Space-time environmental associations in childhood type 1 diabetes. A case-control geographical approach in the Isis-Diab cohort.

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BACKGROUND

Type 1 diabetes (T1D) concordance in monozygotic twin pairs being ~40%, non-heritable factors play a major causal role in this autoimmune disease. T1D has recently increased in young European children. Collecting prospective environmental data in a cohort of millions children-years starting soon after birth seems unpracticable. Retrospective case-control studies are an alternative, if biased controls and recall bias can both be avoided.

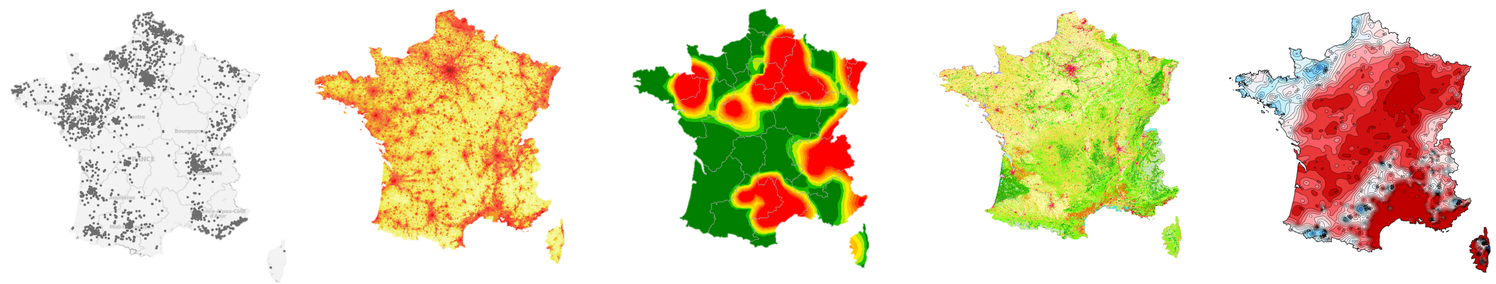
OBJECTIVES

To develop a « virtual control » (VC) geographical approach to unravel environmental factors significantly associated with T1D.

METHODS

3548 children (age-at-onset 7.2±3.7 yrs) with diagnosis after 1984 were analysed.

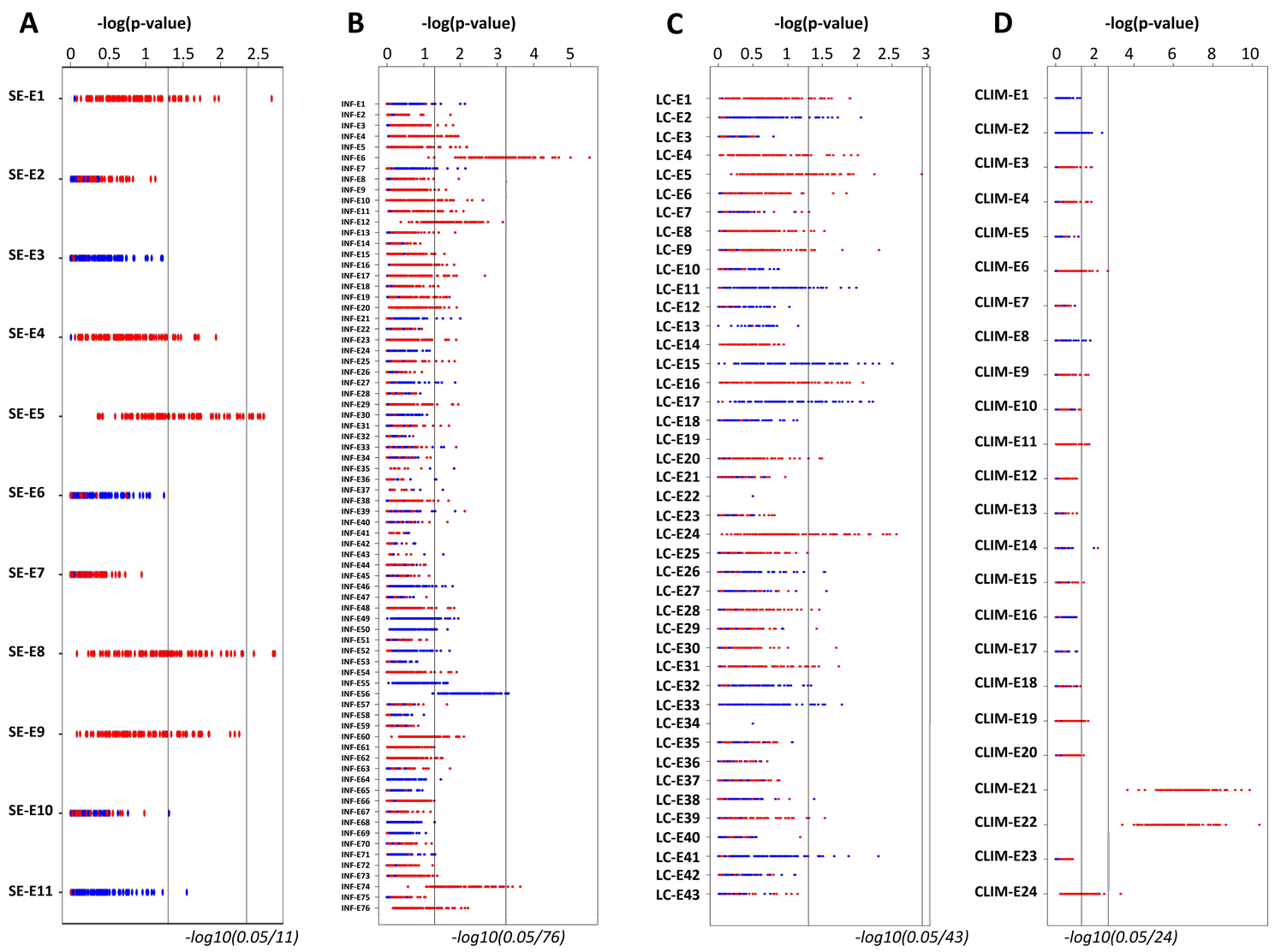
Four dimensions of environmental exposures were tested by mapping socioeconomic, infectious, climatic and land cover databases at the geolocalized address of the child before T1D diagnosis. Levels of exposures were compared between T1D patients and age-matched geographic VCs. A test was considered significant (**) when the median p value computed over 100 comparisons of cases with 100 sets of VCs was below the Bonferroni limit, and indicative (*) of a possible difference when it was <0.05.



	T1D patients	Socioeconomic environment (SE-E)	Infectious environment (INF-E)	Land Cover environment (LC-E)	Climatic Environment (CLIM-E)
Source of information	Isis-Diab	INSEE	French Sentinel System	Corine Land Cover	E-Obs

RESULTS

The socioeconomic and land cover environment of T1D children was comparable to controls. The T1D children showed a greater past exposure to influenza (**) and acute diarrheas (*) and a lower past exposure to varicella (*). T1D children were more frequently exposed to heatwaves (**).



Environmental analysis of T1D in the Isis-Diab cohort. Red/ blue dots indicate that the patients were more/less exposed than the controls. The two lines stand for tests significance at the 0.05 level without (bottom line) and with (upper line) Bonferroni correction for multiple testing. **(A)** Social environment of patients. **(B)** Infectious environment of patients. **(C)** Land Cover environment of patients. **(D)** Climatic environment of patients.

Socioeconomic environment (SE-E)

- SE-E1 Index of urban units
- SE-E2 Unemployment (% of economically active ≥16 years old)
- SE-E3 Blue-collar workers (% of all households)
- SE-E4 White-collar workers (% of all households)
- SE-E5 Non-car ownership (% of all households holds)
- SE-E6 Farmer (% of all households)
- SE-E7 Household overcrowded (households with >1 person per room, % of all households)
- SE-E8 non-home ownership (% of all households)
- SE-E9 Townsend deprivation index (TDI) [23]
- SE-E10 Mean income by year
- SE-E11 Access rate to high school diploma

Climatic environment (CLIM-E)

	Heatwave		Coldspell	
Exposure window	**Absolute**	**Relative**	**Absolute**	**Relative**
Birth-6 months	CLIM-E1	CLIM-E2	CLIM-E3	CLIM-E4
Birth-1yr	CLIM-E5	CLIM-E6	CLIM-E7	CLIM-E8
1yr-2yrs	CLIM-E9	CLIM-E10	CLIM-E11	CLIM-E12
2yrs-3yrs	CLIM-E13	CLIM-E14	CLIM-E15	CLIM-E16
3yrs-4yrs	CLIM-E17	CLIM-E18	CLIM-E19	CLIM-E20
1yr-T1D diagnosis	CLIM-E21	CLIM-E22	CLIM-E23	CLIM-E24

Infectious environment (INF-E)

Exposure window (method)	Influenza like illnesses exposure	Measles exposure	Mumps exposure	Varicella exposure	Acute diarrheas exposure
6 months-1yr (cumulative)	INF-E1	INF-E21	INF-E33	INF-E45	INF-E57
Birth-1yr (cumulative)	INF-E2	INF-E22	INF-E34	INF-E46	INF-E58
1yr-2yrs (cumulative)	INF-E3	INF-E23	INF-E35	INF-E47	INF-E59
2yrs-3yrs (cumulative)	INF-E4	INF-E24	INF-E36	INF-E48	INF-E60
3yrs-4yrs (cumulative)	INF-E5	INF-E25	INF-E37	INF-E49	INF-E61
1yr-T1D diagnosis (cumulative)	INF-E6	INF-E26	INF-E38	INF-E50	INF-E62
6 months-1yr (mean 10 max)	INF-E7	INF-E27	INF-E39	INF-E51	INF-E63
Birth-1yr (mean 10 max)	INF-E8	INF-E28	INF-E40	INF-E52	INF-E64
1yr-2yrs (mean 10 max)	INF-E9	INF-E29	INF-E41	INF-E53	INF-E65
2yrs-3yrs (mean 10 max)	INF-E10	INF-E30	INF-E42	INF-E54	INF-E66
3yrs-4yrs (mean 10 max)	INF-E11	INF-E31	INF-E43	INF-E55	INF-E67
1yr-T1D diagnosis (mean 10 max)	INF-E12	INF-E32	INF-E44	INF-E56	INF-E68
Birth-1yr (winter)	INF-E13	-	-	-	INF-E69
Birth-1yr (summer)	INF-E14	-	-	-	INF-E70
1yr-2yrs (winter)	INF-E15	-	-	-	INF-E71
1yr-2yrs (summer)	INF-E16	-	-	-	INF-E72
2yrs-3yrs (winter)	INF-E17	-	-	-	INF-E73
2yrs-3yrs (summer)	INF-E18	-	-	-	INF-E74
3yrs-4yrs (winter)	INF-E19	-	-	-	INF-E75
3yrs-4yrs (summer)	INF-E20	-	-	-	INF-E76

Land Cover environment (LC-E)

Artificial areas	**Standing forests, semi-natural vegetation, open spaces, bare soils**
LC-E1 Continuous urban fabric	LC-E23 Broad-leaved forest
LC-E2 Discontinuous urban fabric	LC-E24 Coniferous forest
LC-E3 Industrial or commercial units	LC-E25 Mixed forest
LC-E4 Road and rail networks and associated land	LC-E26 Natural grasslands
LC-E5 Port areas	LC-E27 Moors and heathland
LC-E6 Airports	LC-E28 Sclerophyllous vegetation
LC-E7 Mineral extraction sites	LC-E29 Transitional woodland-shrub
LC-E8 Dump sites	LC-E30 Beaches, dunes, sands
LC-E9 Construction sites	LC-E31 Bare rocks
LC-E10 Green urban areas	LC-E32 Sparsely vegetated areas
LC-E11 Sport and leisure facilities	LC-E33 Burnt areas
	LC-E34 Glaciers and perpetual snow
Arable land & permanent crops, Mosaic farmland	**Wetlands**
LC-E12 Non-irrigated arable land	LC-E35 Inland marshes
LC-E13 Permanently irrigated land	LC-E36 Peat bogs
LC-E14 Rice fields	LC-E37 Salt marshes
LC-E15 Vineyards (*)	LC-E38 Salines
LC-E16 Fruit trees and berry plantations	LC-E39 Intertidal flats
LC-E17 Olive groves	
LC-E18 Pastures	**Water Bodies**
LC-E19 Annual crops associated with permanent crops	LC-E40 Water courses
LC-E20 Complex cultivation patterns	LC-E41 Water bodies
LC-E21 Land principally occupied by agriculture, with significant areas of natural vegetation	LC-E42 Coastal lagoons
LC-E22 Agro-forestry areas	LC-E43 Estuaries

CONCLUSIONS

Our exploratory approach with 4 databases provides a proof-of-concept to space-time environment associations studies. Environmental markers (not causes) of T1D can be found. By using more databases, a larger part of a child's environment can be covered.

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Diabetes

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