



GenEpi BioTrain – Wave 3 – Food and Waterborne Diseases

Case study on *Listeria*

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Intended Learning Objectives

Specific objectives of this session:

- 1) Understand foodborne outbreak investigation tools for *Listeria*:
 - Questionnaires
 - Case-control study / case-case study
 - Food traceback techniques
- 2) Establish case definitions for surveillance and outbreak investigations
- 3) Analyze epidemiological surveillance data related to *Listeria* infections
- 4) Acquire knowledge of integrating genomic and epidemiological approaches to enhance *Listeria* surveillance and prevention

Outline

This session consists of the following elements:

- 1) Basic knowledge of *Listeria* and listeriosis epidemiology
- 2) Principles of listeriosis surveillance systems
- 3) Principle of outbreak investigation specific to listeriosis
- 4) Examples

Basic knowledge of *Listeria* and listeriosis epidemiology

- ❑ *Listeria monocytogenes* (Lm): common: soil, food
- ❑ Transmission: foodborne
- ❑ At-risk foods
 - Cheeses and dairy products / deli-meats / smoked fish products / produces
- ❑ At-risk groups
 - Pregnant women / newborn / elderly / persons with comorbidities
- ❑ Clinical presentations
 - Bacteremic / neurolisteriosis / pregnancy-associated
- ❑ Incubation ~ 1 month → implication for investigation of food exposures
 - Bacteremic: Med 2 days (2-12)
 - Neurolisteriosis: Med 8 days (1-14)
 - Pregnancy-associated: Med 23 days (16-67)

Basic knowledge of *Listeria* and listeriosis epidemiology

Burden of listeriosis

Europe



Surveillance Atlas of Infectious Diseases

2022



Region	Reported cases	Case fatality %
EU (without UK)	2740	18,9
Germany	548	
France	451	25
Spain	437	25,7
Italy	347	
Sweden	125	
Denmark	86	
Finland	70	
Czechia	48	29,2
Slovenia	20	5
Ireland	17	8,3
Bulgaria	5	
Luxembourg	4	33,3

France



2nd

leading cause of death from foodborne infection in France

Listeriosis surveillance systems

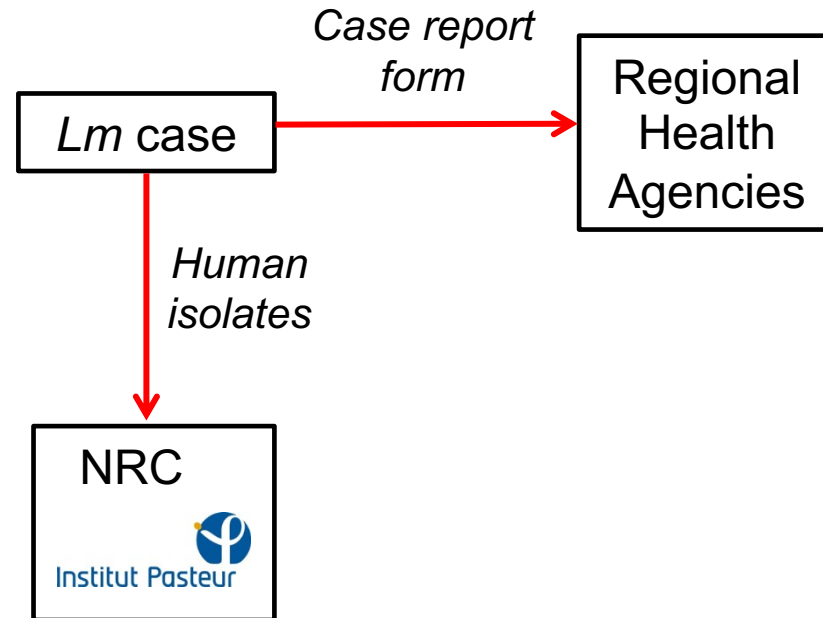
Combination of :

- ❑ Epidemiologic surveillance: collected data should includes:
 - Case characteristics: demographics, presentation, comorbidities, outcomes
 - Food exposure history
- ❑ Microbiologic surveillance: isolates characterization
 - See A. Moura/M. Lecuit presentations
 - cgMLST-typing
 - At least of human isolates
 - Optimized when combined with food/environmental isolates
 - Real-time monitoring for timely detection of clusters/outbreaks

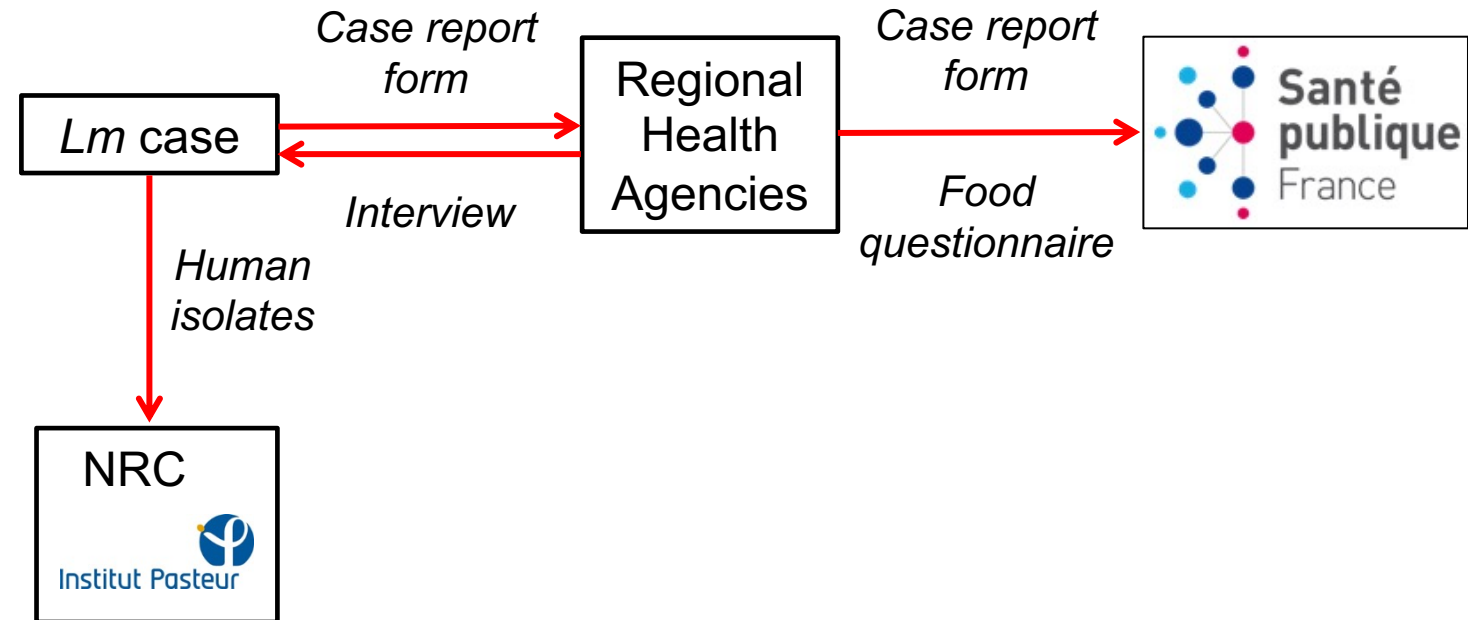
French listeriosis surveillance system



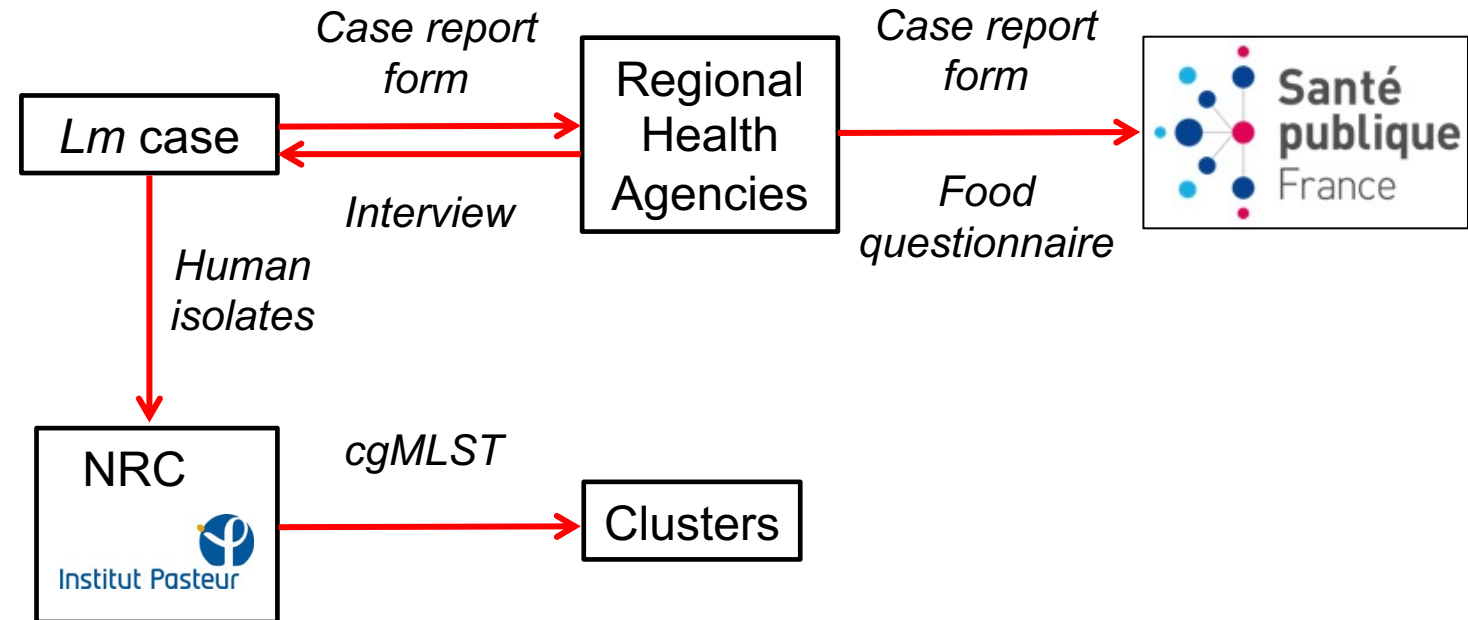
French listeriosis surveillance system



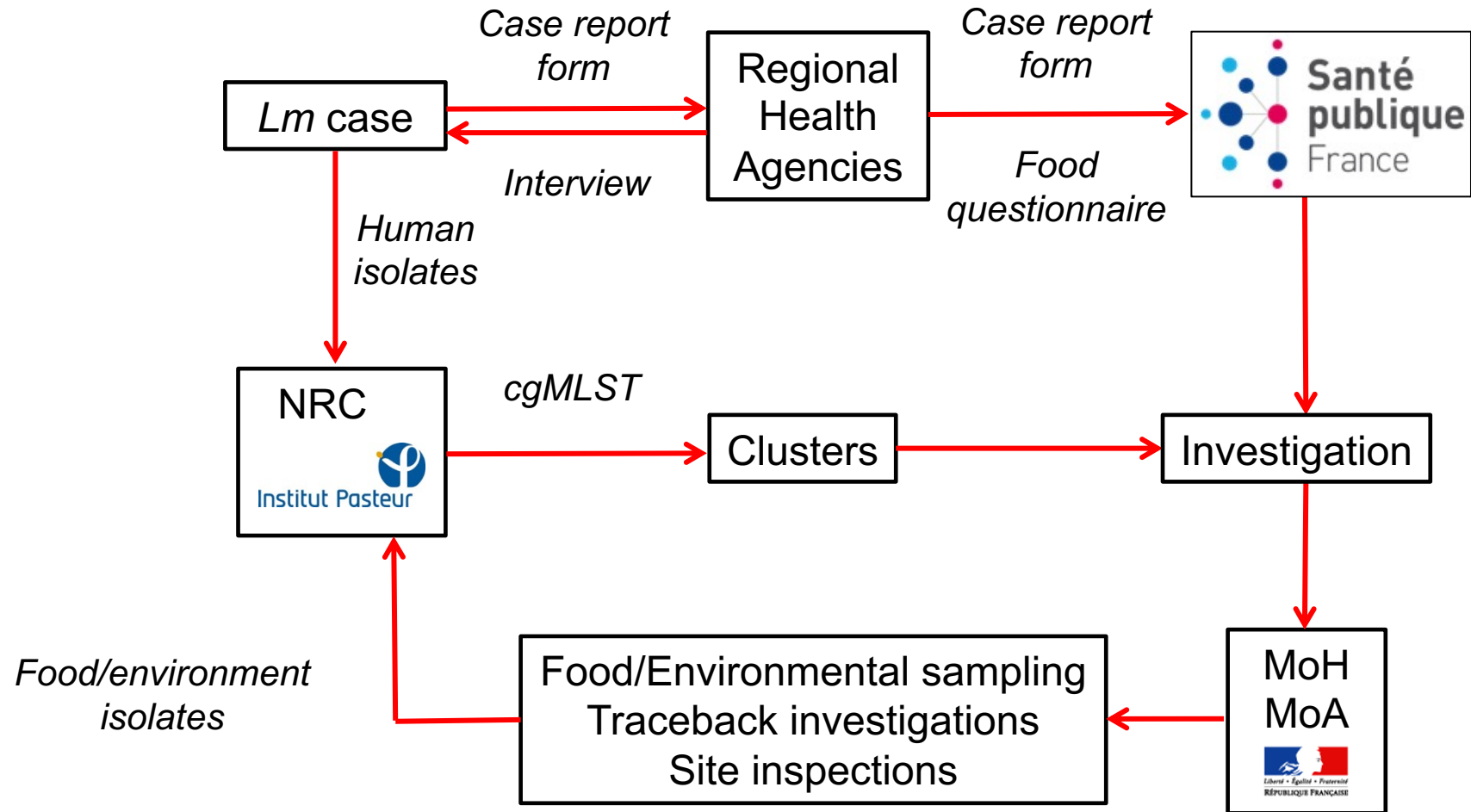
French listeriosis surveillance system



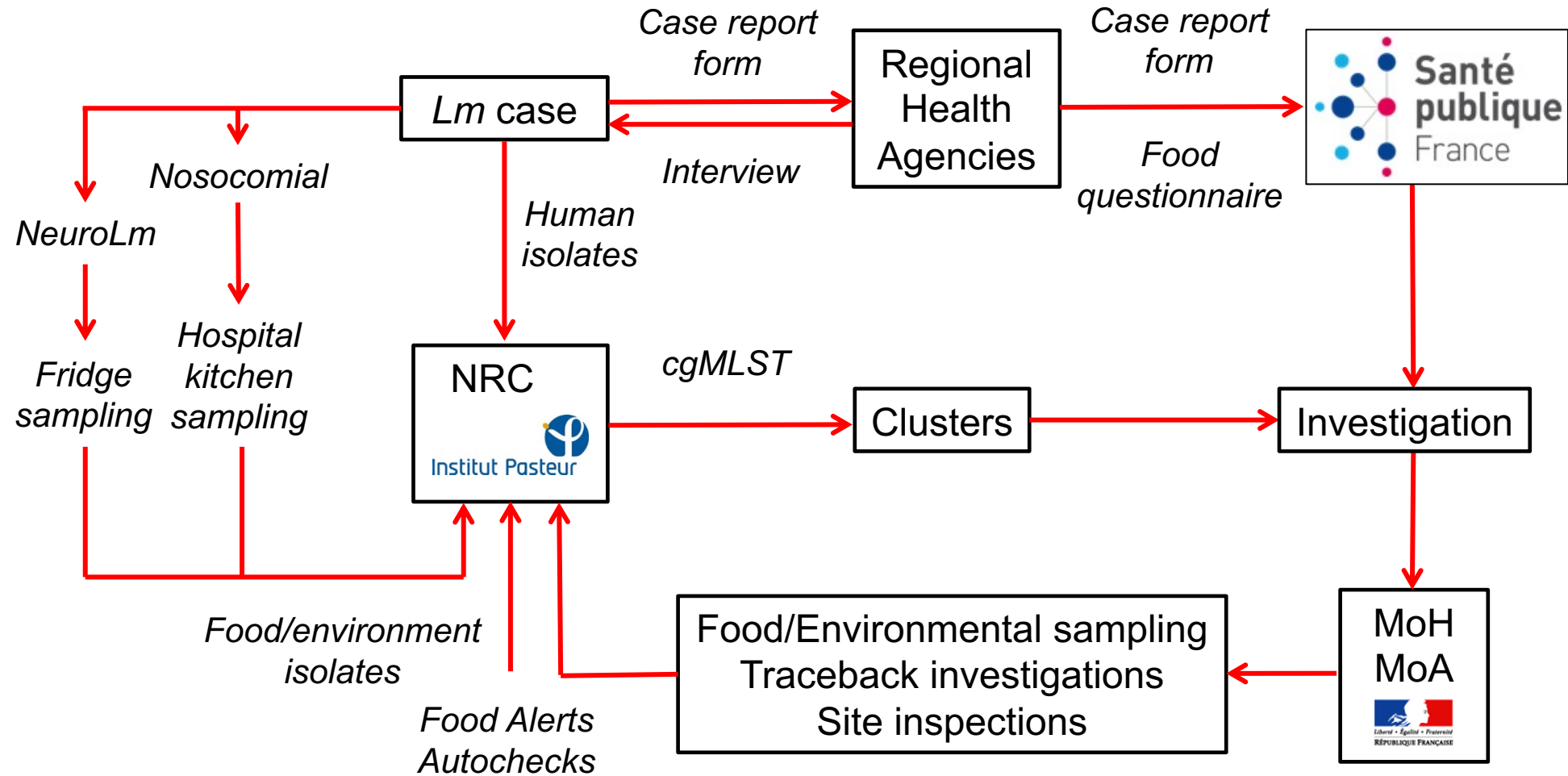
French listeriosis surveillance system



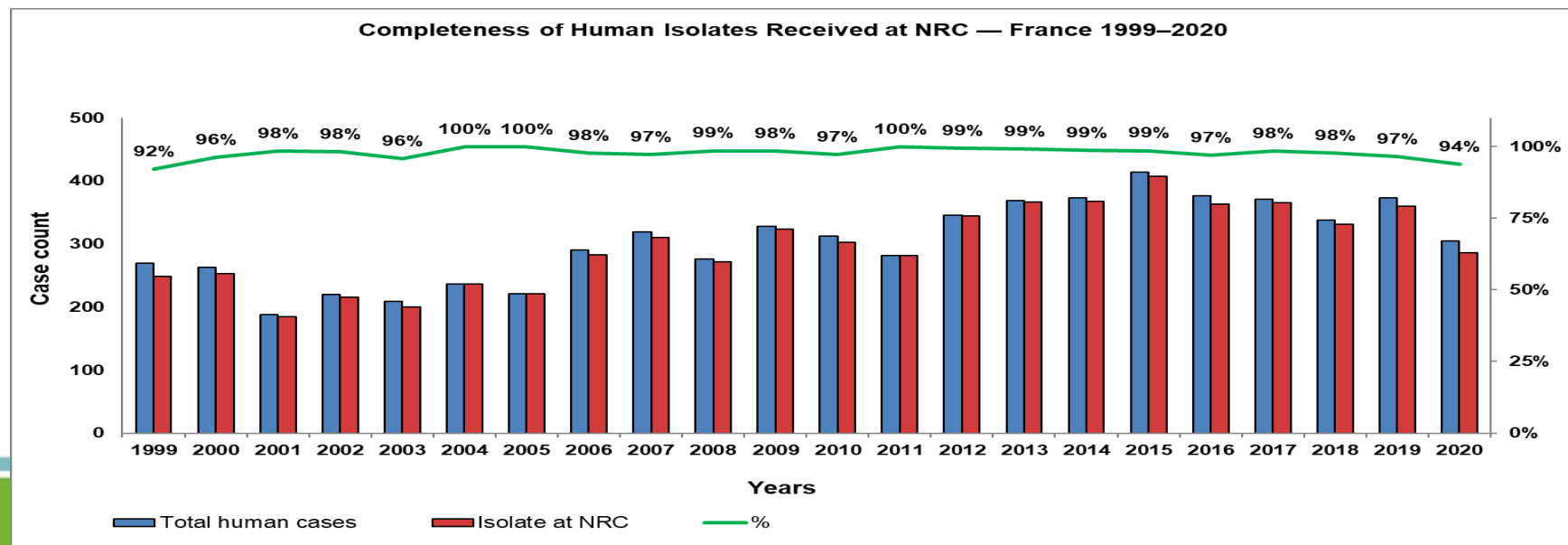
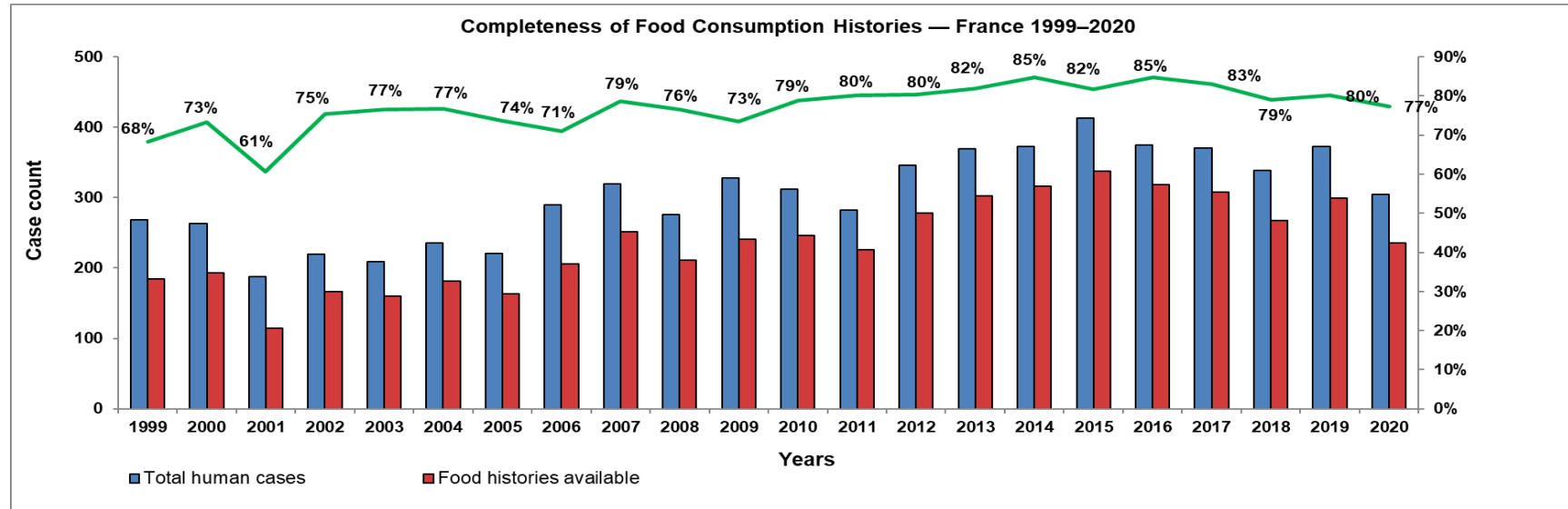
French listeriosis surveillance system



French listeriosis surveillance system



French listeriosis surveillance system



French listeriosis surveillance system



- ❑ cgMLST cluster definition
 - At least 2 similar *Lm* isolates by cgMLST
 - Including at least 1 human isolate
 - Similarity cut-of of 99.6% (i.e. 7 allelic differences out of 1748 allele calls)



French listeriosis surveillance system

- ❑ NRC shares surveillance typing data with partners (Santé publique France, MoAg) on a weekly basis
- ❑ Data are merging with food alert data
- ❑ Cluster analysis is performed in real-time

SUPPORT D'ENREGISTREMENT										VERSION
Centre National de Référence		ENR RL00101-07 - SURVEILLANCE GENOMIQUE CONFIDENTIEL								C
		/				Listeria monocytogenes en 2015-2024			cgMLST = 0: Aucun	
</										

EU *Listeria* and listeriosis surveillance systems



See Mirko Rossi presentation

Epipulse

Item details

[View access settings](#)[< Previous](#)[Next >](#)

ID:	2021-FWD-00099	Type:	Event	Title:	Listeriosis outbreak in Bavaria
Diseases:	Listeriosis	Pathogens:	Listeria monocytogenes	Participating domain:	FWD

[Key information](#)

[Situation Awareness](#) [Comments](#) [Links](#) [Outputs \(upcoming\)](#)

[Create/update comment](#)[View history](#)

Item created on: 2021-11-22 16:42

Item last updated on: 2021-12-06 12:35

Number of reply comments: 12

NCC: Number of confirmed cases: 11

NNC: Number of non-confirmed cases: 0

NCD: Number of confirmed deaths: 1

Show 10 rows

[View comment](#)

<input type="checkbox"/>	Domain	Country / Organisation	Sector	NCC	NNC	NCD	Epidemiological information	Microbiological information	Additional information	Modified time	
<input type="checkbox"/>	FWD	Germany	Public Health	11	0	1	In Germany we have had a listeriosis outbreak since 2015 - 2021, with a total of 11 patient cases. The internal RKI name is Ypsilon1a. 2 males and 9 females between the ages of 51 and 90 years (median 81) were registered. All cases are from Bavaria. Four people died. Food could not yet be identified. We would be interested to know whether other countries have also identified this type of sequence cluster. If you have any questions, please use FG35-Listeriose@rki.de . For microbiological questions, please contact HalbedelS@rki.de			2021-11-22 16:47	Edit
<input type="checkbox"/>	FWD	Denmark	Public Health	0	0			We have no closely related isolates in our database		2021-12-06 12:35	
<input type="checkbox"/>	FWD	Sweden	Public Health	0	0	0		In Sweden, there is no human strain in our collection that matches the outbreaks strains.		2021-12-02 12:26	
<input type="checkbox"/>	FWD	Italy	Public Health	0	0			In Italy, we have no closely related isolates in our database		2021-11-25 14:29	
<input type="checkbox"/>	FWD	Slovenia	Public Health	0	0	0	In Slovenia, we don't have closely related <i>L. monocytogenes</i> isolates in our database. The closest match differs at 35 AD.			2021-11-24 13:58	Manage comments

Descriptive analysis of surveillance data

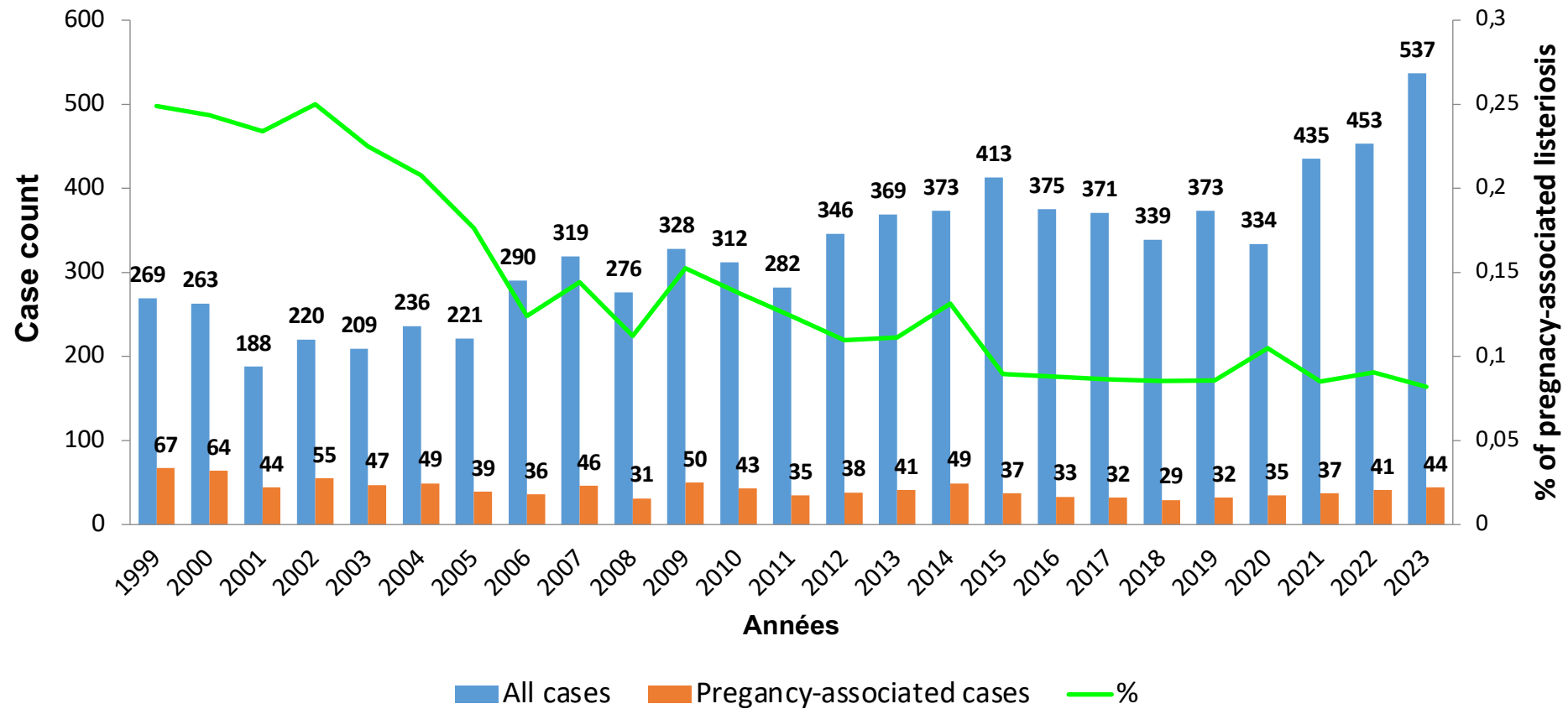
□ Epidemiologic surveillance

- Descriptive epidemiology : cases characteristics: demographics, presentation, outcomes, food consumption history...
- Incidence rates, prevalence, case fatality rates
- Analyses by age, gender, ethnicity... to identify high-risk groups
- Temporal / Geographical analysis to detect trends, seasonality...

→ Useful to describe trends (cases associated with outbreaks/clusters), generate hypothesis, write reports, share findings with public health officials, healthcare providers, and the public to inform control measures and prevention strategies

Descriptive analysis of surveillance data

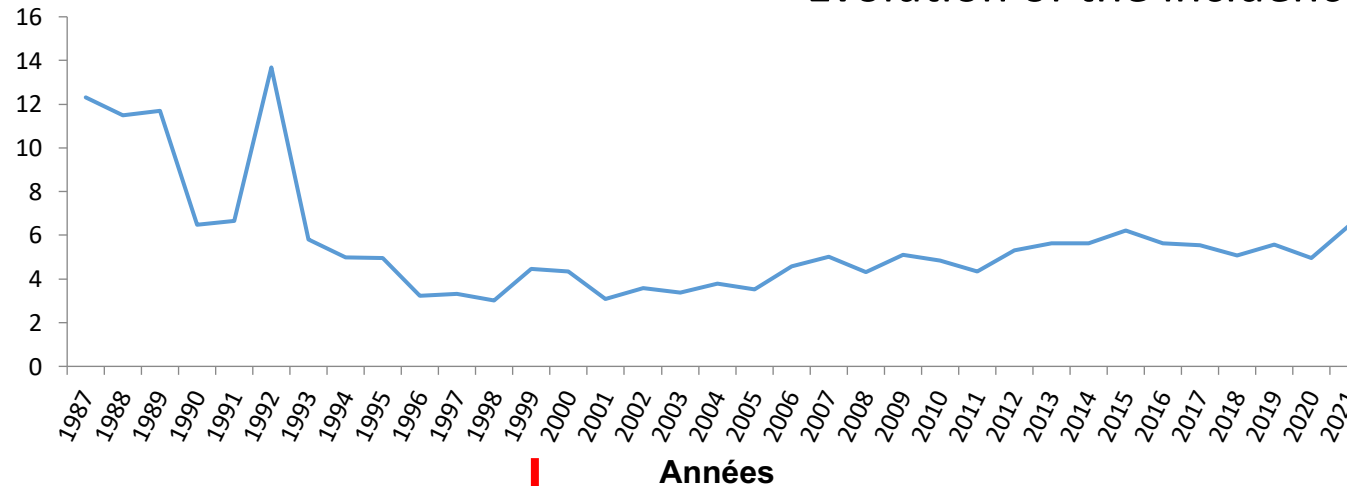
Annual numbers of listeriosis cases and pregnancy-associated listeriosis
France, 1999–2023



Descriptive analysis of surveillance data

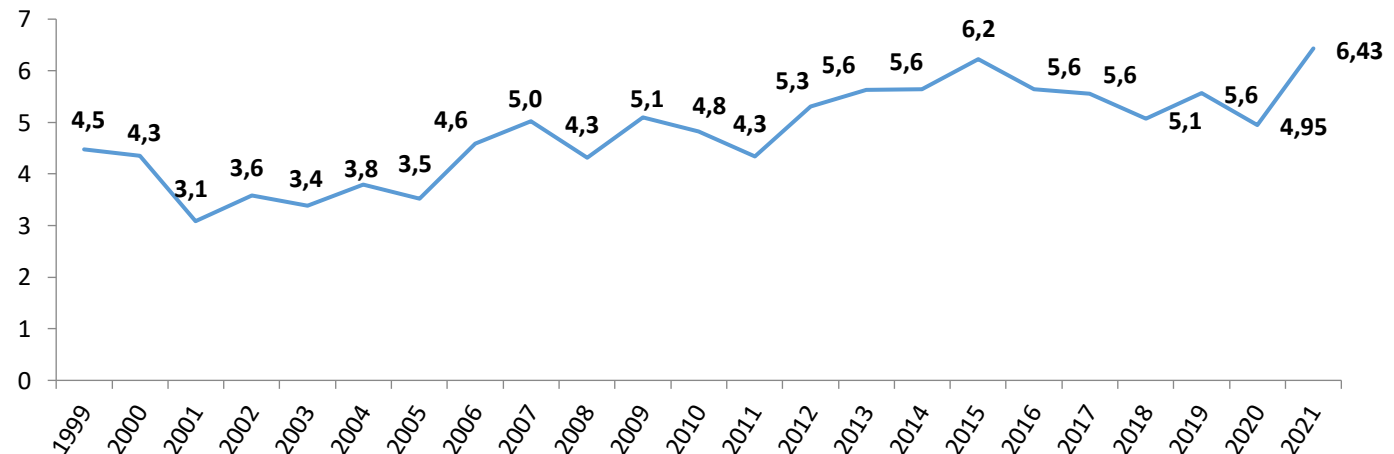
Incidence / million hab.

Evolution of the incidence of listeriosis France, 1987–2021



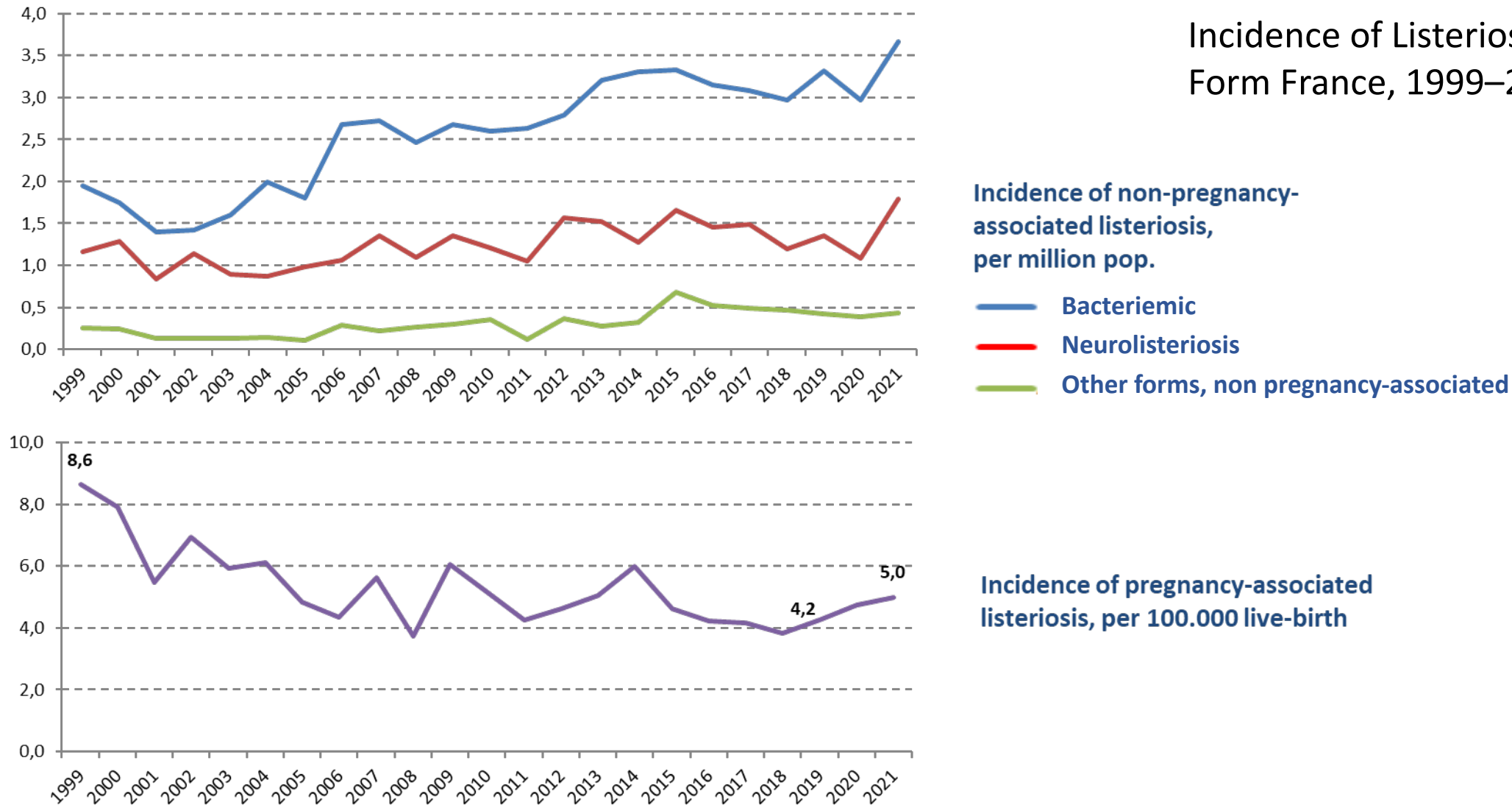
Incidence / million d'hab.

1999-2021



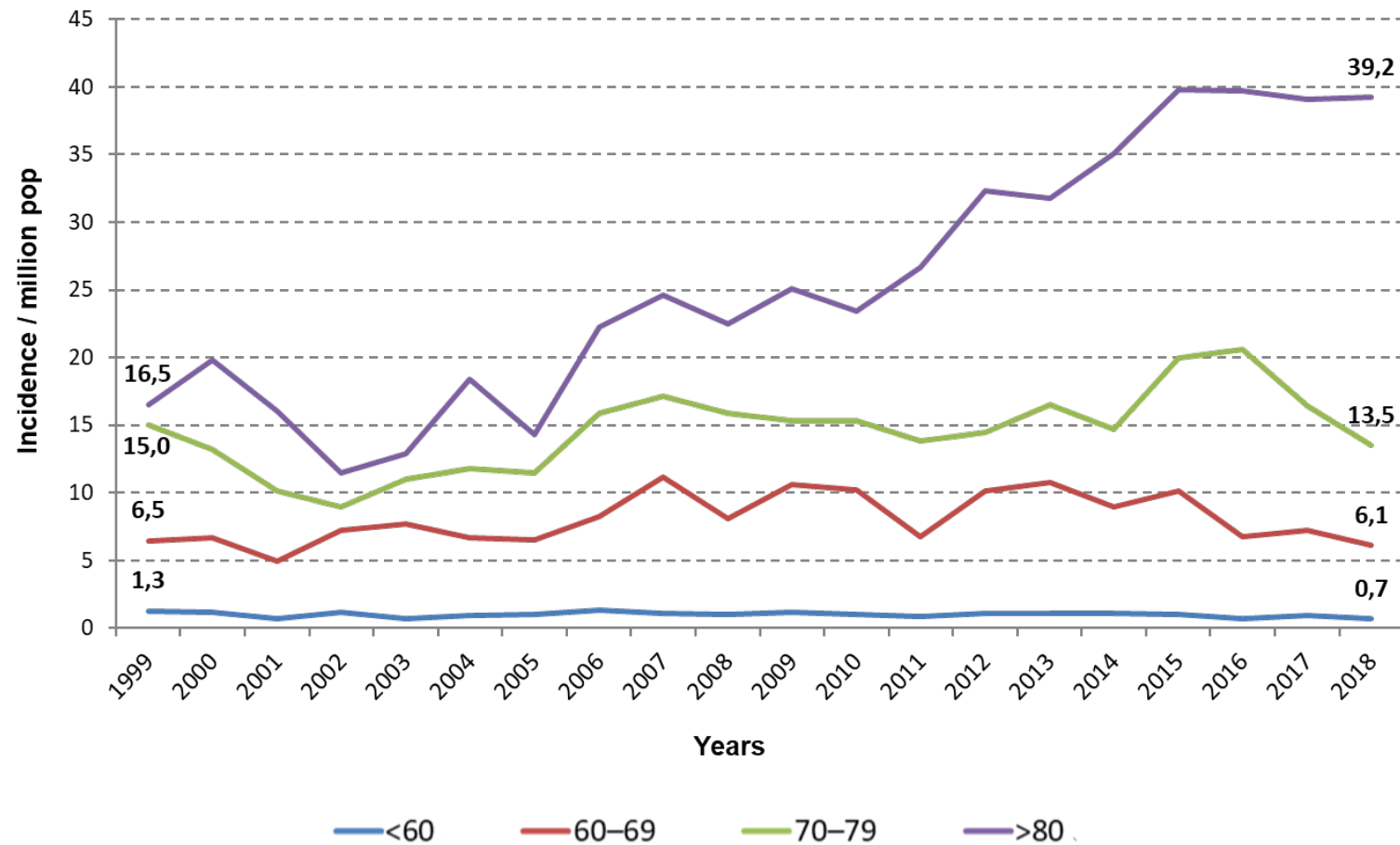
Descriptive analysis of surveillance data

Incidence of Listeriosis by Clinical Form France, 1999–2021



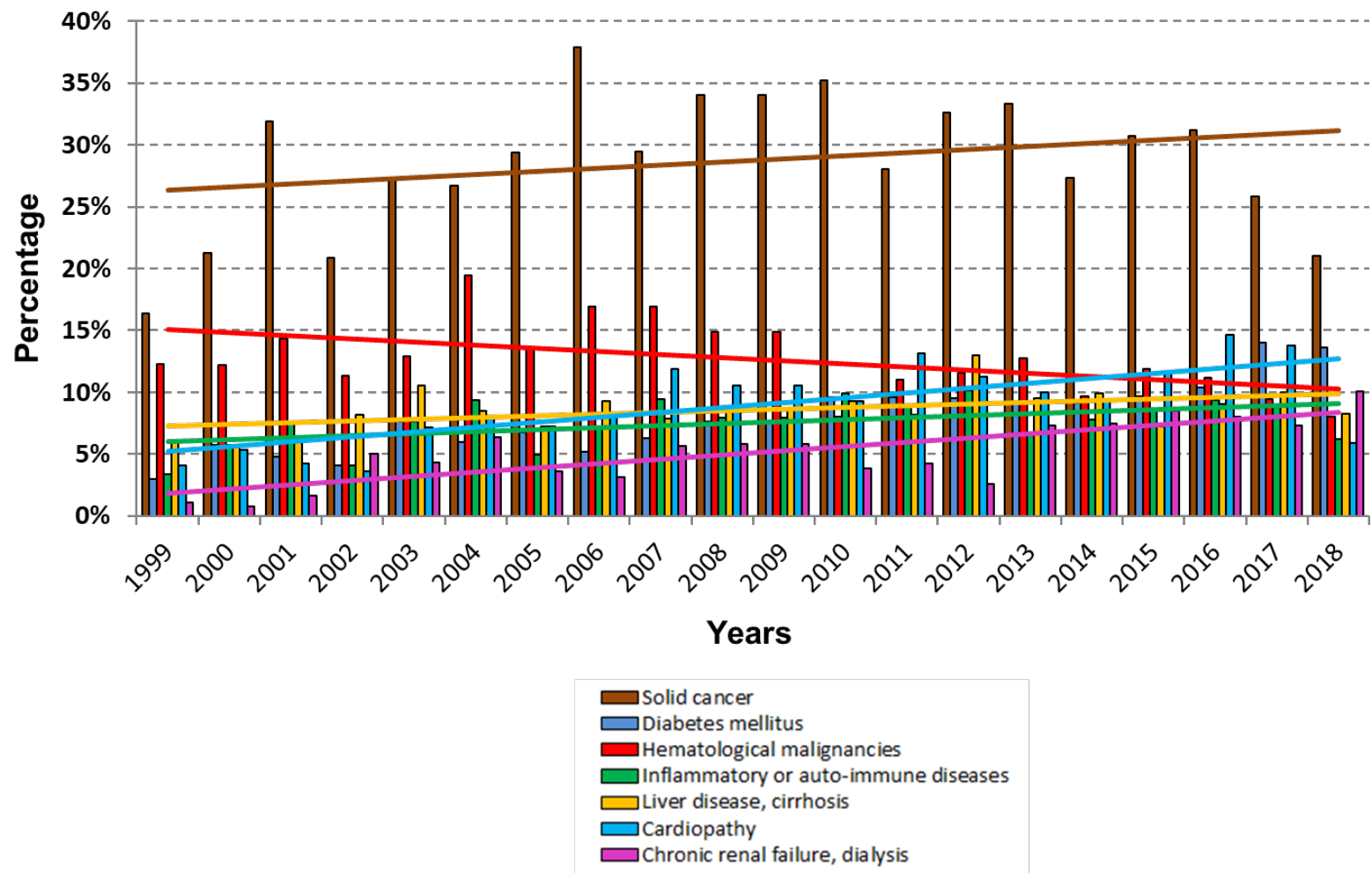
Descriptive analysis of surveillance data

Incidence of non-pregnancy-associated listeriosis by age categories, France, 1999–2018



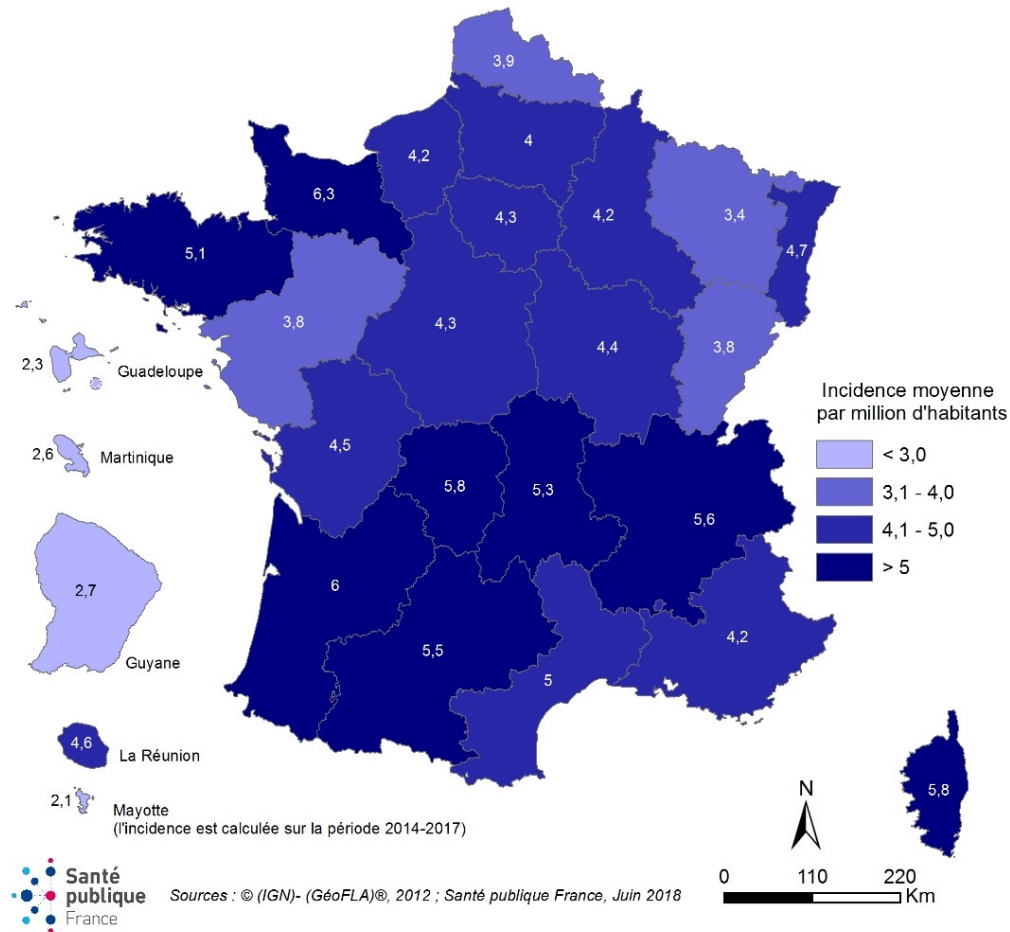
Descriptive analysis of surveillance data

Reported underlying conditions among listeriosis cases, France, 1999–2018



Descriptive analysis of surveillance data

Annual incidence of listeriosis
by region



Cluster/Outbreak detection : Microbiologic surveillance

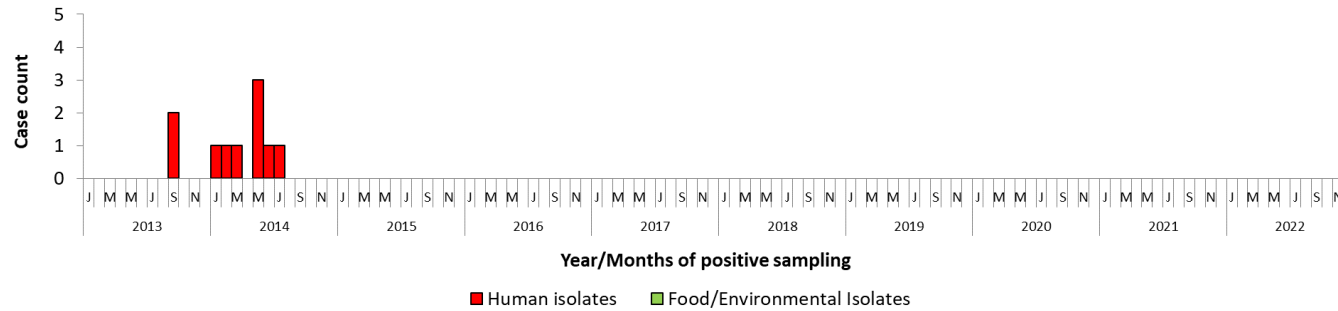
- ❑ Classic 10 steps of an outbreak investigation:
 - 1. Determine existence of an outbreak
 - 2. Confirm diagnosis
 - 3. Develop clear and consistent case definitions
 - 4. Perform case finding
 - 5. Describe time, place, person data (= descriptive epidemiology)
 - 6. Interview cases and generate hypothesis
 - 7. Test hypothesis (= analytical epidemiology)
 - 8. Perform further studies (microbiological, trace-back)
 - 9. Inform risk managers, advise on control measures
 - 10. Disseminate findings, conduct evaluation

Cluster/Outbreak detection and investigation

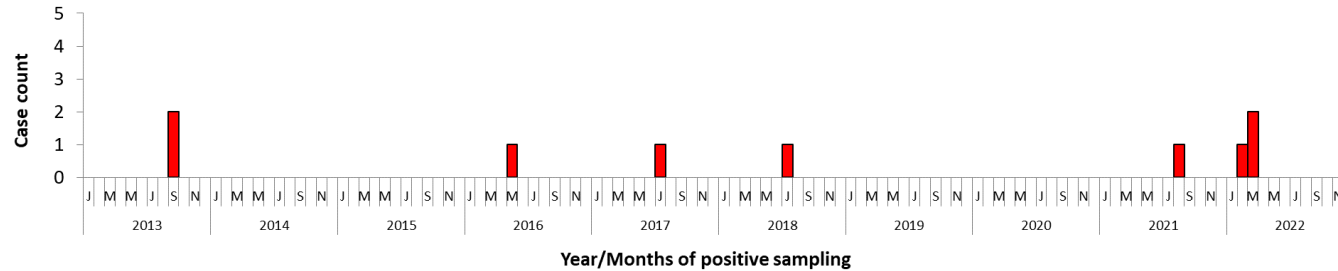
- ❑ In the microbiologic surveillance era : clusters/outbreak are predominantly (but not only) identified by microbiology surveillance
 - ❑ Case definition “easily” defined
 - Confirmed cases: *Lm* infection with outbreak strain (define by cgMLST)
 - Possible/suspected cases (pending typing): might be investigated, but not really efficient
 - Time/place might be specify
 - ❑ So
 - 1. Determine existence of an outbreak
 - 2. Confirm diagnosis
 - 3. Develop clear and consistent case definitions
 - 4. Perform case finding
 - 5. Describe time, place, person data
- are solved steps

Cluster/Outbreak detection and investigation: various situations

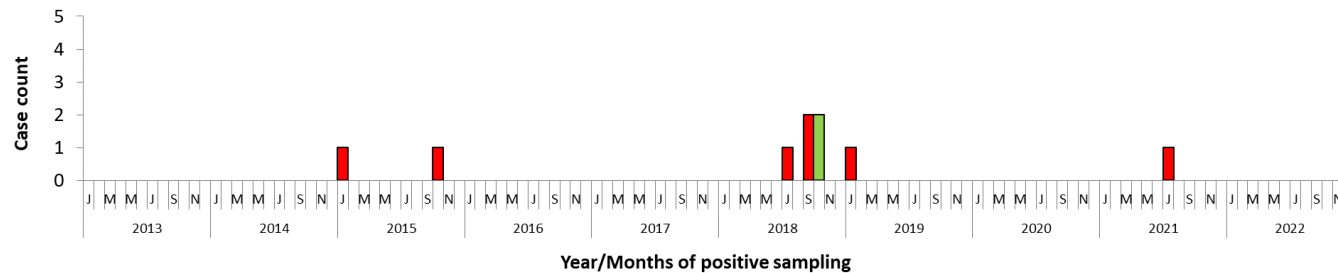
Human Cases and Food/Environmental Isolates by Year/Months of Positive Sampling



1. Point source contamination



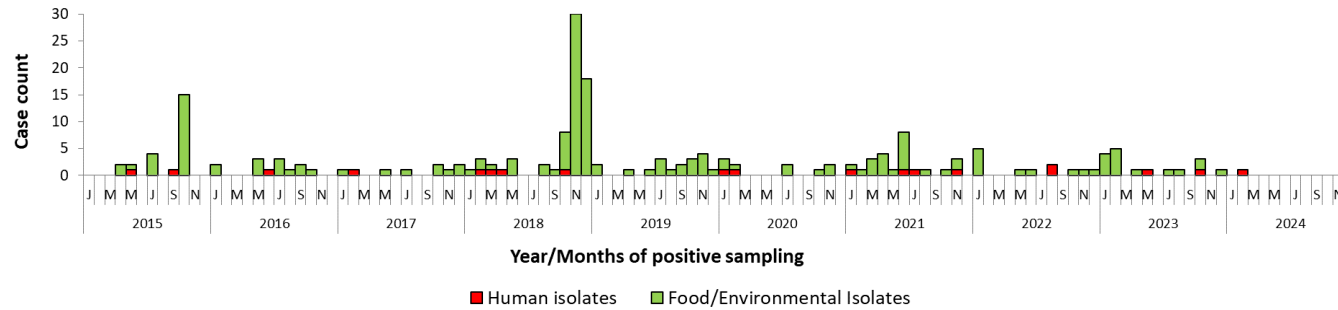
2. Persistent contamination or re-introduction



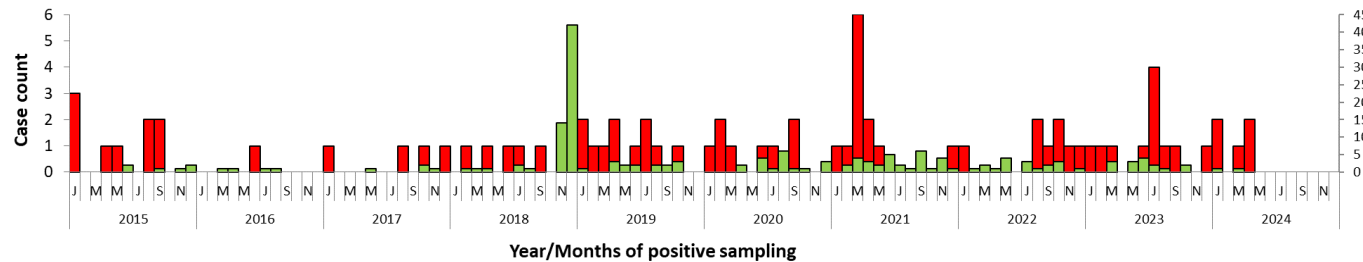
3. Association with food/environmental isolates

Cluster/Outbreak detection and investigation: various situations

Human Cases and Food/Environmental Isolates by Year/Months of Positive Sampling



4. Predominant F/E isolates

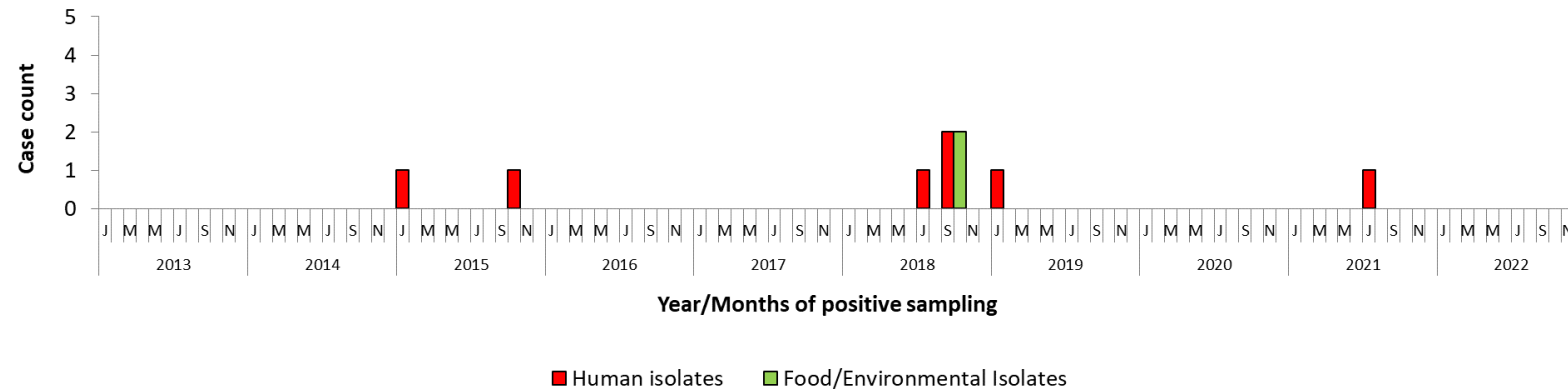


5. Complex clusters

But many others...

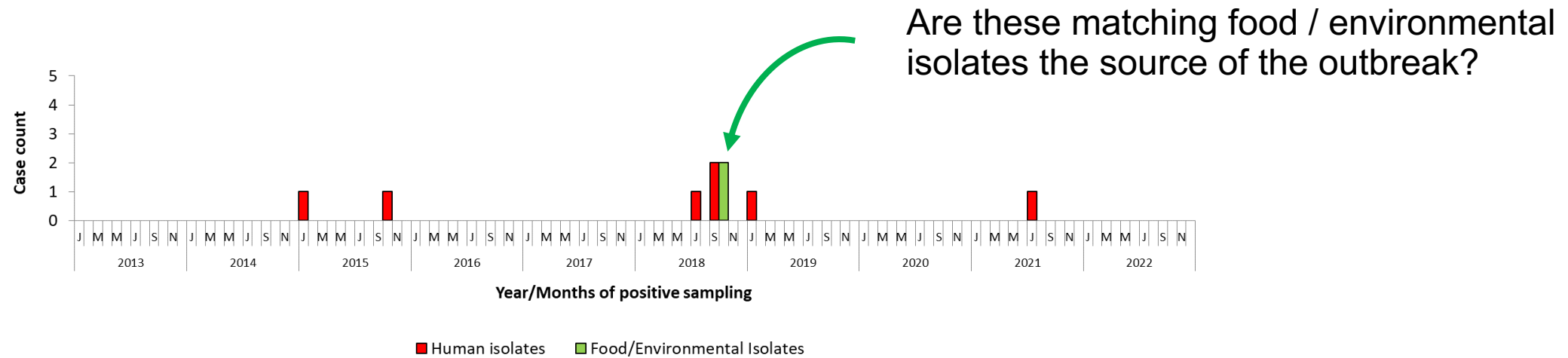
Listeriosis Clusters/Outbreaks Next Steps : identifying sources?

❑ Is matching sufficient?



Listeriosis Clusters/Outbreaks Next Steps : identifying sources?

❑ Is matching sufficient?



Identifying sources requires: Epidemiology

❑ Classic 10 steps of an outbreak investigation:

- 1. Determine existence of an outbreak
- 2. Confirm diagnosis
- 3. Develop clear and consistent case definitions
- 4. Perform case finding
- 5. Describe time, place, person data (= descriptive epidemiology)
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- 7. Test hypothesis (= analytical epidemiology)
- 8. Perform further studies (microbiological, trace-back)
- 9. Inform risk managers, advise on control measures
- 10. Disseminate findings, conduct evaluation

Principle of listeriosis outbreak investigation: 1) Interviews

- ❑ Assess food exposures of outbreak-associated cases and compare them with food exposures of a control group
 - ❑ *Listeria* characteristics drive investigation issues:
 - Given long incubation period / increase age / high CFR → obtaining food history is often difficult / potential recall bias, availability or accuracy of interviewing proxys
 - Compare with foodborne pathogens with short incubation period (*Salmonella*, *STEC*...), interviewing outbreak cases once the outbreak is recognized can be problematic
- Importance of getting high-quality real-time interview to minimize recall bias

Listeriosis food exposure questionnaire

- ❑ Should include known at-risk foods and newly identified vehicles
- ❑ Constantly evolving
- ❑ Evidence-based selected items if possible (food alerts, documented contaminated products)
- ❑ Administered in real-time so that cases food consumption history already available when cases are identified as being part of a genomic cluster
 - Feasibility depending on allocated resources
 - In-person interviews / phone interviews / online surveys

Listeriosis food exposure questionnaire

FROMAGES ET PRODUITS LAITIERS

J'aimerais maintenant vous poser quelques questions concernant les fromages et les produits laitiers que vous auriez pu consommer pendant cette période.
Pouvez-vous m'indiquer, les magasins où vous avez effectué vos achats :

1

2

3

4

5

6

7

8

Au cours des 30 jours ayant précédé le début de vos symptômes, avez-vous consommé :
(Si oui, préciser les marques, les lieux d'achat, ou de consommation, par ex. cantine, restaurant..., et le conditionnement, si applicable : (E)mballé, à la coupe, issus de l'agriculture (B) biologique, (S)urgelé, (M)aison.

	O	?	N	
145	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Camembert, si oui, préciser :
146	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	au lait cru
147	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	au lait pasteurisé
148	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Coulommiers, si oui, préciser :
149	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	au lait cru
150	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	au lait pasteurisé
151	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Brie, si oui, préciser :
152	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	au lait cru
153	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	au lait pasteurisé
154	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Comté
155	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Gruyère
156	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Beaufort
157	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Cantal
158	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Salers
159	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Emmental ou Gruyère acheté en magasin
160	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Emmental ou Gruyère acheté rapé
161	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Appenzel
162	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Gouda
163	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Mimolette
164	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Morbier
165	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Leerdammer
166	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Munster
167	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Pont-l'Évêque
168	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Livarot
169	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Maroilles
170	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Neuchâtel
171	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Saint-Nectaire
172	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Reblochon
174	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Raclette
175	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Foies gras

CHARCUTERIES ET PRODUITS CARNES

J'aimerais maintenant vous poser quelques questions concernant les charcuteries et les viandes que vous auriez pu consommer pendant cette période.
Pouvez-vous m'indiquer, les magasins où vous avez effectué vos achats de charcuteries et de viandes, (préciser les noms, villes) :

1

2

3

4

5

6

7

8

Au cours des 30 jours ayant précédé le début de vos symptômes, avez-vous consommé :
(Si oui, préciser les marques, les lieux d'achat, ou de consommation, par ex. cantine, restaurant..., et le conditionnement, si applicable : (E)mballé, à la coupe, issus de l'agriculture (B) biologique, (S)urgelé, (M)aison.

	O	?	N		Marques	Lieux d'achat (N°) ou de consommation	Conditionnement (E / C / B / S / M)
244	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	pate ou mousse de foie			
245	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	pate de campagne			
246	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	pate de volaille			
247	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	pate de lapin			
248	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	pate en croûte			
249	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	autre(s) pate(s), préciser :			
250	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	foie gras			
251	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	rillettes, si oui, préciser :			
252	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	rillettes de porc			
253	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	rillettes d'oie			
254	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	rillettes de canard			
255	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	autres rillettes			
256	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	andouilles (charentaises)			
257	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	jambon blanc (essayer de préciser au maximum la marque et le lieu d'achat)			
258	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	jambon de pays (cru ou fumé), si oui, préciser :			
259	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	jambon de Bayonne			
260	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	jambon Serrano			
261	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	autre jambon cru			
262	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	jambon de volaille			
263	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	jambonneau			
264	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	mortadelle			
265	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	speck			
266	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	pancetta			
267	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	bacon			
268	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	viande des grisons			
269	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	charcuterie corse, si oui, préciser :			
270	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	coppa			
271	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	lardon			

Santé publique France

Maladies

Exploitation des données

Utilisateurs et droits

Référentiel des maladies

m.tourdjman(Toronto)

Enregistrer

Enregistrer et terminer la saisie

Oui

Ne sait pas

270

Coppa

Bacon

Speck

Pâté de campagne

Oui

Ne sait pas

Non

245 Pâté de campagne

166 Munster

162 Gouda

145 Camembert

267 Bacon

265 Speck

656 OK pour rappel

655 Autres preuves d'achats

654 Carte de fidélité ok

653 Carte de fidélité

654 Milkshake

653 Glace ou sorbet artisanal

650 Pomme d'amour

640 Pâtisseries artisanales

639 Crèmes dessert

34

Principle of listeriosis outbreak investigation: 2) Analytic Epi Case-control study?

- ❑ Constitution of a control group can be difficult: in classic case-control study, controls should:
 - Be free from the disease / outcome of interest
 - Be selected from the same population as cases → same geographic area / same period
 - Have potential similar exposure
 - Have similar potentiality to develop the disease
 - ❑ Specific at-risk groups for listeriosis make selection of control group difficult
 - Matching criteria: age category, comorbidities, period of contamination (seasonal foods),, geographic areas (regional foods)...
- Traditional case-control studies difficult for *Lm* outbreaks: almost never done
- Case-case studies

Principle of listeriosis outbreak investigation: 2) Analytic Epi

Case-case study

- ❑ Compare food consumption frequencies of outbreak cases with food consumption frequencies of sporadic listeriosis cases in selected time / place
 - Background rate readily available
 - Comparable groups

However, for small clusters case-case studies might not provide useful information

Limitation: selection of control based on typing can introduce other bias

Aliments consommés	Cas n=7	Témoins n=23	OR	IC95%	P
Brie	7 (100%)	12 (52%)	5,5	0,5-276	0,11
Brie au lait cru	6 (86%)	2 (9%)	63	3,6-3023	0,0001
Chèvres	4 (57%)	11 (48%)	1,5	0,19-12,11	0,67
Emmental/Gruyère	4 (57%)	7 (30%)	3	0,38-25,7	0,2
Saumon fumé	4 (57%)	12 (52%)	1,2	0,16-10,23	0,82
Saucisson sec	5 (71%)	8 (35%)	4,7	0,6-56,7	0,09
Camembert	5 (71%)	17 (74%)	0,9	0,01-11,7	0,9
Lardons	6 (86%)	11 (48%)	6,5	0,6-325,6	0,08
Jambon blanc	7 (100%)	19 (83%)	1,3	0,1-72,4	0,85

Principle of listeriosis outbreak investigation: 3) Hypothesis generation using Binomial probability calculation

	<i># cases with exposure</i>	<i>% cases with exposure</i>	<i>Cumulative Probability</i>		<i>Cumulative Probability (exponential)</i>	<i>P (exactly that many hits)</i>
	31	100%	0.0000		1.326E-07	0.00000
sample size	30	97%	0.0000		2.874E-06	0.00000
31	29	94%	0.0000		3.029E-05	0.00003
	28	90%	0.0002		2.069E-04	0.00018
	27	87%	0.0010		1.031E-03	0.00082
background rate	26	84%	0.0040		3.999E-03	0.00297
60.0%	25	81%	0.0126		1.257E-02	0.00857
	24	77%	0.0330		3.299E-02	0.02041

By chance alone, how likely are we to find x of n people (or more) eating a given product?

Requires sources of background rates estimates : interviews!

Principle of listeriosis outbreak investigation: 4) Traceback investigations

- ❑ Traceback more and more useful to confirm hypothesis from questionnaires
- ❑ Exploit any proofs of purchase available
 - Loyalty cards data
 - Internet purchases
 - Brand / lot numbers collected during house visit
 - Collect them during interview
- ❑ Investigation of supplier information
- ❑ Investigation of distribution patterns

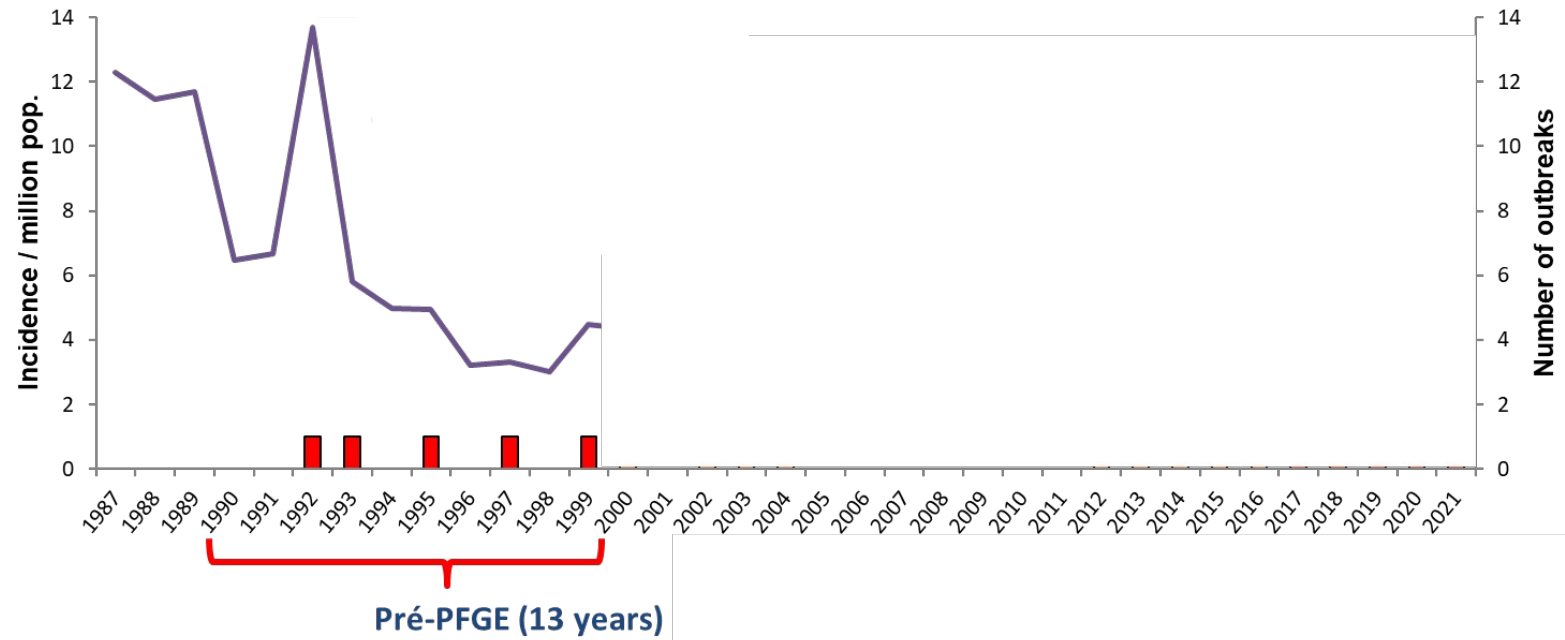
- ❑ Close collaboration with regulatory agencies:
 - To launch site investigations for a lower level of epi evidence
 - To investigate suspected products distribution sites (was product distributed in places patronized by cases?)

Principle of listeriosis outbreak investigation: 5) Food and Environmental testing

- ❑ Inspect food production facilities, processing methods, distribution channels, and storage practices to identify potential sources of contamination
- ❑ Sample suspected foods identified by epi
- ❑ Get autocheck when possible
- ❑ Get isolates from food alerts (including RASFF?)
- ❑ Integration into a joint database in a timely manner AND with relevant metadata: food item, producer identifier, etc...
- ❑ Systematic integration of isolates implicated in recalled products?
- ❑ Other isolate sources: fridge testing / Hospital inspection for cases suspected to be hospital-acquired

IMPORTANCE OF THE RELEVANT METADATA

Impact of genomic on cluster detection



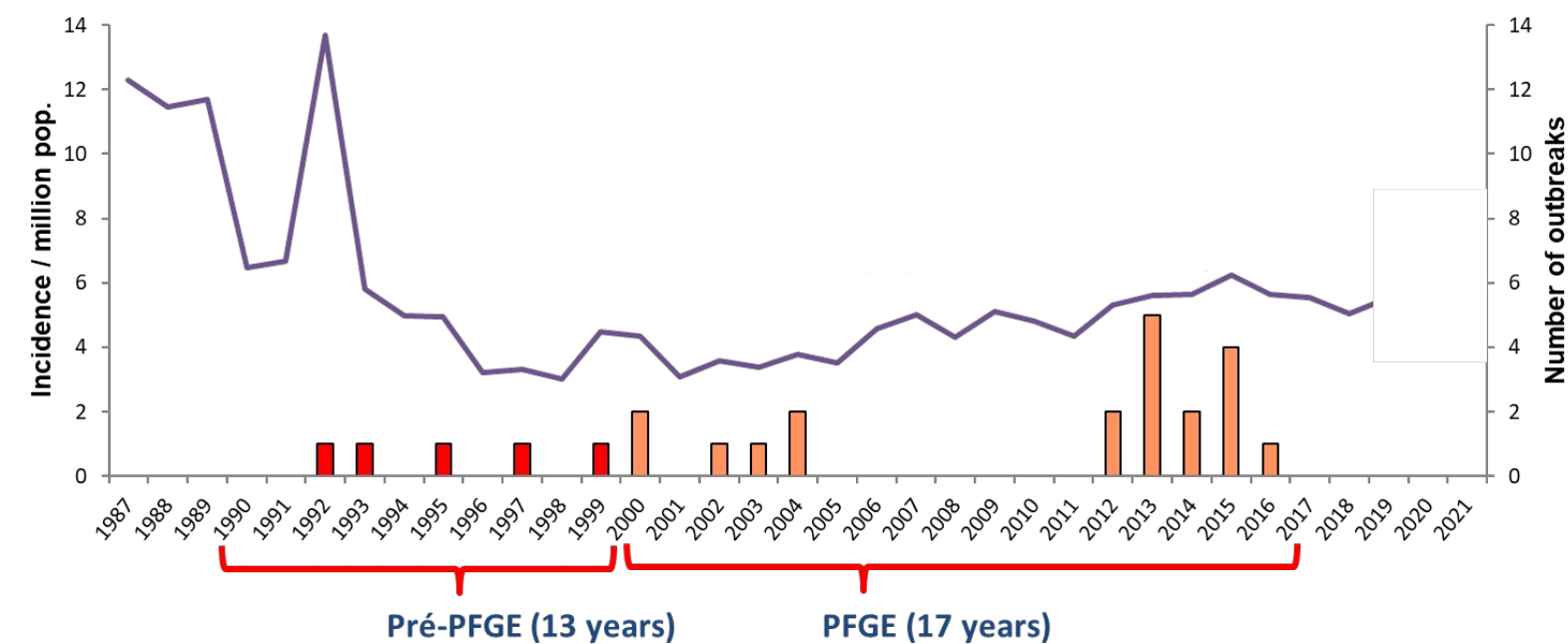
Investigated clusters

Identified outbreaks 5

Mean nb outbreak/year 0,4

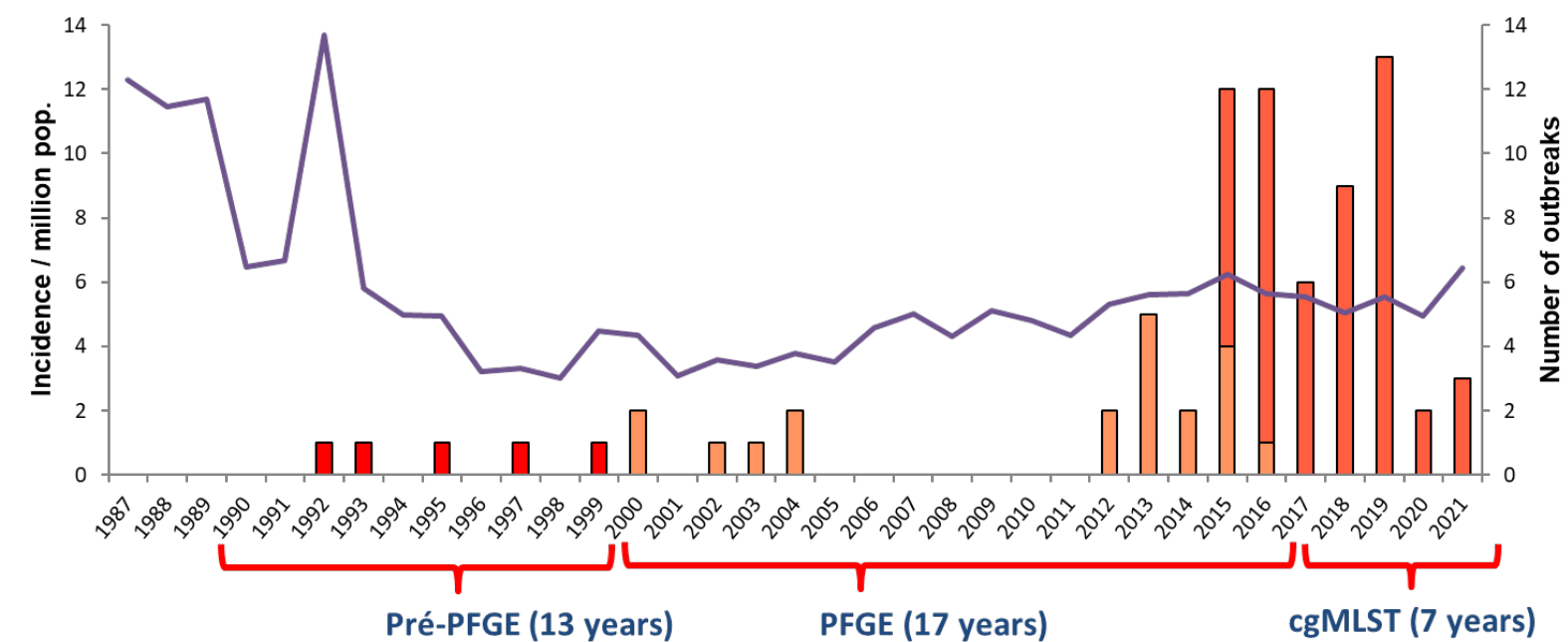
Med nb case/outbreak 36

Impact of genomic on cluster detection



Investigated clusters	202	
Identified outbreaks	5	20 (10%)
Mean nb outbreak/year	0,4	1,2
Med nb case/outbreak	36	6

Impact of genomic on cluster detection

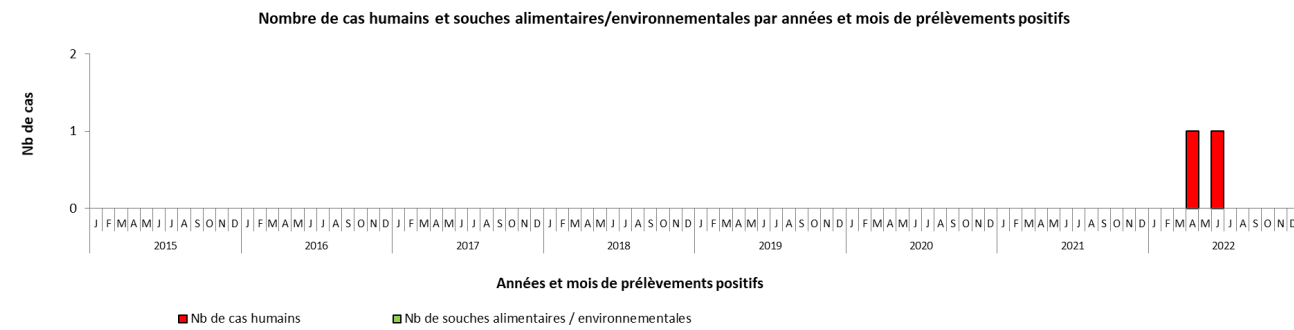


2024 : 652 clusters followed

Investigated clusters		202	440
Identified outbreaks	5	20 (10%)	83 (19%)
Mean nb outbreak/year	0,4	1,2	12
Med nb case/outbreak	36	6	2

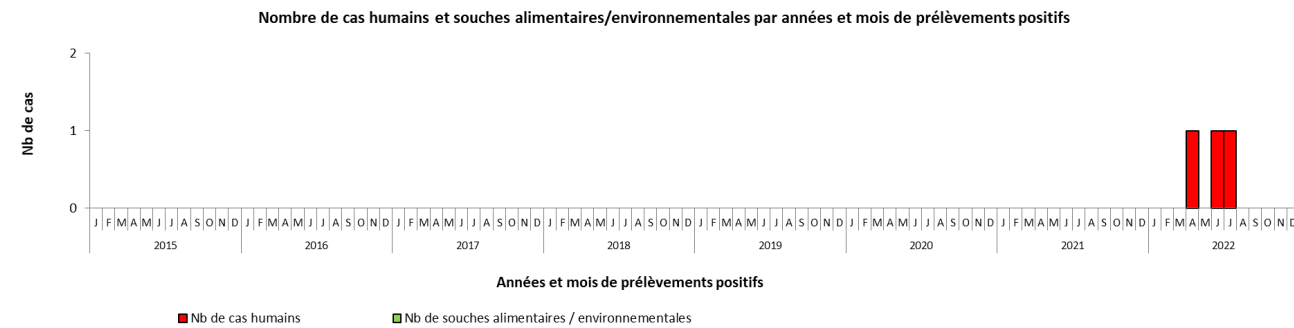
Example 1
**Outbreak of Listeriosis Associated with Consumption
of Vegan Cheese**

Alert and investigations



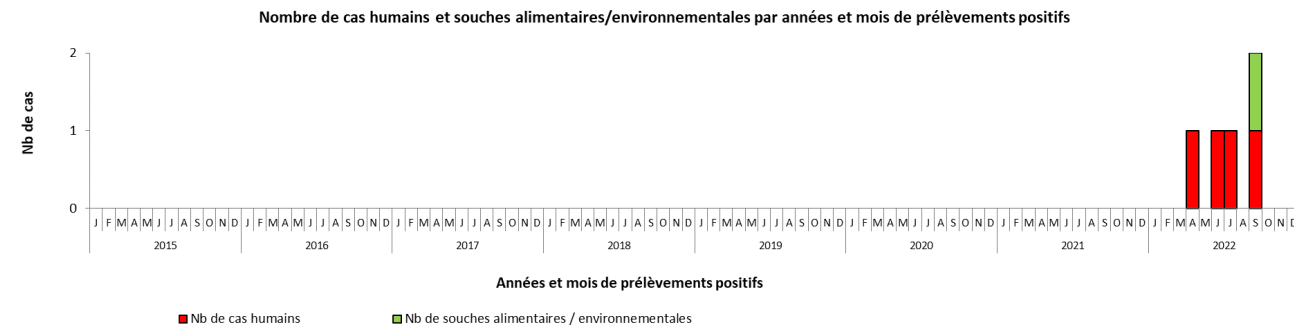
- ❑ 07/2022: cluster of 2 cases, including 1 reporting consumption of a recalled vegan cheese-like product and 1 with vegan habits

Alert and investigations



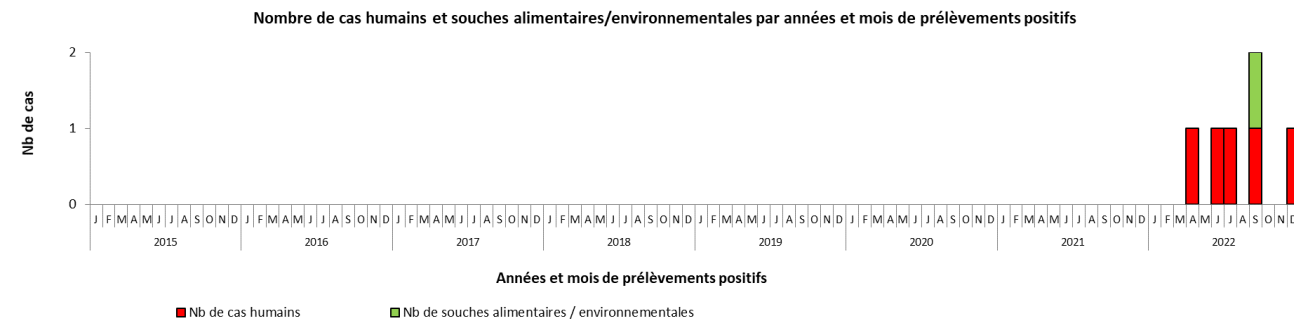
- ❑ 07/2022: cluster of 2 cases, including 1 reporting consumption of a recalled vegan cheese-like product and 1 with vegan habits
- ❑ 08/2022 : 1 additional case, interview found exposure to the recalled product
- ❑ Exported product: no food isolate available from recalled products

Alert and investigations



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- ❑ 10/2022 : 1 additional case, interview/traceback suggested ongoing contamination
- ❑ Isolate recovered from testing in Belgium (RASFF) confirmed similarity
- ❑ Plant inspection suggested control measures were taken

Alert and investigations



- ❑ 07/2022: cluster of 2 cases, including 1 reporting consumption of a recalled vegan cheese-like product and 1 with vegan habits
- ❑ 08/2022 : 1 additional case, interview found exposure to the recalled product
- ❑ Exported product: no food isolate available from recalled products
- ❑ 10/2022 : 1 additional case, interview/traceback suggested ongoing contamination
- ❑ Isolate recovered from testing in Belgium (RASFF) confirmed similarity
- ❑ Plant inspection suggested control measures were taken
- ❑ 12/2022 : 1 additional case triggered further inspection and confirmed ongoing contamination
- ❑ Facility closed. EpiPulse 2022-FWD-00102 identified 3 additional cases : Belgium, Germany, Netherlands, all reporting product consumption

Outbreak of Listeriosis Associated with Consumption of Vegan Cheese

N ENGL J MED 390;15 NEJM.ORG APRIL 18, 2024

Overview

- ❑ In total : 8 cases between Apr 2002 and Dec 2022, 4 EU countries
- ❑ 6 pregnancy-associated / 1 neurolisteriosis / 1 bacteremic
- ❑ All clinical isolates genetically closely related (1 allelic difference; type L2-SL475-ST504-CT11461)
- ❑ Consumers information especially pregnant women about risk associated with consumption of vegan cheese substitutes
- ❑ New vehicle, identified by epi, confirmed by genomic

CONSO

LISTERIA: DES PRODUITS VÉGÉTAUX JAY & JOY AYANT PROVOQUÉ DES "ACCOUCHEMENTS PRÉMATURÉS" RAPPELÉS

Le 20/01/2023 à 12:56

NATURALIA

Rappels produits

LE 16/01/2022

JAY&JOY

Communiqué de presse

Paris, le samedi 21 janvier 2023 - La société Jay&Joy, ses fondateurs et ses salariés, viennent d'être informés de cas de contamination par *Listeria* après ingestion de certains produits des gammes végétales, Jil et Joséphine. Nous présentons nos plus vives excuses aux personnes ayant été touchées et à leurs proches.

Immédiatement, le 14 janvier dernier, par mesure de précaution la société a procédé de façon volontaire au retrait / rappel de ses produits pour contrôles (<https://rappel.conso.gouv.fr/fiche-rappel/9072/interne>). Par sécurité, un arrêté de retrait a été pris ultérieurement, le 16 janvier dernier.

Nous sommes en contact constant avec les services de la Préfecture et de Santé Publique France. Toutes les mesures correctives prescrites dans le communiqué des services de la Préfecture et de Santé Publique France sont déjà en cours d'application. Certaines attendent la validation des services de la Préfecture et de Santé Publique France.

Les cas qui viennent d'avoir été mis en évidence (<https://rappel.conso.gouv.fr/fiche-rappel/9072/interne>).

Il a été convenu le vendredi 16 janvier dernier de ce :

A date, tous les rappels produits.

Très mobilisée depuis la fabrication de façon différents.

Chaque lot de fabrication transmis à la DDP de la Préfecture et de Santé Publique France.



Après cinq cas de listériose, la crèmerie végétan Jay&Joy assure que la sécurité est sa priorité

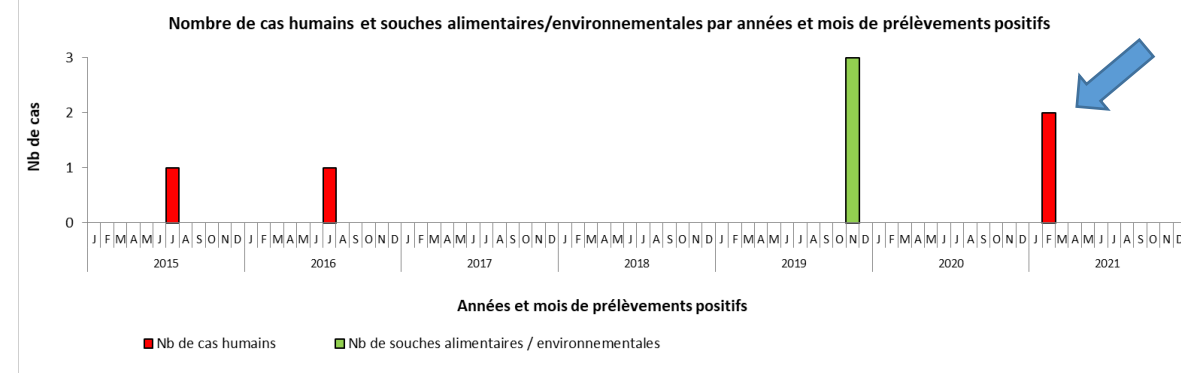
leparisien.fr/01-2023-SQ6Z6FBDNJCFNGKJXYAKJOVSQ.php

24 janvier 2023

Example 2

**Fatal neonatal listeriosis following *L. monocytogenes*
horizontal transmission in pediatric ward: cluster of 2 cases**

Alert and investigation



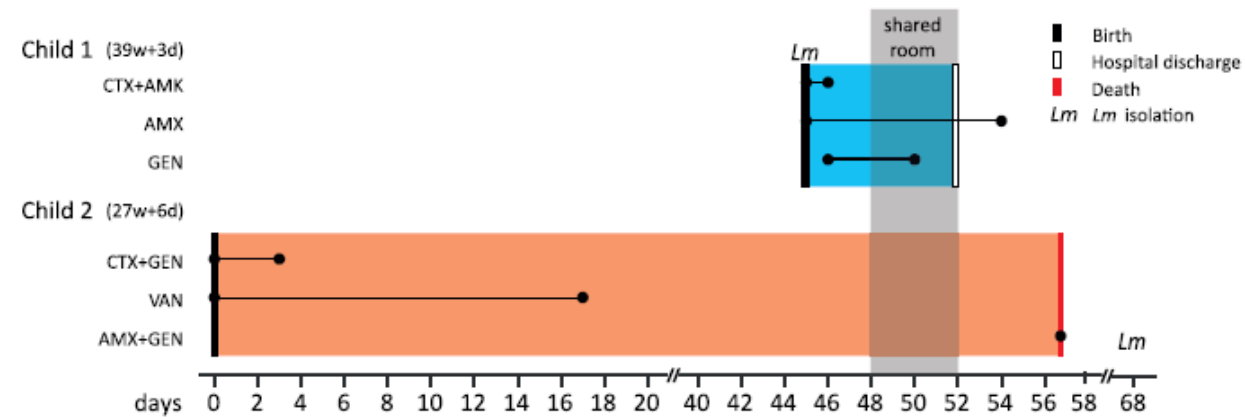
- ❑ Feb 2021 : 2 separate reports of neonatal cases from same hospital, eventually cgMLST matching
- ❑ Case #1: born on Feb 2 at 39+3 weeks of gestation
 - Stained amniotic fluid and maternal fever during labor
 - At birth : fever (38.8C), respiratory distress, sepsis
 - *Lm* cultured from placenta, gastric aspirate, maternal vaginal samples
 - Treated in neonatal ICU: Amoxicillin 9 days + Gentamicin the first 4 days
 - After 2 days of Amoxicillin: transferred to the neonatal unit in a double room.
 - Favorable outcome
- ❑ Case #2: born prematurely on Dec 25, 2020 at 27+6 weeks of gestation
 - No sign of infection, favorable evolution, transferred in neonatal unit at 32 WG, first in a single room for 2 weeks, then in double room together with case #1 for 4 days, then in single room for 4 days
 - Condition deteriorated at 35 WG: fever and refractory septic shock with fatal outcome
 - Post-mortem CSF sample grew *Lm*.

Alert and investigation

❑ Cases were unrelated until sequencing results

❑ Investigation

- Both cases were breastfed by their mothers.
- Parents used disposable gloves and gowns
- Infants shared bathtub, scale, and changing table, which were cleaned and disinfected by parents according to local decontamination procedures
- No recent changes in staff or procedures reported
- No *Lm* was found in the environment, including samples from the changing table, bath syphon, scale, and parents' toilet samples
- Both isolates were cgMLST type L1-SL4-ST4-CT1339, genosero group IVb, hypervirulent CC4, 2 AD, 2 SNP
- Additional oral inoculation experiments in adult and neonatal mice show that neonates are susceptible to a low *Lm* inoculum and this susceptibility results from the immaturity of the neonatal gut microbiota



Alert and investigation

Article

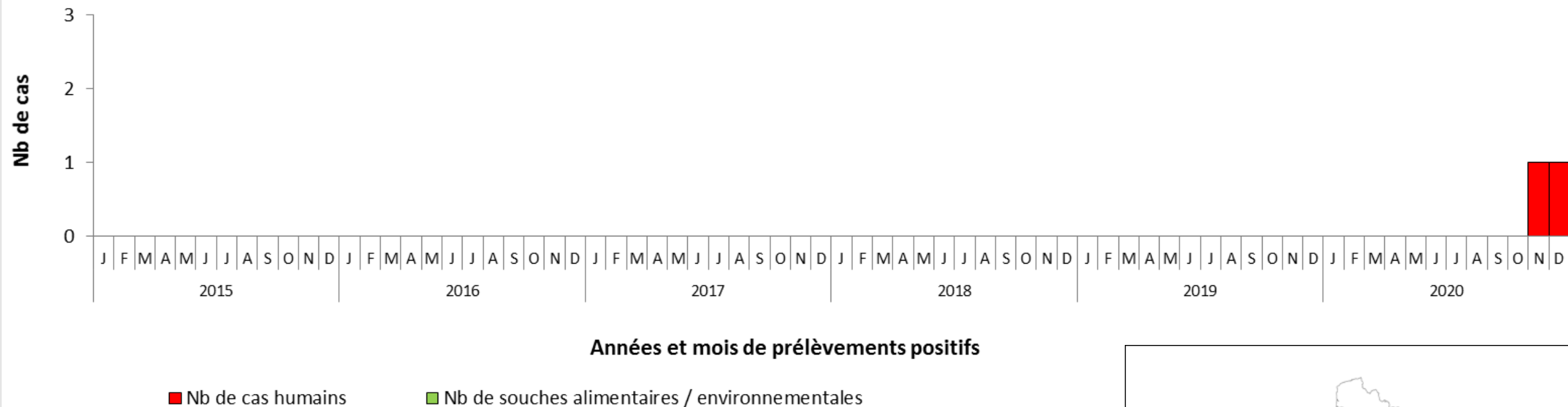
Fatal neonatal listeriosis following *L. monocytogenes* horizontal transmission highlights neonatal susceptibility to orally acquired listeriosis

- ❑ Infected neonates should be isolated for as long as they shed *Lm* in their feces to avoid horizontal transmission and its dire consequences
- ❑ Identified by epi, secondarily confirmed by genomic, triggering investigation and recommendations.

Example 3

An outbreak unfolding...

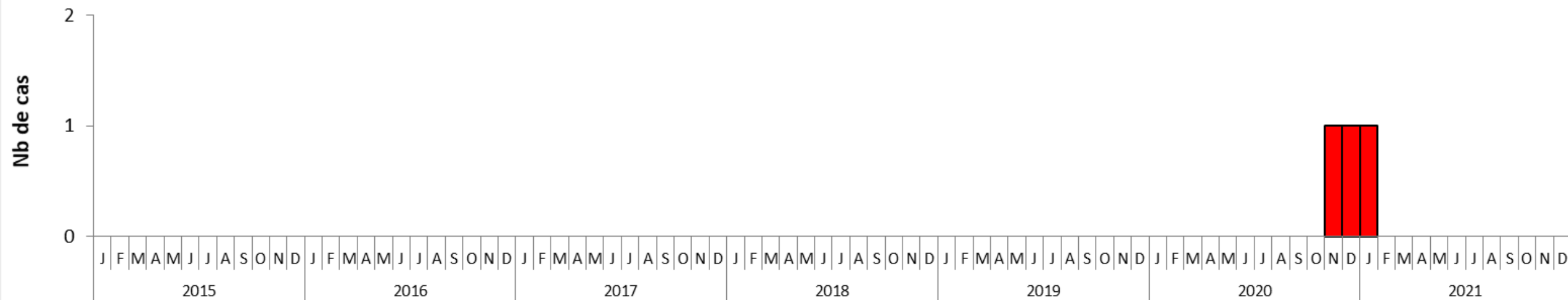
Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs



- ❑ Dec 21, 2020: 2 cases, no common source



Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs

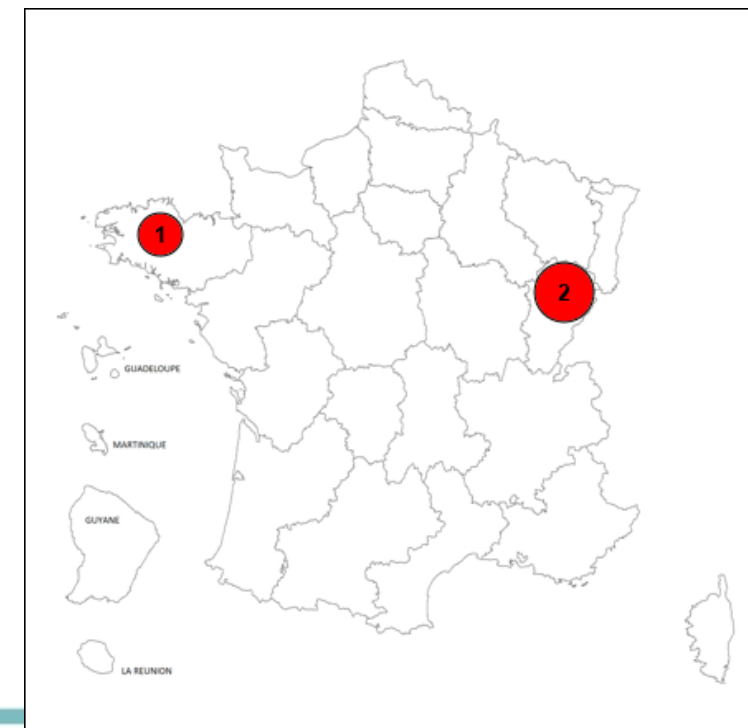


Années et mois de prélèvements positifs

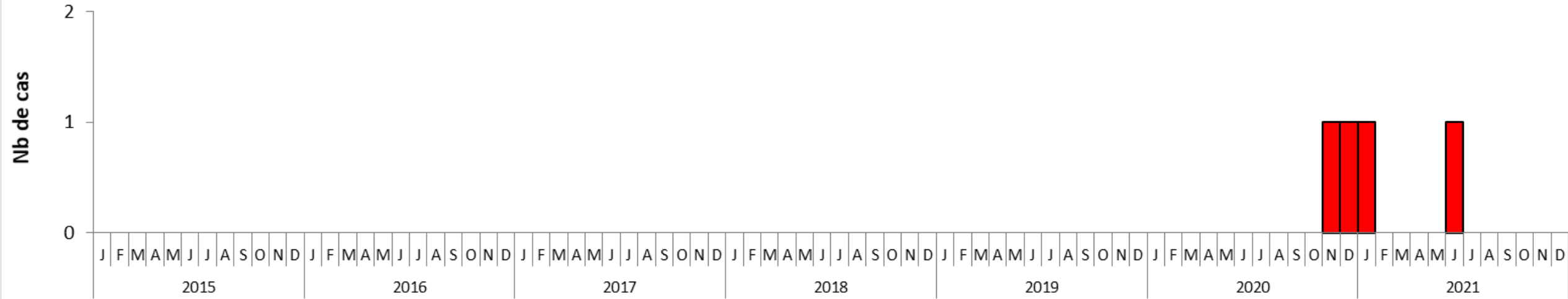
■ Nb de cas humains

■ Nb de souches alimentaires / environnementales

- Feb 2, 2021: 3 cases, no common source



Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs

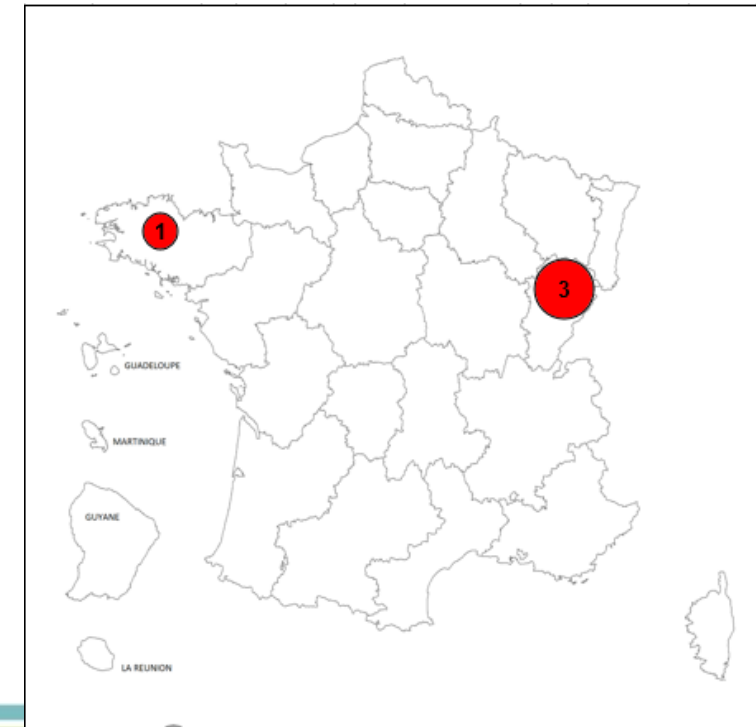


Années et mois de prélèvements positifs

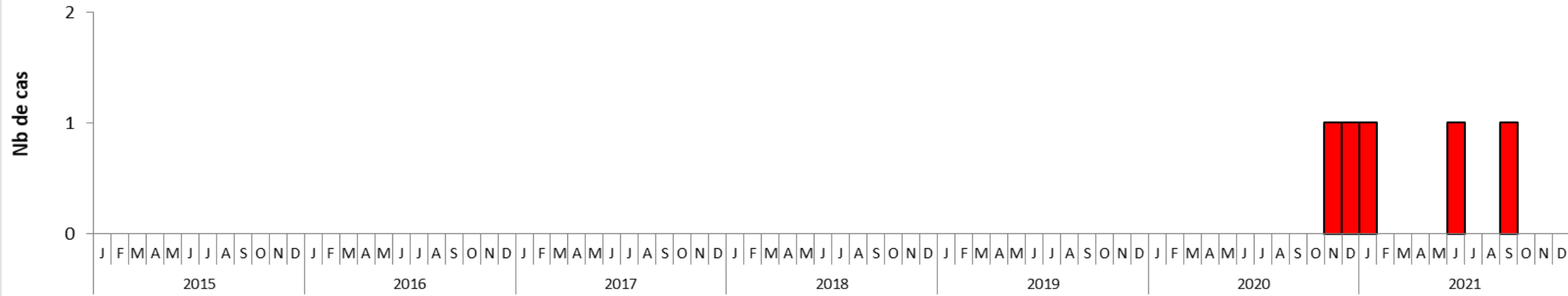
■ Nb de cas humains

■ Nb de souches alimentaires / environnementales

- Jul 7, 2021: 4 cases, no common source



Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs

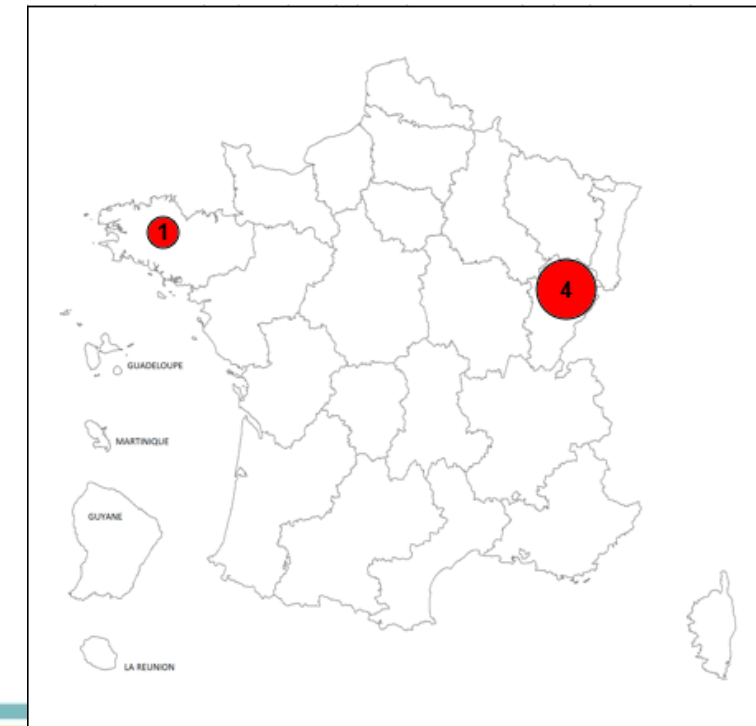


Années et mois de prélèvements positifs

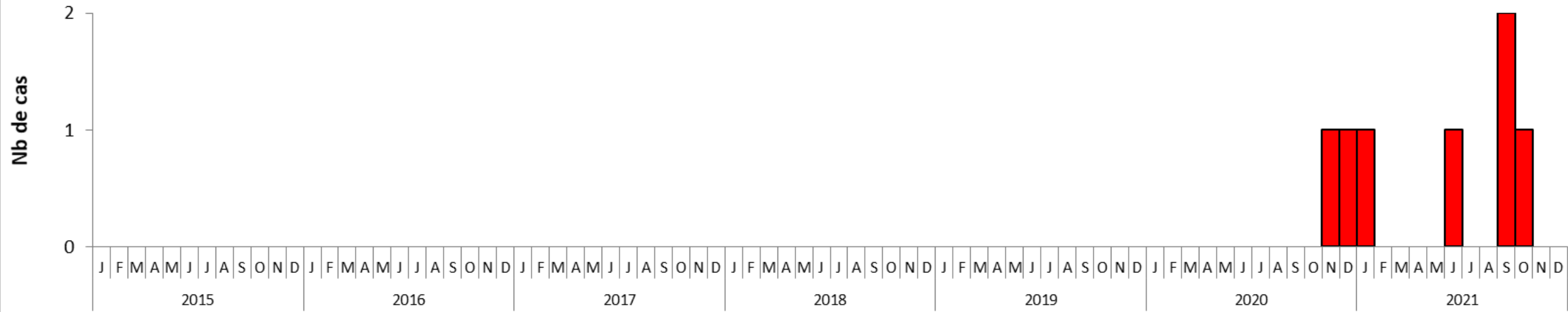
■ Nb de cas humains

■ Nb de souches alimentaires / environnementales

- Oct 7, 2021: 5 cases, no common source



Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs

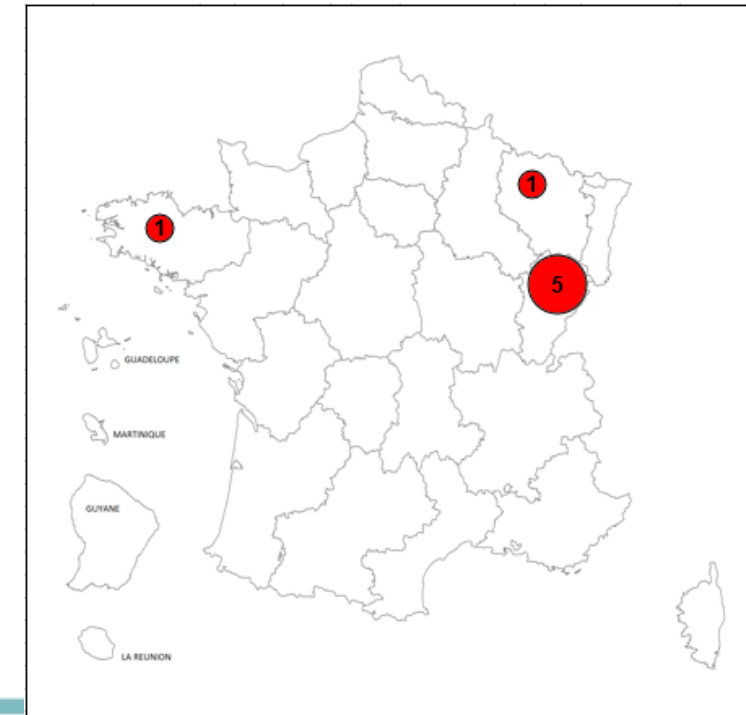


Années et mois de prélèvements positifs

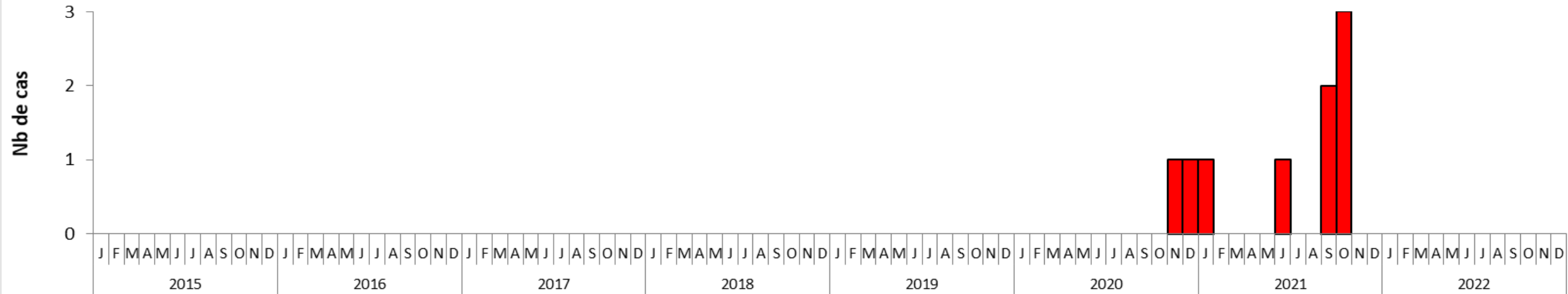
■ Nb de cas humains

■ Nb de souches alimentaires / environnementales

□ Nov 9, 2021: 7 cases, no common source



Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs

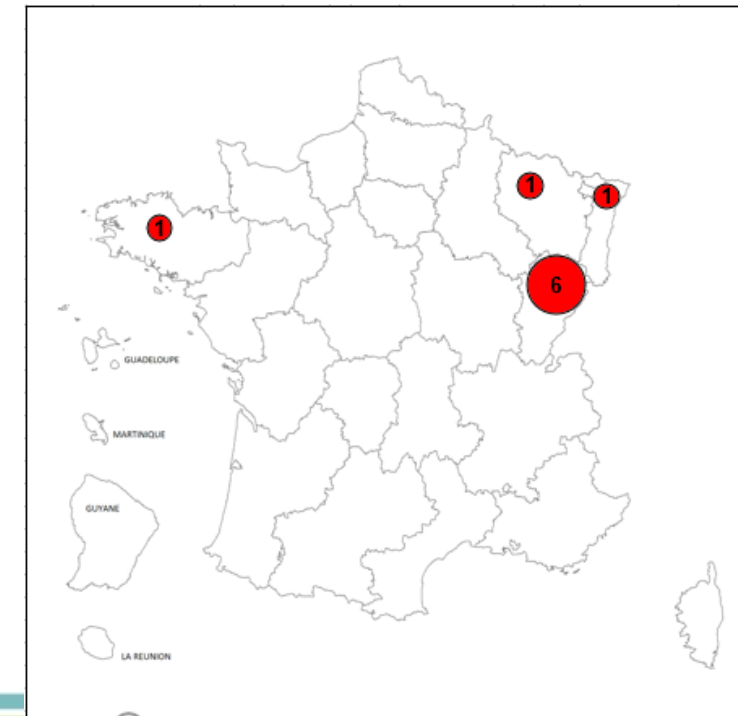


Années et mois de prélèvements positifs

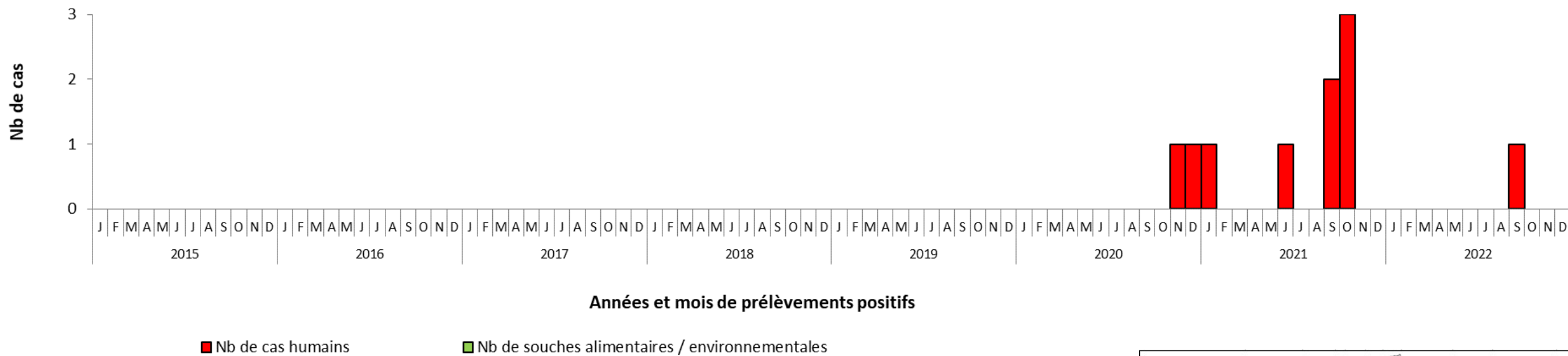
■ Nb de cas humains

■ Nb de souches alimentaires / environnementales

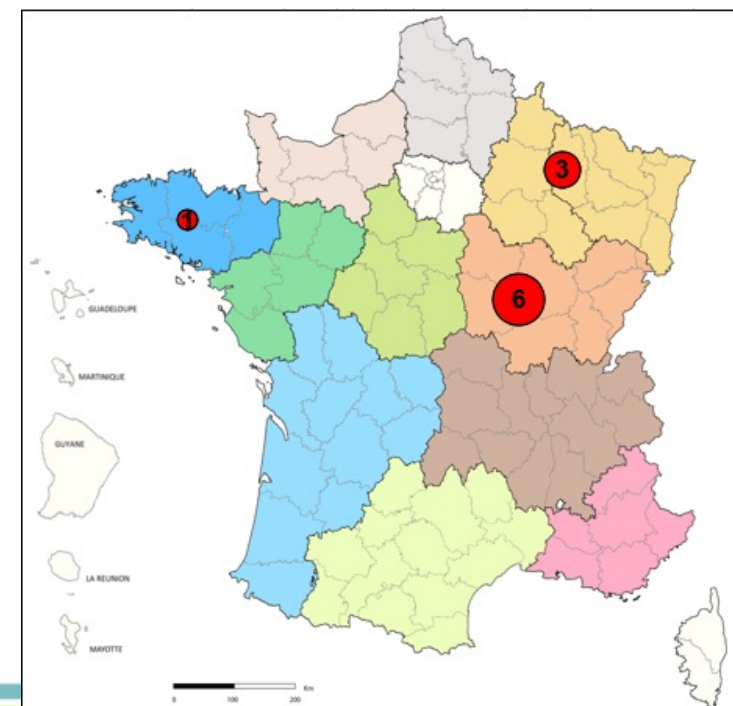
□ Jan 3, 2022: 9 cases, no common source



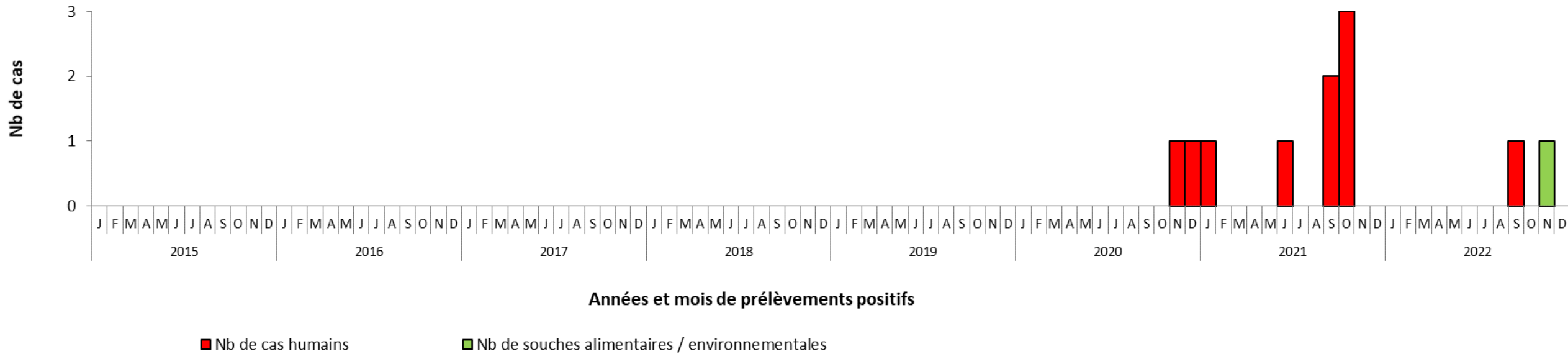
Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs



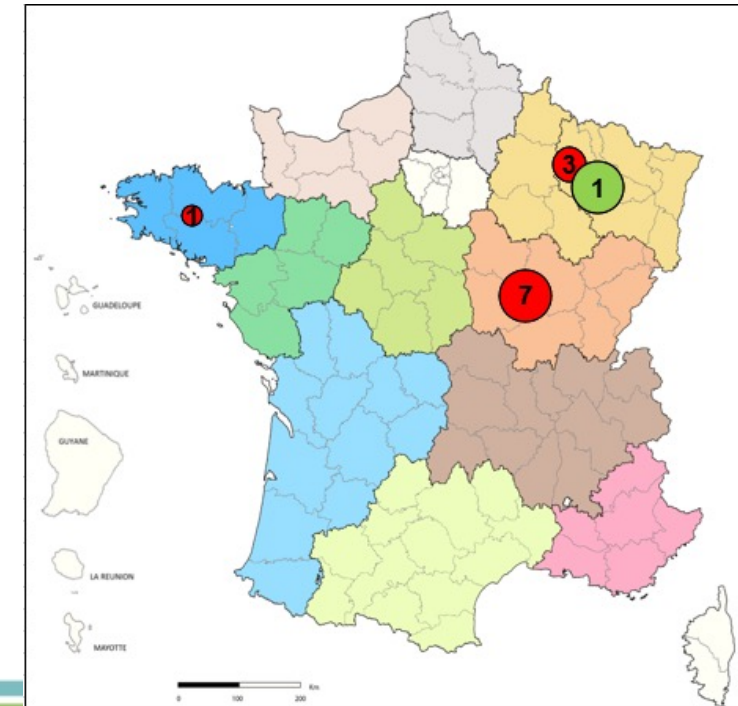
- Oct 10, 2022: 10 cases, no common source



Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs



- ❑ Dec 12, 2022: 10 cases, 1 food isolate from Munster cheese tested as part of a local food alert involving a local producer
- ❑ 3/10 reported Munster consumption, from different market, no traceback possible
- ❑ Additional information needed about the alert



Années et mois de prélèvements positifs

■ Nb de cas humains ■ Nb de souches alimentaires / environnementales

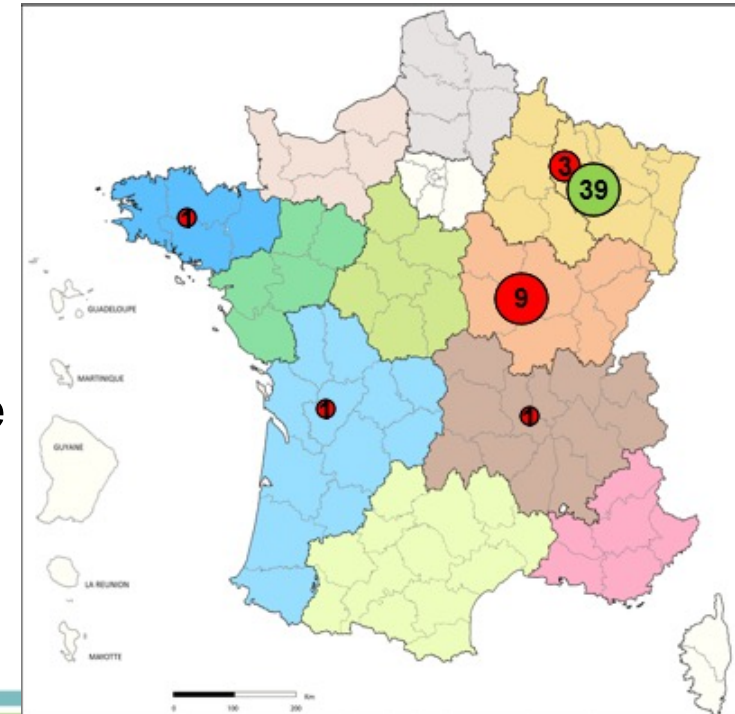
Année	Mois	Nb de cas humains	Nb de souches alimentaires / environnementales
2020	Déc	1	0
2021	Jan	1	0
2021	Fév	1	0
2021	Mars	1	0
2021	Avr	0	0
2021	Mai	0	0
2021	Juin	0	0
2021	Juillet	1	0
2021	Avr	2	0
2021	Sept	3	0
2022	Oct	0	0
2022	Nov	1	0
2022	Déc	0	2
2023	Jan	0	17

-

Nombre de cas humains et souches alimentaires/environnementales par années et mois de prélèvements positifs

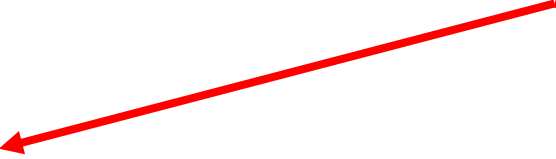


- ❑ Dec 23, 2023: 15 cases, additional food isolates from the facility
- ❑ 2 confirmed exposures to the implicated cheeses
- ❑ No specific measures taken from the investigation beside surveillance

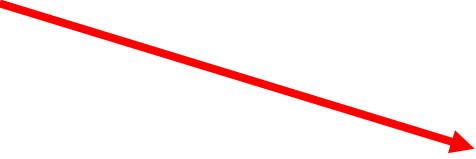


- ❑ Detailed food questionnaires / interviews are crucial but not always sufficient
- ❑ Recall bias
- ❑ Product sold to different local markets with no labeling
- ❑ Product distributed under different brand names
- ❑ Importance of food testing and combined databases

- ❑ From a public health perspective: for « identified » sources: importance to distinguish :



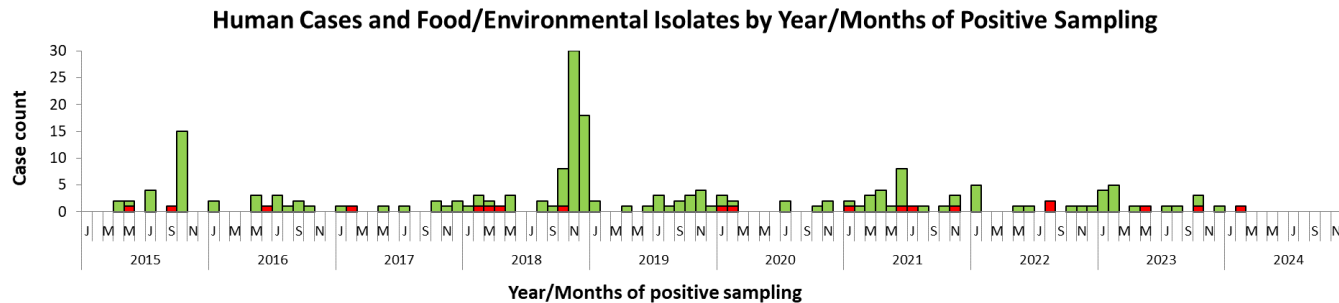
clusters with source identified
and measures taken based on
surveillance & investigation



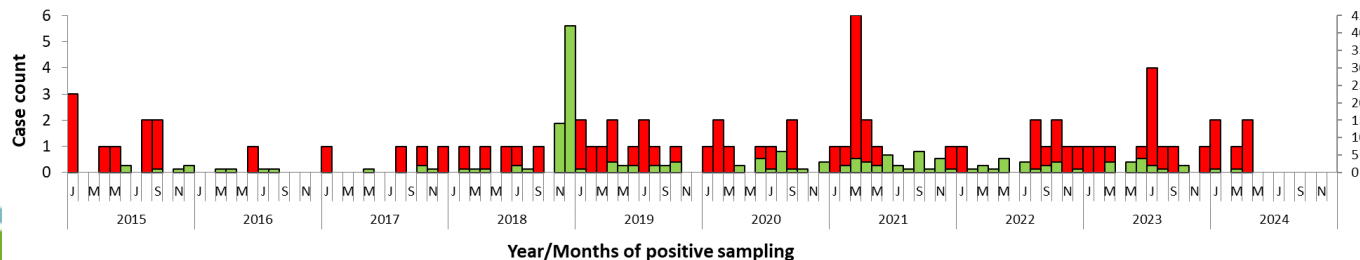
cluster with source identified based on
food surveillance and measures already taken
not based on surveillance & investigation

Pitfall of genomically-defined clusters

- ❑ Multistrain contamination can be difficult to link to a single producer as clusters might be independently analysed: importance of METADATA
- ❑ Complex clusters: hard to solve, possible multiple sources within a single cluster
- ❑ With growing number of food/isolates in the database, hypothesis generation can be complex



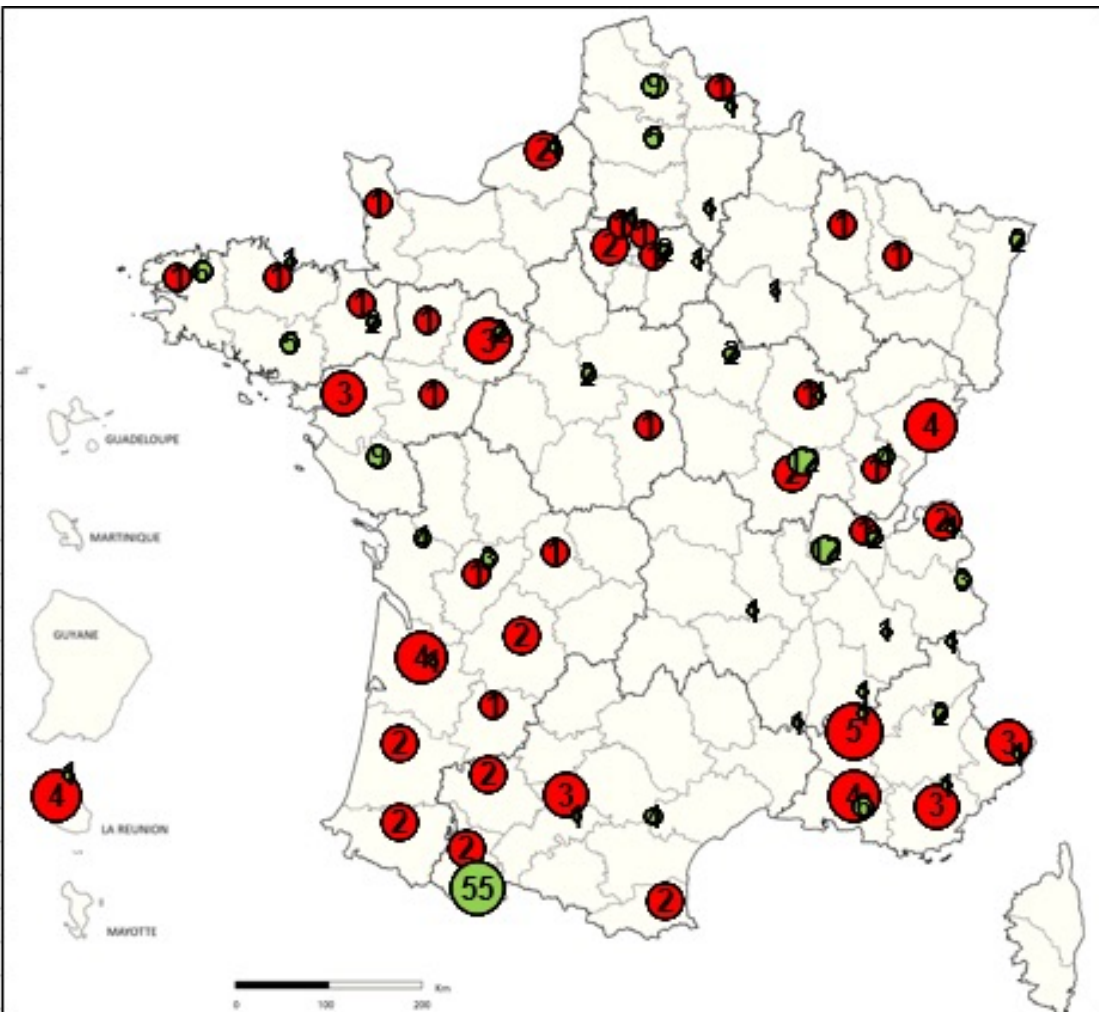
4. Predominant F/E isolates



5. Complex clusters

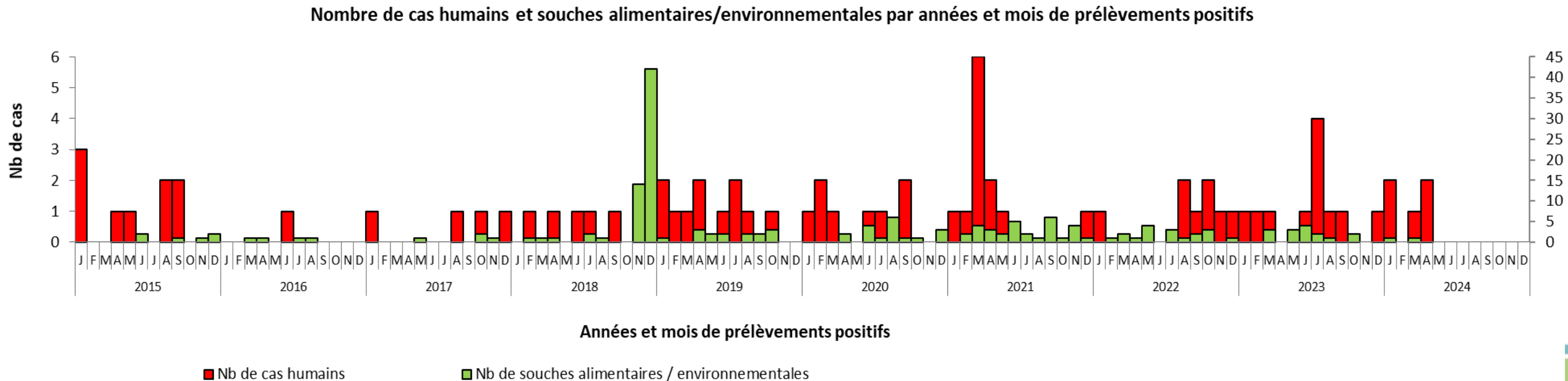
Pitfall of genomically-defined clusters

- ❑ Complex clusters: what do we do?



Pitfall of genomically-defined clusters

- ❑ Complex clusters: what do we do?
- ❑ 76 cases spanning from Jan 2015 to Apr 2024



Pitfall of genomically-defined clusters

- ❑ Complex clusters: what do we do?
- ❑ 76 cases spanning from Jan 2015 to Apr 2024
- ❑ 155 food isolates + 26 environmental isolates from XXX different foods (all the spectrum of at-risk foods), involving ZZZ producers

Conclusion & Discussion

Specific objectives

- 1) Understand foodborne outbreak investigation tools for *Listeria*:
 - Questionnaires → **extended, real time**
 - Case-control study → **no in real life**
 - Case-case study → **Yes**
 - Binomial approach → **Yes**
 - Food traceback → **Yes +++ in real time to pile up information**
- 2) Establish case definitions for surveillance and outbreak investigations → ...
- 3) Analyze epidemiological surveillance data related to *Listeria* infections → ...
- 4) Acquire knowledge of integrating genomic and epidemiological approaches to enhance *Listeria* surveillance and prevention → **Yes +++ but for hypothesis generation, NEED EPIDEMIOLOGY. MATCHES ≠ OUTBREAKS**

Acknowledgements

The creation of this training material was commissioned by ECDC to Institut Pasteur with the direct involvement of Mathieu TOURDJMAN from Santé publique France, the French Public Health Agency

Acknowledgments to:

French National Reference Center for *Listeria*, Pasteur Institute, Paris: Marc Lecuit, Alexandre Leclerc, Pierre Thouvenot, Alexandra Moura

French Ministry of Agriculture: Sophie Belichon, Nathalie Fredriksen

Santé publique France: Isabelle Billecoq, Edith Laurent, Jet de Valk