Clinical Infectious Diseases

MAJOR ARTICLE

Unusual Initial Abdominal Presentations of Invasive Meningococcal Disease

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Background. Invasive meningococcal disease (IMD) is recognized as septicemia and/or meningitis. However, early symptoms may vary and are frequently nonspecific. Early abdominal presentations have been increasingly described. We aimed to explore a large cohort of patients with initial abdominal presentations for association with particular meningococcal strains.

Methods. Confirmed IMD cases in France between 1991 and 2016 were screened for the presence within the 24 hours before diagnosis of at least 1 of the following criteria (1) abdominal pain, (2) gastroenteritis with diarrhea and vomiting, or (3) diarrhea only. Whole-genome sequencing was performed on all cultured isolates.

Results. We identified 105 cases (median age, 19 years) of early abdominal presentations with a sharp increase since 2014. Early abdominal pain alone was the most frequent symptom (n = 67 [64%]), followed by gastroenteritis (n = 26 [25%]) and diarrhea alone (n = 12 [11%]). Twenty patients (20%) had abdominal surgery. A higher case fatality rate (24%) was observed in these cases compared to 10.4% in all IMD in France ($P = .007$) with high levels of inflammation markers in the blood. Isolates of group W were significantly more predominant in these cases compared to all IMD. Most of these isolates belonged to clonal complex 11 of the sublineages of the South American-UK strain.

Conclusions. Abdominal presentations are frequently provoked by hyperinvasive isolates of meningococci. Delay in the management of these cases and the virulence of the isolates may explain the high fatality rate. Rapid recognition is a key element to improve their management.

Keywords. abdominal; meningococcal disease; typing; serogroup; whole-genome sequencing.

Symptômes précurseurs des IIM

- Symptômes précoces, peu spécifiques
- Au Chili, en 2012:
  - Diarrhée dans 36% des cas d'IIM de sérogroupe W
  - Diarrhée chez 56% des patients décédés contre 27% des survivants (p=0,034)

  Moreno et al, Rev Chilena Infectol, 2013
- 7 cas de gastro-entérites avec IIM dues à la souche W ST-11, chez des adolescents au Royaume-Uni dont 5 décès **Campbell et al, Euro Surv, 2016**

	Percentage of children (95% CI)	Median hour of onset
Clinical features present in >50% of children		
Fever	93·9% (89–98)	1
Drowsiness	81·1% (74–88)	7
Nausea or vomiting	76·4% (67–84)	4
Irritability	66·6% (57–75)	4
Haemorrhagic rash	61·0% (51–70)	13
Poor appetite or feeding	59·9% (50–70)	5
Clinical features present in 20–50%		
General aches	48·5% (39–58)	7
Confusion or delirium*	45·1% (36–55)	16
Cold hands and feet	43·2% (33–53)	12
Headache*	40·5% (31–50)	0
Leg pain	36·7% (28–47)	7
Neck pain or stiffness	35·0% (26–44)	13
Photophobia	27·5% (19–36)	15
Sore throat or coryza	23·6% (15–32)	5
Clinical features present in <20%		
Abnormal skin colour	18·6% (11–27)	10
Floppy muscle tone†	18·3% (12–26)	13
Bulging fontanelle‡	11·5% (5-18)	15
Breathing difficulty	10·8% (5–18)	11
Seizure	9·8% (4–16)	17
Unconsciousness	9·5% (4–15)	22
Increased thirst	8·1% (3–14)	8
Diarrhoea	6·6% (2–12)	9

Percentages and median hours of onset are standardised to UK case-fatality rate. *Data only available for children aged >1 year. †Data only available for children aged <5 years. ‡Data only available for children aged <1 year.

Table 3: **Overall frequency and time of onset of clinical features of meningococcal disease in children before hospital admission**

Thompson et al, Lancet, 2006

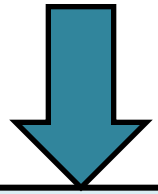
Présentation abdominale des IIM, un diagnostic sous-estimé?

Objectif :

Décrire sur les plans clinique, biologique et bactériologique, une large cohorte de patients avec une présentation abdominale d'une IIM confirmée adressés au CNRMH de Paris

Méthodes

Ensemble des IIM en France de 1991-2016 : **11979 cas**



Critère d'inclusion :

Diagnostic d'**IIM** confirmé
ET
Au moins un symptôme abdominal dans les 24 h précédant le diagnostic parmi:
-Douleur abdominale seule
-Diarrhée seule
-Gastro-entérite

114 cas

Exclusion **n =9** :
-Constipation : **3**
-Diarrhée 24 h après le diagnostic: **2**
-Cirrhose : **2**
-Salpingite : **1**
-Traumatisme abdominal :**1**

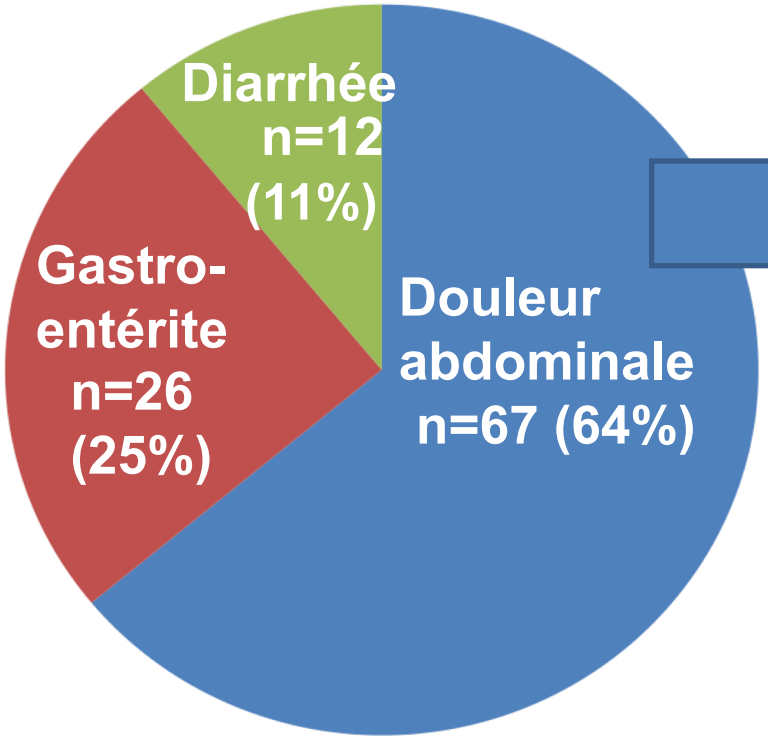
105 cas

Cas confirmés par culture
n =92

Cas confirmés par PCR
n = 13

Douleur abdominale : le symptôme le plus fréquent

n=105 cas
58 ♀ 47 ♂
52 enfants (de 2 mois à 18 ans)
53 adultes (de 19 ans à 91 ans)
Âge médian de 19 ans (Q1 6,5- Q3 50)



Chirurgie abdominale
n=20 (20%)

Taux de mortalité des présentations abdominales= **24%** *versus* **10%** pour toutes les formes d'IIM **(p=0.007)**

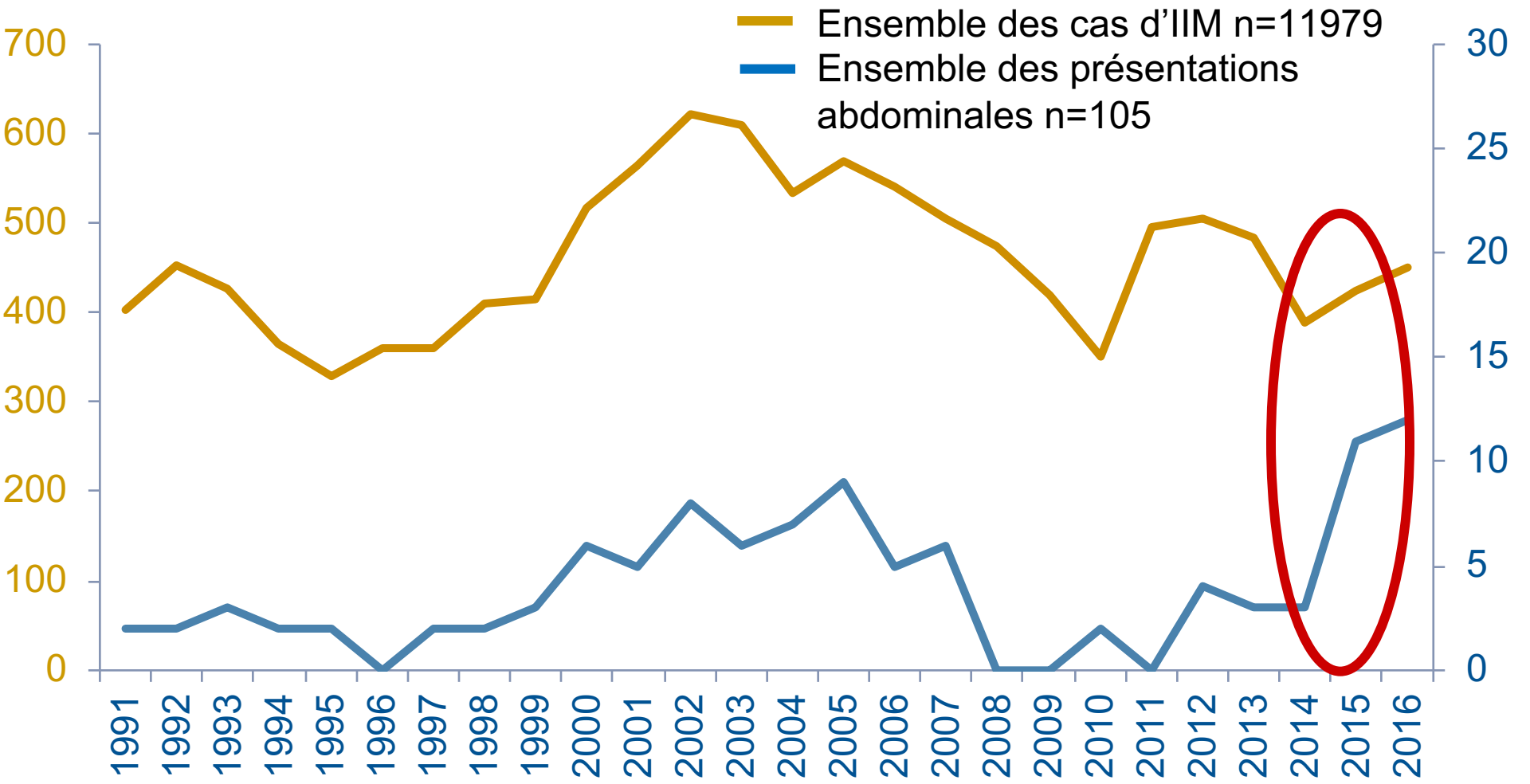
Populations pédiatrique/adulte

n = données disponibles*	**Population totale n=105**	**Enfants n=52**	**Adultes n =53**
Manifestations digestives, n (%)			
Douleur abdominale, n (%)	**67 (64)**	**34 (65)**	**33 (62)**
Gastro-entérite, n (%)	26 (25)	12 (23)	14 (26)
Diarrhée seule, n (%)	12 (11)	6 (12)	6 (11)
Chirurgie digestive n (%)	**20 (20)** (n *=100)	**12 (24)** (n * =50)	**8 (21)** (n* = 38)
Autres symptômes :			
Purpura, n (%)	**30 (36)** (n* = 84)	**17 (38)** (n *= 45)	**13 (33)** (n*= 39)
Syndrome méningé n (%)	**41 (51)** (n* = 81)	**27 (64)** (n* = 42)	**14 (36)** (n*= 39)
Antibiotiques avant l'admission n(%)	**39 (68)** (n* = 56)	**21 (76)** (n*= 29)	**18 (64)** (n*=28)
Décès, n (%)	**19 (24)** (n* =79)	**6 (16)** (n* =37)	**13 (25)** (n*=41)

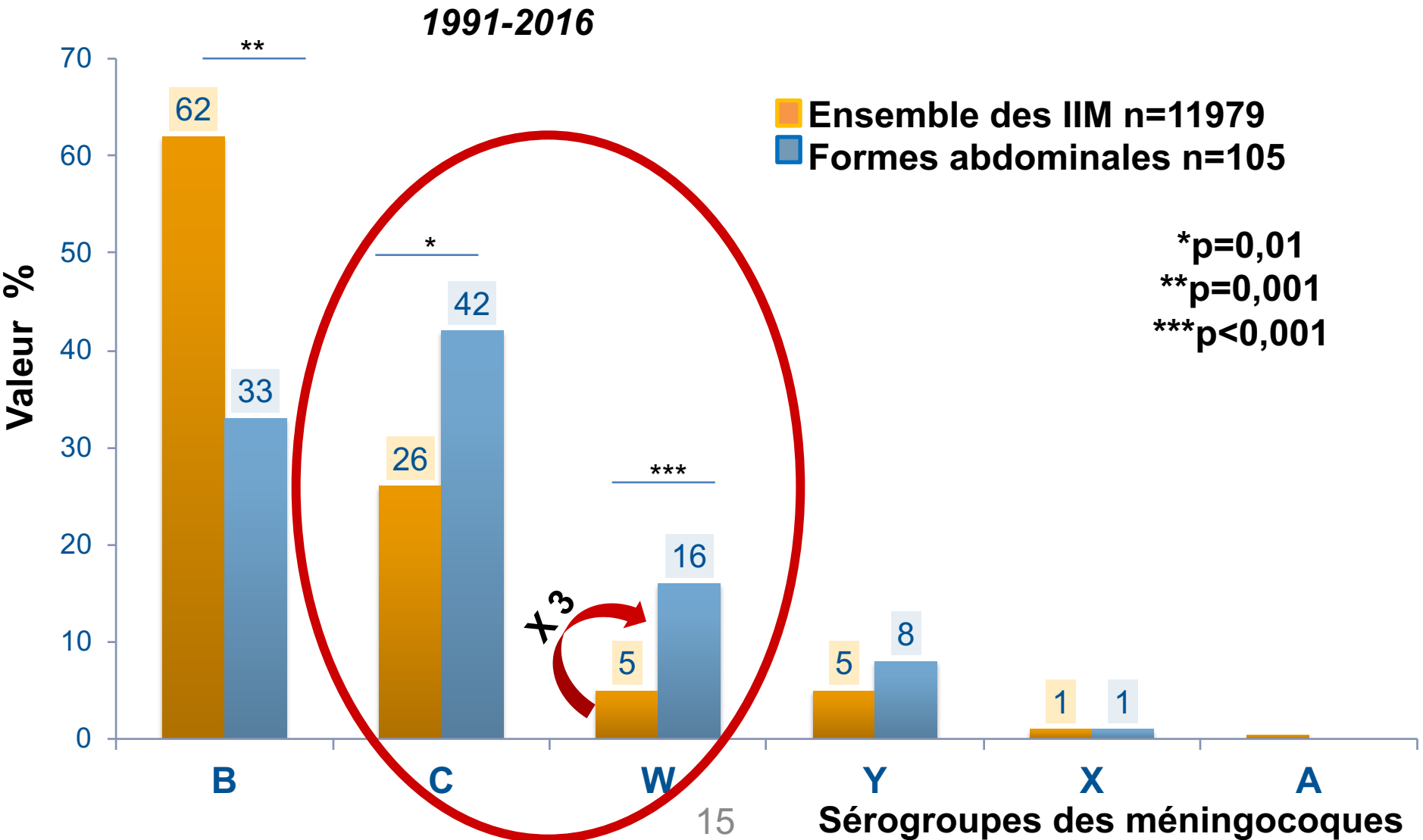
Une réponse inflammatoire importante

Paramètres biologiques	
C-Reactive Protein, (écart type) mg/l, (n=58)	**198** (±140)
Leucocytes /mm³ (n= 61)	**15044.8** (± 9893.7)
Polynucléaires neutrophiles /mm³ (n=47)	**11866.1** (± 9347.4)

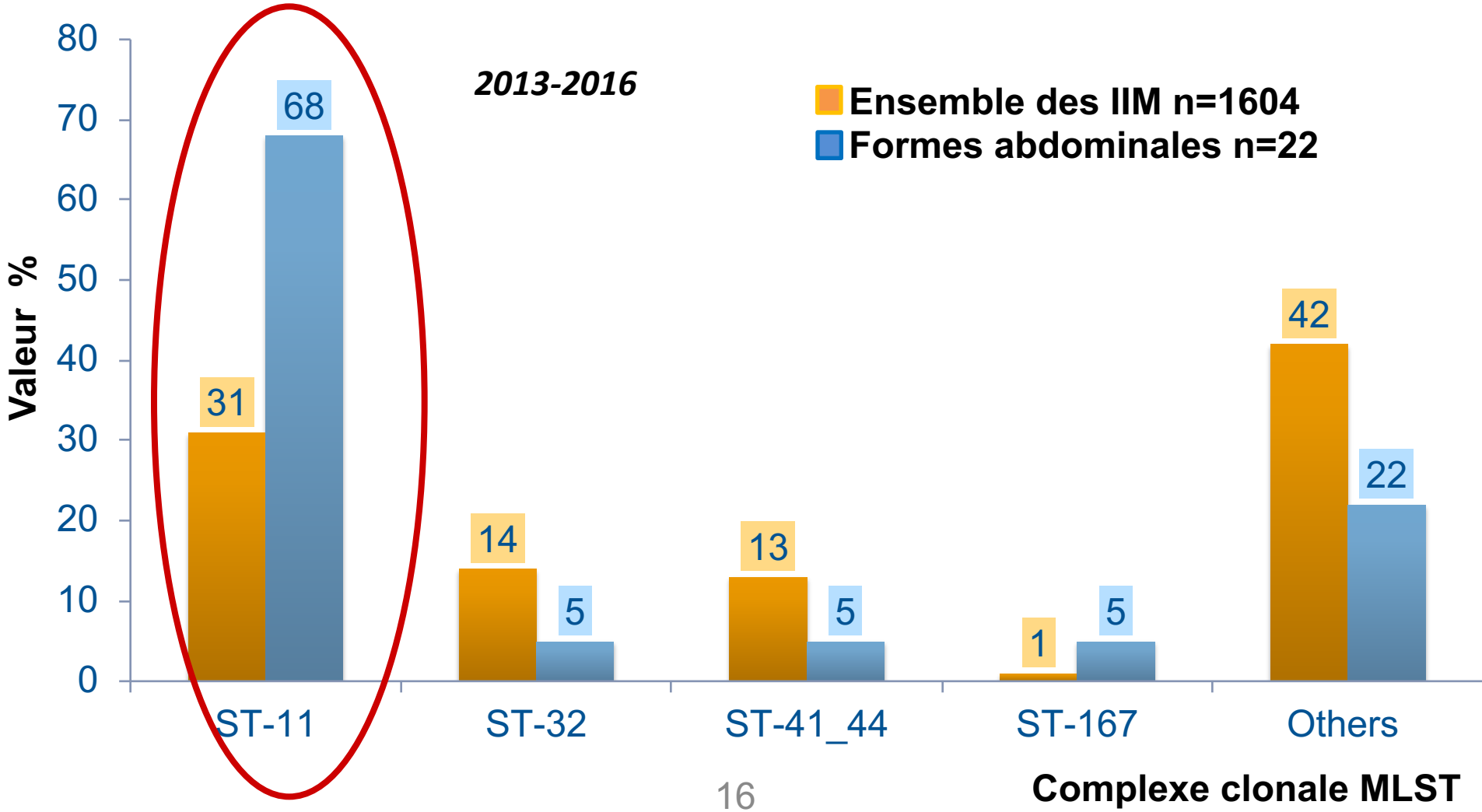
Distribution des présentations abdominales d'IIM entre 1991 et 2016



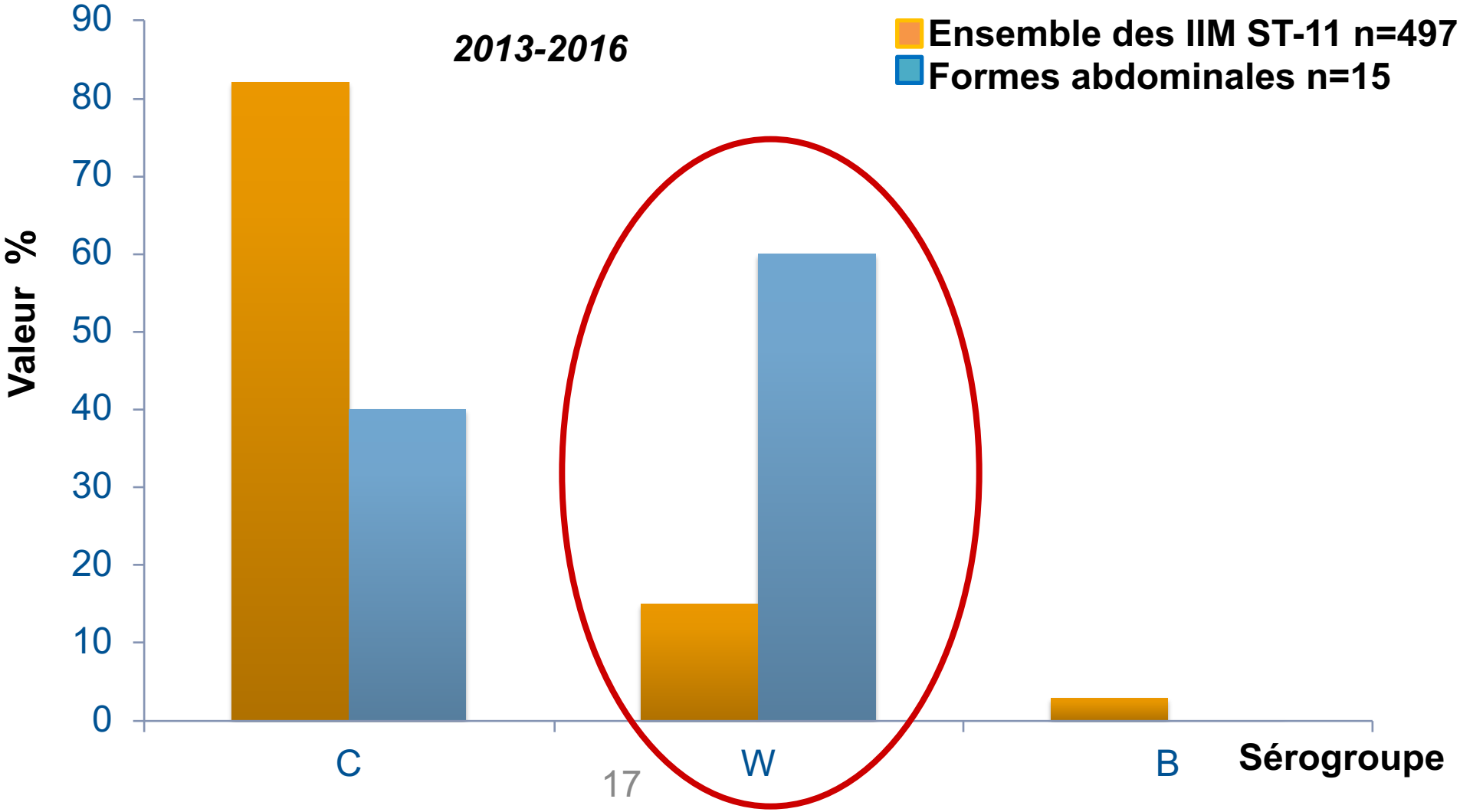
Quels sont les sérogroupes des cas de présentation abdominale d'IIM ?



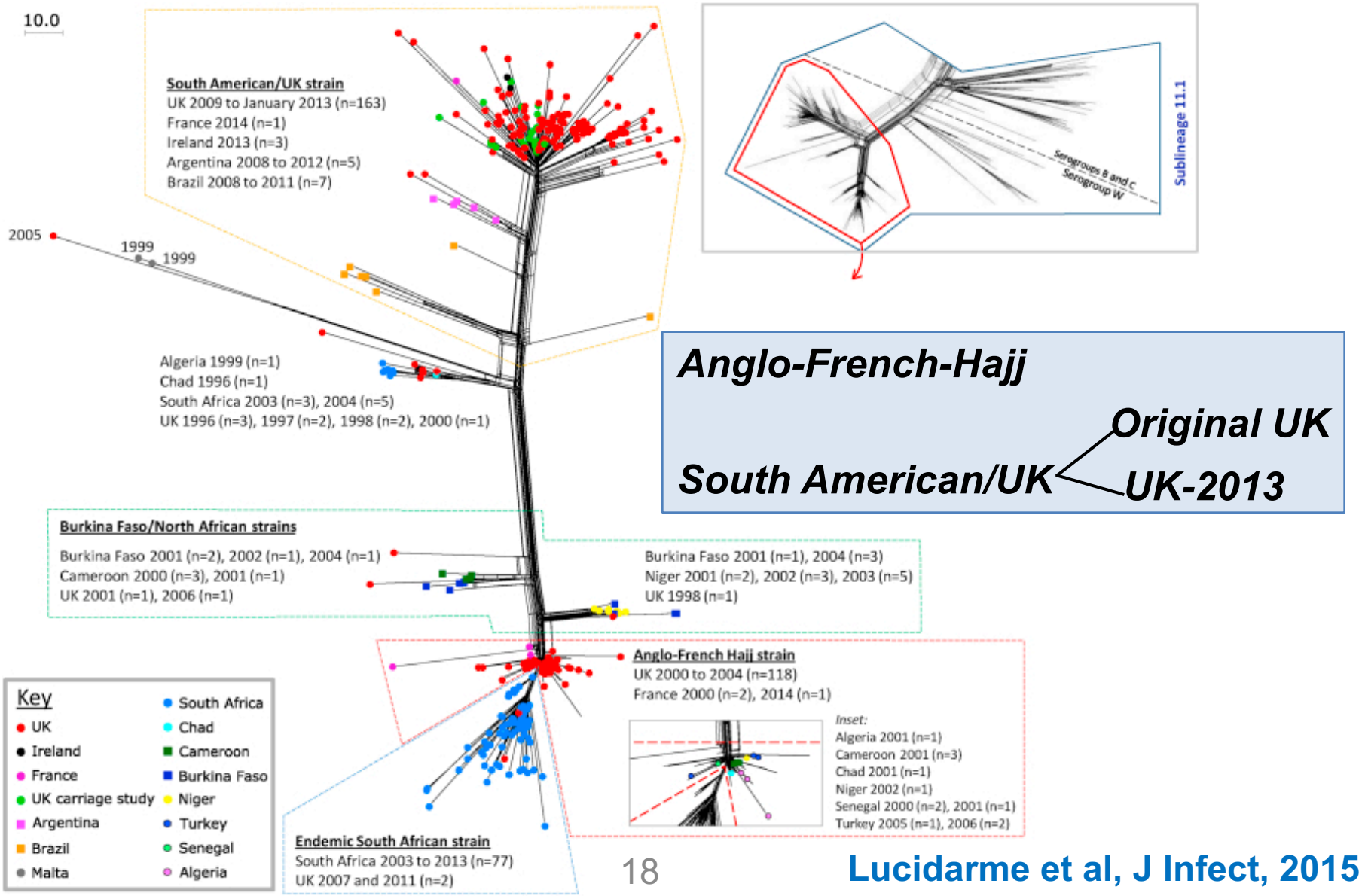
Quels sont les complexes clonaux des cas de présentation abdominale d'IIM ?



Présentation abdominale d'IIM et complexe ST-11

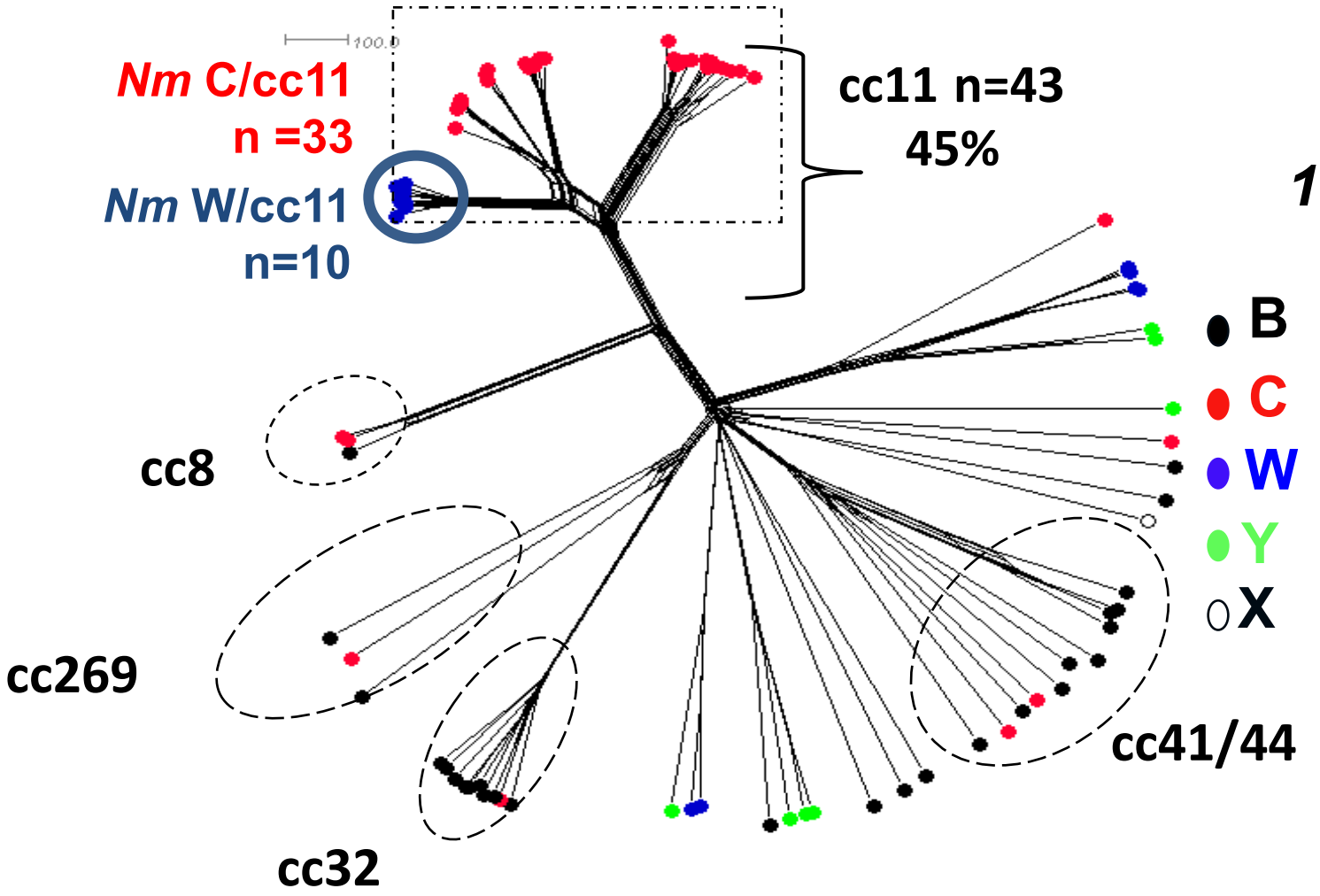


Expansion W ST-11 : Différentes lignées



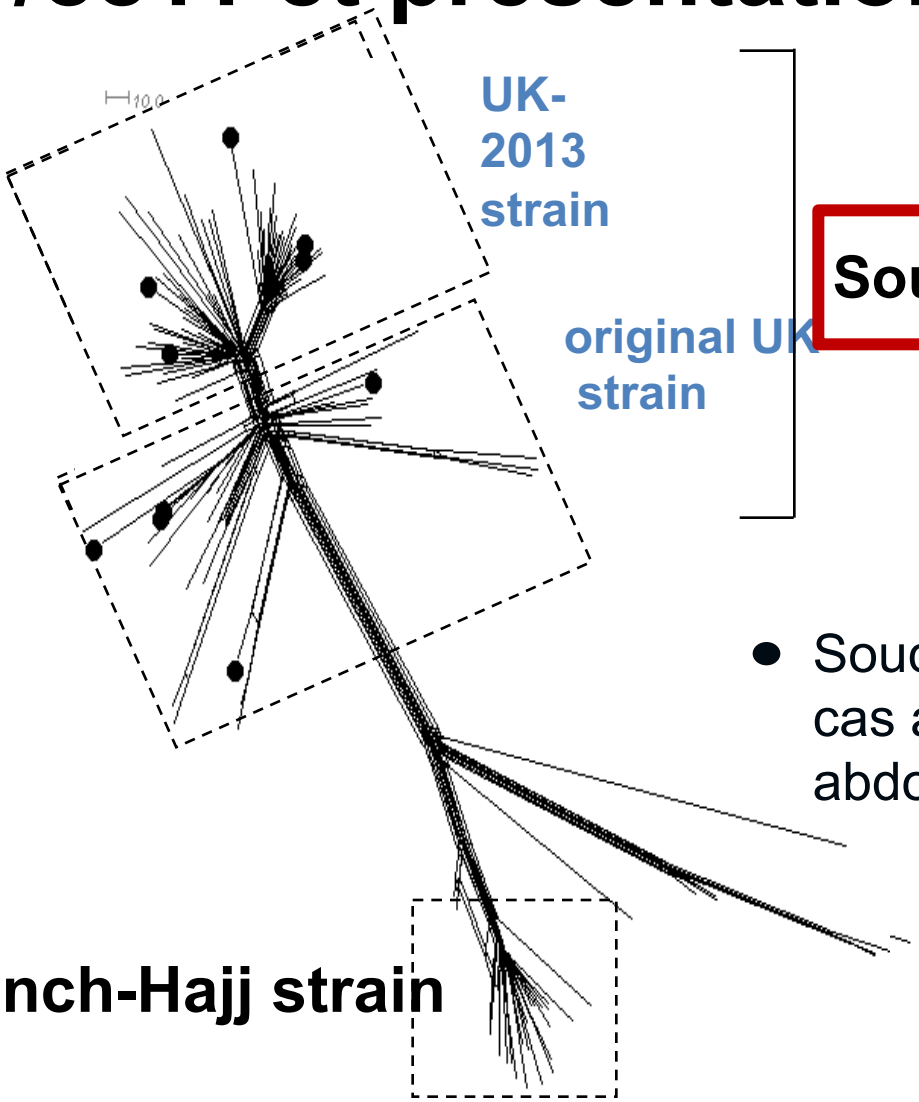
Lucidarme et al, J Infect, 2015

Analyse phylogénétique



77% des souches appartiennent à un complexe hyper-invasif

*Nm*W/cc11 et présentation abdominale



- Souches de *Nm*W/cc11 des cas avec présentation abdominale

Core genome Tree : Toutes les souches de *Nm*W/cc11 isolées de 2010 à 2016

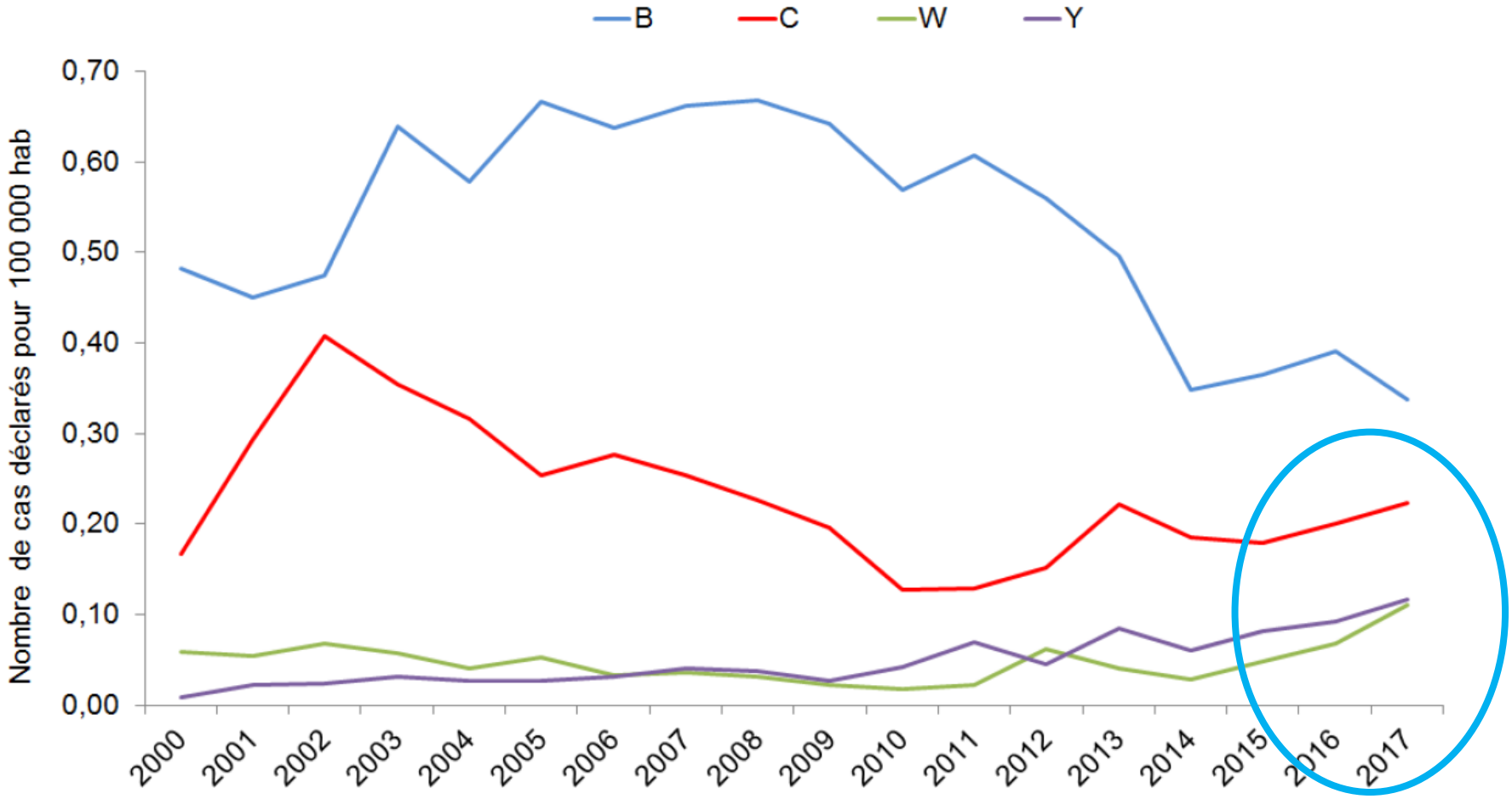


Figure 6 : Taux de notification des infections invasives à méningocoque liées aux principaux sérogroupes, France entière, 2000-2017