Incidence and spatial trends of idiopathic central precocious puberty in France: a nationwide study

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Introduction

A large number of known or suspected Endocrine Disrupting Chemicals (EDCs) are present ubiquitously in the environment and in consumer products, usually in trace amounts. Low doses exposures of the general population to some EDCs are now proven in France. Early exposure to EDCs could affect the development of reproductive functions: Idiopathic Central Precocious Puberty (ICPP) is a pathology increasingly studied for its possible causal link with EDC exposure.

The aim of this study, based on a nationwide health administrative database, was to estimate the incidence of ICPP and to analyse its spatial trends in France.

Methods

Data source

All data were provided by the DCIR (Inter-Scheme Consumption Data), a specific database included in the French National Health Insurance Information System (SNIIRAM).

DCIR contains individual, anonymous and exhaustive data on all reimbursements for patient health expenditure. It covers all those affiliated to a health insurance scheme - approximatively 98% of the French population (66 million inhabitants in 2010). Drugs are identified using their Anatomical Therapeutic Classification (ATC) codes.

Data are available for the last three and current year. An anonymous social security identification number (NIR) allows the identification of multiple health expenditure occurrences for each patient.

Population and case definition

The study population consisted of girls less than 9 years and boys less than 10 years, in metropolitan France, having a reimbursement for a Central Precocious Puberty (CPP) drug treatment, during the period 2011-2013. CPP drug treatments were identified by at least one reimbursement of Gonadotropin-Releasing Hormone (GnRH) agonist (triptorelin, leuprorelin, buserelin).

Cases with specific known causes of precocious puberty, such as central nervous system lesions (tumour or malformation) or peripheral endocrine tumours (ovarian, testicular, or adrenal) were excluded from the study to be specific of ICPP. Such cases were identified by linking drug reimbursement data with medical information from hospital data and other medication reimbursements (hydrocortisone).

Data analysis

ICPP counts per district were computed for girls, all ages and by age group]0-7],]7;8],]8;9], and boys all ages.

Spatial distribution of the cases was assessed by applying 4 different models: a simple average implying an overall homogeneity over the whole country; an unstructured heterogeneity implying true difference in rates unrelated to their neighbourhoods; a model with spatial heterogeneity implying that the rate observed in one place is influenced by the rates from its neighbourhood; and finally, a model with unstructured and spatial heterogeneity, combining the two previous models and their implications. Model choice was based on Deviance Information Criteria (DIC). National and regional incidences were predicted based on the best selected model, using the French population census data from the National Institute of Statistics and Economic Studies (Insee).

The model's results were transferred in the GIS software ArcGIS 10.0 (©ESRI) in order to chart the spatial variations of the incidence of ICCP. A map was created for each group by gender and age, using a manual classification of values.

Results

Incidence in girls

A total of 3 519 girls were identified with an ICPP from 2011 to 2013, corresponding to about 1 173 new cases in girls per year in metropolitan France. The female incidence was 2.68 per 10,000 girls under 9 years old ([95% CI 2.55, 2.81]). The incidence, and its 95% CI, by age per 10,000 girls, was 0.62 [0.57, 0.69] in the group]0-7] years old, 9.56 [8.84, 10.26] in the group]7-8] years old and 11.7 [10.89, 12.57] in the group]8-9] years old.

Incidence in boys

A total of 352 boys were identified with an ICPP, corresponding to about 117 new cases per year in metropolitan France. The male incidence was 0.24 [95% CI 0.21, 0.27] per 10,000 boys under 10 years old. There was a female predominance in the incidence of ICPP (female-to-male ratio 10:1).

Spatial distribution

For girls, all ages or by group, or boys all ages, the best model according to DIC, was a pure spatial heterogeneity. Predictive regional incidences, girls all ages, ranged from 0.95 to 12.39 per 10,000 girls (figure 1). We observed an excess of incidence from south-west (Midi-Pyrénées region) to east (Rhône-Alpes region) of France. Similar patterns were observed over the different age groups within girls (figure 2), and incidence in the Midi-Pyrénées region was especially high in the group]8-9] years old. For boys, we observed similar patterns by geographical distribution to those of girls (figure 3).

FIGURE 1 Predictive incidence rates of ICPP in French districts, girls under 9 years old. Based on medication reimbursement, 2011-2013

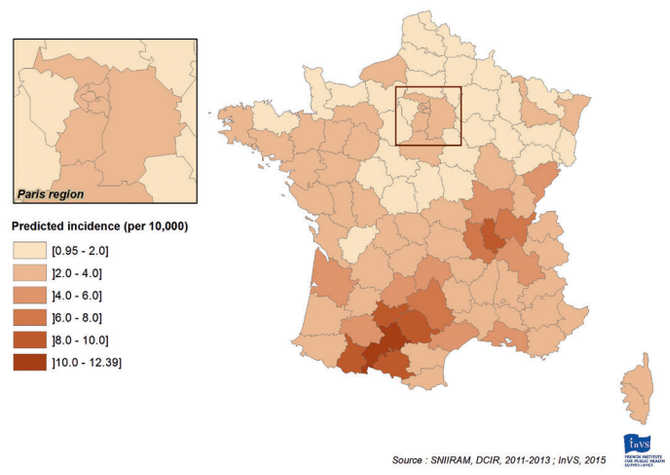


FIGURE 2 Predictive incidence rates of ICPP in French districts by age group

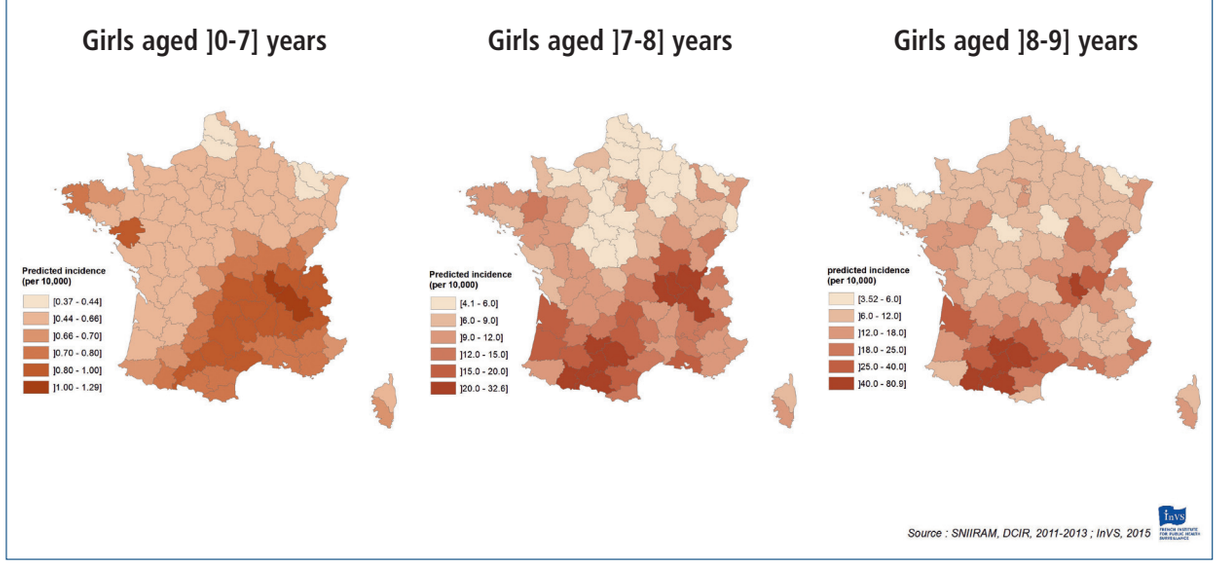
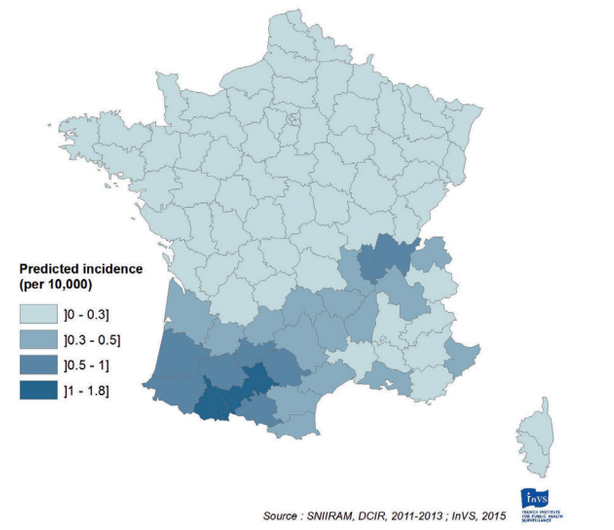


FIGURE 3 Predictive incidence rates of ICPP in French districts, boys under 10 years old. Based on medication reimbursement, 2011-2013



Conclusion

These results are based on a nationwide epidemiologic study: data collected target very specific treatments of ICPP, cover most of the study population (98%) and thus are suitable for analysing spatial trends. In a next step, access to data for a period of ten years will make spatio-temporal analysis possible over a longer period at a national level.

Our results for ICPP incidence for both gender are consistent with those previously published in Denmark [1], to our knowledge the only other country in which ICPP incidences are available at a national level.

The part of variance explained by the spatial heterogeneity related to the 3 age groups is nearly equivalent. However, this does not mean that factors explaining this heterogeneity are the same for the 3 groups. Spatial heterogeneity has to be discussed in terms of known and suspected risk factors (obesity, environmental exposures…), variations in medical practices or unknown risk factors of ICPP. Spatial heterogeneity must be further analyzed.

Reference List

[1] Teilmann G, Pedersen CB, Jensen TK, Skakkebaek NE, Juul A. Prevalence and incidence of precocious pubertal development in Denmark: an epidemiologic study based on national registries. Pediatrics 2005;116:1323-8.

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