Association of environmental markers with childhood type 1 diabetes mellitus revealed by a long questionnaire in a case-control study

Balazard F [1,2], Le Fur S[3,2], Valtat S[2], Isis-Diab collaborative group, Valleron AJ[2], Bougnères P[3,2]
[1]: Sorbonne Universités, UPMC [2]: INSERM U1169
[3]: Department of pediatric endocrinology, Hôpital Bicêtre, Kremlin-Bicêtre,

Background
T1D incidence is increasing due to unknown environmental factors.

Objectives
We investigated environmental markers for association to T1D by conducting a case-control study. We used a **very long questionnaire with 845 questions** exploring all aspects of environment that are likely to be recalled.

Methods
Controls were recruited by the cases among their friends. This was taken into account in a first analysis by performing matched tests.
In this first analysis, we excluded cases who could not recruit their own control, We performed a second analysis with those cases included. For that second analysis, we controlled for social class, age, urban and rural environment using stratification on a propensity score.
We corrected for multiple testing. The Bonferroni threshold was used for the propensity analysis and the less conservative False Discovery Rate threshold was used for the matched analysis. This is because the matched analysis controls biases more thoroughly. Results that pass both thresholds are reported.

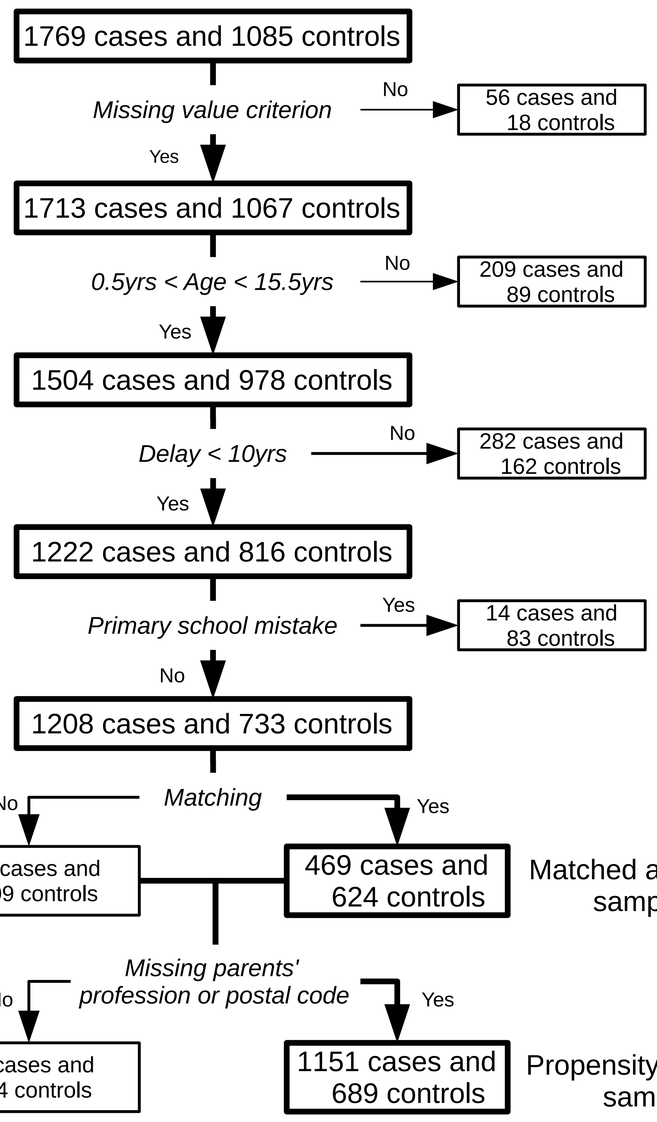

Fig. 1 Flowchart of the samples definition. Delay refers to the time between diagnosis and questionnaire reception. Participants have made the primary school mistake if they answered that they went to primary school even though their reference age is smaller than 5.5 years. The two samples on which analyses were performed are in the bottom right corner.

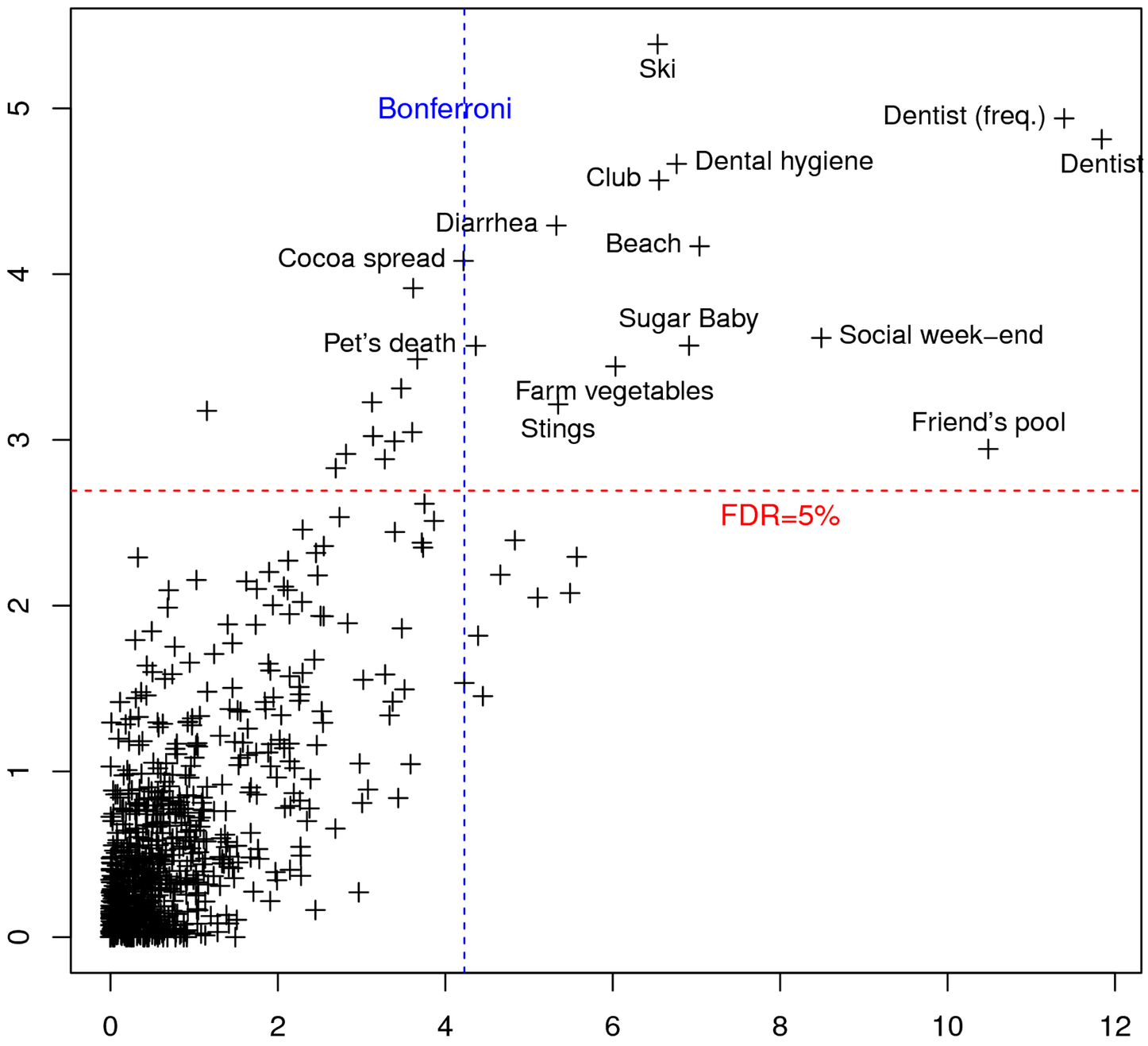

Fig. 2: Comparison of the results of the two analyses. -log10(p-value) of the two analyses plotted against each other. The most associated variables in both analysis are in the top right corner. The Bonferroni threshold for the propensity analysis is the vertical line. The false discovery rate threshold for the matched analysis is the horizontal line. A more lenient statistical control is used for the matched analysis as it is less prone to bias. All variables passing both thresholds are labeled (top right corner). All the significant associations are protective.

Results
Results are shown in Fig. 2. All significant variables have a negative association with T1D.
We offer no interpretation of the results.
Nevertheless, we note that cocoa spread contains a large proportion of palm oil that is an important source of tocotrienol. Tocotrienol has been shown in murine models to affect NLPR3 [1] which may play a role in T1D pathogenesis [2].

Conclusions
These findings are novel and may open new areas of investigation for T1D environmental research. However they need to be confirmed in other childhood T1D cohorts.

Conflict of interest :
The authors declare no conflict of interest.

References :
1. Kim et al.: Suppression of NLRP3 inflammasome by γ-tocotrienol ameliorates type 2 diabetes. *J Lipid Res* 2016
2. Hu et al.: NLRP3 deficiency protects from type 1 diabetes through the regulation of chemotaxis into the pancreatic islets. *Proc Natl Acad Sci U S A* 2015

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Diabetes
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