Integrated and predictive approach for identifying determinants of health changes: the role of nutrition

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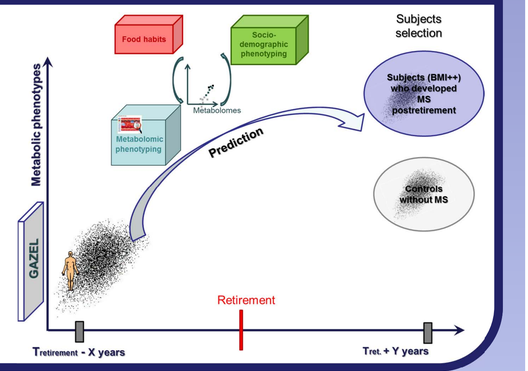
INTRODUCTION

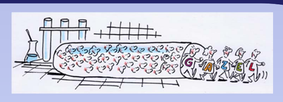
The overall objective of the DIAPASON project is to develop accurate and robust markers of the evolution of health status toward metabolic syndrome (MetS), and to determine to what extent nutrition is a major determinant, using a multidisciplinary approach, putting together sociology, epidemiology, nutrition, statistics, and computer science. The project uses the French population-based GAZEL cohort, an on-going epidemiological study set up in 1989 (~20,000 volunteers) among employees of the French national Gas and Electricity Company. The study consists in integrating demographic, socioeconomic, clinical, and biological data (from annual questionnaires, including food frequency questionnaires (FFQs)) to analyze food trajectories between 1998 and 2009.

Primary goal: Development of a model for predicting the onset of MetS among at risk retired subjects.
Secondary goal: Study in a more heterogeneous population undergoing a life transition (retirement) during the study period.



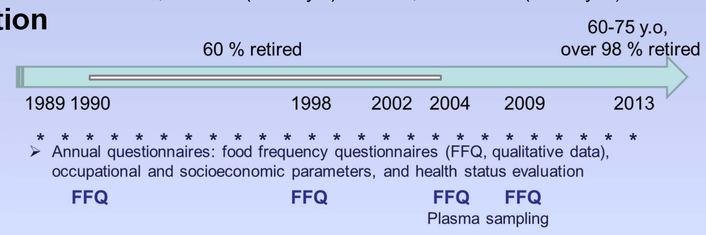
Subjects

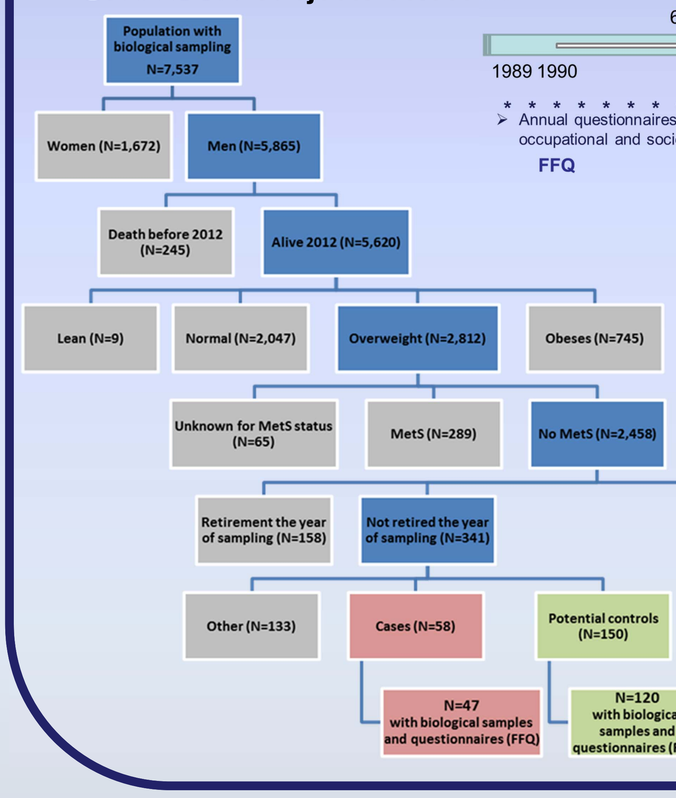
The GAZEL COHORT



Over 20,000 participants recruited in 1989;
~ 15,000 men (40-50 y.o) and ~ 5,600 women (35-50 y.o.)

- DIAPASON subjects selection





Inclusion:
- Without MetS (NCEP criteria)

End of the study (2008-2012):
- **Case** = subjects with ≥ 2 risk factors (**declared** diabetes, hypertension, dyslipidemia)
- **Controls** paired on:
  - Age (years): [52; 55[, [55; 58[and [58; 64[
  - BMI (kg/m²): [25; 28[and [28; 30[

Methods

• Epidemiological methods

❖ **Analysis on the GAZEL cohort of the parameters from the annual questionnaires**

- Selection of a subpopulation (9,042 subjects) corresponding to the DIAPASON criteria
- Determination of relevant and not redundant food items in the annual questionnaires: 22 food items
- For each different food items, rare answers (<5%) were merged

❖ **Construction of Foods Patterns with Multiple Correspondence Analysis (MCA) on the GAZEL cohort**

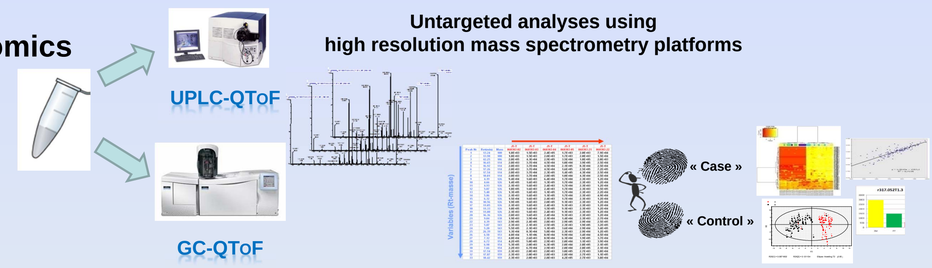
- Development of MCA on the 1998 variables and construction of Food Patterns
- Projection of the 2004 and 2009 variables on the MCA based on the 1998 variables
- Analysis of score means evolution from 1998 to 2009

❖ **Analysis on the DIAPASON subjects**

- Recovery of factorial scores for all DIAPASON subjects : *112 subjects (Cases and Controls) for the Principal Analysis / 94 subjects (Cases and Controls) for the Secondary Analysis*.
- Analysis of score mean evolution for the DIAPASON subjects

• Metabolomics

Untargeted analyses using high resolution mass spectrometry platforms



• Integration and modeling

Variables:
- LC- and GC-MS metabolomic data
- Socioeconomic parameters
- Phenotypic data
- Synthetic variables for food habits

➢ Characterization and discrimination of phenotypes
Identification of subjects with the same patterns
Identification of (bio)markers of these groups

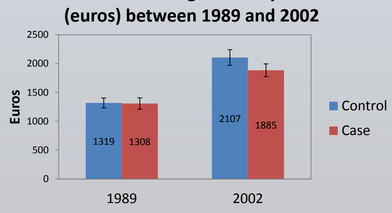
➢ Prediction of the evolution towards these phenotypes
Are the identified (bio)markers predictive?

RESULTS

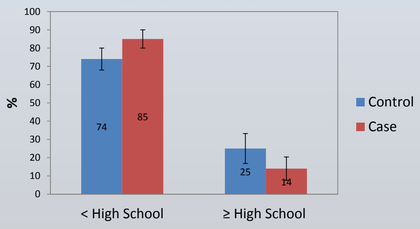
• Subjects characterization

The socio-economic results are presented for the principal analysis of the DIAPASON subjects

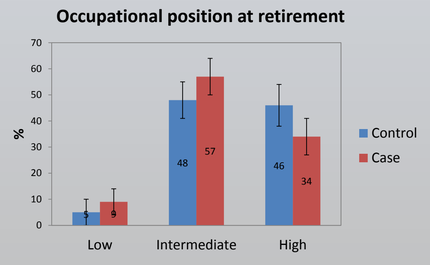
Evolution of average monthly income (euros) between 1989 and 2002



Educational Level



Occupational position at retirement



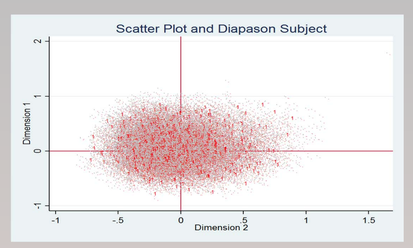
Control subjects of the principal analysis do not have significantly different monthly income and school levels, neither professional evolution than Case subjects.

• Food pattern determination

❖ **Multiple Correspondence Analysis (MCA) on 22 food items:**

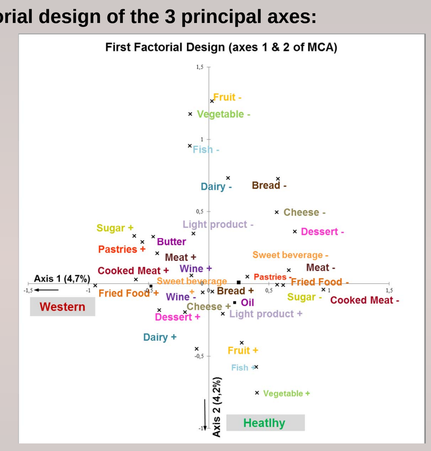
Red Meat, Poultry, Fish, Cooked Meat, Eggs, Fried Food, Fat type, Light Products, Milk, Dairy, Cheese, Bread, Vegetables, Raw vegetables, Starchy Food, Fruits, Desserts, Pastries, Sugar, Coffee, Sweet Beverages, Wine

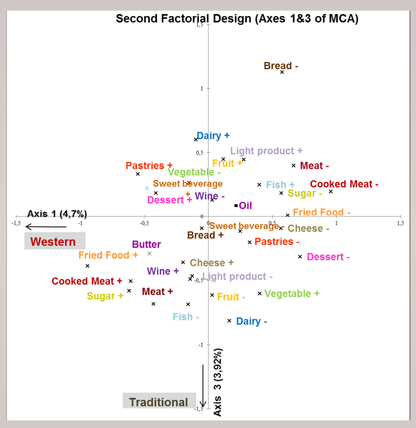
❖ **Scatter Plot of the whole GAZEL cohort and the DIAPASON subjects (in red):**



The DIAPASON subjects are representative of the whole GAZEL cohort

❖ **Factorial design of the 3 principal axes:**





3 Axes

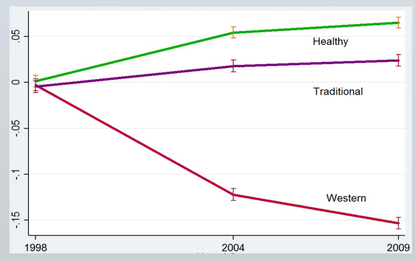
- Western: fat and sweet products
- Healthy: healthy foods (vegetables, fruits...)
- Traditional: cooked and traditional French diet (rich in wine, cheese, vegetables, low in dairy, fish and fruits)

• Food pattern trajectories

❖ **Mean score evolution between 1998 and 2009 for the whole GAZEL cohort**

Factorial scores have been reversed for more readability

Over time:
- The mean score is increased on the Healthy axis
- The mean score is increased on the Traditional axis
- The mean score is decrease on the Western axis

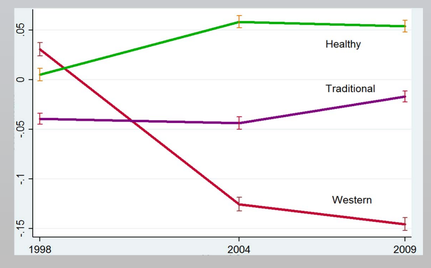


Subjects of the GAZEL cohort improve their food habits over time

❖ **Mean score evolution between 1998 and 2009 for the DIAPASON subjects**

DIAPASON *subjects from the two analyses (principal and secondary)*

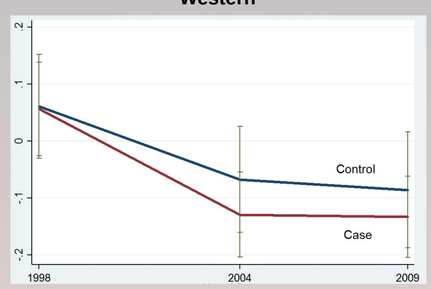
Over time:
- The mean score is increased on the Healthy axis
- The mean score is increased on the Traditional axis
- The mean score is decrease on the Western axis



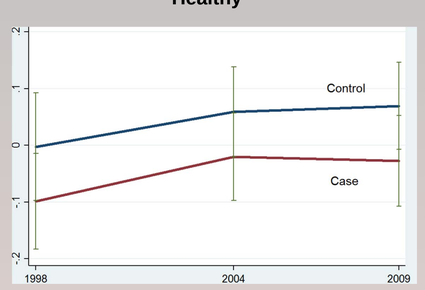
The DIAPASON subjects improve their food habits over time; they follow the trend of the whole GAZEL cohort

❖ **Mean score evolution between 1998 and 2009: Case-Control comparisons (principal analysis)**

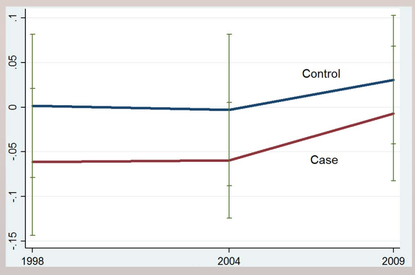
Western



Healthy



Traditional



- The Case-Control analysis of the factorial scores shows that Case and Control subjects' food habits follow the same trends over time.
- Cases and Controls' scores on the various patterns are not significantly different.
- In a supervised model (mixed model), the difference between Cases and Controls was not statistically significant (p=0.06 for the Healthy diet).

CONCLUSION

❖ From annual FFQs, three food patterns were identified on the whole **GAZEL** cohort: Western, Healthy and Traditional French diets. The analysis between 1998 and 2009 revealed different food trajectories according to dietary pattern, towards healthier food habits.

❖ The DIAPASON sub-cohort was found representative of **GAZEL** regarding food patterns and food trajectories. Comparison between Cases and Controls showed no significant differences between the two groups regarding food habits and socioeconomic characteristics. This could probably be explained by the small sample size.

❖ Supervised multidimensional models will be built to provide new tools for a better stratification of at-risk populations. Integration of socioeconomic parameters with the most relevant food patterns and discriminant metabolomic biomarkers will allow analyzing the role of nutrition as determinant and modulator in MetS etiology. All this will contribute to develop more personalized nutritional advices towards MetS prevention.

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