Supplemental Material

Association between Residential Proximity to Viticultural Areas and Childhood Acute Leukemia Risk in Mainland France: GEOCAP Case-Control Study, 2006–2013

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Figure S4. Non-linear logistic regression model of the association between viticulture density and risk of childhood lymphoblastic leukemia in the *Occitanie* region (exposure assessment based on polygons associated with CLC and RPG **(a)** and with RPG alone **(b)**).

Table S1 – Distribution of the controls with respect to the geocoding uncertainty and the size of urban unit

	Size of urban unit (inhabitants)				Total
	<5,000 N=11,948	**5,000-19,999** N=4,534	**20,000-99,999** N=5,127	**≥100,000** N=18,587	N=40,196
Uncertainty < 100 m	**65.9%**	**79.8%**	**87.1%**	**93.0%**	**82.6%**
(1) entrance of the residential plot	48.8%	59.0%	65.1%	70.7%	62.1%
(2) projection toward the road	11.3%	9.0%	8.8%	7.0%	8.7%
(3) interpolation between neighboring addresses.	5.8%	11.8%	13.2%	15.3%	11.8%
Uncertainty ≥ 100 m	**34.1%**	**20.2%**	**12.9%**	**7.0%**	**17.4%**
(4) in the middle of the street	5.5%	5.8%	5.3%	3.2%	4.5%
(5) in the middle of an urban residential neighborhood	0.2%	1.2%	1.3%	1.1%	0.9%
(6) in the middle of a rural hamlet	26.1%	11.8%	5.1%	1.9%	10.6%
(7) at the town hall of the municipality	2.3%	1.4%	1.2%	0.8%	1.4%
All controls	**100%**	**100%**	**100%**	**100%**	**100%**

N: number of controls

Table S2 - Distribution of controls according to viticulture density (based on CLC and RPG and on RPG alone), FDep deprivation index, average daily UV radiation level, and length of major roads within 150 m, data for Figure S2.

	Viticulture density											
	RPG and CLC						RPG alone					
	0	]0; 0.005[	[0.005;0 .034[	[0.034;0 .119[	[0.119;0 .308[	[0.308;0 .928]	0	]0; 0.003[	[0.003;0 .012[	[0.012;0 .036[	[0.036;0 .086[	[0.086;0 .678]
FDep deprivation index												
[-6.7;-1.2[	7,557	114	111	123	87	48	7,626	102	94	84	80	54
[-1.2;-0.2[	7,115	189	157	177	186	215	7,228	159	143	144	168	197
[-0.2;0.5[	7,110	202	166	176	176	209	7,201	176	160	181	158	163
[0.5;1.3[	6,996	181	222	202	221	217	7,103	168	188	190	199	191
[1.3;5.4]	7,395	119	148	127	134	116	7,472	108	128	114	108	109
Average daily UV radiation level (J/cm^2)												
[85.5;94.6[	7,853	59	37	37	37	17	7,887	61	30	30	18	14
[94.6;99.3[	7,636	67	81	81	96	78	7,664	79	85	95	64	52
[99.3;101.2[	7,860	50	45	37	23	24	7,870	47	35	25	34	28
[101.2;109.6[	6,927	277	188	218	202	227	7,058	245	157	173	175	231
[109.6;136.5]	5,897	352	453	432	446	459	6,151	281	406	390	422	389
Length of major roads within 150m (m)												
0	25,410	629	617	617	620	642	25,754	553	551	538	562	577
]0;203.6[	2,137	39	33	49	44	30	2,167	35	39	35	28	28
[203.6;275.2[	2,142	44	43	32	34	36	2,167	33	36	30	35	30
[275.2;299.3[	2,144	30	38	40	40	40	2,163	28	28	44	37	32
[299.3;437.6[	2,118	39	44	37	50	45	2,140	42	35	39	39	38
[437.6;1967.2]	2,222	24	29	30	16	12	2,239	22	24	27	12	9

RPG: Graphic Parcel Register, CLC: Corine Land Cover, Fdep: French municipality deprivation index

Table S3 - Association between childhood lymphoblastic acute leukemia and indicators of proximity to vines, by age group (GEOCAP inclusions 2006-2013, GIS-based assessment of exposure based on RPG and CLC sources).

	0-6 years old				7-14 years old			
	Controls (N=18,707)	Cases (N=1,958)	OR (95%CI) [1]	p[2]	Controls (N=21,489)	Cases (N=1,130)	OR (95%CI) [1]	p[2]
Presence of vines within 1000 m								
No vines, no other crops, UU[3] ≥100,000 inhabitants	4,276	395	0.83 (0.61,1.12)		4,338	228	0.92 (0.63,1.34)	
No vines, no other crops, UU[3] <100,000 inhabitants	485	53	1 (Ref)		565	32	1 (Ref)	
No vines, other crops[4] ≤ 1000 m but none ≤ 500 m	2,354	258	0.98 (0.72,1.34)		2,619	122	0.82 (0.55,1.22)	
No vines, other crops[4] ≤ 500 m	9,815	1067	0.97 (0.73,1.30)		11,729	629	0.94 (0.65,1.36)	
Possible presence of vines ≤ 1000 m[5]	220	29	1.20 (0.74,1.95)		235	15	1.13 (0.60,2.13)	
Probable presence of vines ≤ 1000 m[6]	1,557	156	0.90 (0.65,1.25)		2,003	104	0.92 (0.61,1.38)	
Density of viticulture within 1000 m[7]								
RPG and CLC (sensible indicator)			1.04 (0.98,1.10)	0.10			1.05 (0.98,1.13)	0.08

RPG: Graphic Parcel Register, CLC: Corine Land Cover

[1] Odds ratio (OR) and 95% confidence interval (CI) estimated by unconditional logistic regression adjusted for age categories (<1,[1-4],[5-6],[7-9],[10-14]).
[2] one-sided p-values for the slope parameter in the quantitative analysis with the density of vines within 1000 m
[3] size of urban unit (UU);
[4] at least one plot identified by RPG or CLC with a crop different from vines
[5] at least one vine plot identified by CLC, but no vines identified with RPG
[6] at least one vine plot identified by RPG
[7] OR associated with a 10% increase in viticulture density.

Table S4 – Association between the density of viticulture and the risk of acute lymphoblastic leukemia in the *Occitanie* region - Parameter estimates and 95% confidence interval (CI) in 11 density categories[1] of viticulture density (based on polygons associated with CLC and RPG and with RPG alone), data for Figure S4.

RPG and CLC					RPG alone				
Median viticulture density[1]	controls	cases	beta[2]	95% CI[2]	Median viticulture density[1]	controls	cases	beta[2]	95% CI[2]
0	2008	163	-1.94	-2.15;-1.72	0	2130	170	-1.94	-2.15;-1.72
0.001	125	6	-2.38	-3.22;-1.54	0.001	108	10	-1.74	-2.41;-1.06
0.008	128	3	-3.28	-4.44;-2.13	0.004	114	4	-2.80	-3.81;-1.80
0.022	122	9	-2.13	-2.87;-1.40	0.010	114	4	-2.86	-3.87;-1.85
0.049	124	6	-2.41	-3.25;-1.57	0.018	110	8	-1.98	-2.72;-1.24
0.103	123	7	-2.21	-2.99;-1.43	0.030	107	10	-1.76	-2.43;-1.09
0.173	118	12	-1.63	-2.26;-1.01	0.044	111	6	-2.30	-3.14;-1.45
0.256	123	7	-2.32	-3.10;-1.54	0.063	110	7	-2.31	-3.15;-1.47
0.340	122	8	-2.15	-2.88;-1.41	0.094	111	6	-2.33	-3.17;-1.49
0.445	110	20	-1.18	-1.68;-0.68	0.142	105	12	-1.56	-2.18;-0.94
0.602	120	10	-1.86	-2.53;-1.19	0.269	103	14	-1.32	-1.91;-0.73

RPG: Graphic Parcel Register, CLC: Corine Land Cover

[1] the first category grouped children with no viticulture area within 1000 m of their geocoded address, and the following 10 categories corresponded to deciles of viticulture density

[2] parameter estimate and 95% confidence interval for each category of viticulture density

Figure S1- Joint distribution of size of urban unit and viticulture density (exposure assessment based on polygons associated with CLC and RPG **(a)** and with RPG alone **(b)**) in controls.
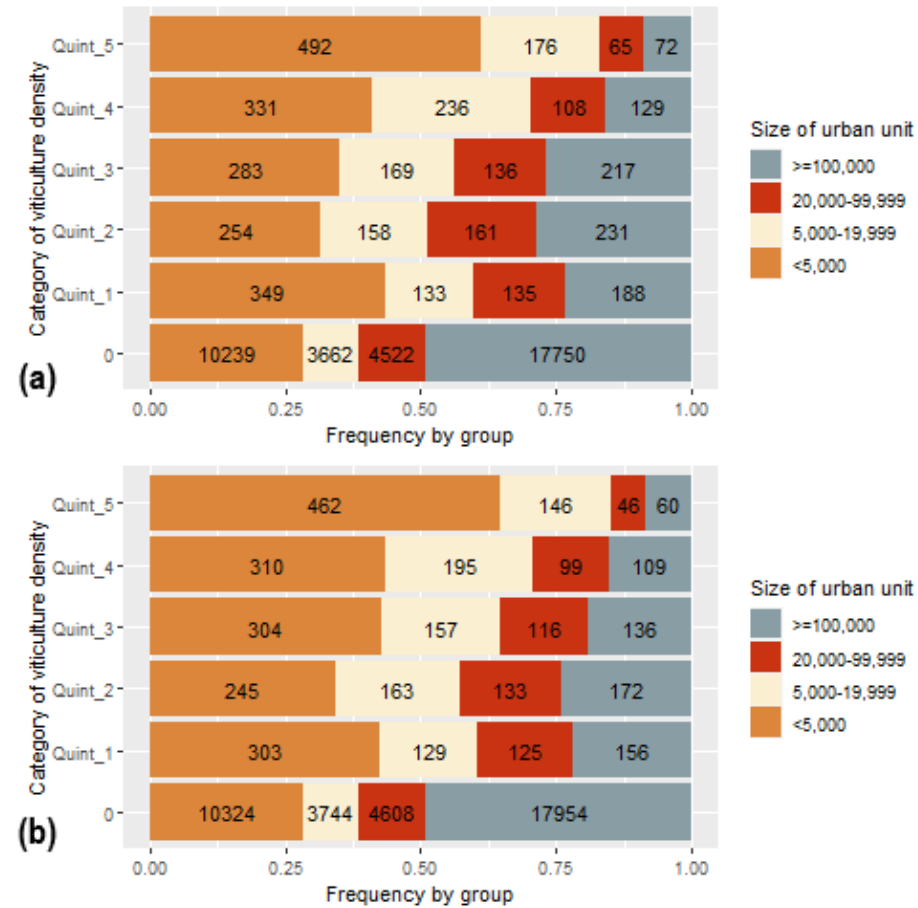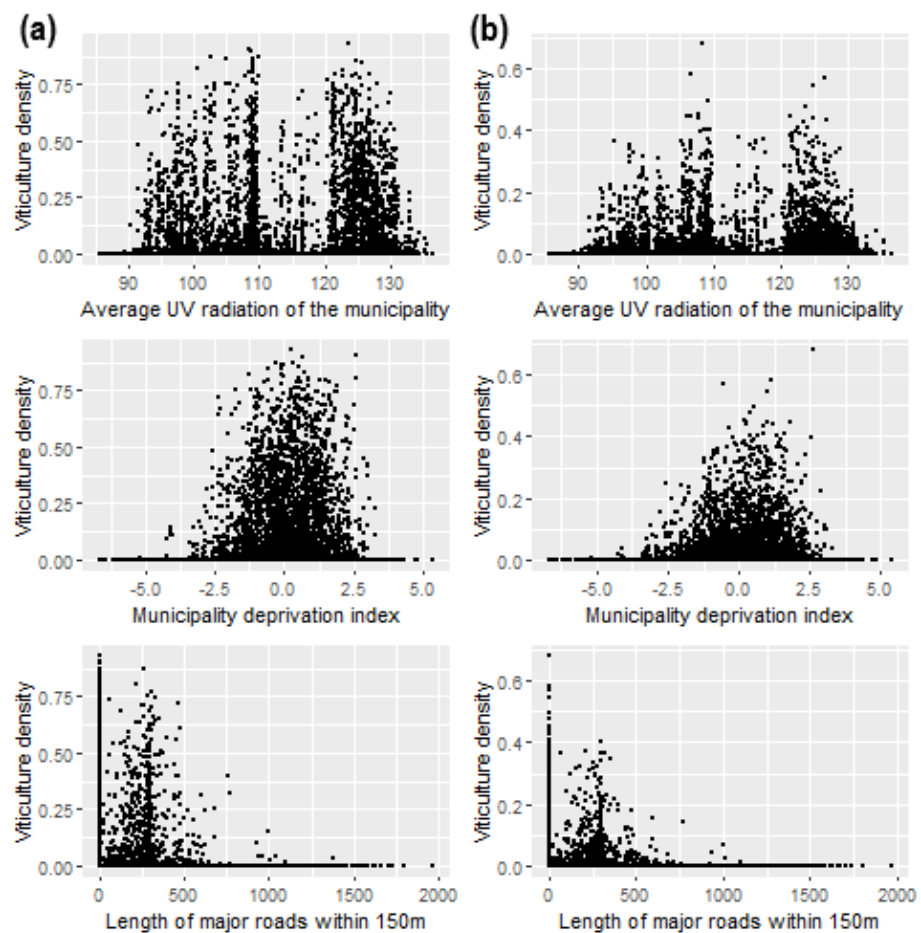

RPG: Graphic Parcel Register, CLC: Corine Land Cover

Notes: The controls were divided into 6 categories of exposure: unexposed children (no viticulture within 1000 m of the address) + quintiles of viticulture density for exposed children.

Quintiles defining categories in (a): 0.5%, 3.4%, 11.9%, 30.8%

Quintiles defining categories in (b): 0.3%, 1.2%, 3.6%, 8.6%

Figure S2 – Joint distribution of viticulture density (exposure assessment based on polygons associated with CLC and RPG **(a)** and with RPG alone **(b)**) and three potential confounding factors (FDep deprivation index of the municipality, average daily UV radiation level in the municipality, length of major roads within 150 m of the address) in controls.
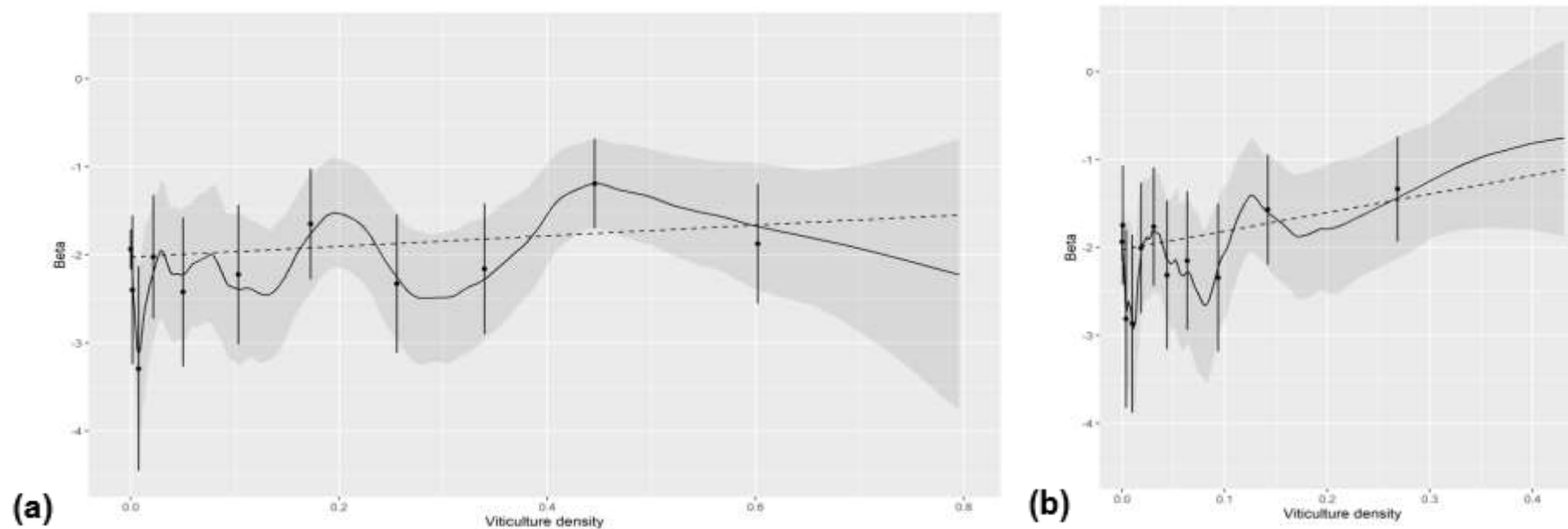

RPG: Graphic Parcel Register, CLC: Corine Land Cover
Data from Table S2.

Figure S3 – Viticultural density in the municipalities of the French regions, calculated as the proportion of the municipality areas dedicated to viticulture
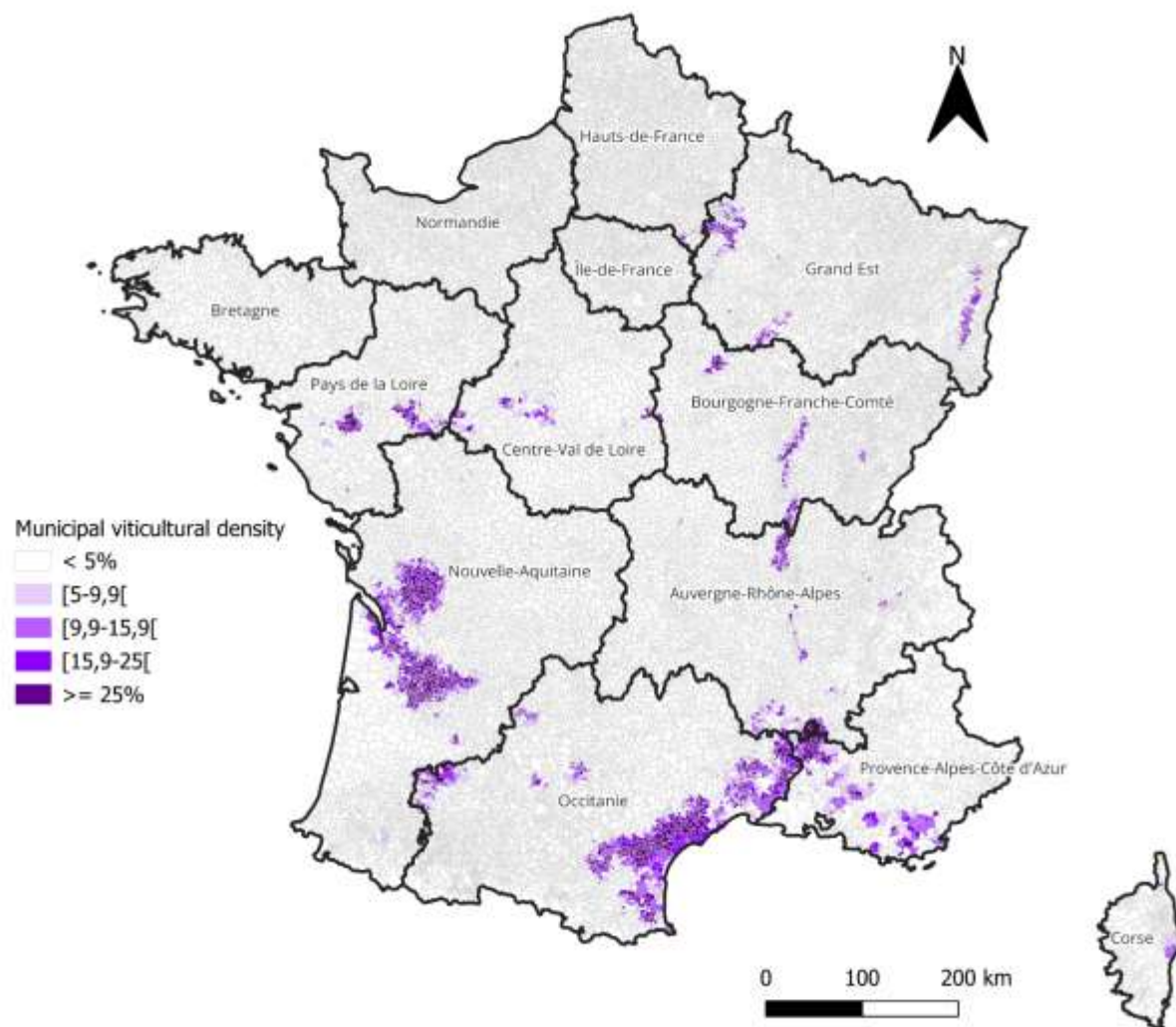
Map generated by our team using agricultural census data, municipality boundaries (DataGouv France with © information from OpenStreetMap contributors under the ODbL license) and QGIS 3.28 software.

Figure S4 – Non-linear logistic regression model of the association between viticulture density and risk of childhood lymphoblastic leukemia in the *Occitanie* region (exposure assessment based on polygons associated with CLC and RPG **(a)** and with RPG alone **(b)**)

RPG: Graphic Parcel Register, CLC: Corine Land Cover
Notes: The solid line shows the LOESS model fit with 95% confidence interval ribbon; the dotted line shows linear model fit; the vertical bars show the parameter values and 95%CI for 11 categories (non-exposed children + 10 decile categories of viticulture density for the exposed children) estimated with a qualitative model.
Data from Table S4.