PMSI Analysis

Epidemiology and misdiagnosis of porphyria in FRANCE: A PMSI database analysis

Report

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TABLE OF CONTENTS

1 BACKGROUND INFORMATION

1.1 Context

Alnylam is developing a new drug for the treatment of acute hepatic porphyria.

Porphyrias constitute a group of hereditary metabolic diseases characterized by intermittent neuro-visceral manifestations, cutaneous lesions or by the combination of both. We report below the ICD-10 classification for these conditions.

(E80) Disorders of porphyrin and bilirubin metabolism

- (E80.0) Hereditary erythropoietic porphyria
  - Erythropoietic protoporphyria
  - Erythropoietic porphyria, congenital
  - Gunther's disease
  - Erythropoietic porphyria
  - Erythropoietic coproporphyria
- (E80.1) Porphyria cutanea tarda
  - Sporadic porphyria cutanea tarda
  - Familial porphyria cutanea tarda
- (E80.2) Other porphyria
  - Acute intermittent porphyria
  - Hereditary coproporphyria
  - Variegate porphyria
  - Chester porphyria
  - Porphyria, hepatic
  - Pseudoporphyria
  - Toxic porphyria
  - Hepatoerythropoietic porphyria
  - Porphyria, NOS

Beside this classification, one can differentiate two categories of porphyria:

- Acute porphyrias (acute intermittent porphyria, variegate porphyria, aminolevulinic acid dehydratase deficiency porphyria and hereditary coproporphyria)
- Chronic porphyrias (congenital erythropoietic porphyria, porphyria cutanea tarda, and erythropoietic protoporphyria).

Acute porphyrias are targeted by the treatment developed by Alnylam. The ICD-10 code for this disease is E80.2. This code includes several conditions like hereditary coproporphyria, acute hepatic porphyria, hereditary coproporphyria, variegate porphyria etc. Acute hepatic porphyria can be treated with Hemine (Normosang®): this treatment is given during hospital stays by intravenous infusions.

1.2 The PMSI database

The PMSI database contains all hospital stays for one year in private and public medical establishments managing acute care (over 30 million stays in 2016).

The main available variables are: identification of medical establishment, sex and age of patient, if the patient deceased, all diagnosis (ICD X of the WHO) with a main diagnosis (reason of the hospitalisations), related diagnosis if the main diagnosis is a treatment (ex: chemotherapy) and associated diagnoses that were relevant for the management of the patient, the length of stay including the duration of the stay in intensive care units, all medical procedures (using the French CCAM classification), where the patient comes from and where he will be discharge (at home or in other medical unit). Death is known when the patient died during the stay (N = 296,090 in 2016 on 594,000 estimated deaths).

Medications and medical devices consumption that are registered on a specific formulary named "additional list of drugs" are also available. The reason is that hospitals could charge the Sickness Funds on top of the DRG for these products.

Today, the databases are available from 2009 now on. The 2017 database is le last year available, since July 2018.

Table 1 : Main variables of the MSO PMSI database

Data Element	PMSI
ICD X : main, related and secondary diagnoses	X
Medical procedures codes (CCAM)	X
Hospital (name)	X
Type of hospital (private, public, teaching status, general hospital)	X
Anonymous code of patient	X
Patient age	X
Gender	X
DRG	X
LOS (including day care hospital, less than 48 hours)	X
Patient origin (home, other hospital…)	X
Patient disposition (rehab, skilled nursing …)	X
From FINESS database	
Location of hospital	
Address	

Data Element	PMSI
Medications and medical devices	X

2 OBJECTIVES

The objectives of this analysis are to:

- Estimate the annual incidence of other porphyria (ICD10 code E80.2) for the year 2017 and a description of these patients by age and gender groups and severity stages (hospitalizations and deliveries of Normosang);
- Estimate the prevalence of other porphyria on December 31st 2017 by age and gender groups, severity stages and by geographical areas;
- Report the hospitalizations' procedures and conditions related to misdiagnoses before the diagnosis of other porphyria.

3 METHODS

3.1 Selection criteria

3.1.1 For the incidence calculation

Incident patients were defined as patients aged between 12 and 65 years old:

- With
  - at least one primary diagnosis of porphyria (ICD-10 codes: E80.2) from January 1st, 2017 until December 31st, 2017 (observation year);

    OR

  - At least one delivery of Normosang between January 1st, 2017 and December 31st, 2017;

  And

- No diagnosis of porphyria in the previous years, spanning from January 1st, 2009 until December 31st, 2016 (pre-observation years) (Figure 1).

Two sensitivity analyses were performed with the following inclusion criteria:

1. sensitivity analysis 1:

   Patients aged between 12 and 65 years old with:

   a. at least 2 diagnosis of porphyria, with at list one as a primary diagnosis from January 1st, 2017 until December 31st, 2017 (observation year);

      OR

   b. At least one delivery of Normosang between January 1st, 2017 and December 31st, 2017;

   And

No diagnosis of porphyria in the previous years, spanning from January 1st, 2009 until December 31st, 2016 (pre-observation years) (Figure 1).

2. sensitivity analysis 2:

   Patients aged between 12 and 65 years old with:

   a. at least 2 diagnosis of porphyria, coded either primary or secondary diagnosis, from January 1st, 2017 until December 31st, 2017 (observation year);

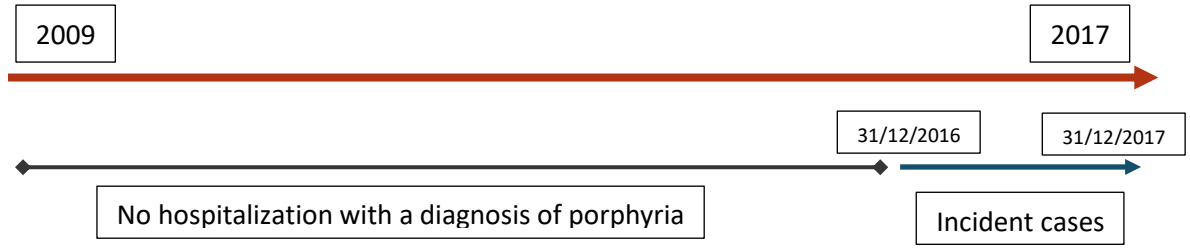
      OR

   b. At least one delivery of Normosang between January 1st, 2017 and December 31st, 2017;

   And

      No diagnosis of porphyria in the previous years, spanning from January 1st, 2009 until December 31st, 2016 (pre-observation years) (Figure 1).

Figure 1: Selection of incident porphyrias



3.1.2 For the prevalence calculation

Prevalent patients were defined as patients with at least one diagnosis of porphyria (primary diagnosis with the ICD-10 codes: E80.2 or delivery of Normosang) in the period of January 1st, 2009

Patients who deceased before December 31st 2017 were excluded from the prevalence[1].

Two sensitivity analyses were performed with the same criteria as for the incidence calculation.

3.1.3 For the hospitalizations, procedures and conditions related to misdiagnoses before the diagnosis of AHP

Two groups of patients were included for this analysis:

- Patients with acute porphyria;
- A control group of matched patients (on age, gender and year of hospitalization) not suffering from porphyria.

Acute porphyria patients

For this analysis, the population was restricted to patients who were treated with Hemine (NORMOSANG®) between 2015 and 2017 or hospitalized twice with an ICD10 code of porphyria as a main or secondary diagnosis (E80.2) between 2015 and 2017.

Incident patients were selected for the years 2015, 2016 and 2017 by excluding patients who were treated with this drug or hospitalized with an ICD10 code of porphyria as the main or secondary diagnosis (E80.2) in the preceding years (2014 and before).

Control group

A control group of patients was selected by matching them to the AHP patients on the following criteria:

- Year of hospitalization;
- Age at time of the hospitalization;
- Gender.

Patients treated with Hemine (NORMOSANG®) AND/OR who had a diagnosis of porphyria (ICD-10 code E80.2) between 2011 and 2017 were excluded from this group.

To increase the power of the comparison, 10 matched patients were selected for each AHP patient.

[1] Note that only deaths that occurred during an hospital stay are recorded in the PMSI.

3.2 Analysis

3.2.1 incidence and prevalence of porphyria

Annual incidence in 2017 and prevalence are reported in number and percentages.

Prevalent estimations are stratified by:

- Age categories (age on December 31st, 2017);
- Gender;
- Geographical French regions for prevalent patients;
- Severity of porphyria (hospitalizations and deliveries of Normosang).

Severe porphyria was defined as:

- Patients with at least one traditional hospitalization (> 1 day, i.e. at least one overnight stay) in 2017 with a primary diagnosis of E80.2 (other porphyria) AND an emergency department visit as the modality of entry in the hospital;

  Or

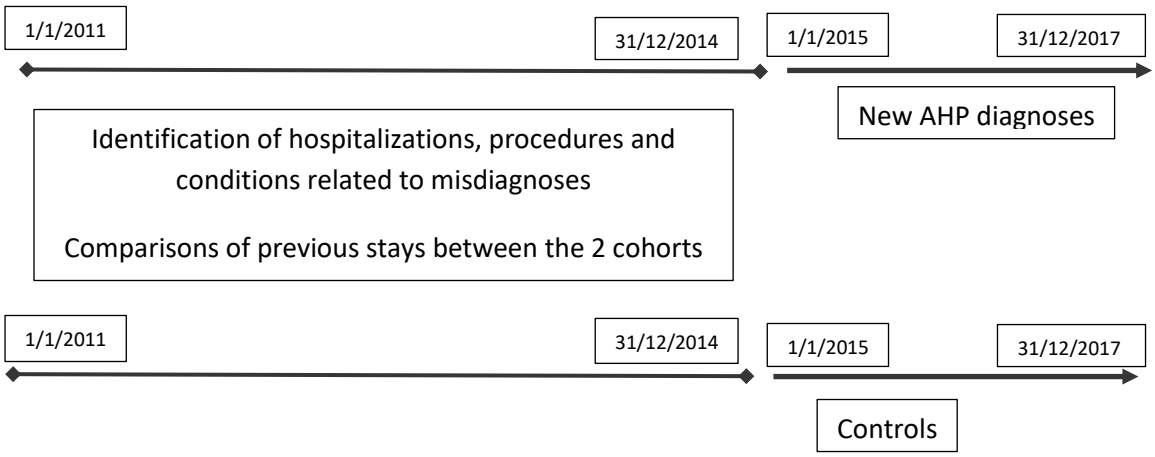
- Patients with at least one traditional hospitalization with Normosang® treatment. However, patients treated with Normosang® as a preventive treatment were identified and excluded: patients with at list 6 one-day stays per year (without overnight stay) with this drug.

3.2.2 Hospitalizations, procedures and conditions related to misdiagnoses before the diagnosis of AHP

The 2 groups of patients selected for this analysis (see chapter 3.1.3) were followed up retrospectively as 2 historical cohorts (Figure 2). The hospitalizations that occurred in the 5 years preceding 2015, 2016 and 2017 for patients respectively identified in these 2 years were examined in terms of:

1) Conditions (ICD-10 codes);
2) Procedures (French CCAM classification);
3) Disease related groups.

Figure 2: Hospitalizations, procedures and conditions related to misdiagnoses before the diagnosis of AHP



For both populations (AHP and control group), we compared the proportions of patients between diagnosed AHP patients and controls and report the p-value of these comparisons. All ICD-10 diagnoses (primary or secondary), *groupe homogènes de maladies* (Disease related groups) and procedures were compared between both categories of patients, with the odds ratio of having the code according to the group (AHP / controls) and the p-value of the comparison.

As an exploratory analysis, a classification models was built based on hospitalization data (diagnosis - ICD10 codes; procedures - French CCAM classification; Disease related groups). The main objective of this analysis was to classify patients into two groups: patients with porphyria and patients without porphyria. Through the selection procedure, we already know if the patient is a carrier of the disease and we therefore used supervised machine learning algorithms.

4 RESULTS

4.1 incidence of porphyria

On December 31st 2017, 294 patients were hospitalized at least once between 2009 and 2017 for porphyria as the primary diagnosis or with a delivery of Normosang®. Among those 294 subjects, 24 were hospitalized for the first time in 2017 with a diagnosis of porphyria or a delivery of Normosang®.

The incidence of the condition was therefore estimated as 24 for the year 2017.

As the French population was 67 million in 2017 (2), we can estimate the crude incidence of porphyria at 0.036 per 100,000 person years.

The 2 sensitivity analyses lead to the following results:

- Sensitivity analysis 1: 14 patients were identified, and the estimated prevalence is 0.021 per 100,000 per year;
- Sensitivity analysis 2: 20 patients were identified, and the estimated prevalence is 0.030 per 100,000 per year.

Table 1 report the description of the patients in terms of age and gender. Among the 24 incident patients, 25% were males and they are 35.9 years old on average. 8.3% of these patients are below 18 years old, 79.2% are between 18 and 50 years old, 11.5% between 56 and 65 years.

Table 1; Description of the incident patients (age and gender)

	Total
Incident population with porphyria	**24 (100,0%)**
Sex	
Male	6 (25,0%)
Female	18 (75,0%)
Age on December 31st 2017 (years)	
Number (response rate)	24 (100,0%)
Mean (SD)	35,9 (13,2)
Median / Min / Max	35,5 / 15,0 / 62,0
Quartile 25 / Quartile 75	25,5 / 43,5

[2] https://www.insee.fr/fr/statistiques/3305173

	Total
Age on December 31st 2017 in classes	
12-17 years	2 (8,3%)
18-25 years	4 (16,7%)
26-30 years	3 (12,5%)
31-35 years	3 (12,5%)
36-40 years	3 (12,5%)
41-45 years	4 (16,7%)
46-50 years	2 (8,3%)
56-60 years	1 (4,2%)
61-65 years	2 (8,3%)

Table 2 reports the type of hospitalizations of incident patients in 2017 in terms of severity of the disease. Among the 24 incident patients in 2017:

- 37.5 % (9) have been hospitalized through the emergency department of the hospital;
- 50% (12) had a delivery of Normosang® during their hospital stay
- 66.7% (16) were considered as severe patients, defined by either a hospitalization through the emergency department or with a Normosang® treatment.

Table 2: Description of the incident patients (severity)

	Total
Incident population with porphyria	**24 (100,0%)**
Emergency hospitalization for porphyria in 2017	
No	15 (62,5%)
Yes	9 (37,5%)
Number of hospitalizations in 2017 with delivery of Normosang	
0	12 (50,0%)
1	8 (33,3%)
2	3 (12,5%)
6	1 (4,2%)
Number of one-day hospitalizations in 2017 with delivery of Normosang	
0	23 (95,8%)
1	1 (4,2%)
Severity of the disease*	
No	8 (33,3%)

	Total
Yes	16 (66,7%)

4.2 Prevalence of porphyria

According to the flowchart reported in Figure 3, 351 subjects were hospitalized between 2009 and 2017 with a principal diagnosis of porphyria (ICD-10 codes: E80.2). Among those, 57 deceased during an hospital stay before 2017 December 31st. The prevalence of the condition was therefore estimated as 294.

As the French population was 67 million in 2017 ([3]), we can estimate the crude prevalence of porphyria at 0.44 per 100,000.

The 2 sensitivity analyses lead to the following results:

- Sensitivity analysis 1: 188 patients were identified, and the estimated prevalence is 0.28 per 100,000
- Sensitivity analysis 2: 392 patients were identified, and the estimated prevalence is 0.59 per 100,000

There are 2 main limitations to these estimates:

1) Deaths that did not occur during an hospital stay could not be identified and the true number of deaths is therefore above the result presented and the prevalence is overestimated;
2) Patients who were not hospitalized but diagnosed with porphyria and patients who were hospitalized before 2009 could not be identified, which could lead to an underestimation of the result.

[3] https://www.insee.fr/fr/statistiques/3305173

Figure 3: Selection of prevalent porphyrias

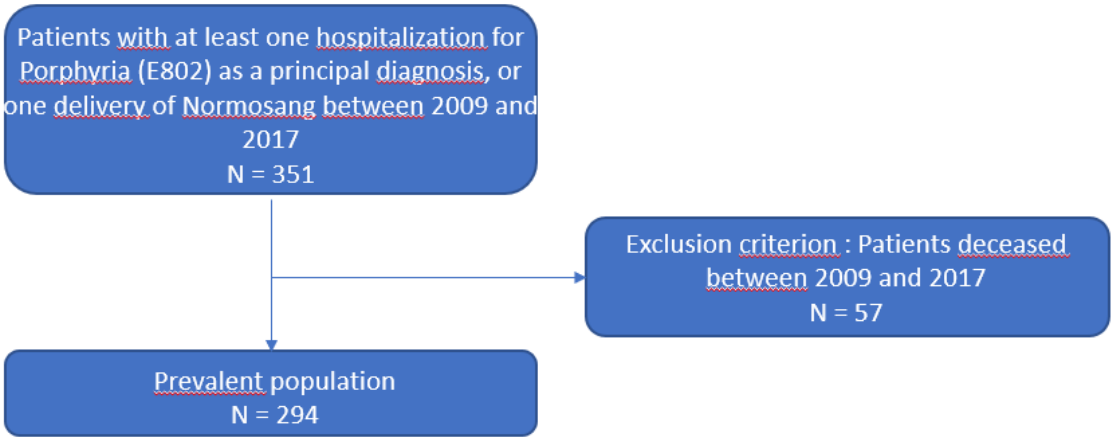


Table 3 report the description of the prevalent patients in terms of age and gender. Among the 294 prevalent patients, 67.3% were women and they are 41.5 year old on average. 3.1% of these patients are below 18 years old, 43.9% are between 18 and 49 years old and 53.1% were between 50 and 65 years old.

Table 3: Description of the prevalent patients (age and gender)

	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
Population	**294 (29,5%)**
Sex	
Male	96 (32,7%)
Female	198 (67,3%)
Age on December 31st 2017 (years)	
Effectif (taux de réponse)	294 (100,0%)
Moyenne (écart-type)	41,5 (12,6)
Médiane / Min / Max	42,0 / 13,0 / 65,0
Quartile 25 / Quartile 75	31,0 / 52,0
Age on December 31st 2017 in classes	
12-17 years	9 (3,1%)
18-25 years	25 (8,5%)
26-30 years	32 (10,9%)
31-35 years	33 (11,2%)
36-40 years	39 (13,3%)
41-45 years	40 (13,6%)

	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
46-50 years	31 (10,5%)
51-55 years	39 (13,3%)
56-60 years	26 (8,8%)
61-65 years	20 (6,8%)

Table 4 reports the repartition of the prevalent patients according to their region of residence.

Table 4: Description of the prevalent patients (region of residence)

	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
Population	**294 (29,5%)**
Most recent residence region	
Ile de France	48 (16,3%)
Auvergne-Rhône-Alpes	33 (11,2%)
Provence-Alpes-Côte-d'Azu	42 (14,3%)
Grand Est	29 (9,9%)
Occitanie	24 (8,2%)
Nouvelle Aquitaine	19 (6,5%)
Bretagne	18 (6,1%)
Pays de la Loire	14 (4,8%)
Bourgogne-Franche-Comté	20 (6,8%)
Hauts de France	13 (4,4%)
Normandie	10 (3,4%)
Centre Val de Loire	12 (4,1%)
Réunion	6 (2,0%)
Guadeloupe	3 (1,0%)
Corse	1 (0,3%)
Etranger	1 (0,3%)
Martinique	1 (0,3%)

Table 5 reports the type of hospitalizations of prevalent patients in 2017 in terms of severity of the disease. Among the 294 prevalent patients in 2017:

- 11.2% (33) have been hospitalized through the emergency department of the hospital for porphyria as a principal diagnosis in 2017 ;
- 16.0% (47) had a delivery of Normosang® during their hospital stay. About half of them (23 on 47) had 1 to 3 hospital stays and 24 had 4 to 68 hospital stays.
- 15.3% (45) were considered as severe patients, defined by either at least one emergency hospitalization for Porphyria as a principal diagnosis in 2017, or one to six hospitalizations with delivery of Normosang in 2017.

Table 5: Description of the prevalent patients (severity)

	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
Population	**294 (29,5%)**
Emergency hospitalization for porphyria as a principal diagnosis in 2017	
No	261 (88,8%)
Yes	33 (11,2%)
Number of hospitalizations in 2017 with delivery of Normosang	
0	247 (84,0%)
1	17 (5,8%)
2	5 (1,7%)
3	1 (0,3%)
4	1 (0,3%)
6	1 (0,3%)
8	1 (0,3%)
13	2 (0,7%)
15	1 (0,3%)
24	2 (0,7%)
26	1 (0,3%)
27	1 (0,3%)
28	2 (0,7%)
29	2 (0,7%)
36	1 (0,3%)
47	1 (0,3%)
48	2 (0,7%)
52	3 (1,0%)
54	1 (0,3%)
59	1 (0,3%)
68	1 (0,3%)
Number of one-day hospitalizations in 2017 with delivery of Normosang	
0	270 (91,8%)

	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
1	2 (0,7%)
6	1 (0,3%)
7	1 (0,3%)
11	1 (0,3%)
13	1 (0,3%)
17	2 (0,7%)
23	1 (0,3%)
24	1 (0,3%)
25	2 (0,7%)
26	1 (0,3%)
28	1 (0,3%)
32	1 (0,3%)
46	3 (1,0%)
52	4 (1,4%)
53	1 (0,3%)
66	1 (0,3%)
Severity of the disease (At least one emergency hospitalization for Porphyria as a principal diagnosis in 2017, or one to six hospitalizations with delivery of Normosang in 2017)	
No	249 (84,7%)
Yes	45 (15,3%)

4.3 Hospitalizations, procedures and conditions related to misdiagnoses before the diagnosis of AHP

Two groups of patients were included for this analysis:

- Patients with acute porphyria;
- A control group of matched patients (on age, gender and year of hospitalization) not suffering from porphyria.

The 2 groups of patients selected for this analysis (see chapter 3.1.3) were followed up retrospectively. The hospitalizations that occurred in the 5 years preceding 2015, 2016 and 2017 for patients respectively identified in these 2 years were examined in terms of:

1) Conditions (ICD-10 codes);
2) Procedures (French CCAM classification);
3) Disease related groups.

Acute porphyria patients

For this analysis, the population was restricted to patients who were treated with Hemine (NORMOSANG®) between 2015 and 2017 or hospitalized twice with an ICD10 code of porphyria as a main or secondary diagnosis (E80.2) between 2015 and 2017.

Incident patients were selected for the years 2015, 2016 and 2017 by excluding patients who were treated with this drug or hospitalized with an ICD10 code of porphyria as the main or secondary diagnosis (E80.2) in the preceding years (2014 and before).

These criteria leaded to the identification of 45 patients.

Control group

A control group of patients was selected by matching them to the AHP patients on the following criteria:

- Year of hospitalization;
- Age at time of the hospitalization;
- Gender.

Patients treated with Hemine (NORMOSANG®) AND/OR who had a diagnosis of porphyria (ICD-10 code E80.2) between 2011 and 2017 were excluded from this group.

To increase the power of the comparison, 10 matched patients were selected for each AHP patient and the total number of matched controls was 450.

4.3.1 Hospitalizations with conditions related to misdiagnoses before the diagnosis of AHP

According to the criteria, 45 porphyria patients have been selected and compared to 450 controls. Among these 45 porphyria patients and the 450 controls, respectively 25 and 286 controls have been hospitalized on the retrospective period.

The results of the analyses are reported in the following tables.

The columns “porphyria cases” and “controls” report the number of patients for whom at least one hospitalization with the codes was identified. We report only codes for which a significant difference is observed between porphyria patients and controls according to the odds ration (OR) confidence interval.

Table 6 reports the ICD10 conditions for which a significant difference between porphyria patients and controls was identified. For example, porphyria patients were more frequently hospitalized with the ICD10 code R10 (Abdominal and pelvic pain) than controls with an odd ratio of 3.9 (CI95% = [1,8; 8.3]).

The codes that have been identified can be categorized in 3 groups (note that the 2 later concern very small number of patients):

- Codes related to symptoms or syndromes:
  - Abdominal and pelvic pain
  - Other disorders of fluid, electrolyte and acid–base balance
  - Headache
  - Malaise and fatigue
  - Pain, not elsewhere classified
  - Other disorders of amniotic fluid and membranes
  - Retention of urine
  - Anaemia in chronic diseases classified elsewhere (excluding these diseases: erythroblastopenia (D60), Other aplastic anaemias (D61), Acute posthaemorrhagic anaemia)
- Codes related to factors influencing health status and contact with health services:
  - Persons encountering health services for other counselling and medical advice (excluding sexual attitude, lifestyle, life-management difficulty, care-provider dependency and medical facilities and other health care);
  - Problems related to care-provider dependency.
- Codes related to Pregnancy, childbirth and the puerperium
  - Maternal care for other known or suspected foetal problems;
  - Other disorders of amniotic fluid and membranes

Finally we did not identify specific diseases which would be more frequently reported for porphyria patients but rather codes related to symptoms / syndromes and codes related to factors influencing health status.

Table 6: Significant main or secondary diagnosis identified during hospitalizations that occurred before 2015 (only diseases with a significant Odds ratio are reported)

ICD10 code	ICD 10 label	Porphyria cases	Controls	OR	95% Confidence interval	
					IC inf	IC sup
R10	Abdominal and pelvic pain	9	27	3,917	1,840	8,3
E87	Other disorders of fluid, electrolyte and acid–base balance	5	4	13,938	3,741	51,9
R51	Headache	4	5	8,683	2,330	32,4
R53	Malaise and fatigue	4	6	7,220	2,036	25,6

Z71	Persons encountering health services for other counselling and medical advice, not elsewhere classified.	4	13	3,280	1,069	10,1
O36	Maternal care for other known or suspected fetal problems	3	5	6,357	1,518	26,6
O41	Other disorders of amniotic fluid and membranes	2	1	20,884	1,893	230,4
R52	Pain, not elsewhere classified	3	4	7,964	1,782	35,6
R33	Retention of urine	2	2	10,419	1,467	74,0
Z74	Problems related to care-provider dependency.	2	2	10,419	1,467	74,0
D63	Anaemia in chronic diseases classified elsewhere*	2	3	6,930	1,157	41,5

* excluding these diseases: erythroblastopenia (D60), Other aplastic anaemias (D61), Acute posthaemorrhagic anaemia (D62)

4.3.2 Hospitalizations with procedures more frequently performed before the diagnosis of AHP

Table 7 reports the procedures that have been identified during the previous hospitalizations before the first diagnosis of porphyria.

The most frequent procedure was an electrocardiogram with 11 porphyria patients having this procedure, compared to 47 controls (OR=2.8 (CI95%=[1.4; 5.4]).

Other most frequent procedures that were significantly more frequent among porphyria patients were radiological exams (mammography, Chest X-ray, ultrasound of the abdomen, X-ray of abdomen and CT scan of the abdomen and small pelvis).

Other procedures concerned less than 3 patients.

Table 7: Significant procedures identified during hospitalizations that occurred before 2015 (only procedures with a significant Odds ratio are reported)

code	procedure	Porphyria cases	Controls	OR	95% Confidence interval	
					IC inf	IC sup
DEQP003	electrocardiogram	11	47	2,774	1,437	5,4
YYYY600	Supplement for digital archiving of a mammogram or a CT or remnographic examination	7	33	2,328	1,029	5,3
ZBQK002	Chest X-ray	7	33	2,328	1,029	5,3
ZCQM008	Transcutaneous ultrasound of the abdomen	5	9	6,125	2,051	18,3
ZCQK002	X-ray of abdomen without preparation	5	10	5,500	1,879	16,1

ZCQH001	CT scan of the abdomen and small pelvis [pelvis], with intravenous injection of contrast material	5	15	3,625	1,317	10,0
AHQP009	Measurement of motor conduction velocities and the amplitude of muscular responses of 5 or more nerves, with study of proximal conduction on at least 4 nerves.	2	1	20,884	1,893	230,4
AHQP012	Measurement of sensory conduction velocities and sensory potential amplitude of 5 or more nerves	2	1	20,884	1,893	230,4
YYYY300	Imaging supplement for interventional radiology performed in the operating room	2	2	10,419	1,467	74,0
JAQM003	Unilateral or bilateral transcutaneous ultrasound of kidney and lumbar region	2	3	6,930	1,157	41,5
JQQJ037	Measurement of the length of the cervical canal of the uterine cervix by vaginal ultrasound	2	3	6,930	1,157	41,5

4.3.3 Hospitalizations with disease related groups more frequently performed before the diagnosis of AHP

Table 8 reports similar results but related to disease related groups (DRGs).

The DRGs for which a significant higher number of patients with porphyria were hospitalized are mostly related to symptoms and general conditions.

Table 8: Significant disease related groups (DRG) identified during hospitalizations that occurred before 2015 (only DRG with a significant Odds ratio are reported)

code	DRG	Porphyria cases	Controls	OR	95% Confidence interval	
					IC inf	IC sup
06M12	Abdominal pain	6	7	9,736	3,270	29,0
10M16	Metabolic disorders	2	1	20,884	1,893	230,4
23M06	Other Factors Affecting Health Status	2	2	10,419	1,467	74,0
01M22	Migraines and headaches	3	6	5,286	1,321	21,1

4.3.4 Utilization of a classification model

The 45 selected patients with acute porphyria were matched with 450 patients based on age, gender, and year of hospitalization. 1506 variables were used, including 689 medical acts (CCAM codes), 553 diagnoses (ICD-10 codes) and 264 homogenous groups of patients (GHM codes).

The random forest method creates random trees to assign patients to a group based on the hospitalization data described before, while trying to minimize the group assignment error. With such imbalanced groups, the algorithm tends to assign every patient to the control group. It was therefore necessary to use an over-sampling method. The Synthetic Minority Over-sampling Technique (SMOTE) was used. It is an over-sampling method which combines the data of random patients from the acute porphyria group with their most similar patients, to create new data: 180 additional patients were created. The random forest analysis was performed on the new sample.

This type of analysis consists in creating various decision trees (1000 in this case), using for each tree a random sampling of the population and the predictors. Then, each observation is assigned to a category (patient or control) based on majoritarian voting from all the trees created.

15% of patients were wrongly assigned to the control group (false negatives) and 4% of the controls were assigned to the acute porphyria group (false positives), with a final out-of-basket error of 8.4%.

The variables used in the analysis were ordered based on their importance for assigning observations to a group (based on Gini importance, or Mean Decrease Impurity). The 10 most important variables are shown in Table 9.

The codes that have been identified are similar to the codes identified in the other analyses, with a greater importance of codes related to pregnancy.

Table 9: 10 most important variables used by the random forests model to assign patients and control to a group.

	Category	Code	Label	Mean decrease in Gini
1	CCAM	JNJP001	Evacuation of a pregnant uterus with medication in the 1st trimester of pregnancy	8.30
2	CIM10	O04	Medical Abortion	7.54
3	GHM	14Z08	Voluntary termination of pregnancy	6.35
4	GHM	01M12	Other nervous system disorders	5.18
5	CIM10	O41	Other amniotic fluid and membrane abnormalities	5.00
6	GHM	06M12	Abdominal pain	4.60
7	CIM10	G93	Other brain conditions	4.44
8	CIM10	Z64	Difficulties related to certain psychosocial situations	4.04
9	GHM	05M16	Coronary atherosclerosis	3.77
10	CIM10	E78	Abnormalities in the metabolism of lipoproteins and other lipidemias	3.75

5 DISCUSSION

Based on the ICD-10 codes that we used, the incidence of porphyria was estimated at 24 patients in 2017, i.e. 0.036 per 100,000 person years (0.021 or 0.030 per 100,000 according to sensitivity analyses.

In 2012, the European Porphyria Network published an article on the result of a study on the epidemiology of inherited porphyria. They collected information prospectively over a 3 year period (2007 to 2009) about the number of newly diagnosed symptomatic patients with an inherited porphyria (335 patients from 11 countries). Prevalence was calculated from the incidence and mean disease duration.

In France, the authors estimated the incidence on a 3 years period at:

- 22 patients for acute intermittent porphyria (0.012 per 100,000 person years);
- 2 patients for hereditary coproporphyria;
- 23 patients for variegate porphyria (0.012 per 100,000 person years).

These estimates are slightly lower than ours if we only consider these 3 diseases. However, the ICD-10 odes that we used include other diseases which would have increased the total incidence for these diseases.

In the same study the authors estimated the prevalence of these diseases at:

- 0.55 per 100,000 for acute intermittent porphyria;
- 0.48 per 100,000 for variegate porphyria.

These estimates are higher than our findings. However, our findings were based on cases that were hospitalized and would then represent more severe cases.

6 ANNEXE – LISTING OF TABLES

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
Population	**392 (39,4%)**	**188 (18,9%)**	**121 (12,2%)**	**294 (29,5%)**
Sex				
Male	140 (35,7%)	40 (21,3%)	22 (18,2%)	96 (32,7%)
Female	252 (64,3%)	148 (78,7%)	99 (81,8%)	198 (67,3%)
Age on December 31st 2017 (years)				
Effectif (taux de réponse)	392 (100,0%)	188 (100,0%)	121 (100,0%)	294 (100,0%)
Moyenne (écart-type)	46,5 (12,7)	41,7 (12,1)	42,5 (11,7)	41,5 (12,6)
Médiane / Min / Max	48,0 / 15,0 / 65,0	42,0 / 15,0 / 65,0	42,0 / 15,0 / 65,0	42,0 / 13,0 / 65,0
Quartile 25 / Quartile 75	36,5 / 57,0	32,0 / 51,0	33,0 / 52,0	31,0 / 52,0
Age on December 31st 2017 in classes				
12-17 years	7 (1,8%)	4 (2,1%)	1 (0,8%)	9 (3,1%)
18-25 years	19 (4,8%)	14 (7,4%)	8 (6,6%)	25 (8,5%)
26-30 years	29 (7,4%)	21 (11,2%)	12 (9,9%)	32 (10,9%)
31-35 years	35 (8,9%)	21 (11,2%)	15 (12,4%)	33 (11,2%)

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
36-40 years	37 (9,4%)	29 (15,4%)	19 (15,7%)	39 (13,3%)
41-45 years	39 (9,9%)	30 (16,0%)	19 (15,7%)	40 (13,6%)
46-50 years	46 (11,7%)	18 (9,6%)	14 (11,6%)	31 (10,5%)
51-55 years	65 (16,6%)	23 (12,2%)	14 (11,6%)	39 (13,3%)
56-60 years	59 (15,1%)	13 (6,9%)	10 (8,3%)	26 (8,8%)
61-65 years	56 (14,3%)	15 (8,0%)	9 (7,4%)	20 (6,8%)
Most recent residence region				
Ile de France	65 (16,6%)	38 (20,2%)	29 (24,0%)	48 (16,3%)
Auvergne-Rhône-Alpes	48 (12,2%)	24 (12,8%)	18 (14,9%)	33 (11,2%)
Provence-Alpes-Côte-d'Azu	36 (9,2%)	25 (13,3%)	10 (8,3%)	42 (14,3%)
Grand Est	38 (9,7%)	15 (8,0%)	8 (6,6%)	29 (9,9%)
Occitanie	31 (7,9%)	16 (8,5%)	10 (8,3%)	24 (8,2%)
Nouvelle Aquitaine	37 (9,4%)	10 (5,3%)	4 (3,3%)	19 (6,5%)
Bretagne	23 (5,9%)	13 (6,9%)	11 (9,1%)	18 (6,1%)
Pays de la Loire	24 (6,1%)	11 (5,9%)	7 (5,8%)	14 (4,8%)
Bourgogne-Franche-Comté	19 (4,8%)	9 (4,8%)	5 (4,1%)	20 (6,8%)
Hauts de France	24 (6,1%)	8 (4,3%)	5 (4,1%)	13 (4,4%)
Normandie	21 (5,4%)	8 (4,3%)	6 (5,0%)	10 (3,4%)
Centre Val de Loire	16 (4,1%)	5 (2,7%)	3 (2,5%)	12 (4,1%)

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
Réunion	4 (1,0%)	2 (1,1%)	1 (0,8%)	6 (2,0%)
Guadeloupe	2 (0,5%)	2 (1,1%)	2 (1,7%)	3 (1,0%)
Corse	2 (0,5%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
Etranger	2 (0,5%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
Martinique	- -	- -	- -	1 (0,3%)
Year of first hospitalization with porphyria or delivery or Normosang				
2009	99 (25,3%)	56 (29,8%)	41 (33,9%)	69 (23,5%)
2010	63 (16,1%)	31 (16,5%)	18 (14,9%)	39 (13,3%)
2011	54 (13,8%)	16 (8,5%)	8 (6,6%)	30 (10,2%)
2012	38 (9,7%)	16 (8,5%)	9 (7,4%)	26 (8,8%)
2013	32 (8,2%)	14 (7,4%)	7 (5,8%)	21 (7,1%)
2014	29 (7,4%)	10 (5,3%)	6 (5,0%)	25 (8,5%)
2015	32 (8,2%)	19 (10,1%)	11 (9,1%)	38 (12,9%)
2016	25 (6,4%)	12 (6,4%)	9 (7,4%)	22 (7,5%)
2017	20 (5,1%)	14 (7,4%)	12 (9,9%)	24 (8,2%)
Severity of the disease (At least one emergency hospitalization for Porphyria as a principal diagnosis in 2017, or one to six hospitalizations with delivery of Normosang in 2017)				
No	351 (89,5%)	147 (78,2%)	84 (69,4%)	249 (84,7%)
Yes	41 (10,5%)	41 (21,8%)	37 (30,6%)	45 (15,3%)

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017

Analyses réalisées par Clément TEISSIER Cemka Eval le 07FEB2020

Etude 2018-295 : Porphyria

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
Population	**392 (39,4%)**	**188 (18,9%)**	**121 (12,2%)**	**294 (29,5%)**
Emergency hospitalization for porphyria as a principal diagnosis in 2017				
No	363 (92,6%)	159 (84,6%)	96 (79,3%)	261 (88,8%)
Yes	29 (7,4%)	29 (15,4%)	25 (20,7%)	33 (11,2%)
Number of hospitalizations in 2017 with delivery of Normosang				
0	345 (88,0%)	141 (75,0%)	74 (61,2%)	247 (84,0%)
1	17 (4,3%)	17 (9,0%)	17 (14,0%)	17 (5,8%)
2	5 (1,3%)	5 (2,7%)	5 (4,1%)	5 (1,7%)
3	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
4	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
6	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
8	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
13	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
15	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
24	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
26	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
27	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
28	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
29	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
36	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
47	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
48	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
52	3 (0,8%)	3 (1,6%)	3 (2,5%)	3 (1,0%)
54	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
59	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
68	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
Number of one-day hospitalizations in 2017 with delivery of Normosang				
0	368 (93,9%)	164 (87,2%)	97 (80,2%)	270 (91,8%)
1	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
6	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
7	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
11	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
13	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
17	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
23	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
24	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
25	2 (0,5%)	2 (1,1%)	2 (1,7%)	2 (0,7%)
26	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
28	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
32	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
46	3 (0,8%)	3 (1,6%)	3 (2,5%)	3 (1,0%)
52	4 (1,0%)	4 (2,1%)	4 (3,3%)	4 (1,4%)
53	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
66	1 (0,3%)	1 (0,5%)	1 (0,8%)	1 (0,3%)
At least one hospitalization in 2017				
No	201 (51,3%)	86 (45,7%)	52 (43,0%)	150 (51,0%)
Yes	191 (48,7%)	102 (54,3%)	69 (57,0%)	144 (49,0%)
At least one hospitalization in 2017 with delivery of Normosang				
No	345 (88,0%)	141 (75,0%)	74 (61,2%)	247 (84,0%)
Yes	47 (12,0%)	47 (25,0%)	47 (38,8%)	47 (16,0%)
At least one hospitalization in 2016 with delivery of Normosang				
No	360 (91,8%)	156 (83,0%)	89 (73,6%)	262 (89,1%)
Yes	32 (8,2%)	32 (17,0%)	32 (26,4%)	32 (10,9%)
At least one hospitalization in 2015 with delivery of Normosang				
No	353 (90,1%)	149 (79,3%)	82 (67,8%)	255 (86,7%)
Yes	39 (9,9%)	39 (20,7%)	39 (32,2%)	39 (13,3%)
At least one hospitalization in 2014 with delivery of Normosang				

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
No	361 (92,1%)	157 (83,5%)	90 (74,4%)	263 (89,5%)
Yes	31 (7,9%)	31 (16,5%)	31 (25,6%)	31 (10,5%)
At least one hospitalization in 2013 with delivery of Normosang				
No	359 (91,6%)	155 (82,4%)	88 (72,7%)	261 (88,8%)
Yes	33 (8,4%)	33 (17,6%)	33 (27,3%)	33 (11,2%)
At least one hospitalization in 2012 with delivery of Normosang				
No	352 (89,8%)	148 (78,7%)	81 (66,9%)	254 (86,4%)
Yes	40 (10,2%)	40 (21,3%)	40 (33,1%)	40 (13,6%)
At least one hospitalization in 2011 with delivery of Normosang				
No	353 (90,1%)	149 (79,3%)	82 (67,8%)	255 (86,7%)
Yes	39 (9,9%)	39 (20,7%)	39 (32,2%)	39 (13,3%)
At least one hospitalization in 2010 with delivery of Normosang				
No	363 (92,6%)	159 (84,6%)	92 (76,0%)	265 (90,1%)
Yes	29 (7,4%)	29 (15,4%)	29 (24,0%)	29 (9,9%)
At least one hospitalization in 2009 with delivery of Normosang				
No	352 (89,8%)	148 (78,7%)	81 (66,9%)	254 (86,4%)
Yes	40 (10,2%)	40 (21,3%)	40 (33,1%)	40 (13,6%)
At least one hospitalization bewteen 2009 and 2017 with delivery of Normosang				

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang	Patients with at least 2 hospitalizations for porphyria, including 1 as principal diagnosis, or delivery of Normosang from 2009 to 2017	Patients with a delivery of Normosang between 2009 and 2017	Patients with at leat 1 hospitalisation for porphyria as principal diagnosis, or delivery of Normosang from 2009 to 2017
No	271 (69,1%)	67 (35,6%)	- -	173 (58,8%)
Yes	121 (30,9%)	121 (64,4%)	121 (100,0%)	121 (41,2%)

Analyses réalisées par Clément TEISSIER Cemka Eval le 07FEB2020

Etude 2018-295 : Porphyria

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang
Population	**392 (100,0%)**
Number of years with hospitalizations with E802 diagnosis or delivery of Normosang	
1	123 (31,4%)
2	152 (38,8%)
3	57 (14,5%)
4	15 (3,8%)
5	9 (2,3%)
6	9 (2,3%)
7	6 (1,5%)
8	4 (1,0%)
9	17 (4,3%)
Years with hospitalizations with E802 diagnosis or delivery of Normosang	
2009	20 (5,1%)
2009 2010	9 (2,3%)
2009 2010 2011	1 (0,3%)
2009 2010 2011 2012	1 (0,3%)
2009 2010 2011 2012 2013	1 (0,3%)
2009 2010 2011 2012 2013 2014	1 (0,3%)
2009 2010 2011 2012 2013 2014 2015	1 (0,3%)
2009 2010 2011 2012 2013 2014 2015 2016 2017	17 (4,3%)
2009 2010 2011 2012 2013 2014 2015 2017	1 (0,3%)
2009 2010 2011 2012 2013 2014 2016	1 (0,3%)
2009 2010 2011 2012 2013 2014 2017	1 (0,3%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang
2009 2010 2011 2012 2014 2017	1 (0,3%)
2009 2010 2011 2013	2 (0,5%)
2009 2010 2011 2013 2014 2015 2016 2017	1 (0,3%)
2009 2010 2011 2014 2015 2016	1 (0,3%)
2009 2010 2011 2014 2016	1 (0,3%)
2009 2010 2011 2015	1 (0,3%)
2009 2010 2012	2 (0,5%)
2009 2010 2012 2013	1 (0,3%)
2009 2010 2014 2015 2016	1 (0,3%)
2009 2010 2014 2016 2017	1 (0,3%)
2009 2010 2015	1 (0,3%)
2009 2011	6 (1,5%)
2009 2011 2012	3 (0,8%)
2009 2011 2012 2013 2014 2015 2016 2017	1 (0,3%)
2009 2011 2014	1 (0,3%)
2009 2011 2014 2017	1 (0,3%)
2009 2012	4 (1,0%)
2009 2012 2013	1 (0,3%)
2009 2012 2014	1 (0,3%)
2009 2013	5 (1,3%)
2009 2013 2015	1 (0,3%)
2009 2013 2017	1 (0,3%)
2009 2014	1 (0,3%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang
2009 2014 2016	1 (0,3%)
2009 2015	2 (0,5%)
2009 2016	4 (1,0%)
2009 2017	2 (0,5%)
2010	11 (2,8%)
2010 2011	16 (4,1%)
2010 2011 2012	3 (0,8%)
2010 2011 2012 2013 2014	1 (0,3%)
2010 2011 2012 2013 2014 2015 2016 2017	1 (0,3%)
2010 2011 2012 2013 2014 2016	2 (0,5%)
2010 2011 2012 2013 2015	1 (0,3%)
2010 2011 2012 2014	1 (0,3%)
2010 2011 2012 2017	1 (0,3%)
2010 2011 2013	1 (0,3%)
2010 2011 2013 2014 2015 2017	1 (0,3%)
2010 2011 2014	1 (0,3%)
2010 2011 2014 2015 2016 2017	1 (0,3%)
2010 2011 2014 2016	1 (0,3%)
2010 2011 2015 2017	1 (0,3%)
2010 2011 2016	1 (0,3%)
2010 2012	5 (1,3%)
2010 2012 2013 2014 2015 2016 2017	1 (0,3%)
2010 2012 2013 2015 2016 2017	1 (0,3%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang
2010 2012 2016	1 (0,3%)
2010 2013	1 (0,3%)
2010 2014	2 (0,5%)
2010 2014 2016	1 (0,3%)
2010 2015	3 (0,8%)
2010 2016	2 (0,5%)
2010 2016 2017	1 (0,3%)
2011	15 (3,8%)
2011 2012	12 (3,1%)
2011 2012 2013	3 (0,8%)
2011 2012 2013 2014 2015 2016 2017	2 (0,5%)
2011 2012 2013 2015 2016	1 (0,3%)
2011 2012 2014	1 (0,3%)
2011 2012 2016	2 (0,5%)
2011 2012 2017	1 (0,3%)
2011 2013	2 (0,5%)
2011 2013 2015	1 (0,3%)
2011 2013 2016	2 (0,5%)
2011 2014	4 (1,0%)
2011 2014 2015	2 (0,5%)
2011 2014 2015 2016	1 (0,3%)
2011 2014 2016	1 (0,3%)
2011 2015	4 (1,0%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang
2011 2015 2016	1 (0,3%)
2011 2016	1 (0,3%)
2011 2017	1 (0,3%)
2012	9 (2,3%)
2012 2013	4 (1,0%)
2012 2013 2014	2 (0,5%)
2012 2013 2014 2015 2016	1 (0,3%)
2012 2013 2014 2015 2016 2017	1 (0,3%)
2012 2013 2015	1 (0,3%)
2012 2013 2016	1 (0,3%)
2012 2014	1 (0,3%)
2012 2014 2015	1 (0,3%)
2012 2014 2016	2 (0,5%)
2012 2015	3 (0,8%)
2012 2015 2016	1 (0,3%)
2012 2015 2017	2 (0,5%)
2012 2016	3 (0,8%)
2012 2016 2017	1 (0,3%)
2012 2017	3 (0,8%)
2013	8 (2,0%)
2013 2014	7 (1,8%)
2013 2014 2015	1 (0,3%)
2013 2014 2015 2016	1 (0,3%)

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang
2013 2014 2015 2016 2017	1 (0,3%)
2013 2014 2015 2017	1 (0,3%)
2013 2014 2017	1 (0,3%)
2013 2015	3 (0,8%)
2013 2015 2017	1 (0,3%)
2013 2016	4 (1,0%)
2013 2017	3 (0,8%)
2014	11 (2,8%)
2014 2015	5 (1,3%)
2014 2015 2016	4 (1,0%)
2014 2015 2016 2017	2 (0,5%)
2014 2016	1 (0,3%)
2014 2017	5 (1,3%)
2015	18 (4,6%)
2015 2016	8 (2,0%)
2015 2016 2017	3 (0,8%)
2015 2017	2 (0,5%)
2016	11 (2,8%)
2016 2017	14 (3,6%)
2017	20 (5,1%)

Analyses réalisées par Clément TEISSIER Cemka Eval le 07FEB2020

Table 2 : Hospitalizations

	Patients with at least 2 hospitalizations for porphyria or delivery or Normosang

Etude 2018-295 : Porphyria