

Monitoring TDS indicators in France: national temporal and spatial trends for sperm quality, testis cancer and urogenital malformations

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Introduction

In utero exposure to endocrine disruptors is suspected to cause the testicular dysgenesis syndrome (TDS): sperm quality impairment, testis cancer and urogenital malformations of the male urinary tract.

We aimed to analyse time and spatial trends on TDS indicators in the French general population, in order to assess whether they were consistent and possibly congruous with TDS hypothesis.

Methods

1-SPERM QUALITY

The data were registered by Fivnat, the professional association in charge of statistics for assisted reproductive technology (ART) in France during the 1989-2005 study period. The source population included 154,712 men, partners of couples undergoing their first ART cycle, aged 20 to 70, and for whom semen concentration, measured on fresh ejaculated semen, was available. Data were provided by 126 different ART centres over the whole French metropolitan territory. The study population was constituted by 26,609 partners of women whose both tubes were absent or blocked. This subsample, randomly selected concerning fertility end points, was considered the closest to the general population. The sperm concentration was regressed on time using a generalised additive model that allowed for non linear relationships and was adjusted on age. Sensitivity analyses were performed on the two successive spermograms available for each individual, and on another subsample of men diagnosed as fertile. In sensitivity analyses, the model was also adjusted for centre, technique, either standard in vitro fertilization (IVF) or intra-cytoplasmic sperm injection (ICSI), and an interaction factor between technique and time was added. Spatial trends analyses are still ongoing.

2-TESTIS CANCER

Data were provided by the French National Hospital Discharge Database (PMSI) from 1998 to 2008. Hospital stays for testis cancer were selected using diagnosis codes based on international classification of diseases codes and surgical procedures. 21,179 hospital stays corresponding to operated testis cancers were selected. Zip code of the patient address at the time of diagnosis was used for spatial analyses.

Using a Poisson model, time trends of annual operated testis cancer rate and its percentage of variation were calculated. Regional variations of operated testis cancer rate were analyzed from 2004 to 2008 using the national mean as a reference value. The rates of operated testis cancer were compared to incidence rates of testis cancer observed in districts where registries are available.

3-UROGENITAL MALFORMATIONS: CRYPTORCHIDISM AND HYPOSPADIAS

Data from PMSI were selected using diagnosis codes and surgical codes for boys under 7 years old over the period 1998-2008. For cryptorchidism, 73,261 and for hypospadias, 32,239 hospital stays were selected during the study period. Zip code of the patient address at the time of diagnosis was used for spatial analyses.

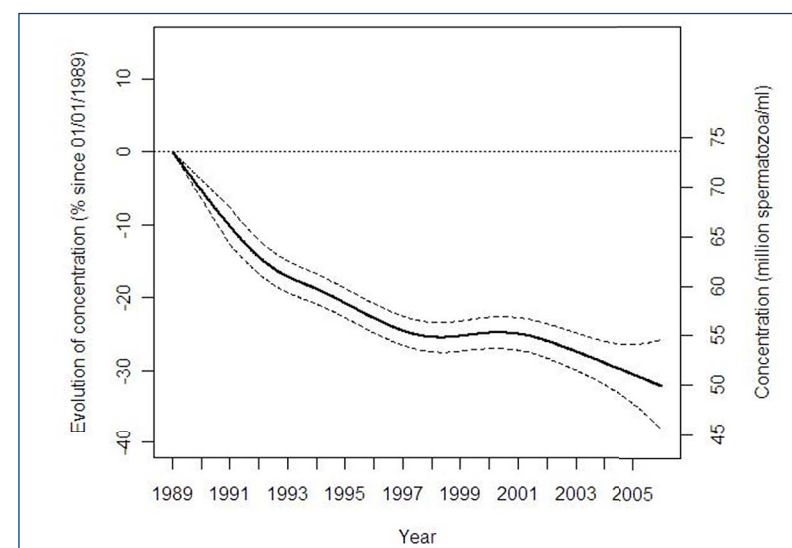
Time trends and regional variations of surgical rates of operated cryptorchidism and hypospadias were analyzed, using the same method as for testis cancer.

Results

1-TIME TRENDS

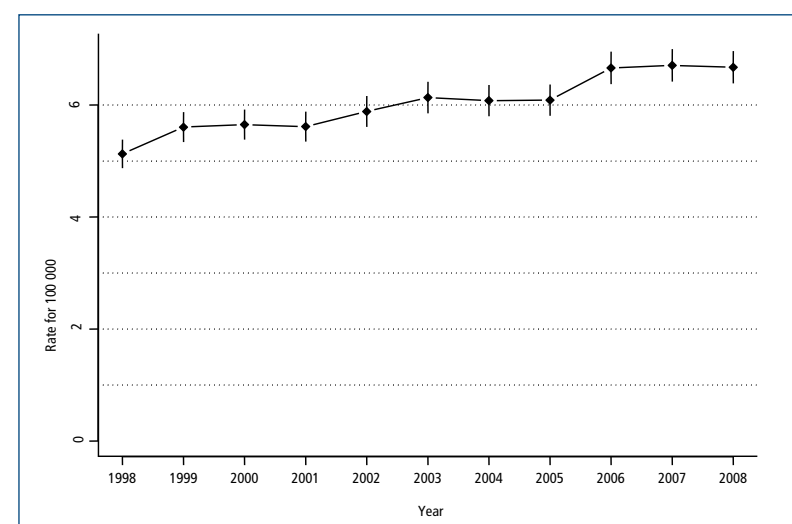
A-Sperm Quality

Average sperm concentration significantly decreased of 1.9% annually from 1989 to 2005.



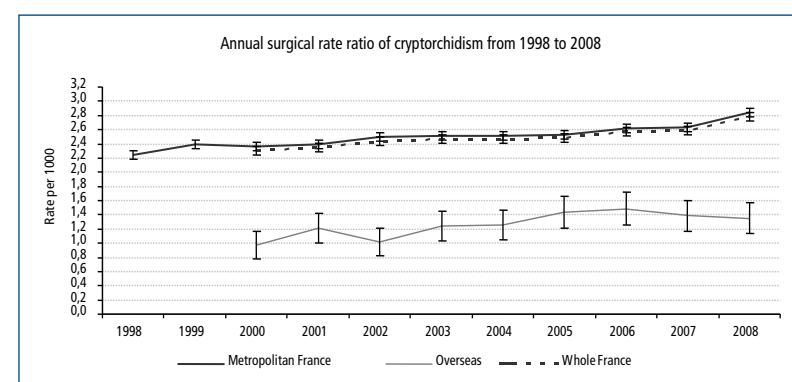
B-Testis cancer

An average annual increase of 2.5% of the rate of testis cancer surgery was observed from 1998 to 2008.



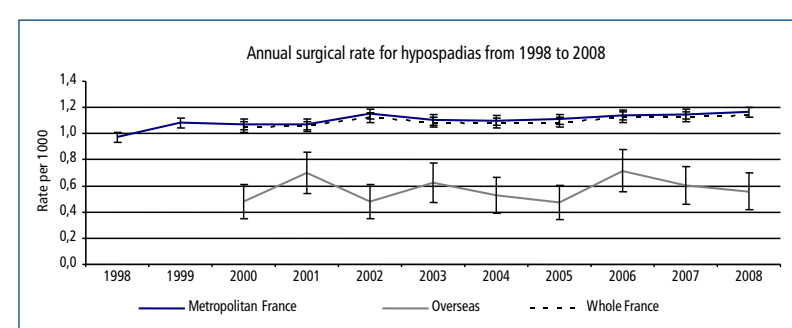
C-Cryptorchidism

The mean annual surgical rate in metropolitan France is 2.51 per 1,000 boys/year. It increases annually by 1.8% [1.4-2.3]. In overseas territories, the rate is much lower, (1.42) but increases annually by 4%.



D-Hypospadias

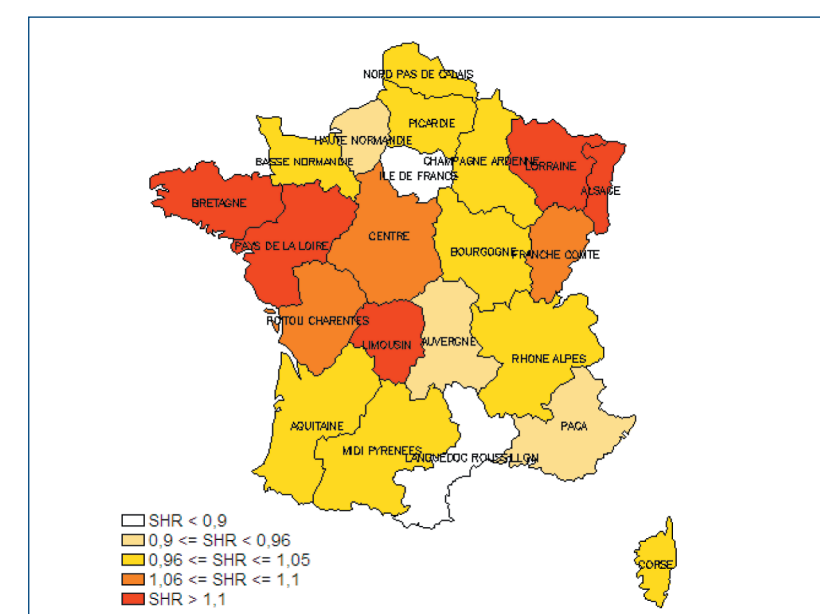
The annual surgical rate in metropolitan France is 1.10 per 1,000 boys/year, and increases annually by 1.2%.



2-SPATIAL TRENDS

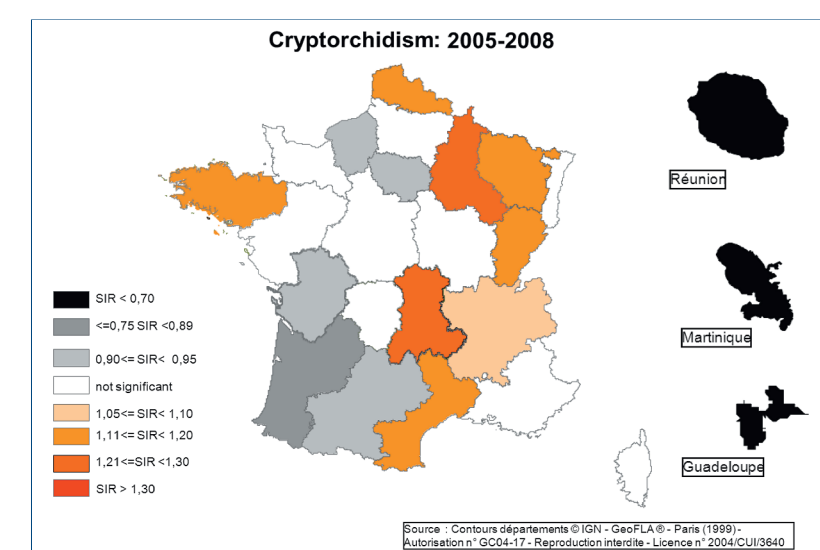
A-Testis cancer

Regional disparity in the rates of patients undergoing surgery was observed (2004-2008). The significantly highest (red color) rates were observed in Alsace, Lorraine, Bretagne and Pays de la Loire, and the significantly lowest (white color) rates in Languedoc Roussillon and Ile-de-France.



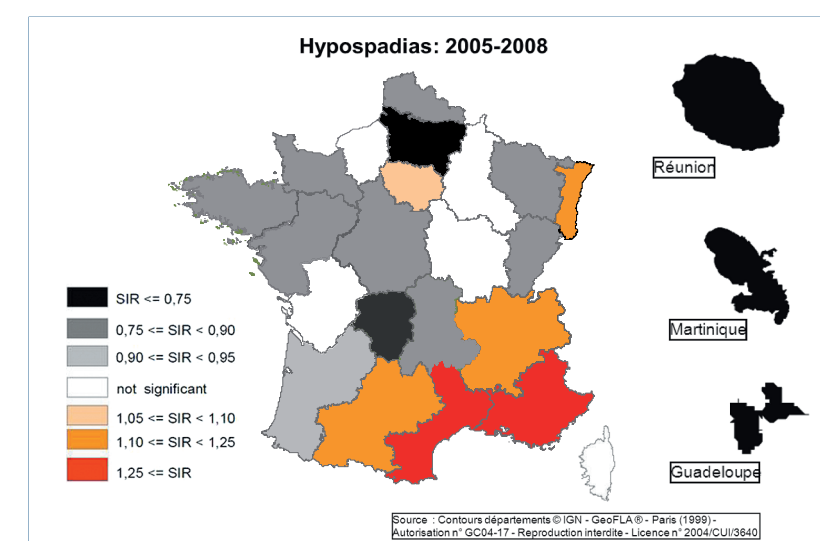
B-Cryptorchidism

The highest incidence ratios compared to the national average are found in Auvergne, Bretagne, Champagne-Ardenne, Franche-Comté, Languedoc-Roussillon, Lorraine and Nord-Pas-de-Calais.



C-Hypospadias

The highest incidence ratios of are found in Languedoc-Roussillon, Provence-Alpes-Côte d'Azur, Alsace and Rhône-Alpes.



Discussion-Conclusion

We aimed to monitor the main indicators associated with the testicular dysgenesis syndrome in France, during substantial periods and in the whole French territory.

In metropolitan France, from 1989 to 2005, time trends in sperm concentration show a significant decrease and, from 1998 to 2008, time trends in testis cancer and urogenital malformations show a significant increase. Results on sperm concentration and testis cancer were robust after sensitivity analysis. Results on urogenital

malformations are less robust because they could reflect a shift of medical practices or a change in coding in the discharge database. Overall, the time trends of these indicators seem consistent and possibly congruous with TDS hypothesis.

Concerning spatial trends, current results do not seem consistent but their interpretation is difficult and the regional scale is probably not the best to take into account environmental exposures. Further works are needed.