Réseau FranceCoag

INSTITUT DE VEILLE SANITAIRE

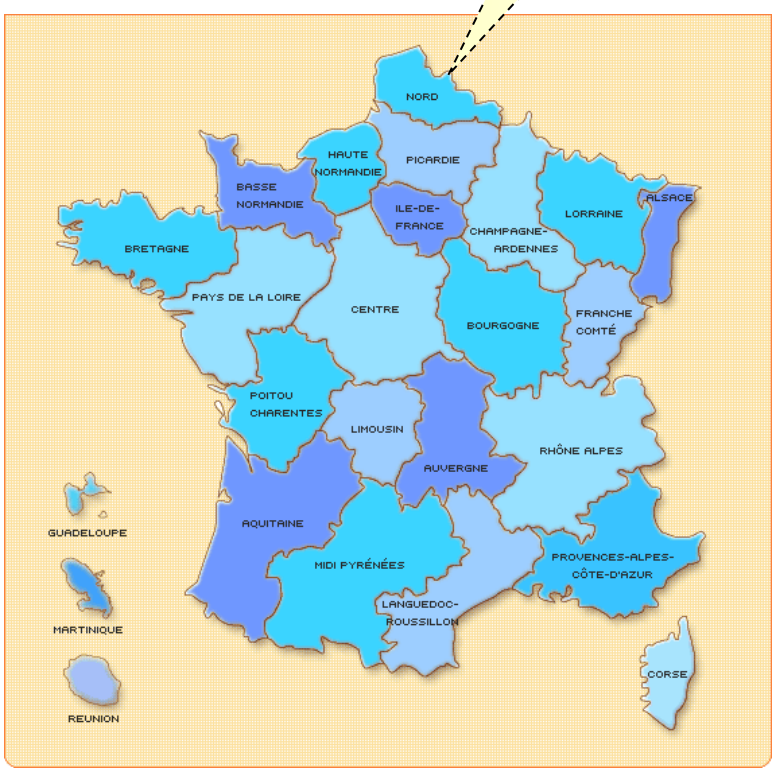
FranceCoag Network

General Background from France

General background in France
Organization - Demography

- 26 administrative regions including 4 oversea regions
- 800 000 births/y (2.01/inh)
- Origin of the population
  - Majority European Caucasian
  - Oversea territories (Caraibean Islands, Indian and Southern Pacific Islands)
  - Multi-ethnic immigration (Maghreb, subsaharian Africa, eastern Asia…)

65 M inhabitants



General background in France
Healthcare System in France

- Several Public Agencies depending on the Ministry of Health
  - Organisation of care supply (DGOS)
  - Drugs regulation and surveillance (ANSM)
  - Public Health Surveillance (InVS)
- Public insurance system with private part
- No restriction for costly care so far thanks to complete reimbursement of drugs and other medical costs in the most costly diseases (long-lasting, serious, rare …)
- National Plans for Rare Diseases leading to the identification of reference centres and networking activities

CR Hémophilie
Centre de Référence et autres déficits hémorragiques constitutionnels

CRMW

1st National plan for rare diseases (2005-2008)

Reference centers have been qualified for Haemophilia & VWD

Haemophilia (H) and Rare Bleeding Disorders (RBD), partnership of 6 centres, coordination in LYON (C Négrier)

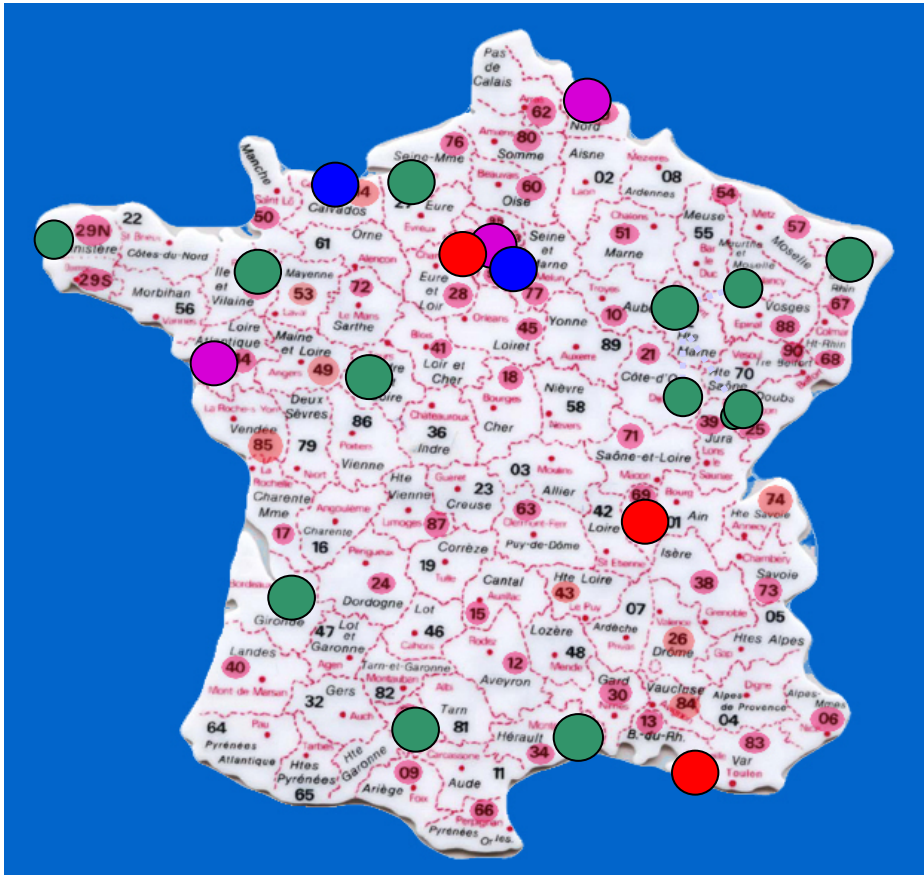
VWD, partnership of 5 centres, coordination in Paris & Lille (A Veyradier, J Goudemand)

Centres for both

Centres associated to the reference centres

The other centres remained secondary centres to maintain the whole network of 36 centres

The association of patients is a partner



Association française des hémophiles

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Design of FranceCoag Network

French Cohort and Registry

History of the French Cohort

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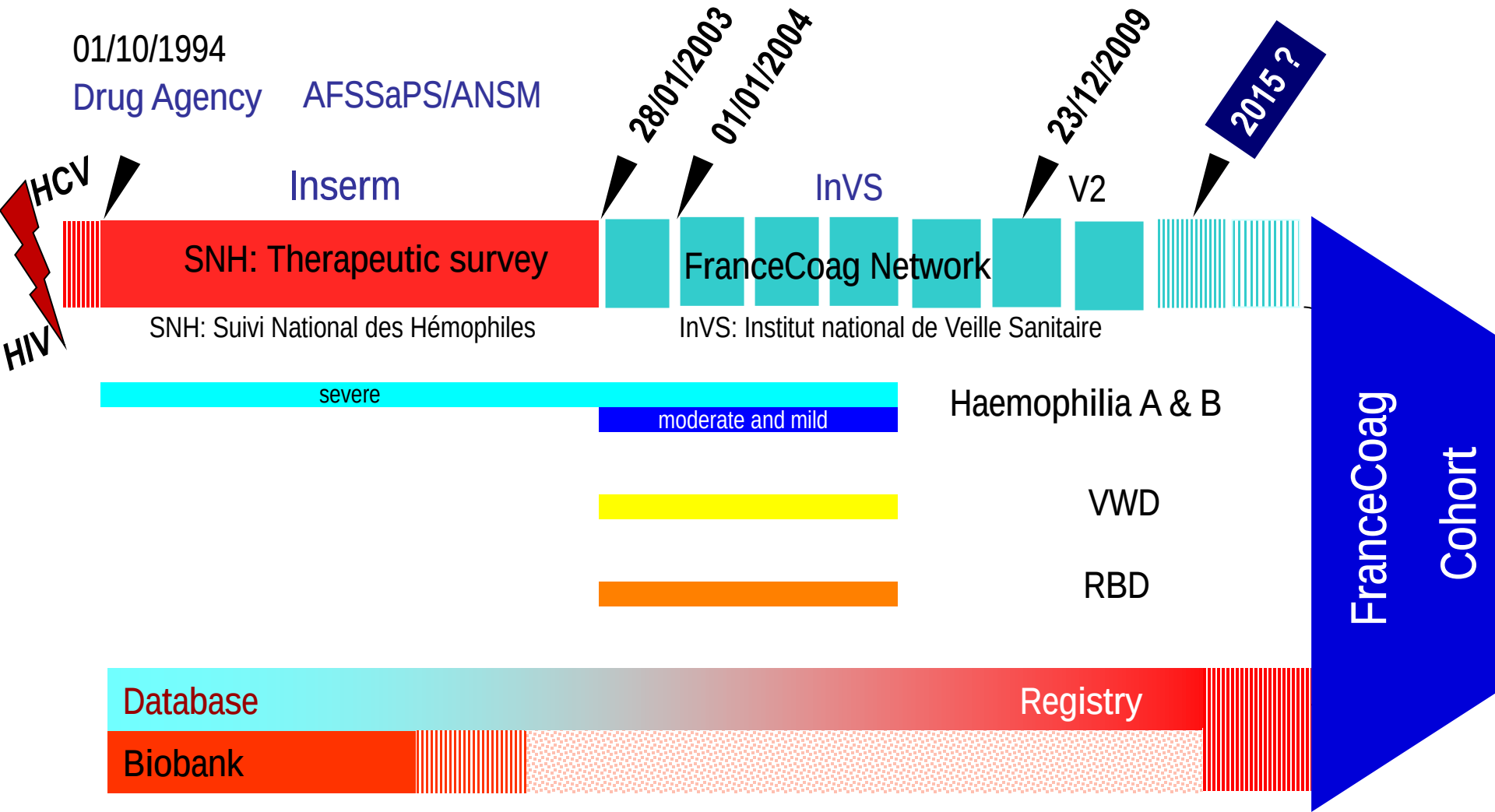
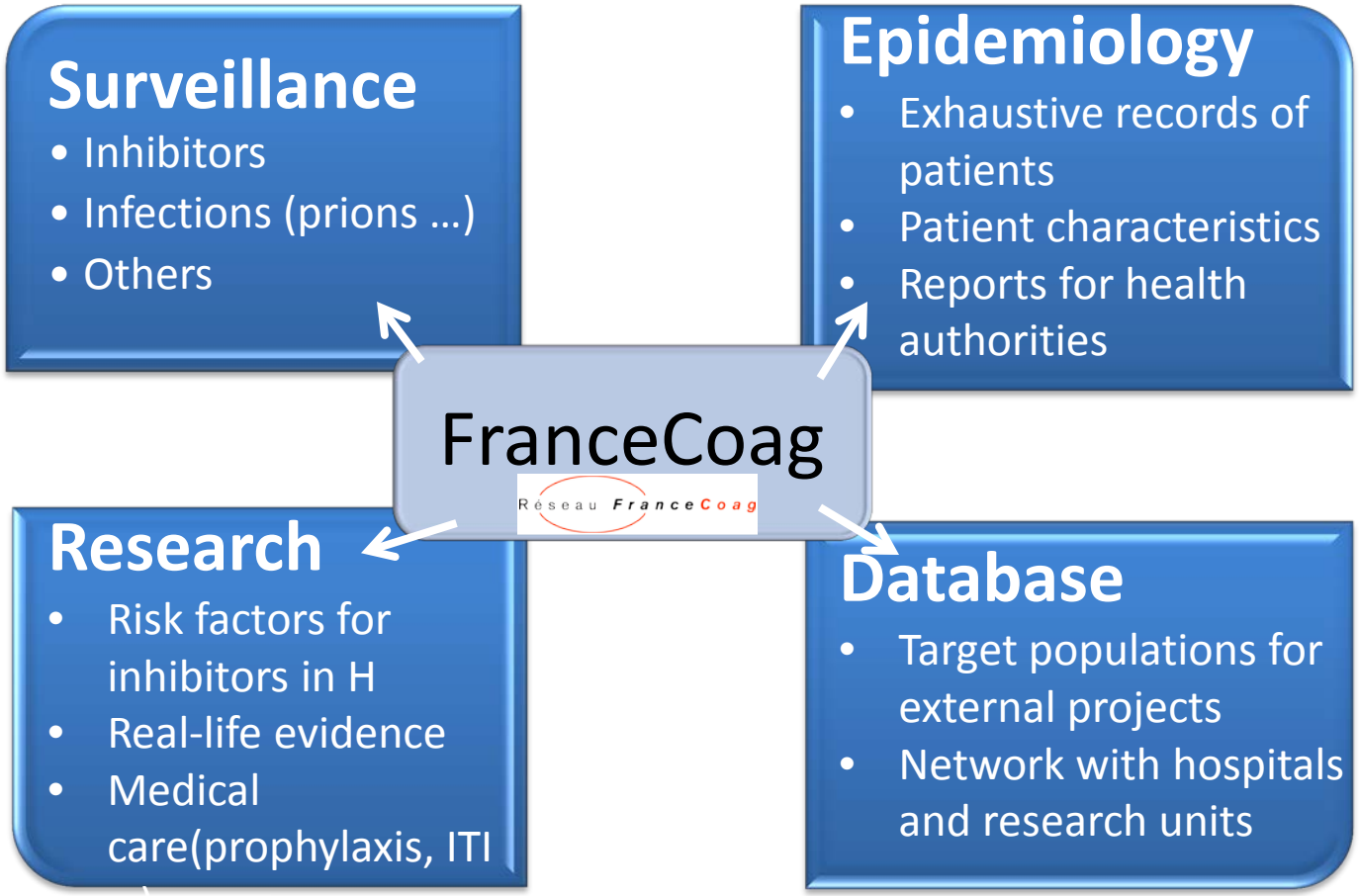


Specific aims of FranceCoag



Partners

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- **Coordinating Centre**

  Currently located in the Department of Chronic Diseases and Injuries (DMCT) of National Institute for Public Health Surveillance (InVS)

- **Steering Committee** including representatives of all the partners:
  - Clinicians and Health care professionals from HTC (CoMETH)
  - Coordinators of Reference centres for haemophilia and VWD
  - National Institute for Public Health Surveillance
  - Other Health institutions: DGOS, Agency for drugs (ANSM)
  - National Institute on Health and Medical Research (Inserm)
  - Association of patients : AFH

Scientific experts in various fields and data managers are invited to the steering committee meetings

Methods

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- **National Cohort survey:**
  - database
  - biobank collection for cells and plasma
- **Including a Pups Cohort**
  - for children with severe (<1%) and moderate (<2%) haemophilia with the knowledge of the complete information as regards the treatment,
  - exhaustive: ***all children born from the 1/01/2000***
  - dedicated to 2 main fields of research (Inhibitors and Prophylaxis)
  - with more detailed information
- **Data registration and management:**
  - information of patients or representative
  - highly secure electronic transmission of anonymised information
  - automatised controls and centre independent monitoring

Inclusion criteria

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Disease	Factor	Inclusion criteria
Haemophilia	FVIII, IX	< 40%
Allied disorders	FI (afibrinogenemia)	< 0.1g/l
	FII, V, VII, X, XIII	< 10%
	FV+FVIII	< 40% FVIIII
	FXI	< 20%
Willebrand	Type 1 & Type 3 VWF:Ag	< 30%
	Types 2 vWF:RCo / VWF:Ag or vWF:CB / VWF:Ag	< 0.7
	2N FVIII:c / VWF:Ag	< 0,5

Information collected

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- **Demographic items :**
  - Gender, date of birth, residence area, date and cause of death
- **Clinical and biological information:**
  - Disease, date and circumstances of diagnosis
  - Family history
  - Inhibitor history
  - History of blood borne infections (HBV, HCV, HIV)
  - Life-threatening and serious bleeds, surgical procedures
  - Highly relevant events since birth (ICH, joint prothesis)
  - Adverse Events and comorbidities
  - Outcome of hepatitis C
  - Replacement therapy : type and amount of product (IU & CED), replacement regimen (prophylaxis, immune tolerance) …
  - Factor level, inhibitor screenings
- **Further step:** genetics for all patients

Additional data set for PUPs

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- More detailed information for inhibitors & prophylaxis concerns:
  - Genetics
  - Ethnicity
  - Family history of inhibitor in case of family history of haemophilia
  - Vaccine
  - Comprehensive data for 75 first ED
  - Comprehensive data for prophylaxis and immune tolerance
  - Central lines
  - Haemarthrosis, target joints, clinical orthopaedic score, …
  - Days in hospital

Web site : *webfc*

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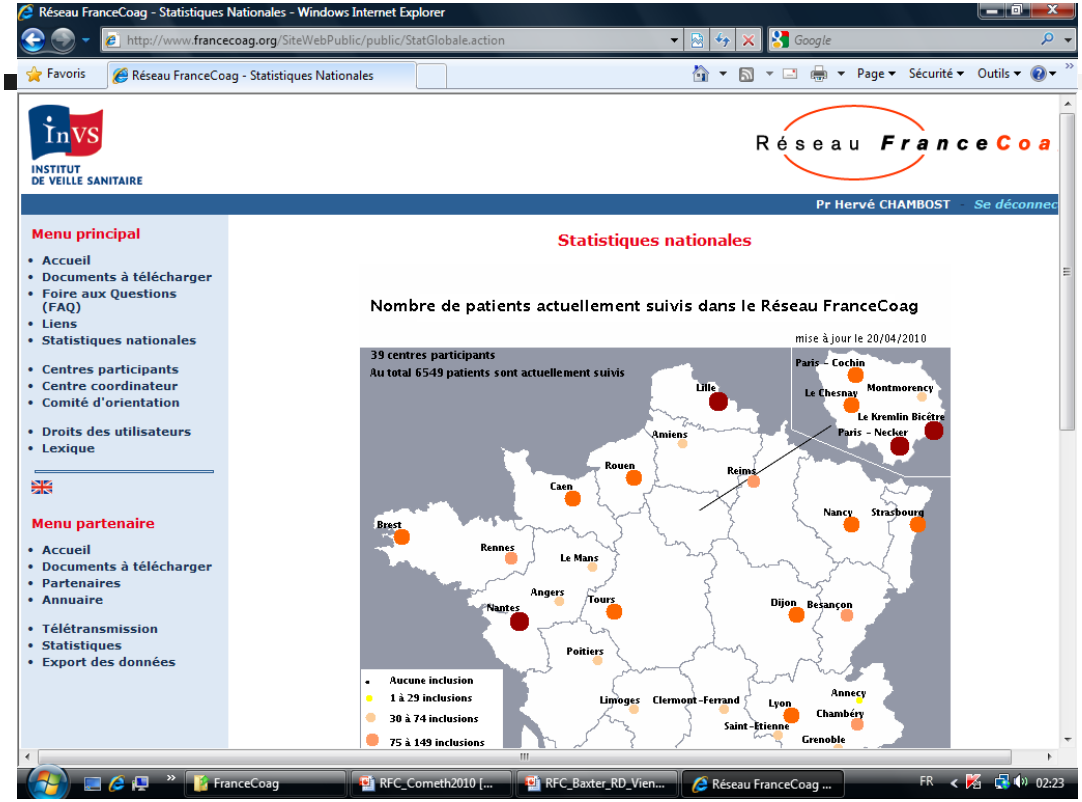

Public access:

- Protocol (summarised in English)
- Global statistics, predefined analysis

http://www.francecoag.org

webfc

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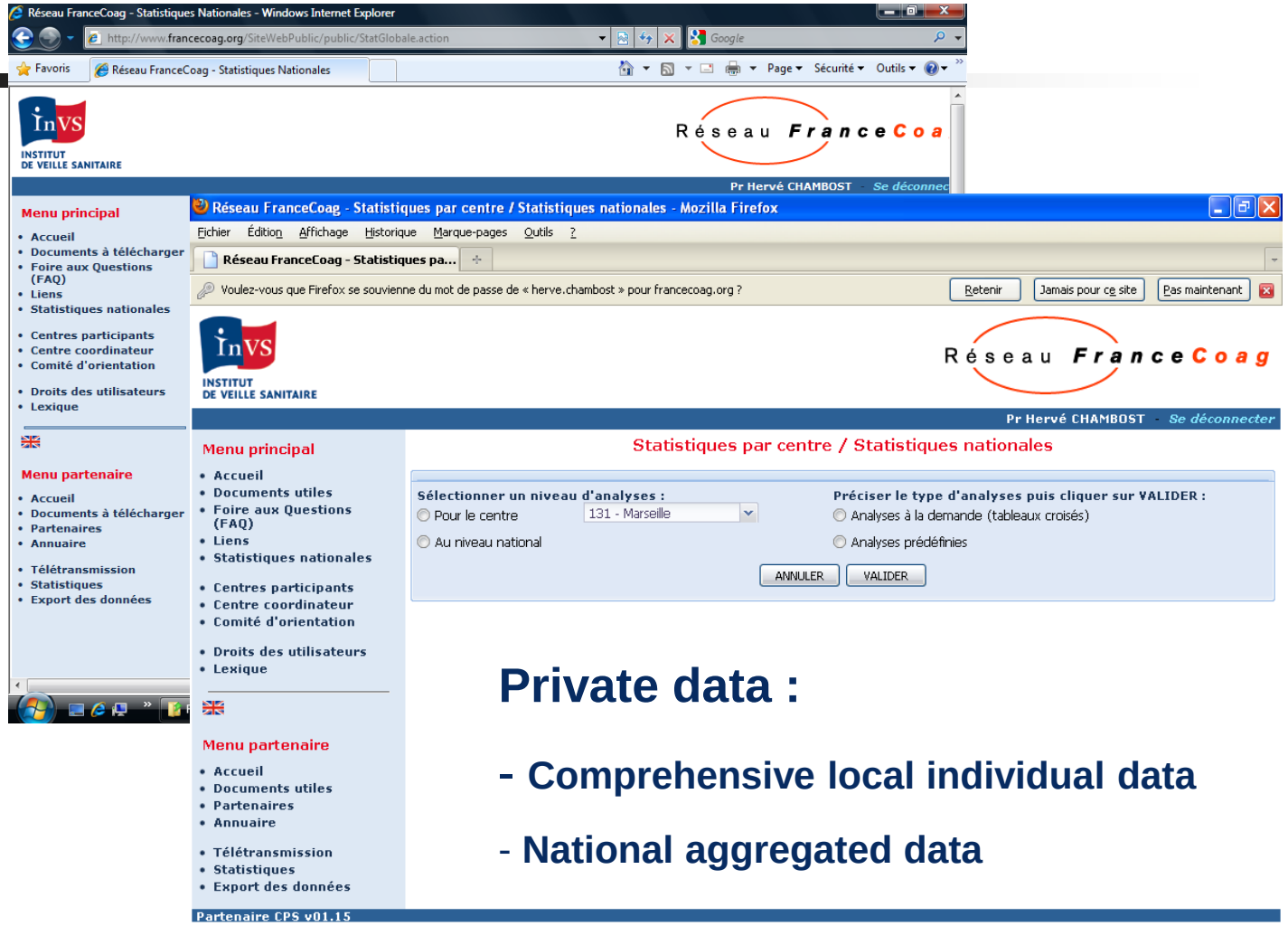

Private data :

- Comprehensive local individual data
- National aggregated data

http://www.francecoag.org

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Results from FranceCoag

On going progression of the Cohort

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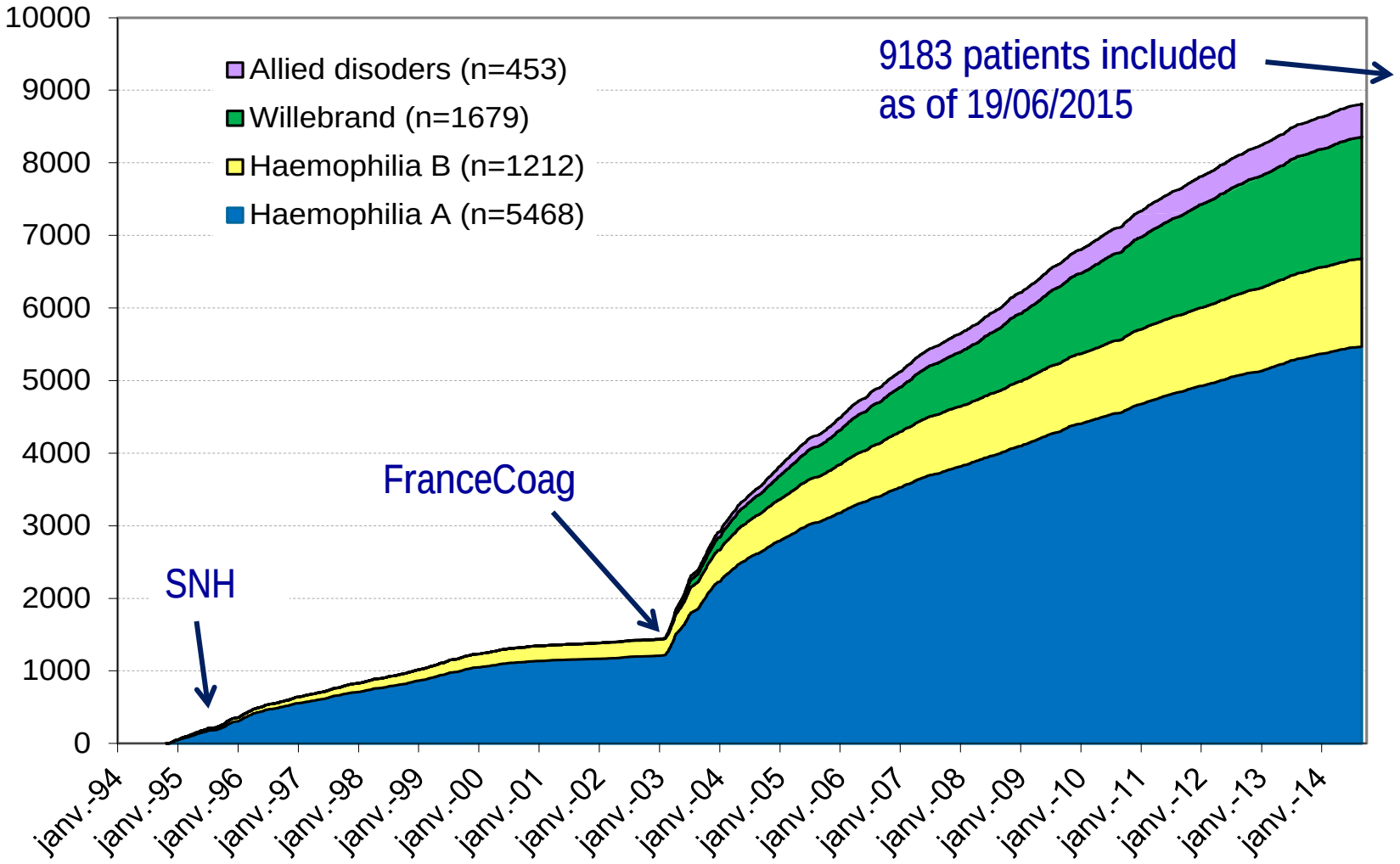

Global results

19th June 2015

9 183 patients included
36 centres

60 037 person year cohort

8 732 patients currently followed
314 died
137 lost of FU

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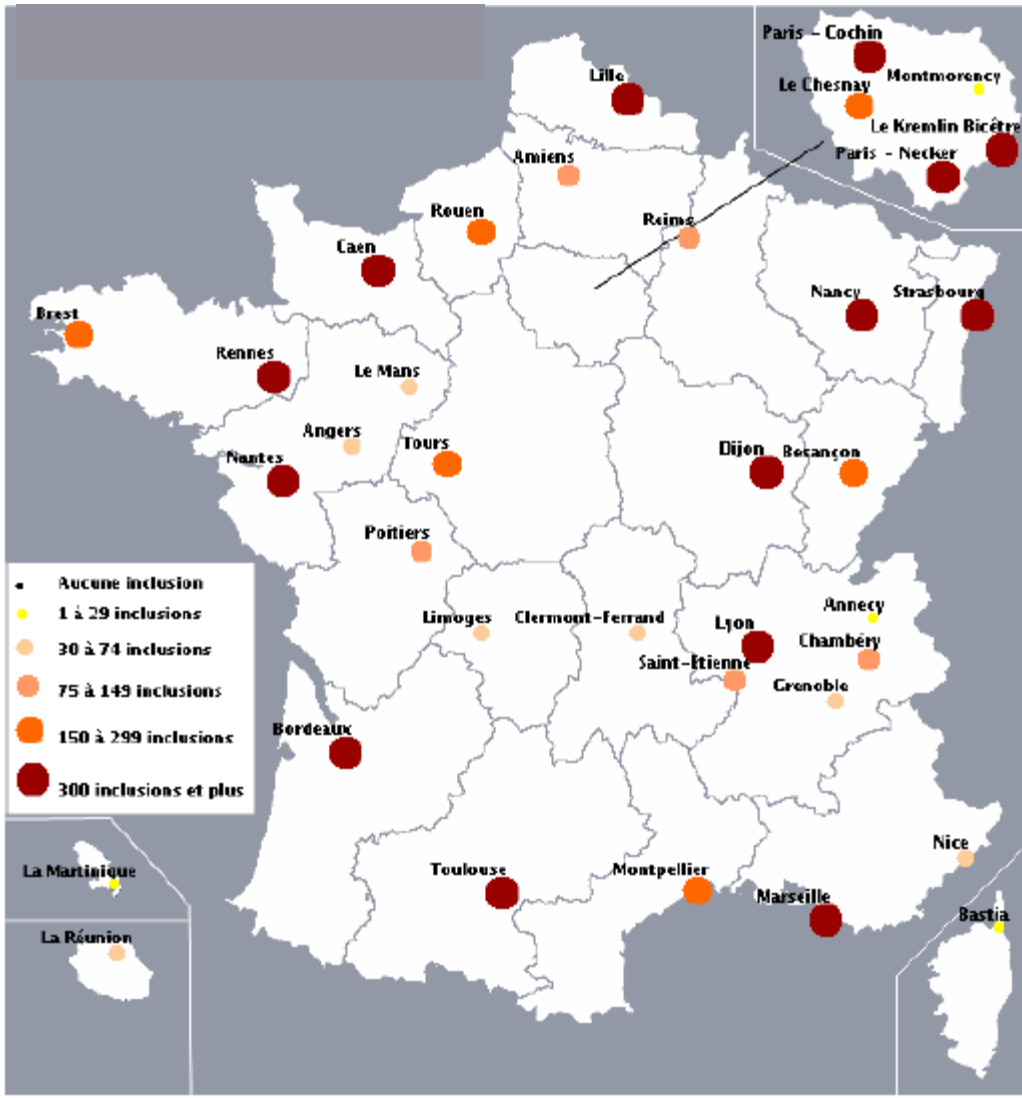
Currently followed population



Source : Réseau FranceCoag, Institut de veille sanitaire (France)

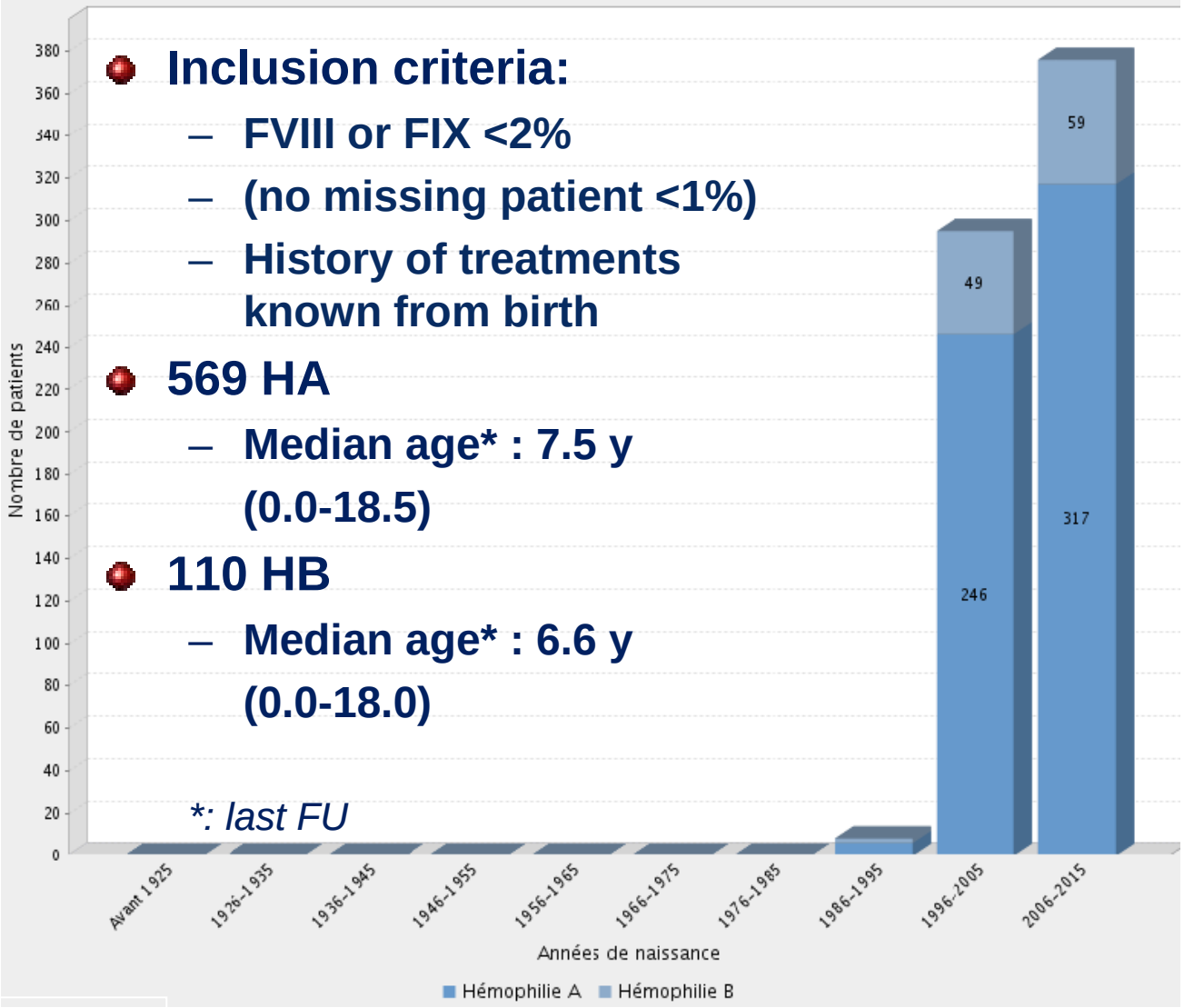
NB : il s'agit de la répartition géographique des patients non décédés ou non perdus de vue à la date de la réactualisation des données et pour lesquels au moins un formulaire a été enregistré.

Pups Cohort

- **Inclusion criteria:**
  - FVIII or FIX <2%
  - (no missing patient <1%)
  - History of treatments known from birth
- **569 HA**
  - Median age* : 7.5 y (0.0-18.5)
- **110 HB**
  - Median age* : 6.6 y (0.0-18.0)

*: *last FU*

n = 679



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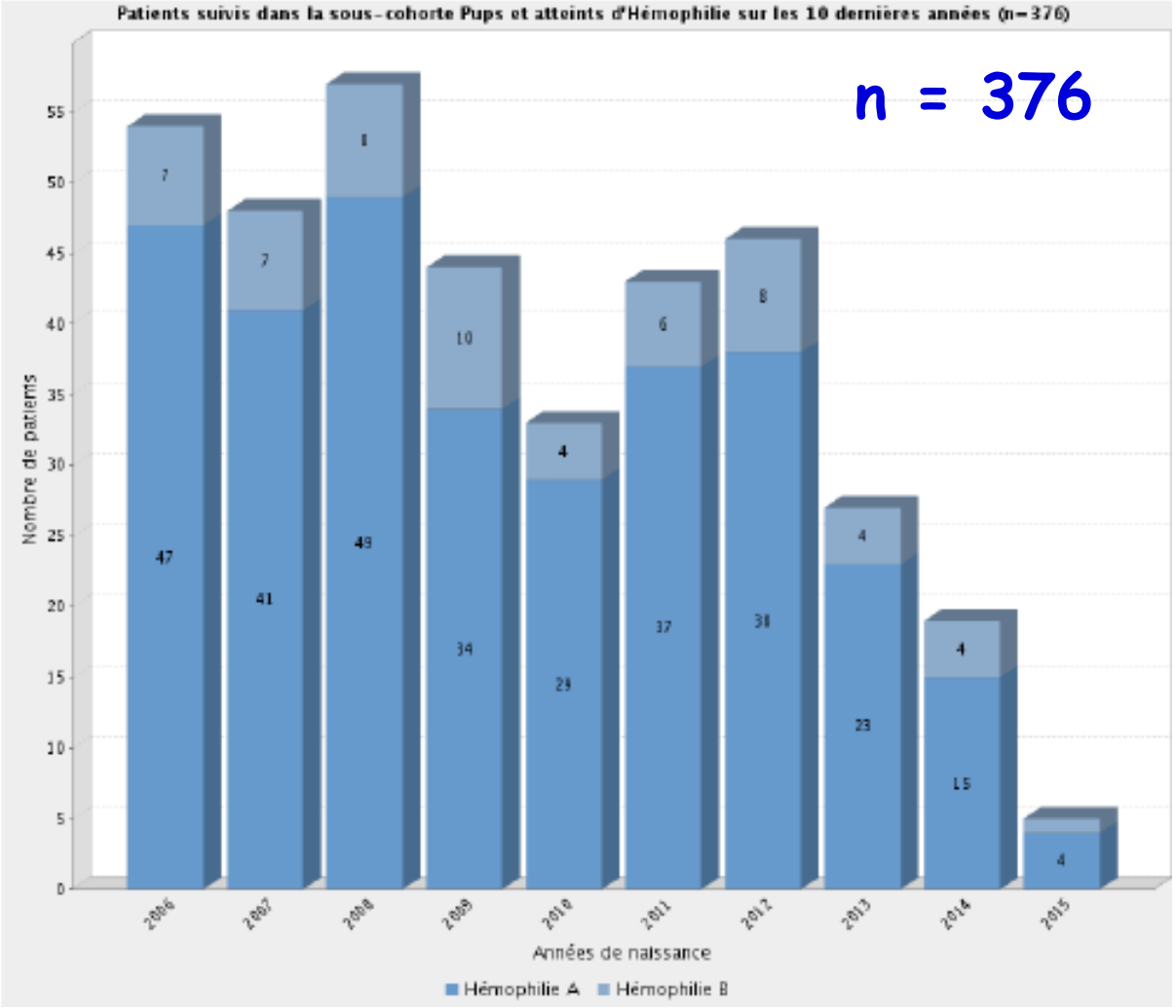
Pups born in the last decade



- **Exhaustiveness since 2000**

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Some Publications from the SNH Period

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Calvez T, Biour M, Costagliola D, et al. The French haemophilia cohort: **rationale and organization of a long-term national pharmacosurveillance system.** Haemophilia 2001;7:82-8.

Gaboulaud V, Parquet A, Tahiri C, et al. Prevalence of IgG antibodies to human **parvovirus B19** in haemophilia children treated with recombinant factor (F)VIII only or with at least one plasma-derived FVIII or FIX concentrate: results from the French haemophilia cohort. Br J Haematol 2002;116:383-9.

Chambost H, Gaboulaud V, Coatmelec B, et al. What factors influence the **age at diagnosis of hemophilia**? Results of the French hemophilia cohort. J Pediatr 2002;141:548-52.

Chambost H, A. Doncarli, M.A. Bertrand, et al. Implementation of a **hepatitis A** prevention policy in haemophiliacs: results from the French cohort. Haemophilia 2007, 13, 712–721

More recent Publications

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THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Use of Clinical Practice Guidelines on Long-term Prophylaxis in Severe Hemophilia in France: A Retrospective Audit

Sandrine Meunier, MD[1], Hervé Chambost, MD, PhD[2], Virginie Demiguel[3], Alexandra Doncarli, PhD[3], Florence Suzan[3], and Marc Trossaërt, MD, PhD[4]

(J Pediatr 2013;162:1241-4).

Regular Article

CLINICAL TRIALS AND OBSERVATIONS

(*Blood.* 2014;124(23):3398-3408)

Recombinant factor VIII products and inhibitor development in previously untreated boys with severe hemophilia A

Thierry Calvez,[1,2] Hervé Chambost,[3,4] Ségolène Claeyssens-Donadel,[5] Roseline d'Oiron,[6] Véronique Goulet,[7] Benoît Guillet,[8] Virginie Héritier,[7] Vanessa Milien,[3] Chantal Rothschild,[9] Valérie Roussel-Robert,[10] Christine Vinciguerra,[11] and Jenny Goudemand,[12] for the FranceCoag Network

Further studies

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Central venous access devices in boys with severe haemophilia: experience from the French PUPs cohort

Arthur Stérin[1], Virginie Demiguel[2], Yves Guillaume[1], Céline Falaise[1], Annie Harroche[3], Yoann Huguenin[4], Sandrine Meunier[5], Vanessa Milien[1], Anne Rafowicz[6], Marc Trossaërt[7], Bénédicte Wibaut[8], Hervé Chambost[1], on the behalf of FranceCoag Network

EAHAD, Helsinki 2015

ISTH 2015 Congress TORONTO JUNE 20-25 Reaching for Unprecedented Peaks

Plasma-derived FVIII products and inhibitor development in previously untreated boys with severe hemophilia A Report of the FranceCoag Network

J. Goudemand, C. Rothschild, R. d'Oiron, V. Demiguel, V. Dalibard, M. Micheaux, P. Lutz, Y. Gruel, C. Vinciguerra, A. Doncarli, H. Chambost, T. Calvez for the FranceCoag Network

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Feedback about FranceCoag Network

Strength of FranceCoag

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- **Comprehensive project**
  - Large partnership
  - Strong adherence of all parties (clinicians, patients, authorities)
- **Increasing cohort (general and Pups)**
- **Quality of data through regular monitoring**
- **Exhaustiveness for Pups**
  - Qualified as “registry” in november 2011 (National committee for Rare Diseases)
- **Long lasting public funding**
- **Improvement of care and practices through participation**
- **Biobanking**
  - Project aimed by surveillance with secondary research objective
- **Research projects**

Weakness of FranceCoag

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- **Complex project**
  - ✘ Difficulty to operate
  - ✘ Heterogeneity of objectives: lack of global adhesion of the coordinating agency
- **Public funding and regulations**
  - ✘ No complementary private partnerships till now limiting the possibilities for research projects
- **Publications :** Insufficient rating till a recent period
- **Interoperability** ?? multiple collection systems (national/international)
- **Platelet disorders not included**
- **Biobanking**
  - ✘ No long lasting project due to the cost and the lack of precise and realistic objective

Evolution of the project

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- **Transfer of the coordination and budget from a national agency to an academic structure (University Hospital / Reference Centre)**
  - Stronger clinical governance
  - Extension to platelet disorders
  - Continuation of a registry (exhaustiveness of inclusions), with cohorts of special interest (PUPs +++)
  - Renewal of public funding
  - Partnership with agencies to carry on surveillance objectives
  - Diversified partnership (institutional research units, firms or other private partners) to stimulate research projects
  - Favour homogenization of data set collection and interoperability of systems, for example by a limitation of adverse events and comorbidities registred to consensual fields (inhibitors, thrombosis, cancer, ...)
  - Education