/E; CI: 95% Confidence Interval; UAA: total utilized agricultural area

¹ The crop density in a municipality is defined as the ratio of the area used for the crop over the total area of this municipality (based on national agricultural census data);

² Average crop density weighted by the pediatric population at risk living in the municipalities of the category;

³ Number of statistical units, defined as "municipalities x period" in each category;

⁴ p-value of the tests (chi-square test of heterogeneity between categories of agricultural density, departure from log-linearity test, one-sided test of the regression coefficient in the semi-quantitative model (H_0 : slope = 0 vs H_1 : slope >0);

⁵ SIRR (for $\Delta x = 10\%$) = Relative Standardized Incidence Ratio with 95% confidence limits: Multiplicative variation of the SIR for a 10% increase in the crop density derived from a log-linear Poisson regression model adjusted to the observations (the outcome is the observed number of cases by municipality x period; the offset is the expected number of cases; and the independent covariate is the crop density).

Table S 12 The ten most common crops grown in France and the USA in 2000¹

France		USA		
	Area (ha)	%	Area (ha)	%
Wheat	5 235 110	18.8	Soybeans	29 299 493
Industrial crops	2 105 200	7.6	Corn	27 612 210
Maize	1 753 870	6.3	Wheat	18 421 479
Barley	1 521 930	5.5	Cotton	5 040 884
Rapeseed and Turnips	1 176 100	4.2	Sorghum	2 733 813
Grapes	883 660	3.2	Barley	1 625 095
Sunflower seeds	722 870	2.6	Vegetables	1 496 845
Dry pulses	475 390	1.7	Rice	1 294 053
Sugar beets	409 060	1.5	Oats	808 132
Vegetables	240 810	0.9	Sunflower	741 973
Potatoes	157 820	0.6	Sugar beets	552 713
Total Agricultural land	27 856 310		Total Agricultural land	335 667 601

¹ 2000 World Census of Agriculture, Main results and Metadata per country (1996-2005), FAO development series, Rome 2010