Italian involvement in the outbreak

G Scavia

Istituto Superiore di Sanità (ISS)

National Reference Lab. for E.coli - Rome (Italy) – Italian National Registry for HUS

11 Workshop of the EURL for E.coli
Rome, 10-11 November 2016

STEC outbreak in Romania, 2016

From the rumors of the web…

STIRI › Sănătate

Ministrul Sanatatii, despre cazul copiilor bolnavi din Arges: "Sunt frustrat ca nu ave… starea bebelusilo…

pubblicato il 19/feb/2016 13:52

Romania, 7 bambini di Arges ancora ricoverati. Analisi sulla…

Tre restano in terap…

Mi piace 0 face…

internazionali, sta indagar…
potrebbe essere la causa…

The Romania Journal
Your reliable online news about Romania

POLITICS | BUSINESS | SOCIETY & PEOPLE | WORLD | SPARE TIME | TRAVEL | SPORTS | FILES

BREAKING NEWS: Razvan Murgeanu, former presidential adviser for Traian Basescu, remanded by DNA

Home / SOCIETY & PEOPLE / HEALTH / UPDATE: Second child dies in the case of Argeș County haemolytic uremic syndrome, 10 babies hospitalized. Negative results for orange samples

UPDATE: Second child dies in the case of Argeș County haemolytic uremic syndrome, 10 babies hospitalized. Negative results for orange samples

to search type and hit enter

RECENT COMMENTS

Lactate Br?det owner: Under the Romanian law, none of our employees is sick - The Romania Journal: [...] New accusations related to Br?det cheese. 3 employ...

After Snoop Dogg made it famous, Bogata village launches touristic promotion site - The Romania Journal: [...] It offers as well information on the Internet spee...

After Snoop Dogg made it famous, Bogata village launches touristic promotion site - The Romania Journal: [...] Snoop Dogg's check-in mistake on Instagram made Bo...

King Mihai discharged, transported to his private residence in Switzerland - The Romania Journal: [...] King Mihai has been admitted to a medical clinic i...

New accusations related to Br?det cheese. 3 employees diagnosed with E.coli. Romanian baby hospitalised in Italy with food poisoning. - The

STEC outbreak in Romania (1):
… to information from the ECDC

ECDC Extranet | EPIS FWD Epidemic Intelligence Information System Food- and Waterborne Diseases and Zoonoses

Search this site…

Home | News | Molecular Typing Cluster Investigations | Urgent Inquiries | Documents | Users | Search

You are here: EPIS > FWD > Urgent Inquiries > Unusual cluster of severe diarrhoea with HUS

Urgent inquiry: Unusual cluster of severe diarrhoea with HUS

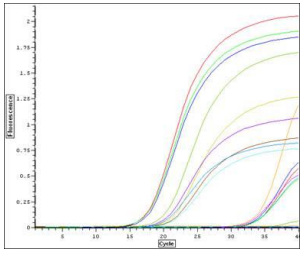
Epidemiological and microbiological information

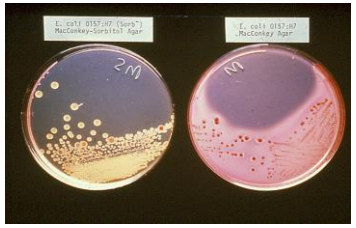
UI ID: UI-345 | **Country or institution:** Romania | **Disease:** unknown | **Pathogens:** unknown | Open map

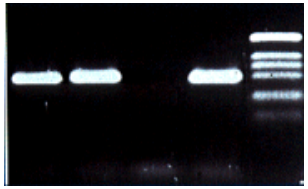
ECDC/EFSA: Multi-country outbreak of STEC infection associated with HUS
http://ecdc.europa.eu/en/publications/

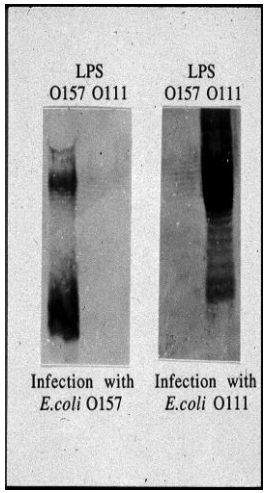
HUS and STEC infection in Italy

- **Laboratory diagnosis of STEC infection by:**
  - ✓ Direct examination of feces for Free Stx (Vero cell assay) and Stx genes (Real Time PCR)
  - ✓ STEC isolation
  - ✓ Detection of serum antibodies against the LPS of E. coli O157, O26, O103, O111, O145 (ELISA)

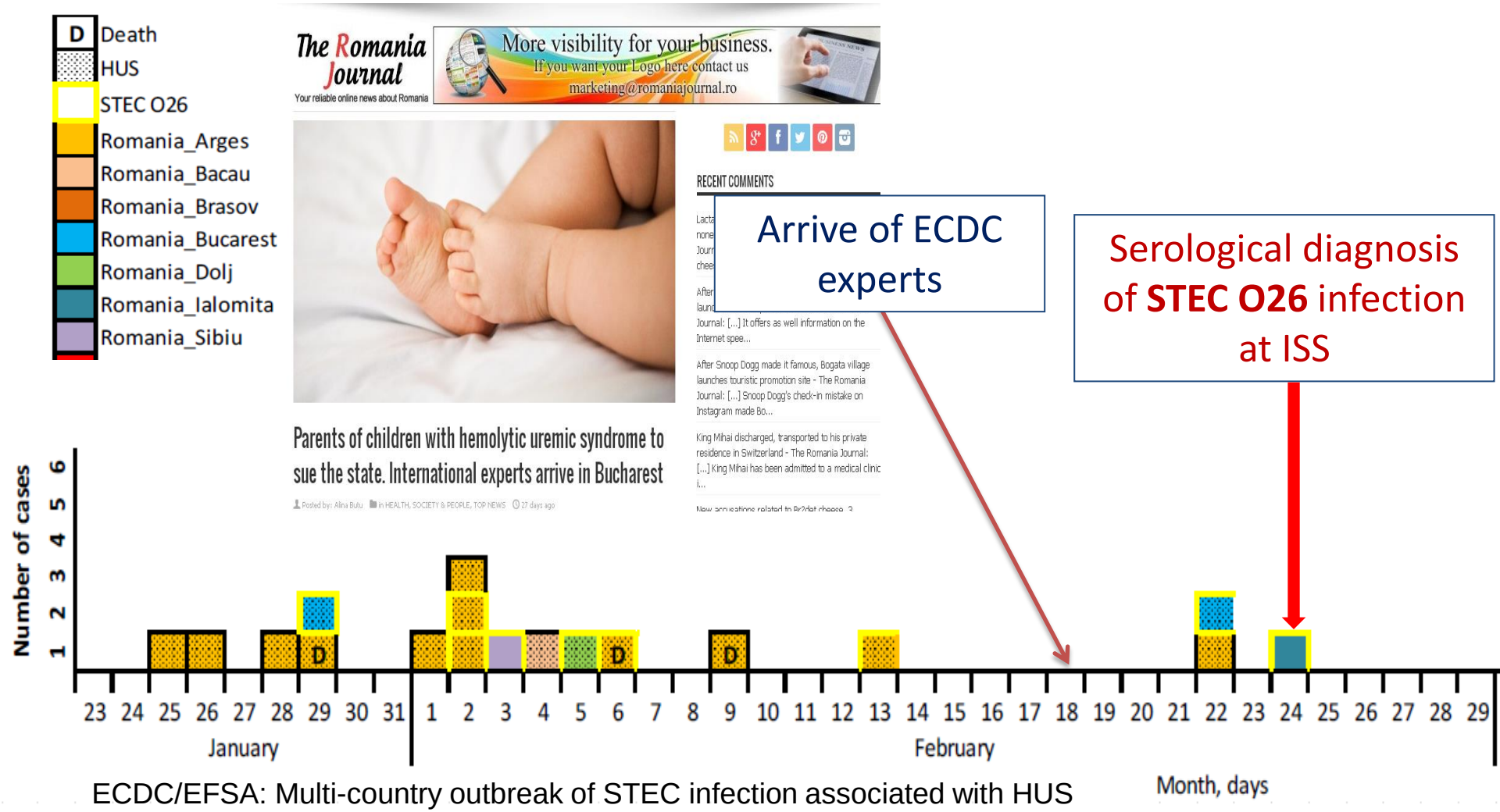








STEC outbreak in Romania (2):
January – February 2016



ECDC/EFSA: Multi-country outbreak of STEC infection associated with HUS
http://ecdc.europa.eu/en/publications/

STEC outbreak in Romania (3):
precautionary RASFF for cheese (NEWS)

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Directorate G: Crisis management in food, animals and plants
Unit DDG2.G5.: Alert, traceability and Committees

RASFF
Rapid Alert System for Food and Feed

Brussels, 9 March, 2016

RASFF
NEWS

FOOD
INFORMATION EXCHANGE

NEWS: 16-811
ORIGINAL NOTIFICATION

SUBJECT: PRECAUTIONARY VOLUNTARY WITHDRAWAL OF MILK PRODUCTS FROM ROMANIA

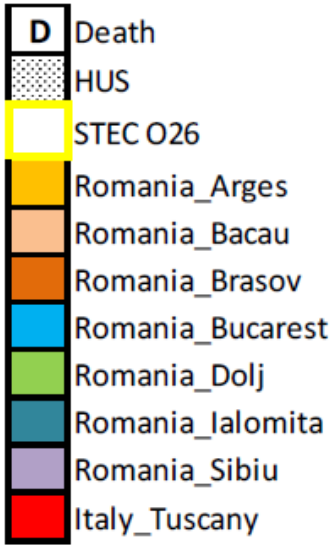
PAGES: COVER PAGE (1) + 6 + 9 file(s) attached

EMAIL: saute-rasff@ec.europa.eu

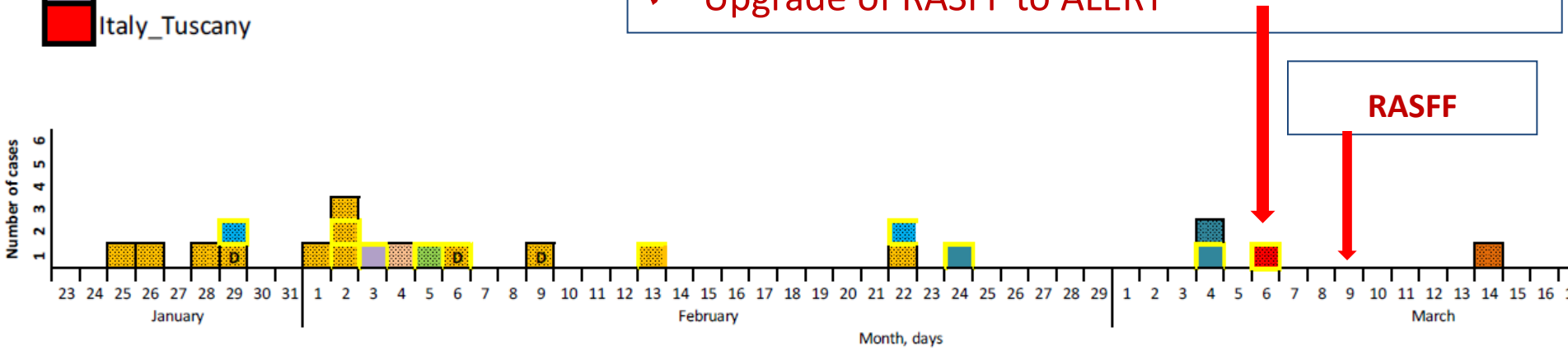
official control on the market - distribution to other member countries - withdrawal from the market
Product distributed to Belgium, Germany, Italy and Spain
notification flags: BE D/DE D/ES D/IT D/RO N
producer: SC Bradet SRL (Romania)
There is no epidemiological information suggesting a clear link between the cheese and patients. The Romanian contact point provided information to the ECCP that there were no unfavourable results in relation to the batches distributed to the other Member States. In the E. coli O26 strain isolated from the "incriminated products" no virulence genes were detected.

STEC outbreak in Romania / Italy (1):

January – March 2016



- ✓ 14/3/16: HUS case in Italy reported (6/3 onset of illnes)
- ✓ STEC O26 infection
- ✓ Consumption of cheese from Romania
- ✓ Same brand as the RASFF !
- ✓ Cheese positive for STEC O26
- ✓ Upgrade of RASFF to ALERT



ECDC/EFSA: Multi-country outbreak of STEC infection associated with HUS

http://ecdc.europa.eu/en/publications/

STEC outbreak Romania (3):
Italy, 2016

Ministero della Salute

Sei in: Home > News e media > Notizie > Notizie dal Ministero > Sicurezza alimentare, casi di Sindrome Emolitico Uremica (SEU) da consumo di prodotti a base di latte dalla Romania

Sicurezza alimentare, casi di Sindrome Emolitico Uremica (SEU) da consumo di prodott
base di latte dalla Romania

15 Marzo 2016

R.it FIRENZE

Firenze, un bambino intossicato da un formaggio contaminato

Il piccolo, 14 mesi, è ricoverato al Meyer. La Asl sta cercando tutti i prodotti della ditta SC Bradet s.r.l. in vendita a Firenze. "Ci può essere Escherichia Coli"

16 Marzo 2016

IL TIRRENO EDIZIONE PISTOIA

Formaggio provoca grave intossicazione, iniziato il ritiro

Dopo il ricovero di un bambino al Meyer, le analisi hanno confermato che la causa potrebbe essere un batterio contenuto nel latticino. Uno dei distributori nazionali del prodotto è in provincia di Pistoia

STEC outbreak in Romania / Italy (1): January - March, April, May…

RAPID COMMUNICATIONS

Early findings in outbreak of haemolytic uraemic syndrom… toxin-pro… February

E Peron [1,2,3], A Zaharia… Rafila [7,10], A Serban [11],
1. European Program… (ECDC), Stockholm,
2. Gastrointestinal, zo… Berlin, Germany
3. These authors cont…
4. National Center for…
5. European Centre fo…
6. Cantacuzino Nation…
7. University of Medic…
8. Department of Nepl…
9. EU Reference Labor…
10. National Institute o…
11. Ministry of Health,

Correspondence: Emili…

Peron E, et al. … toxin-producin…

Italy:
Other 5 HUS cases by STEC O26 from April to August 2016 with link to Romania

Travel related

Food related

A European outbreak case definition: ECDC April - August 2016

Annex 1. European outbreak case definition for multi-country outbreak of STEC infection associated with HUS

The European outbreak case definition defines a case as follows:

A **confirmed case** as:

a resident in Romania

OR

a resident in the EU with an epidemiological link to Romania

AND

with any laboratory confirmation for *E. coli* O26 infection after 15 January 2016

A **probable case** as:

a resident in Romania

OR

a resident in the EU with an epidemiological link to Romania

AND

with clinical haemolytic uremic syndrome (HUS) after 15 January 2016

OR

testing positive for the following STEC virulence genes: *stx*1 and/or *stx*2 and *eae* by PCR after 15 January 2016

OR

testing positive for a *E. coli* serogroup other than O26 after 15 January 2016

Exclusion criteria
Travel history: cases are defined as travelled-associated when travelling out of the EU in the two weeks before symptoms onset or before sampling date if asymptomatic

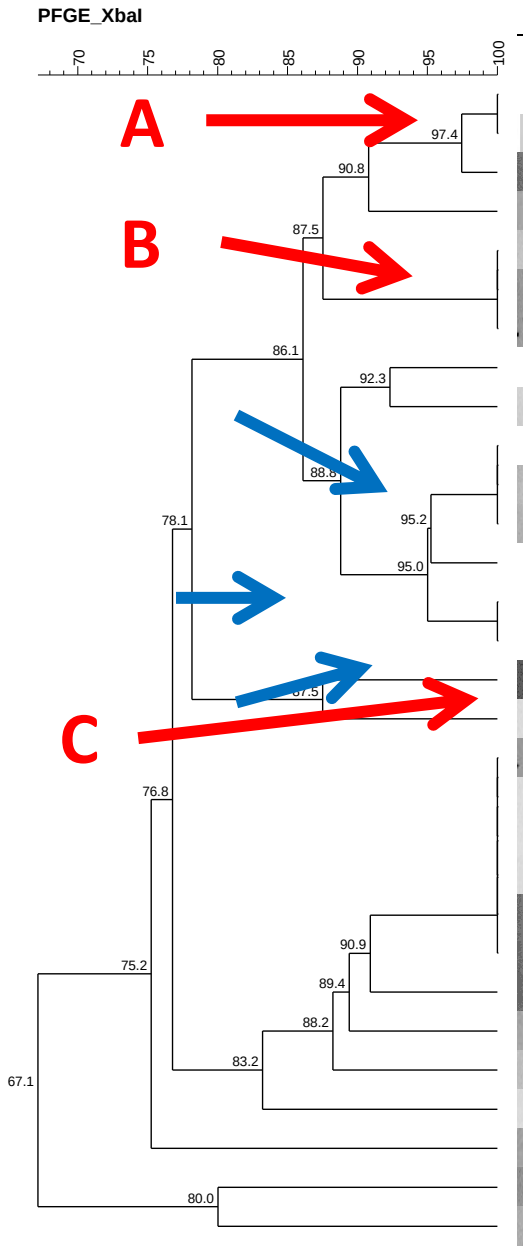
An **epidemiological link** with Romania is defined as:

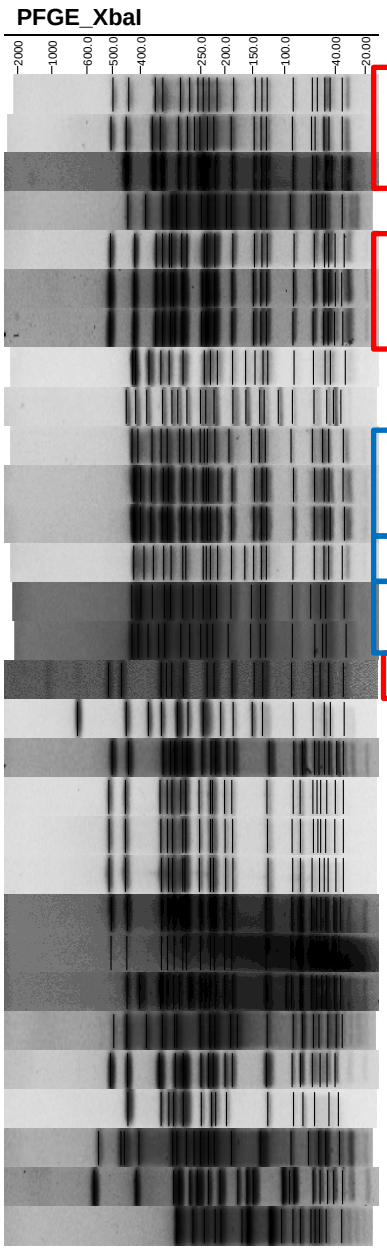
- Travel history to Romania since 15 January
- Close contact with an individual who has a travel history to Romania since 15 January
- Consumption of dairy products produced in Romania after the 15th January

STEC outbreak in Romania / Italy (3):

A total of 10 epidemic cases (5 HUS) in Italy from March to August 2016, according to the EU outbreak case definition

Family cluster #	age (years)	clinical symptoms	Date of onset	Place of residence	Suspected place of exposure to STEC source	Link to Romania	Serum	Vero cell assay	Stool	PFGE available	PFGE Cluster
1	1	**HUS**	mar-16	Tuscany	Italy	**cheese (confirmed)**	**O26+**	-	neg (no bacterial growth)	-	-
	mother	no	-				not tested	+	**E.coli O26, *stx1+, stx2+, eae+***	yes	**A**
	father	**diarrhea**	mar-16				not tested	-	neg	-	-
2	<1	**HUS**	apr-16	Piedmont	Italy	food (cheese) suspected	**O26+**	+	**stx2+ eae+ O26**	ongoing	-
	mother	unknown	-				not tested	neg	***stx2+, eae+, O26* (Real Time PCR)**	-	-
	father	unknown	-				not tested	neg	neg	-	-
	<5 (sister)	unknown	-				not tested	neg	neg	-	-
3	1	**HUS**	may-16	Liguria	Romania	travel	**O26+**	+	**E.coli O26, *stx1+, stx2+, eae+***	yes	**B**
	mother	**diarrhea**	may-16				not tested	+	**E.coli O26, *stx1+, stx2+, eae+***	yes	**B**
	father	no	-				not tested	-	neg	-	-
4	2	**HUS**	jun-16	Lazio	Italy	multiple (Food, PTP)	**O26+**	neg	**E.coli O26, *stx1+, stx2+, eae+***	yes	**B**
	0 (2 months)	no	-				not tested	not tested	not tested	-	-
	6	no	-				not tested	not tested	not tested	-	-
	mother	no	-				not tested	not tested	not tested	-	-
	father	no	-				not tested	not tested	not tested	-	-
	adult (aunt)	**diarrhea, vomiting**	may-16	Romania	?	?	not tested	not tested	not tested	-	-
5	1	**HUS**	jul-16	Lombardy	Italy	food (cheese) suspected	not tested	not tested	**E.coli O26, *stx1+, stx2+, eae+***	yes	**C**
	3 (sister)	**diarrhea**	na				not tested	not tested	not tested	-	-
	mother	**diarrhea**	na				not tested	not tested	not tested	-	-
	father	**diarrhea**	na				not tested	not tested	not tested	-	-
6	5	**HUS**	aug-16	Tuscany	Romania	travel	**O26+**	neg	***stx2+, eae+, O26* (Real Time PCR)**	-	-
	3 (sister)	no	-				not tested	not tested	not tested	-	-
	mother	no	-				not tested	neg	***stx2+, eae+, O26* (Real Time PCR)**	-	-

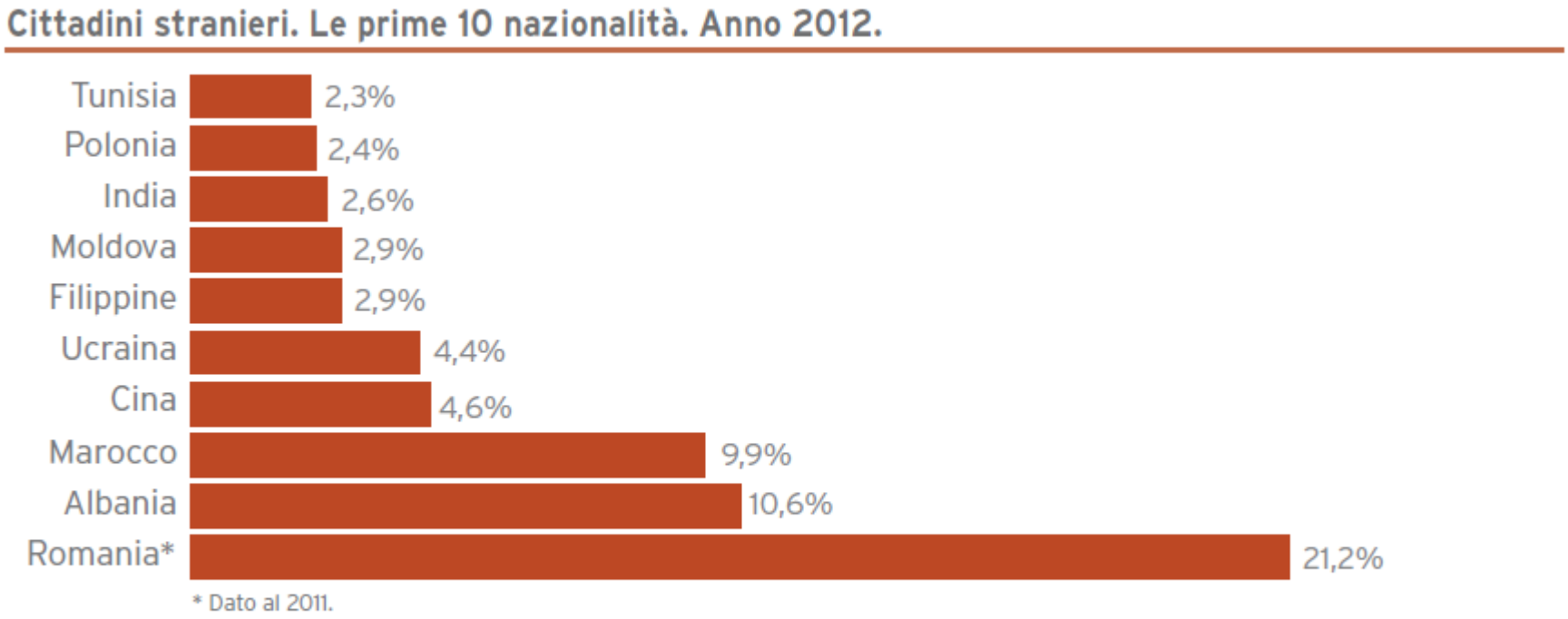




ED 1099	O26	CHEESE (OFFICIAL CONTROL.	vtx1; vtx2	9/05/2016	
ED 1089	O26	CHEESE (LEFTOVER)	vtx1; vtx2	16/03/2.	
ED 1088	O26	HUMAN (MOTHER OF FIRST .	VT1a; VT2a	18/03/2.	
ED 1039	O 26	HUMAN		2015	
ED 1107	O26	HUMAN	vtx2a	2016	
ED 1105	O26	HUMAN (MOTHER-NEFROL.	vtx2	31/05/2.	
ED 1104	O26	HUMAN (CHILD-PEDIATRIC .	vtx2	26/05/2.	
ED 1101	O26	FORMAGGIO	eae+ vtx1+ vt.	2016	
ED 1037	O26	HUMAN	vtx1a	2015	
ED 1102	O26	CHEESE (OFFICIAL CONTROL.	vtx1;vtx2	9/05/2016	
ED 1098	O26	CHEESE (OFFICIAL CONTROL.	vtx1;vtx2	18/04/2.	
ED 1097	O26	CHEESE (OFFICIAL CONTROL.	vtx1;vtx2	18/04/2.	
ED 1100	O26	CHEESE (OFFICIAL CONTROL.	vtx1;vtx2	9/05/2016	
ED 1103	O26	FORMAGGIO	eae+ vtx1+ vt.	2016	
ED 1094	O26	FORMAGGIO	eae+ vtx1+ vt.	2016	
IZSLER_2016-2063.					
ED 1036	O 26	HUMAN		2015	s
ED 1068	O26	BOVINE	VT2a	2016	
ED 1032	O 26	ANIMAL (ovino)	vtx2a	2015	s
ED 1031	O 26	ANIMAL (ovino)	vtx2a	2015	s
ED 1027	O 26	HUMAN	vtx2a	2015	s
ECC 537	O26	BOVINE	VT2a	2016	
ECC 536	O26	BOVINE	VT2a	2016	
ECC 535	O26	BOVINE	VT2a	2016	
ED 1069	O 26	BOVINE	vtx2a	2016	
ED 1111	O26	HUMAN	vtx2a	2016	
ED 1035	O 26	HUMAN	vtx2a	2015	
ED 1043	O 26	HUMAN		2015	S
ED 1106	N.T.		eae+ vtx2+	2016	
ED 1041	O 26	HUMAN		2015	S

Main citizenship of foreign population in Italy (Census 2011)

Source: ISTAT – Caritas 2013 (www.istat.it)



FONTE: Caritas e Migrantes. XXIII Rapporto Immigrazione 2013. Elaborazione su dati ISTAT.

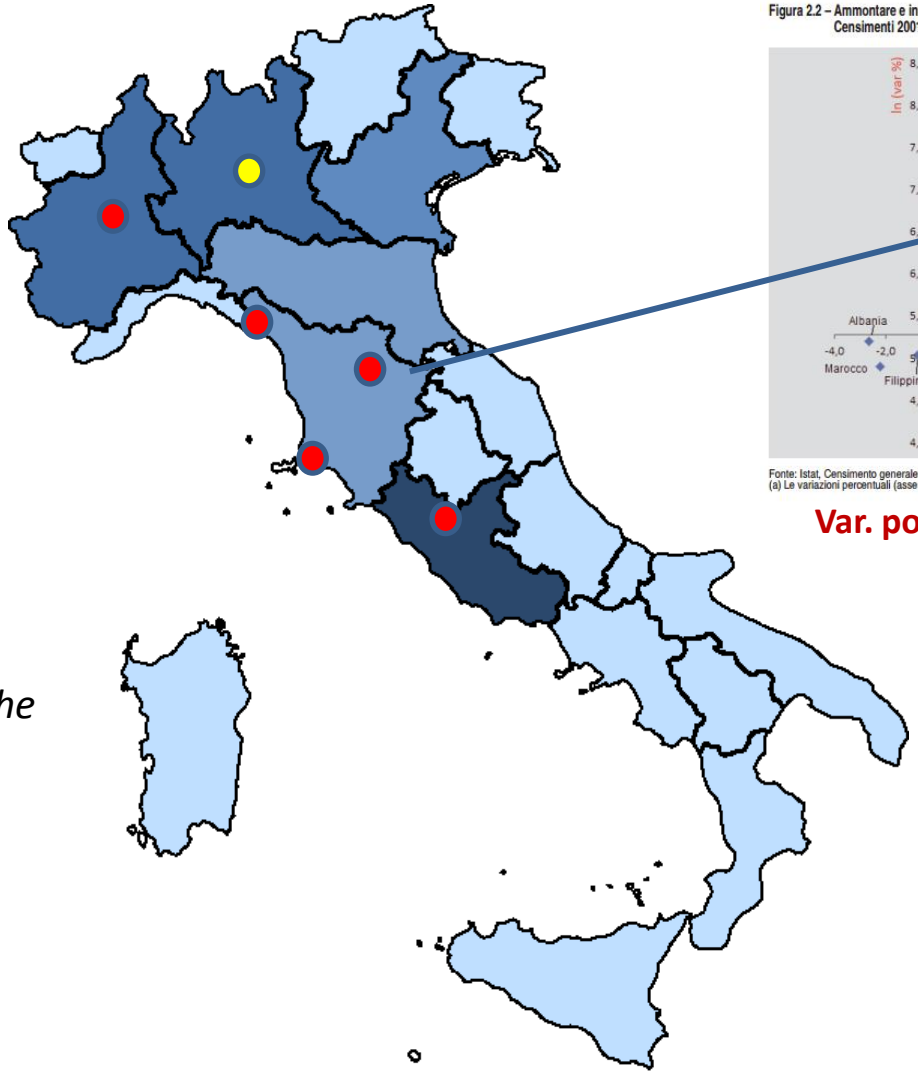
Regional distribution of Romanian population in Italy, 1 January 2015 (1)

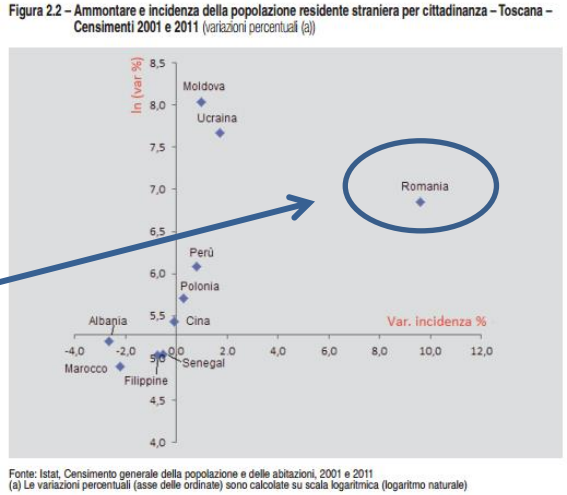
Source: http://demo.istat.it/str2015/index.html

*Population (*1,000)*

- 0 - 55
- 56 - 110
- 111 - 165
- 166 - 210
- 211 - 265

Case of HUS linked to the Romanian outbreak





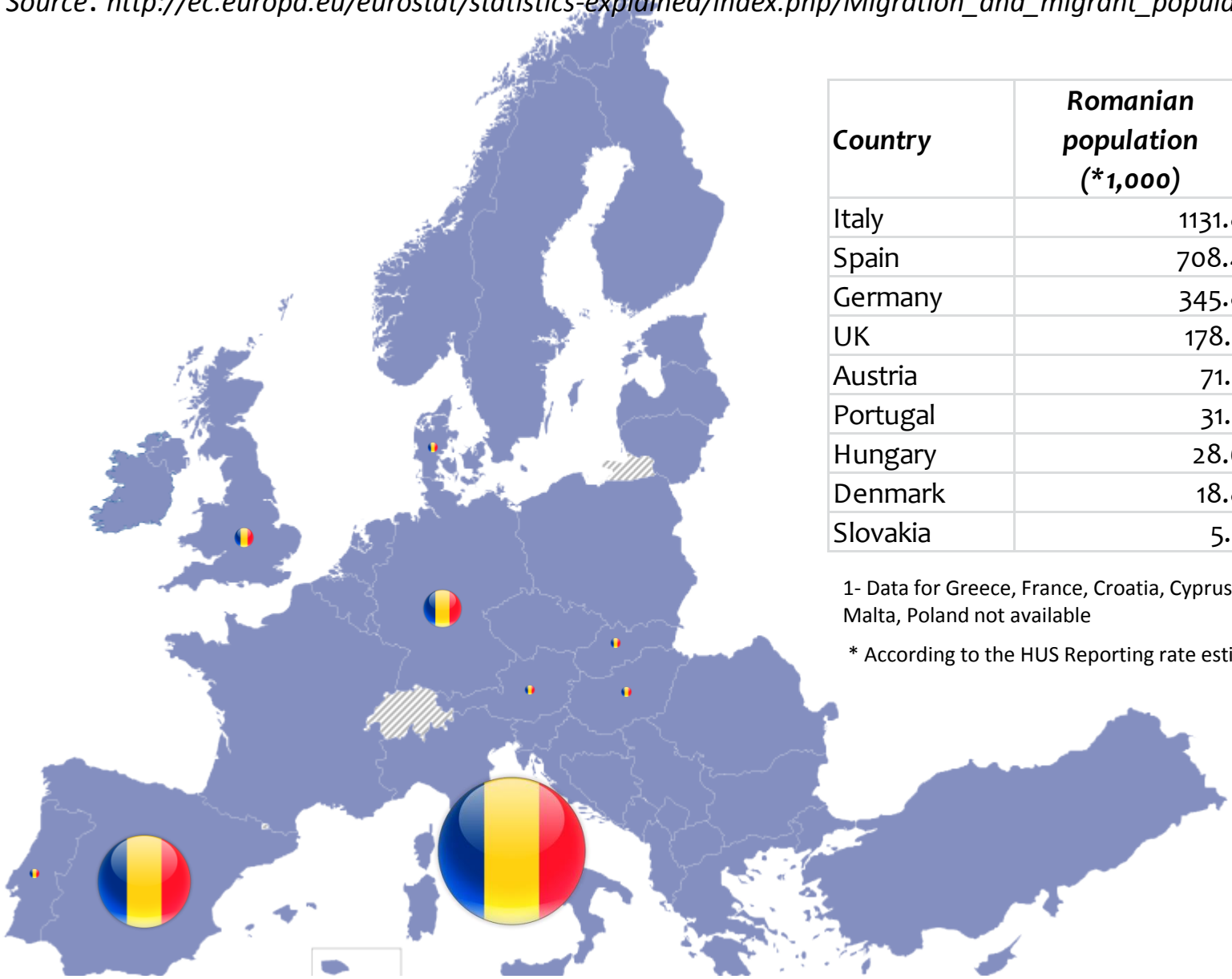
Var. population (%) 2001 - 2011

Cumulative HUS Reporting Rate in the Italian population from Romania, 2016: 0,44 cases *100,000

Why cases linked to Romania have only been reported from Italy ?

Main countries of citizenship and birth of the Romanian population, 1 January 2015 (1)

Source: *http://ec.europa.eu/eurostat/statistics-explained/index.php/Migration_and_migrant_population_statistics*



Country	Romanian population (*1,000)	Expected HUS cases (n)*
Italy	1131.8	
Spain	708.4	**3.1**
Germany	345.8	**1.5**
UK	178.3	**0.8**
Austria	71.3	**0.3**
Portugal	31.5	**0.1**
Hungary	28.6	**0.1**
Denmark	18.8	**0.1**
Slovakia	5.3	**0.0**

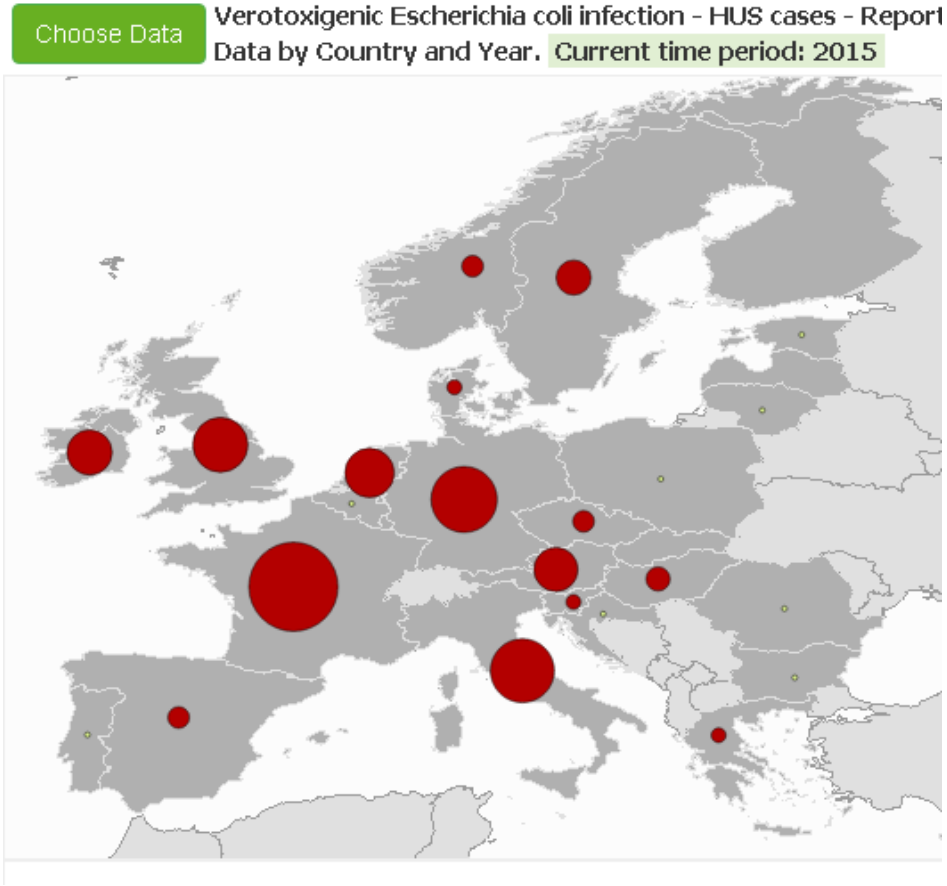
1- Data for Greece, France, Croatia, Cyprus, Luxembourg, Malta, Poland not available

* According to the HUS Reporting rate estimated Italy

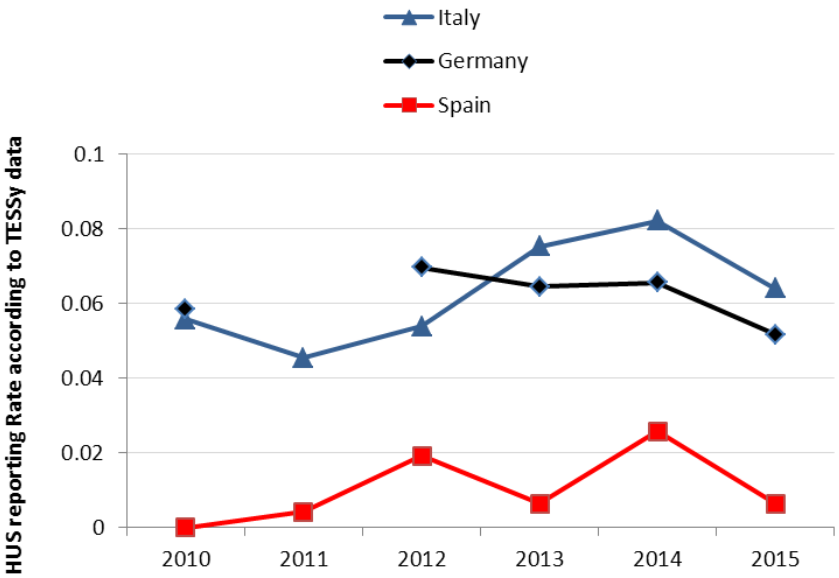
A different distribution of the Romanian population in the EU MSs?

STEC/HUS cases reported to the TESSy (ECDC)

http://ecdc.europa.eu/en/data-tools/atlas/pages/atlas.aspx



HUS reporting rate by year, according to TESSy data in Italy, Germany, Spain



A different sensitivity of the HUS reporting to TESSy ?

The Italian Registry for HUS - 1

Pediatric Nephrology Unit

Active since 1988, the HUS Registry (2005) is coordinated by:

- Italian National Public Health Institute (ISS)
- Italian Society for Pediatric Nephrology (SINEPE)

The network includes **14 Units of Pediatric Nephrology** which permanently participate to the Registry

Supported by:

- Italian Society for Nephrology (SIN)

Collaborating laboratories:

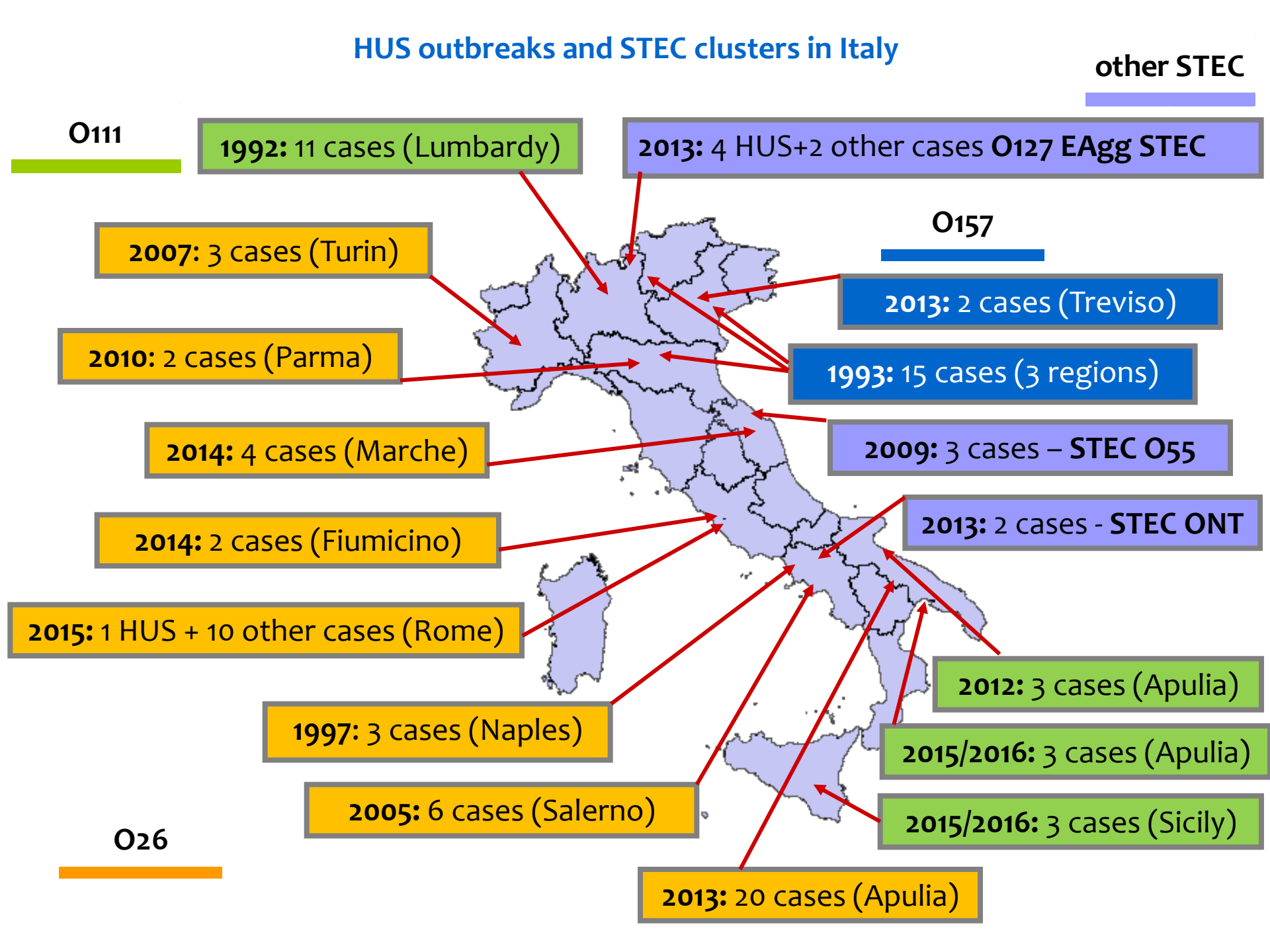
- **STEC:** National Reference Laboratory for E.coli, Rome
- **Host genetic factors:** Istituto Mario Negri, Bergamo
- **Kinetic of Shiga-toxin:** University of Bologna, Bologna

Feed-back to:

- Regional and National Public Health Authorities
- European Center for Disease Prevention and Control (ECDC)

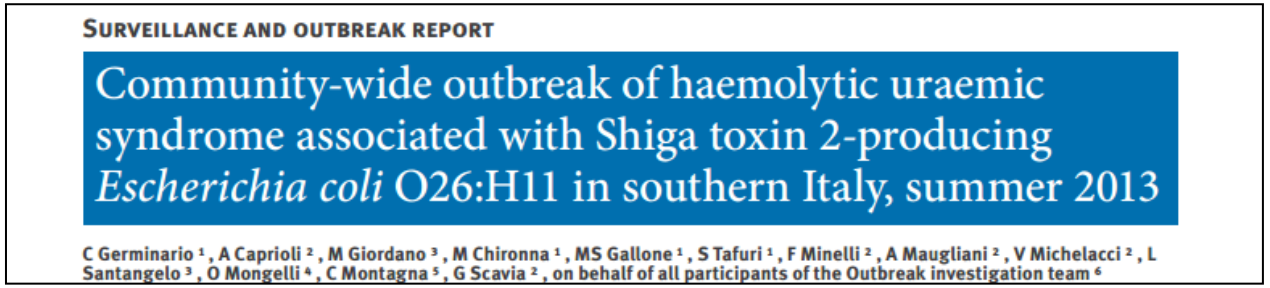
www.iss.it/seu

HUS outbreaks and STEC clusters in Italy



Common findings between the Romanian (2016) and the Italian (2013) HUS-STEC outbreaks

- Prolonged , general outbreaks in the community
- Outbreak cases scattered across wide geographic areas
- Both residents and travel-associated cases included
- Similar number of cases involved, and patients' characteristics (age, clinical picture)
- Primarily associated with HUS and high severity of clinical course
- STEC O26 carrying (*stx1*), *stx2* and *eae* was the main but not the only STEC strain involved (O157 in Romania, O80 and ONT in Italy)
- No single PFGE profiles of the STEC O26 strains isolated from the outbreak cases
- Cheese: confirmed / suspected to be the implicated vehicle.
- Failure of tracing-back to a single product
- Failure of tracing-back to a primary source/reservoir of STEC infection



SURVEILLANCE AND OUTBREAK REPORT

Community-wide outbreak of haemolytic uraemic syndrome associated with Shiga toxin 2-producing *Escherichia coli* O26:H11 in southern Italy, summer 2013

C Germinario [1], A Caprioli [2], M Giordano [3], M Chironna [1], MS Gallone [1], S Tafuri [1], F Minelli [2], A Maugliani [2], V Michelacci [2], L Santangelo [3], O Mongelli [4], C Montagna [5], G Scavia [2], on behalf of all participants of the Outbreak investigation team [6]

The outbreak heritage in Italy: STEC testing of cheese and dairy, 2014.

	Food category										
Samples tested	**Bovine meat [a]**	**Ovine and goat meat [a]**	**Other ruminants meat [b]**	**Pig meat**	**Other meat [c]**	**Mixed meat**	**Milk and dairy products [d]**	**Raw milk [e]**	**Fruit and vegetable**	**Seeds [f]**	**Other food**
n	4,930	192	41	1,599	2,885	2,42	6,097	901	1,975	1,023	1,786
Country	**Proportion (%) of total samples tested**										
AT	1.9	3.6	97.6	1.8	14.6		2.8	4.8	10		1.6
BE	27.7				8		9.3	37.6	33.4	44.2	8.2
CH	0.6						3.6				
CY		1		0.3							
CZ	3.3			10.6					1.9	0.7	
DE	14.2	21.9		17.3	9.2	88.4	18.8	38.7	2.7	11.3	43
DK											
EE								7		0.1	0.1
ES	7.2	19.8		4.1	20.5		0.5		8	2.7	6.4
FI											
FR							17.3			24.3	
GB		6.3			0.1	11.6	2.4	3.3	3		
HU	2.2								6.3	4.6	
IE	1.1	1		0.6	1.3		0.1	0.2	1	0.4	3.7
IT	4.3	22.9	2.4	22.4	34.4		45.1	0.7	20.7		23.9
LV				0.9	3.3					3.9	
NL	13.5	23.4		37.9	2.5			0.9	7.9	4.2	2.1
PL	23			2	0.5						
PT	1			2.1	0.3				0.4		
SE					<0.1						0.1
SI					5.3			6.7	2.9	3.5	0.7
SK					<0.1		<0.1	0.1	1.7		10.5

Conclusions

- Transnational outbreak in a transnational community!!
- Importance of epidemic risk communication
- HUS sentinel event → importance in publichealth and added value of sindromic surveillance
- In the era of WGS, serological testing still play a role!!
- Critical importance of close cooperation between public health and food safety authorities and support bodies at both European level, national and regional level
- Importance of a strong coordination of the investigation activities and the dissemination of information
- Importance of early warning systems (EPIS, EWRS, RASFF) for quick response
- STEC O26 (stx2+) in cheese and dairies: an emerging threat

Thank you

Alfredo Caprioli, Fabio Minelli, Antonella Maugliani, Valeria Michelacci, Rosangela Tozzoli, Stefano Morabito, Paola Chiani, Marco Materassi, Marina Vivarelli, Licia Peruzzi, Gianluigi Ardissino, Mario Luini, Stefano Bilei