

Temporal and spatial trends of precocious puberty in France: a feasibility study

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Introduction

Precocious puberty (PP) is defined as the development of secondary sexual characteristics before the age of 8 in girls and 9 in boys. The prevalence is about 10 times higher in girls than in boys (Carel and Leger, 2008). The disease is mostly due to the activation of the pituitary-gonadal axis (central PP) with no identified cause. Early environmental exposure to endocrine disrupting chemicals (EDC) seems to impair sexual development and could play a causal role (Blanck *et al.*, 2000; Vasiliu *et al.*, 2004; Sharpe and Skakkebaek, 1993). Female PP incidence is suspected to have increased in some countries (US and Europe, Teilmann *et al.* 2005). Very few studies have been published on the incidence of PP at the scale of a whole country. Therefore a better knowledge on the epidemiology of PP is needed.

The objective of this study is to assess the feasibility of monitoring temporal and spatial trends of PP in France based on existing data found in medical-administrative databases.

Methods

DATA SOURCES

We collected data from two national medical-administrative databases:

1. The French Hospital Discharge Database (*Programme de médicalisation des systèmes d'information-PMSI*) which provides medical information about hospital-admitted patients in France, including discharge diagnoses encoded according to ICD-10.
2. The French national health insurance information system (*Système national d'information inter-régimes de l'Assurance maladie-Sniiram*). The Sniiram consists of several specific schemes that cover 97% of the French population (64.7 million inhabitants in 2010): the general scheme that covers all French employees (insured and beneficiaries) represents 75% of the population; farmers/agricultural workers and beneficiaries (~6%), independent occupations and beneficiaries (~5%).

The French healthcare system contains data about:

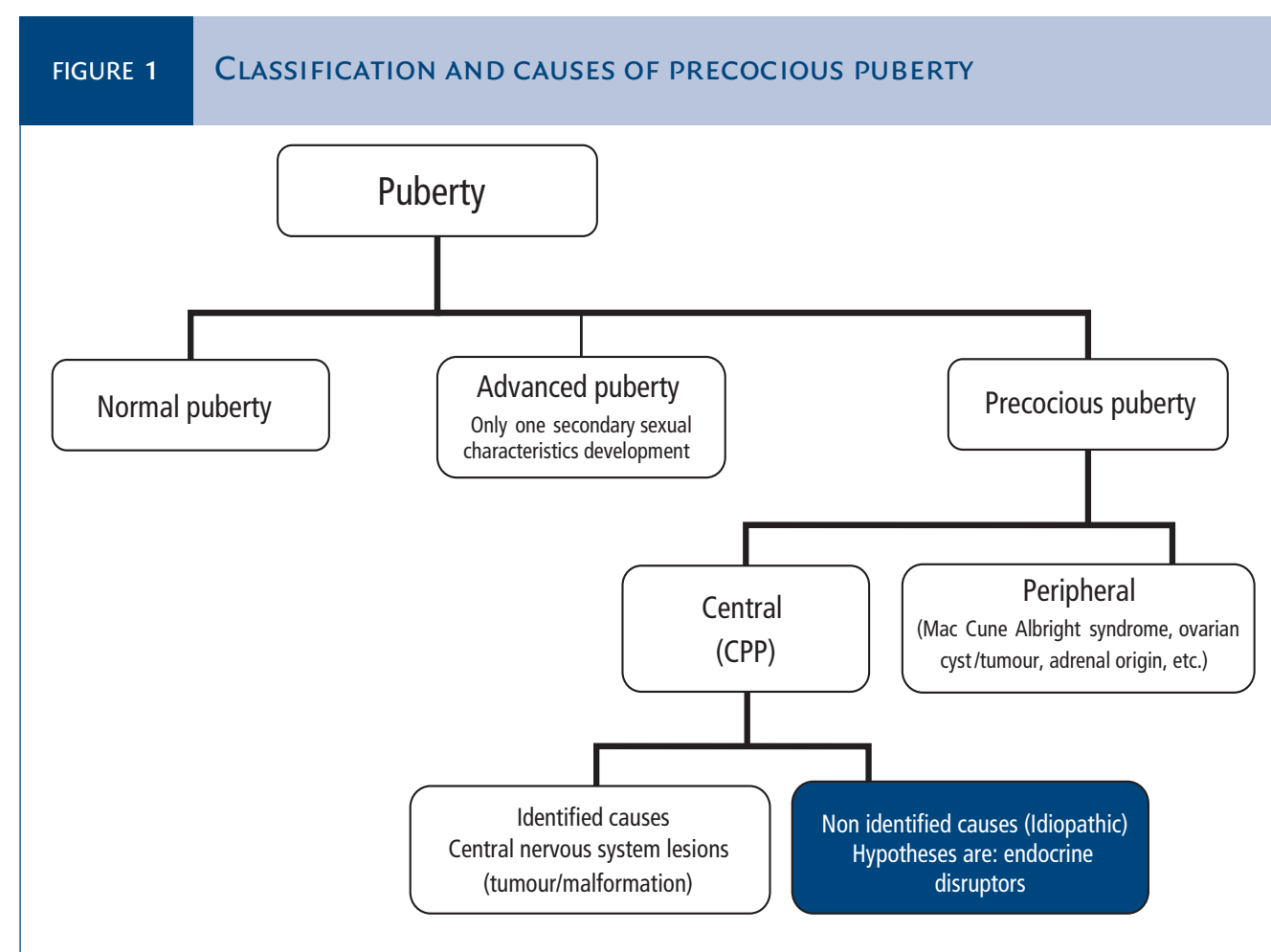
- all reimbursements for patient health expenditure, including drugs prescribed by healthcare professionals;
- patient's status with respect to full reimbursement of medical care related to a severe and costly long term disease (LTD), encoded according to ICD-10.

Data are individualized, anonymous and exhaustive. Zip codes of patients' residence are available. For farmers/agricultural workers and independent occupations, LTD data are aggregated by sex, age group and district of residence. Information from these databases can be linked provided that specific rules are respected.

EVALUATION OF PP

The diagnosis of puberty disorders in children is conducted using the Gonadotropin Releasing Hormone (GnRH) test, generally in a hospital during a one-day-care. Depending on the results of the test and other diagnosed diseases, the causes of precocious puberty can be determined (figure 1, Brauner, 2006; Carel and Leger, 2008). ICD-10 codes relating to the evaluation of this pathology are: E30.1 (Precocious puberty) or E22.8 (Other hyperfunction of pituitary gland).

- Information about suspicion of PP available from the French Hospital Discharge Database



MEDICAL MANAGEMENT OF PP

GnRH agonists are recommended in the treatment of central PP (CPP) in girls younger than 9 years old and in boys younger than 10 (Carel and Leger, 2008). The duration of the treatment is about 2-3 years.

- Information about treatment for PP available from the French healthcare system

INSURANCE MANAGEMENT OF PP

PP can be considered, if accepted by the insurance system, as a "severe and costly long-term disease (LTD)", thus entitling the patient to be fully reimbursed of the related costs. In such cases, the causes of LTD is encoded as (ICD 10) E30.1 or E22.8.

- Information about LTD for PP available from the French healthcare system

CASE DEFINITION

Children hospitalized, treated or in LTD for idiopathic central precocious puberty, before the age of 9 for girls and the age of 10 for boys, in France. PP with identified causes, as central nervous system lesions (tumour or malformation) or peripheral endocrine tumours (ovarian, testicular, or adrenal) are excluded, using ICD codes from the PMSI.

CALCULATION OF INCIDENCE

For the 3 PP management steps (evaluation, medical and insurance management), we calculated annual incidence rates as the first occurrence of the event (suspicion/treatment/LTD) reported to the total number of children in France, using the French population census data from the National Institute of Statistics and Economic Studies (Insee).

Results

TABLE	DESCRIPTION OF EACH DATA SOURCE		
	Evaluation Suspicions of PP	Medical Management Treatments for PP	Insurance Management LTDs for PP
Databases	French Hospital Discharge Database – PMSI –	French National Health Insurance Information System – SNIIRAM –	French National Health Insurance Information System – SNIIRAM –
Type of data	Medical information about patients admitted to hospital Suspicion of precocious puberty First hospitalization with diagnoses discharge encoded E301, E228 (ICD-10)	Reimbursements for patient health expenditure prescribed by healthcare professionals Idiopathic central precocious puberty First reimbursement for a GnRH agonist	Severe and costly long-term disease (LTD) Pathological precocious puberty First declaration of LTD encoded E301, E228 (ICD-10)
Study population	Girls aged 0-9 years Boys aged 0-10 years Whole of France, 2006-2011	Girls aged 0-9 years Boys aged 0-10 years Whole of France, 2011-2012	Girls aged 0-9 years Boys aged 0-10 years for salaried workers; 0-9 yrs for others French employees, 1988-2011 Agricultural occupations: Metropolitan France, 2007-11 Independent occupations: Metropolitan France, 2009-11
Zip code	✓	✓	✓ For agricultural and independent occupations, only district of residence
Social data (Universal health care coverage)	✓	✓	✓ Not for agricultural and independent occupations
Data coverage (regarding the study population)	~60%	~97%	~30% (over French employees)
Data completeness	100% of hospitalizations	100% of drug reimbursements prescribed by healthcare professionals	100% of LTDs

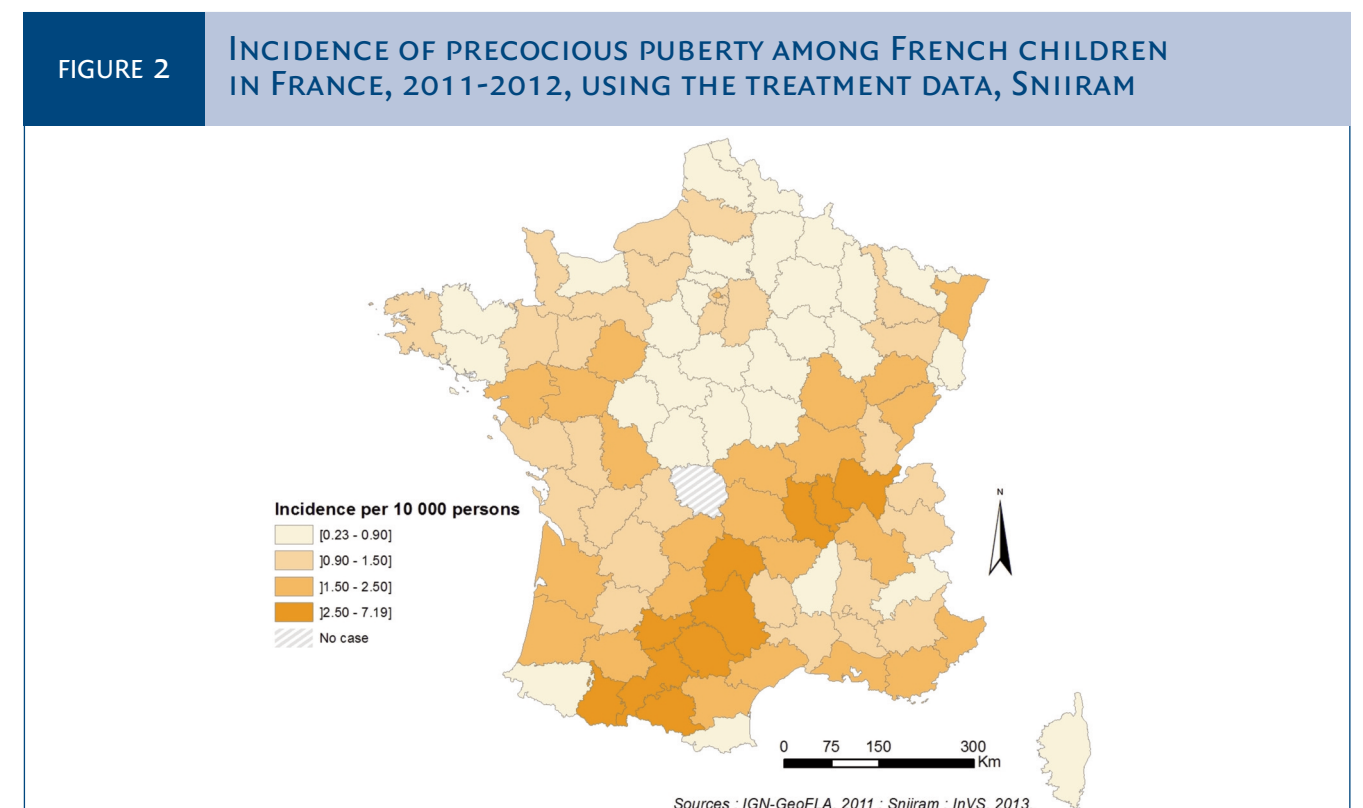
PRELIMINARY EPIDEMIOLOGICAL RESULTS

- Suspicion (2006-2011)

From 2006 to 2011, a total of 9,472 children were registered in French hospitals for a suspicion of precocious puberty. 91% were girls. During this period, the yearly number of new suspicions varied between around 1,400 (1.9/10,000) to 1,700 (2.3/10,000), whole of France.

- Treatment (2011-2012)

In 2011 and 2012, a total of 2,728 children were registered in the French national health system for a treatment of idiopathic precocious puberty. 90% were girls. The number of new cases was 1,288 (1.5/10,000) in 2011 and 1,440 (1.5/10,000) in 2012, whole of France. Spatial trends are represented on figure 2.



- LTD (1988-2011)

Around 4,000 children were registered with a LTD related to precocious puberty between 1988 and 2011. Between 2004 and 2011, data were available for only 45 districts throughout France (Metropolitan France and overseas departments). Furthermore, by linking treatment data with LTDs data, only one third of the children receiving a treatment for PP were in LTD of precocious puberty.

Conclusion

This feasibility study and the first preliminary results show that epidemiological surveillance of precocious puberty can be conducted in France based on medical-administrative databases.

- Data on treatments are the most specific, covering the largest study population (97%), and the most complete for studying spatial trends of idiopathic central precocious puberty. However, as of today, data are available over a short period of time, and are therefore not useful for studying temporal trends. Despite its specificity, the use of these treatments for other indications might occur in the future and would confound future analysis.
- Data of LTDs are specific, available over a long period, but seem to cover only one third of the target population. Thus spatial and temporal trends must be interpreted with great care due to interfering biases, such as varying coverage over space and time due to e.g. changes in practices.
- Hospitalization data are not reliable enough. On one hand, they tend to overestimate the number of cases because they trace suspicions of precocious puberty, on the other hand they can also underestimate the number of cases since evaluation is not always performed during a hospital stay.

This feasibility study needs to be complemented by other investigations, especially through a capture/recapture study with those 3 sources in order to estimate the total number of cases and assess the specificity of each source.