EPIDEMIOLOGY OF HUMAN PRION DISEASES AND SURVEILLANCE IN ITALY

19th Annual Meeting of the TSE EURL 17-18 October, Torino

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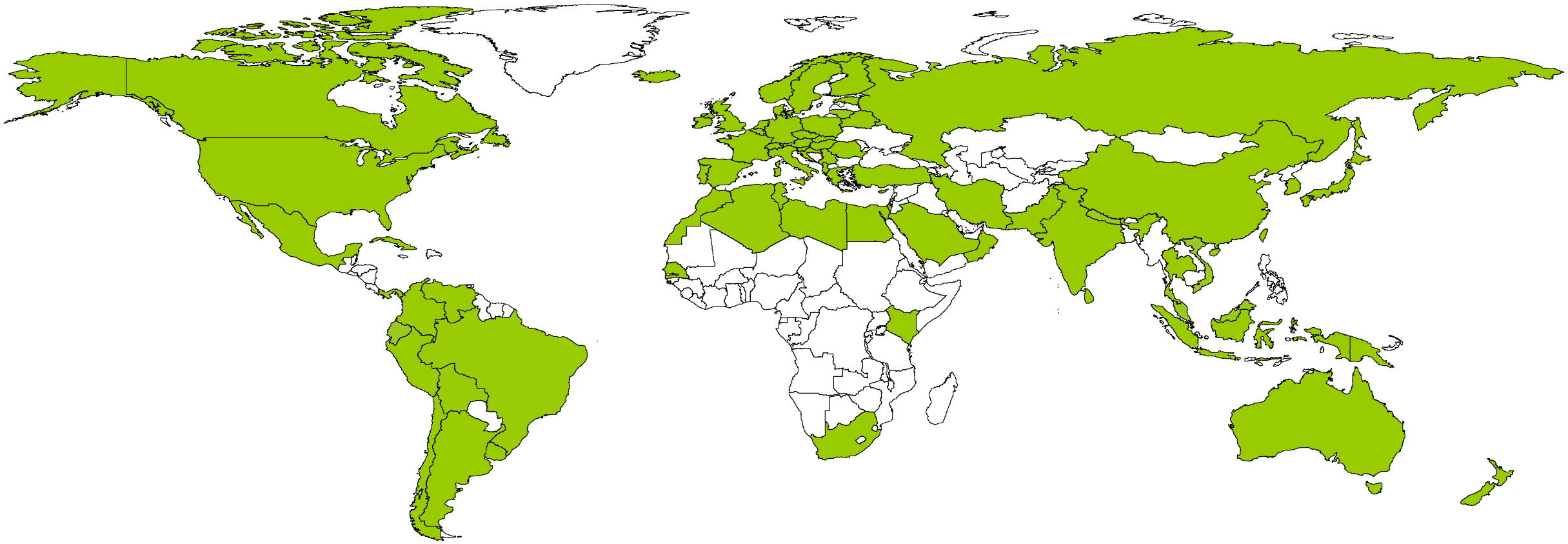
HUMAN PRION DISEASES

Sporadic Creutzfeldt-Jakob disease (CJD)	**- Unknown**
Genetic TSE (genetic CJD, GSS, FFI)	**- Linked to insert/point mutation in the PrP gene (*PRNP*)**
Iatrogenic CJD	**- Linked to medical procedures**
Variant CJD	**- Linked to BSE agent** **- Human-to-human transmission**

Countries reporting CJD

- **Rare disease (1-2 cases per million per year)**
- **Worldwide distribution**
- **Transmissible, however, the majority of cases are sporadic forms**



Masters et al, 1979; Ladogana et al., 2012, updated September 2022

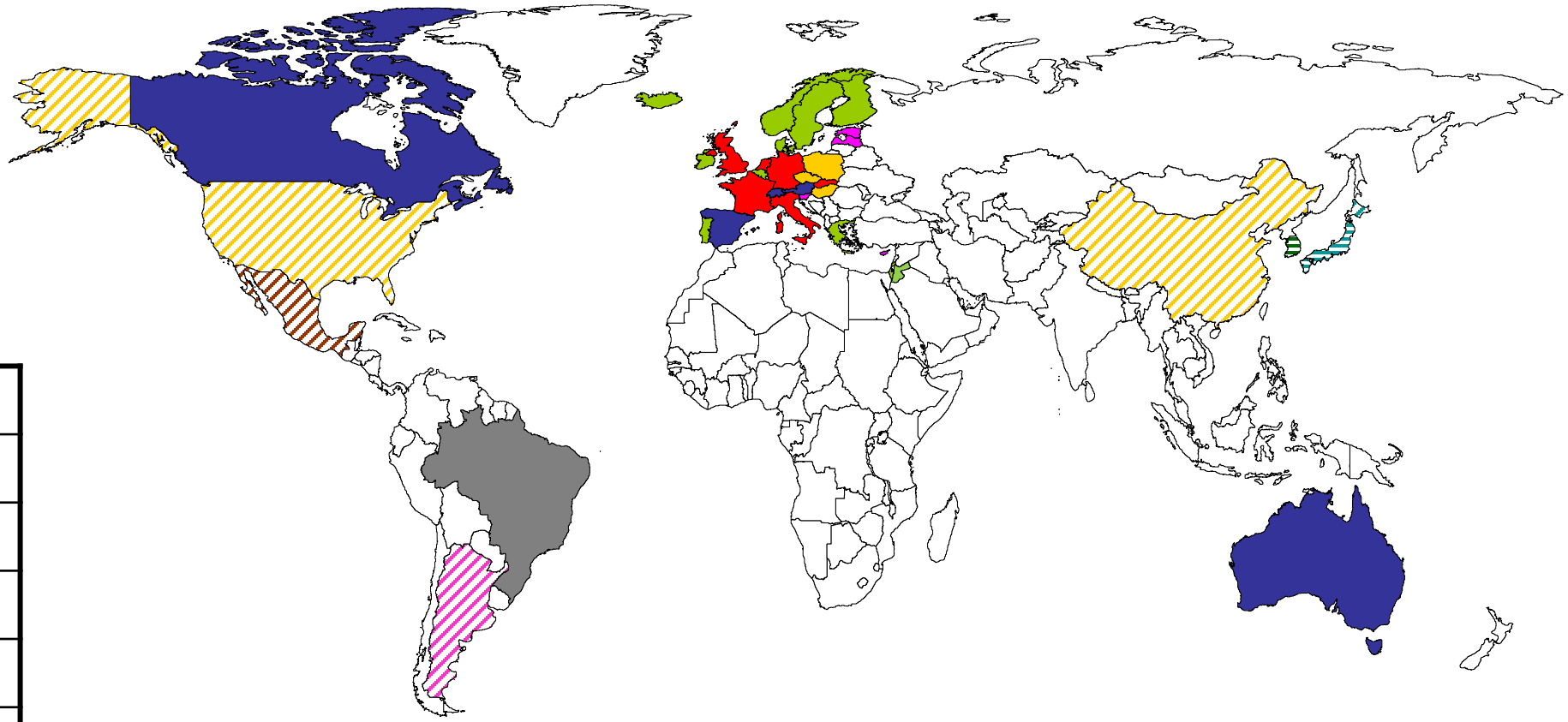
Surveillance of CJD Europe

- A collaborative study of CJD in the European Union was funded by the European Commission through the BIOMED1 and 2 programme in 1993-2003: The European and Allied Countries Collaborative Study Group of CJD (EUROCJD) plus the Extended European Collaborative Study Group of CJD (NEUROCJD)

- DG SANCO (2004-2007) : The European and Associated Countries CJD surveillance network

- ECDC from 2007 to 2021: outsourced to UK Unit as Creutzfeldt-Jakob Disease international surveillance network ended in April 2021

The CJD Surveillance Network in the World



1993	6
1997	11
1998	21
2002	24/26
2004	28/31
2005	28/32
2006	28/33
2009	28/34

Surveillance of CJD in Italy

- Voluntary referral to the CJD Registry 1993-2000

- Mandatory notification to the Registry, Local health offices and Ministry of Health, O.M. 12 February 2001

- Mandatory notification to the Registry, Local health offices and Ministry of Health, D.M. del 21 December 2001

10-1-2002 GAZZETTA UFFICIALE DELLA REPUBBLICA ITALIANA *Serie generale* - n. **8**

DECRETO 21 dicembre 2001.

Sorveglianza obbligatoria della malattia di Creutzfeldt-Jakob.

IL MINISTRO DELLA SALUTE

Surveillance of CJD in Italy

Patient with cognitive decline rapidly progressive

NEUROLOGY Unit
- Neurological examinationn
- Cerebral MRI
- CSF analyses

Suspect PrD

Yes/No PrD

Surveillance Network (Bologna, Milano, Roma, Torino, Verona, Cagliari)
- Cerebral MRI view
- RT-QuIC on CSF and other tissues samples
- *PRNP* sequencing
- Possible Risk factors

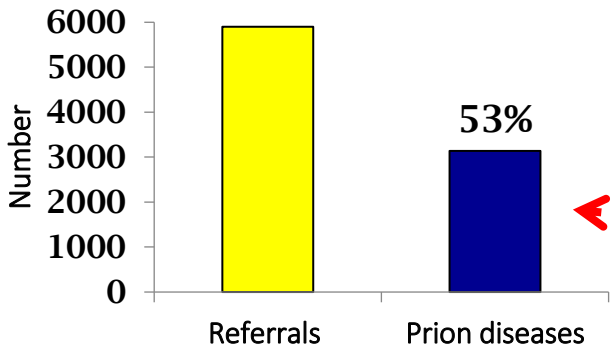
Diagnostic Classification

PrD definite* PrD probable

PrD possible No PrD

Official statistics

Not included in the statistics



*Progressive neurological syndrome **AND** Neuropathologically **or** immunocytochemically **or** biochemically confirmed

History of diagnostic criteria for sporadic CJD

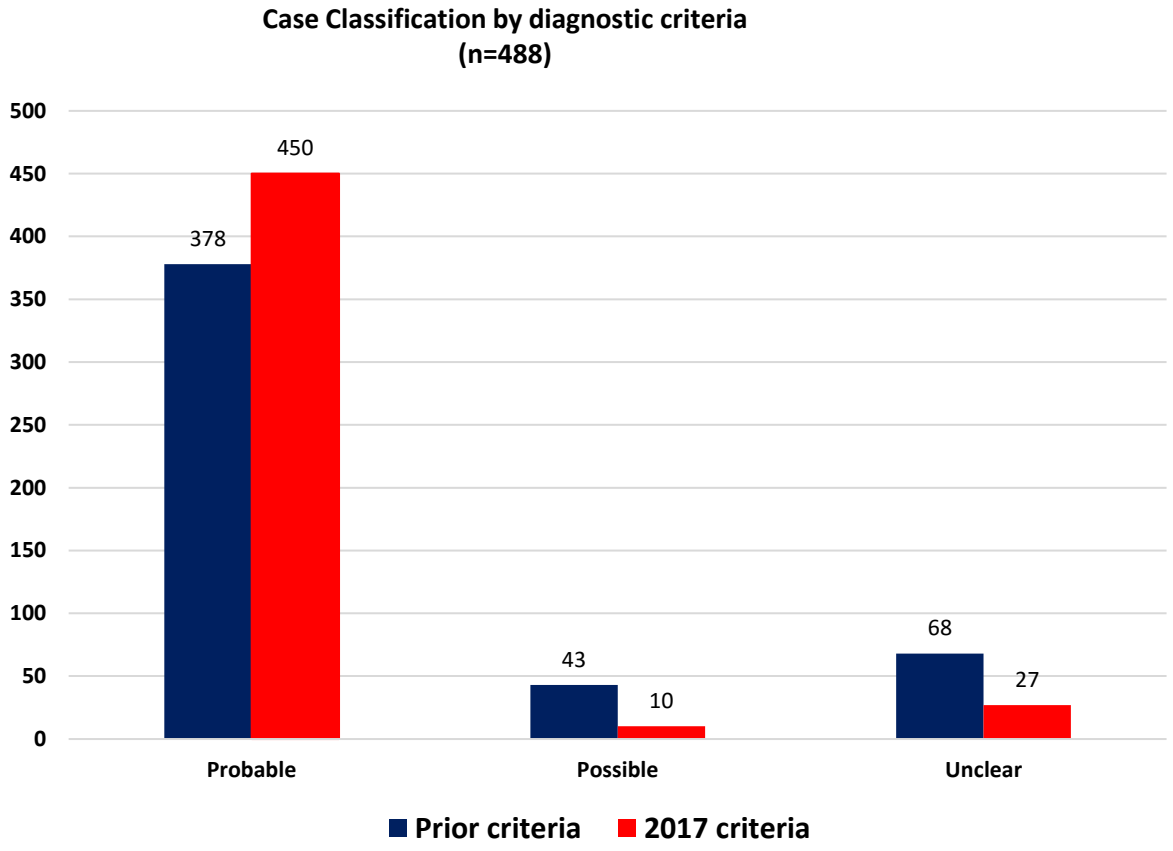
Clinical, diagnostic and instrumental data	Master 1979	EuroCJD 1993	EuroCJD 1998	EuroCJD 2010	EuroCJD 2017
Clinical signs*	+*	+	+	+	+°
Generalized triphasic periodic complexes on EEG	+	+	+	+	+
14-3-3 proteins in the CSF and disease duration < 24 m°			+	+	+
High signal in caudate/putamen on MRI brain scan				+	
High signal in caudate/putamen on MRI brain scan or at least in two cortical regions (temporal, parietal, occipital) in DW o FLAIR					+
RT-QuIC°° in CSF or other body tissues/fluids					+

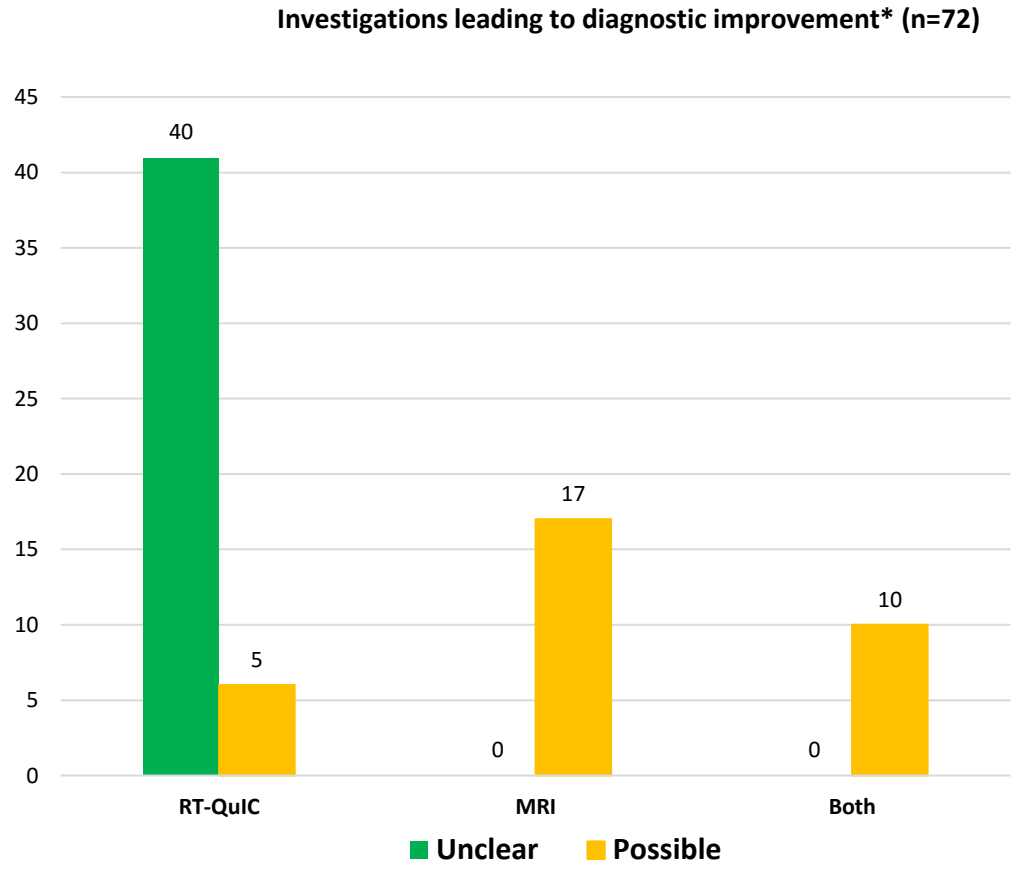
*Rapid progressive dementia + 2 (1 in Master's) of the following signs: myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal, and akinetic mutism features.

° Rapid progressive dementia modified in '**Cognitive decline rapidly progressive'.**

°°If RT-QuIC positive, clinical sign is 'Progressive neurologicas syndrome'.

COMPERISON BETWEEN 2010 AND 2017 DIAGNOSTIC CRITERIA FOR SPORADIC CJD

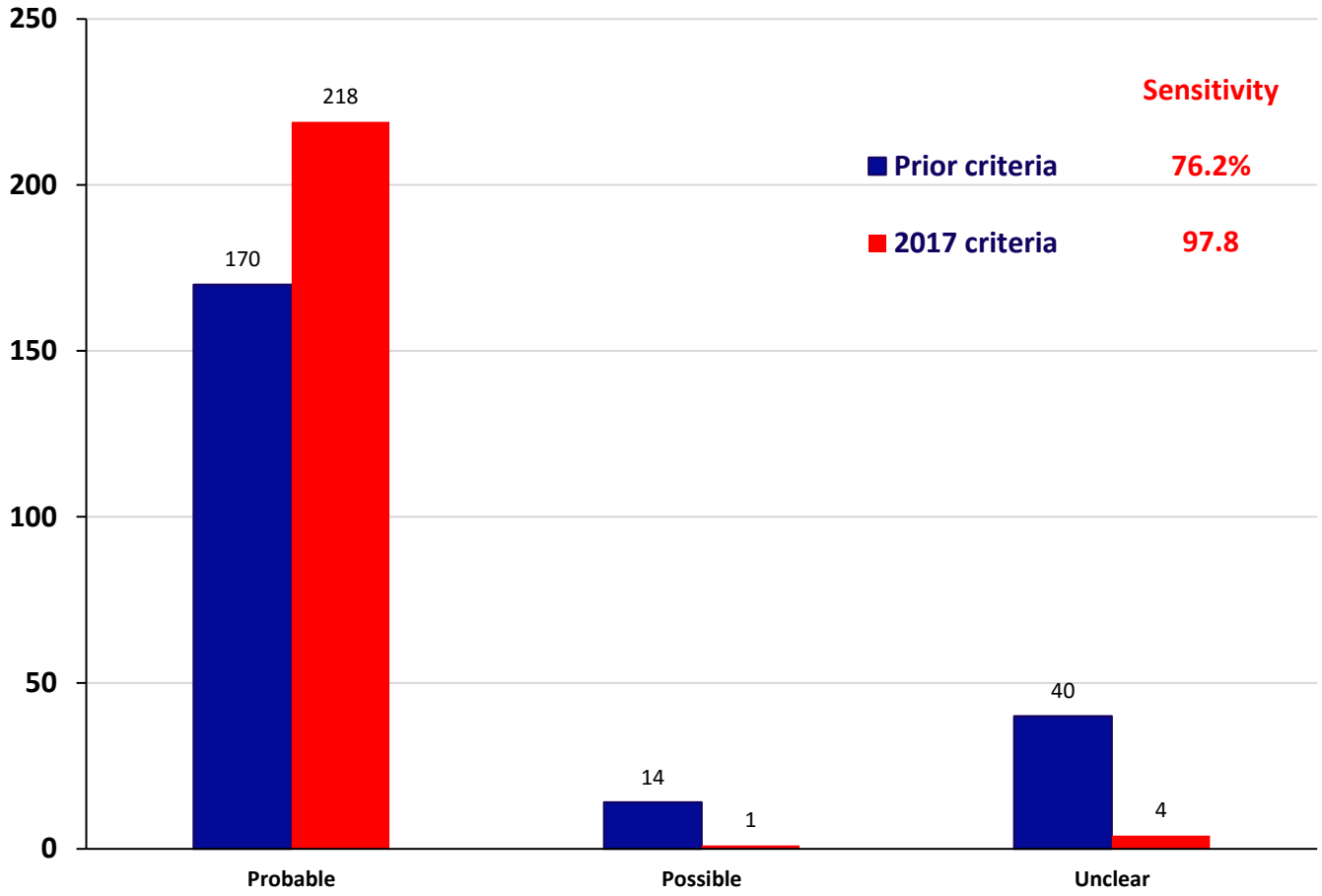




*re-classification as *probable* in subjects previously classified as *possible* or *unclear*

Watson et al., 2022

Sensitivity of Diagnostic Criteria for Sporadic CJD, 2010 *vs* 2017

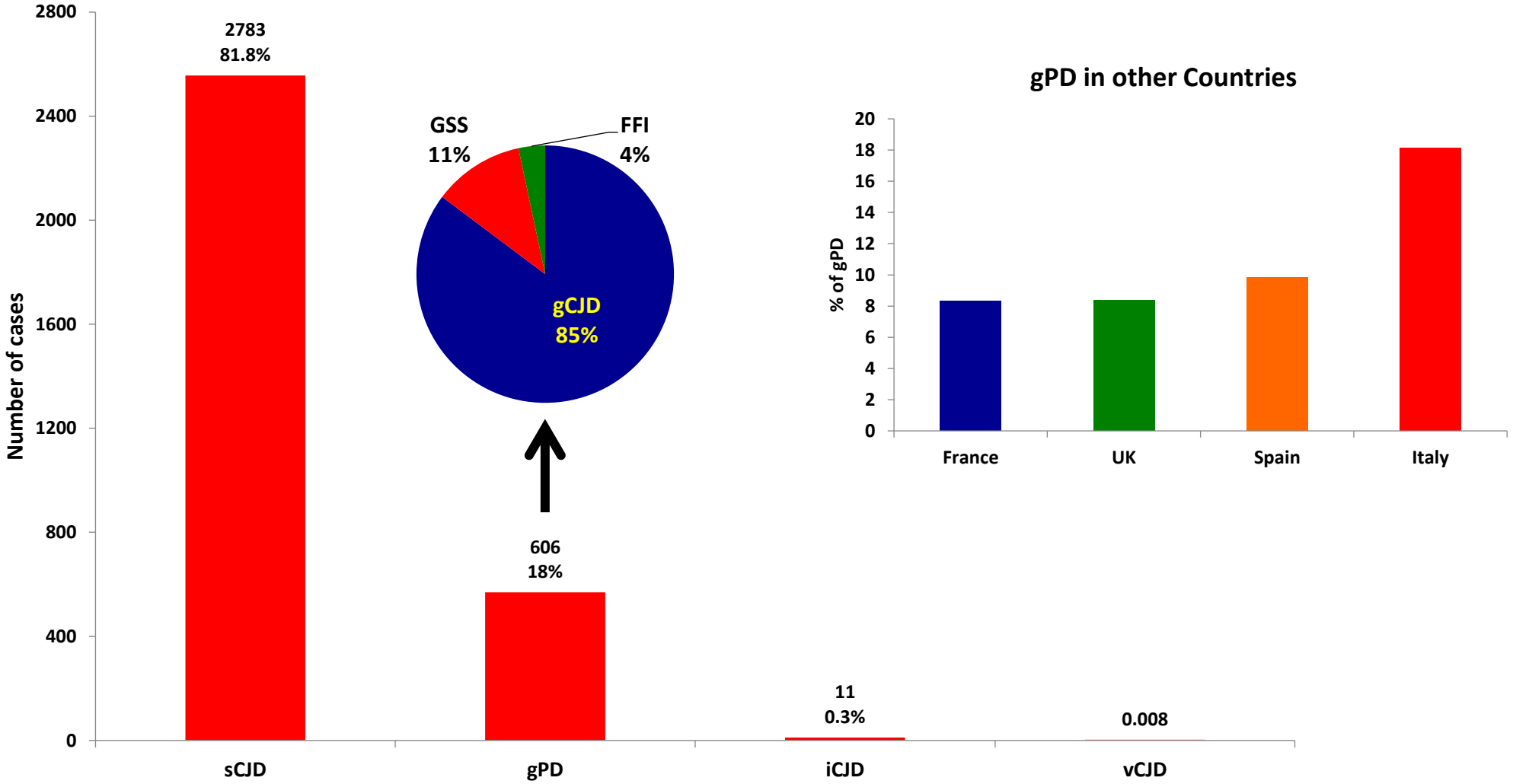


Case classification by prior and updated criteria, cases with full investigation panel performed (n=223)

Watson et al., 2022

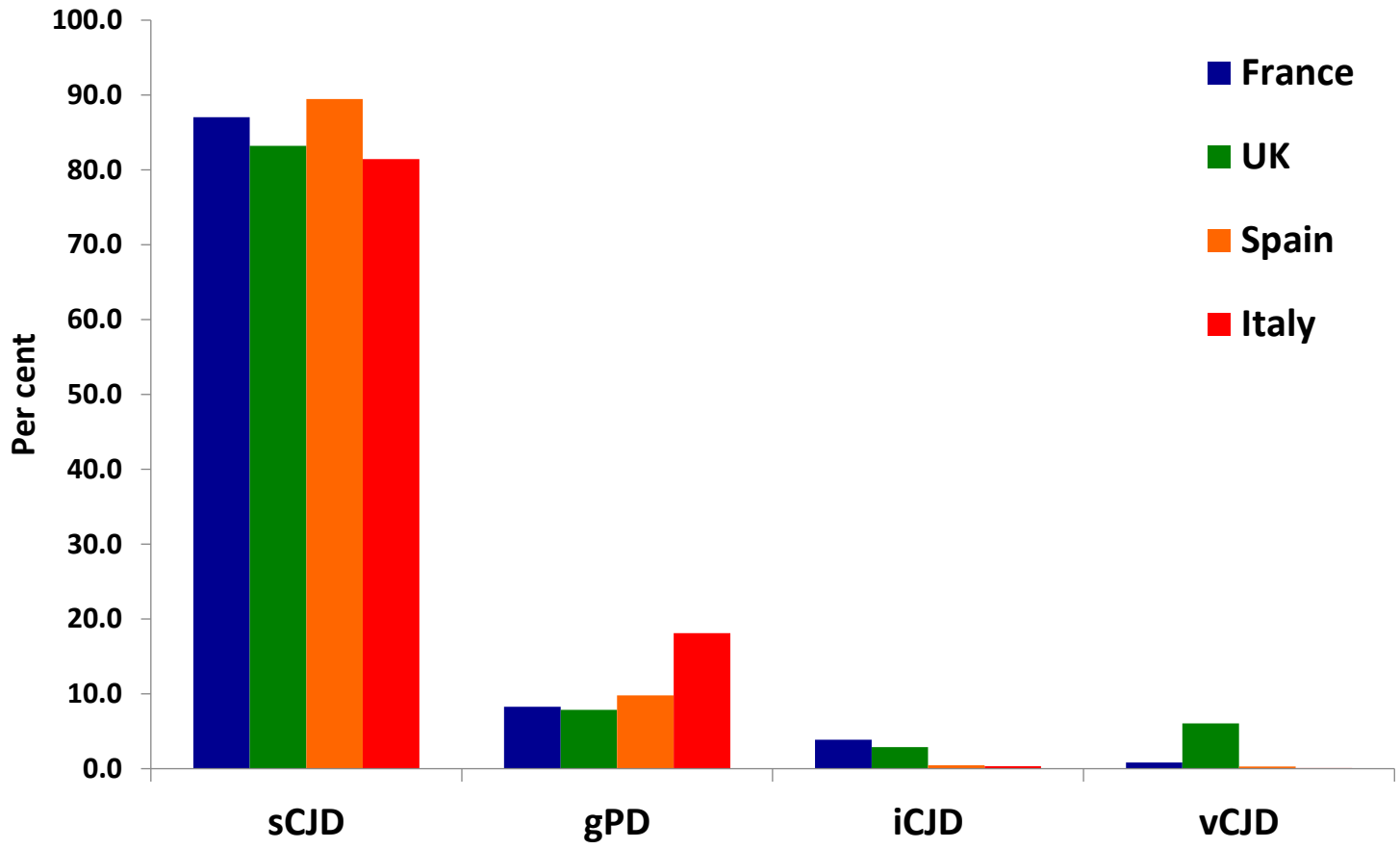
Different forms of Prion Diseases in Italy

(ISS data, 1993-2022°)

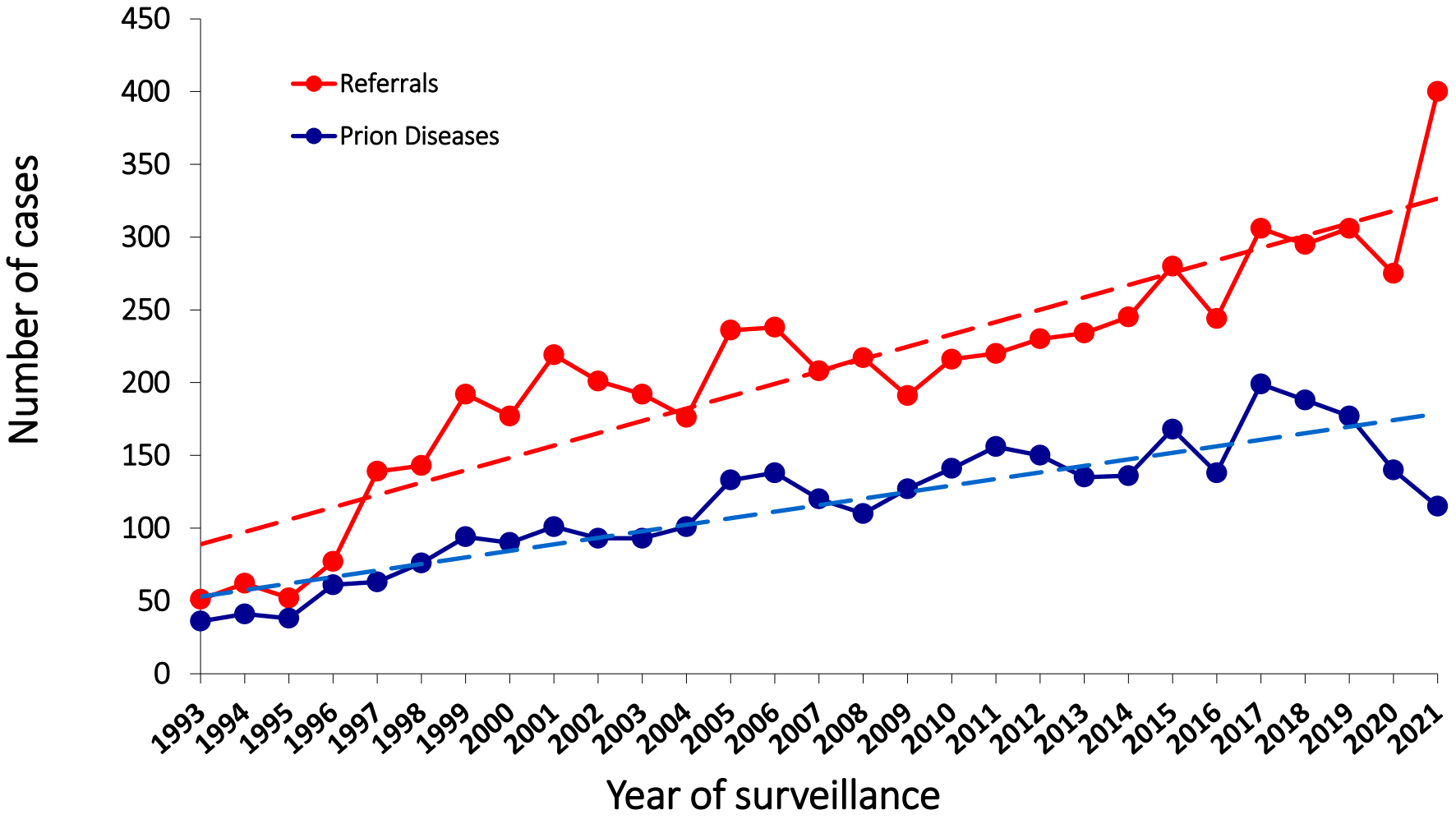


°to 30 settembre 2022; sCJD, sporadic Creutzfeldt-Jakob disease; gPD, genetic Prion Disease; iCJD, iatrogenic CJD; vCJD, variant CJD; gCJD, genetic CJD; GSS, syndrome of Gerstmann-Sträussler-Scheinker; FFI, Fatal familial Insomnia

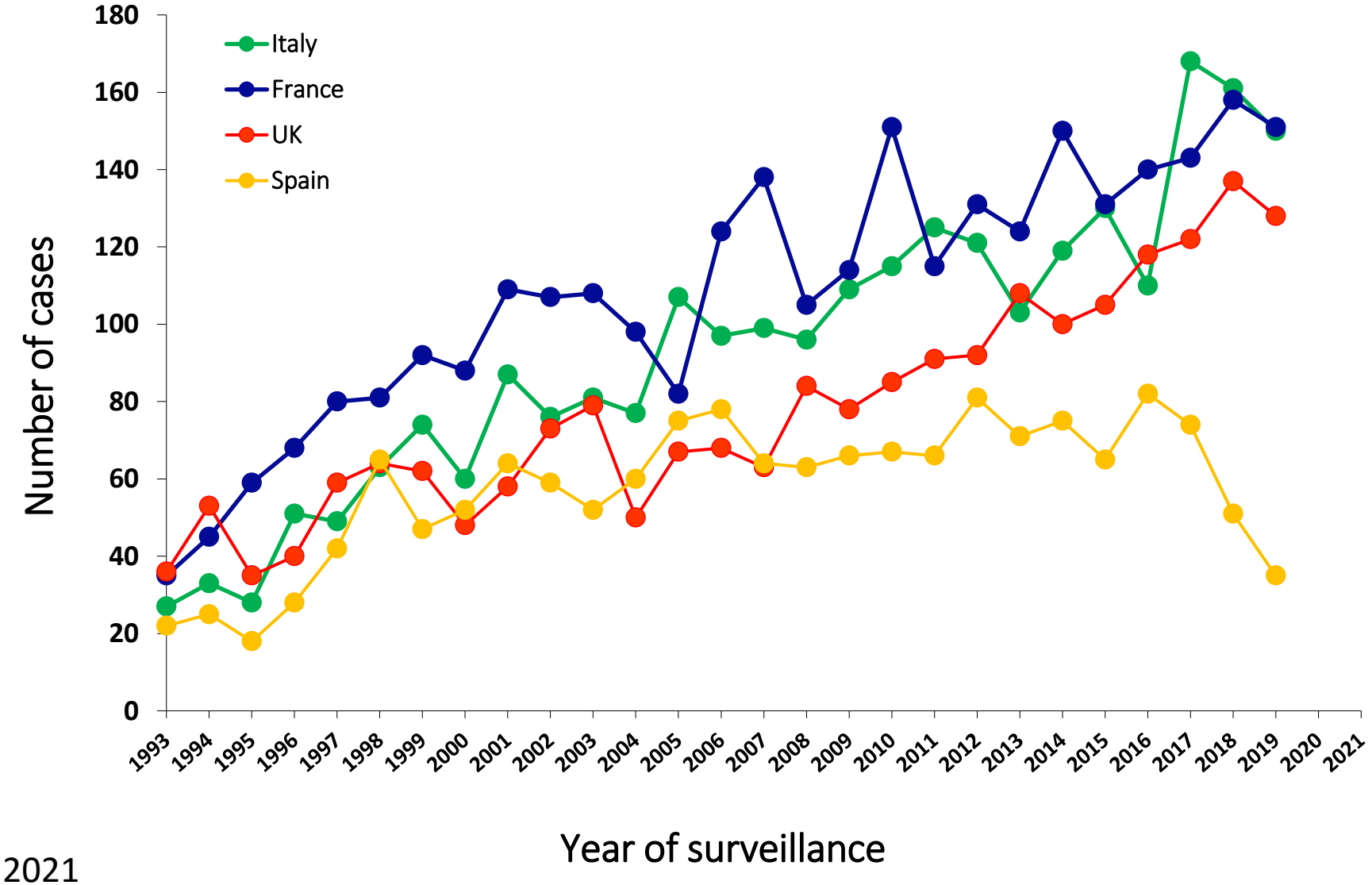
DISTRIBUTION OF PRION DISEASES IN OTHER COUNTRIES
(1993-2021)



Number of referrals and Prion Disease cases in Italy (ISS data, 1993-2021)

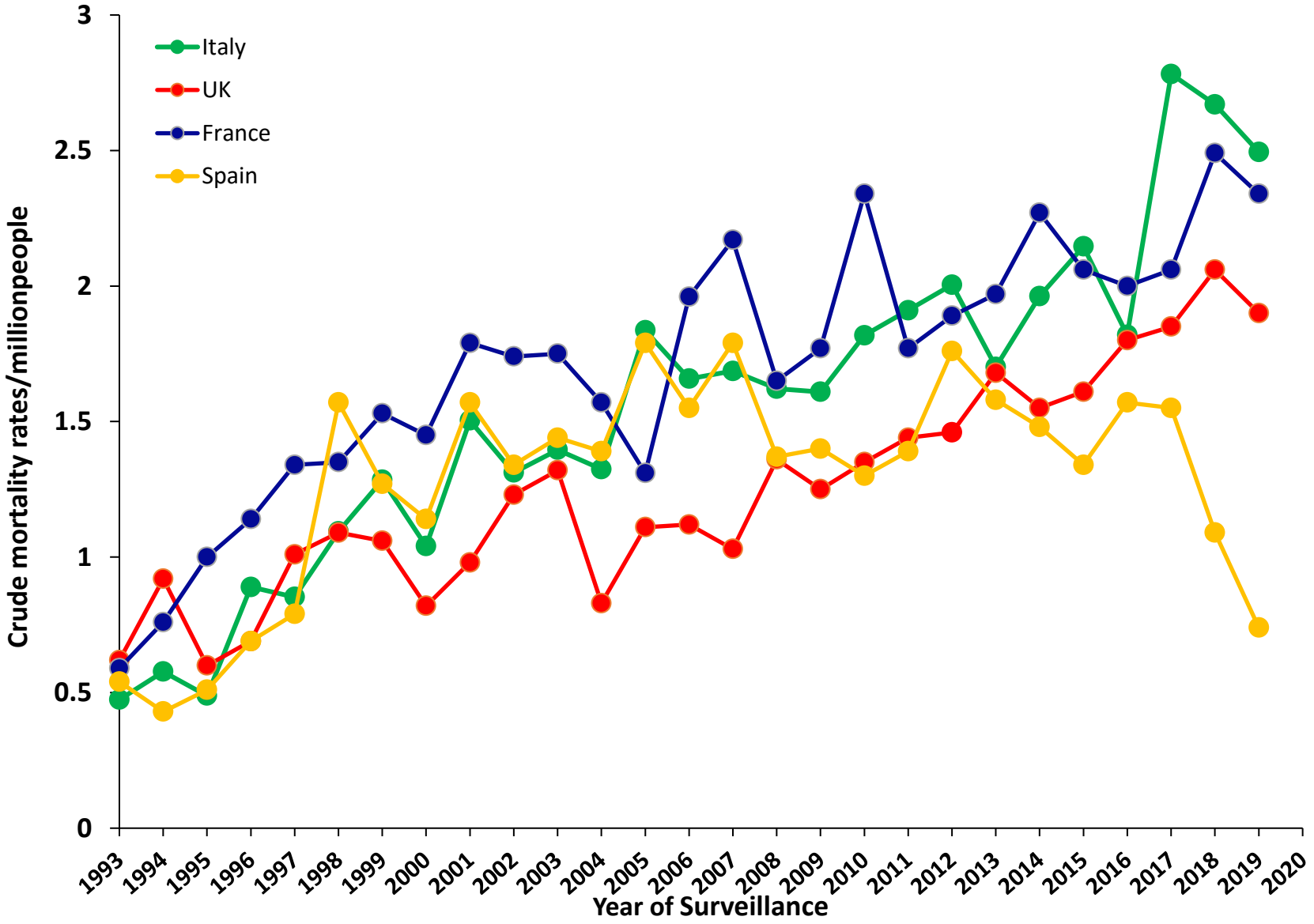


Number of deaths from sporadic CJD in European countries (1993-2019)



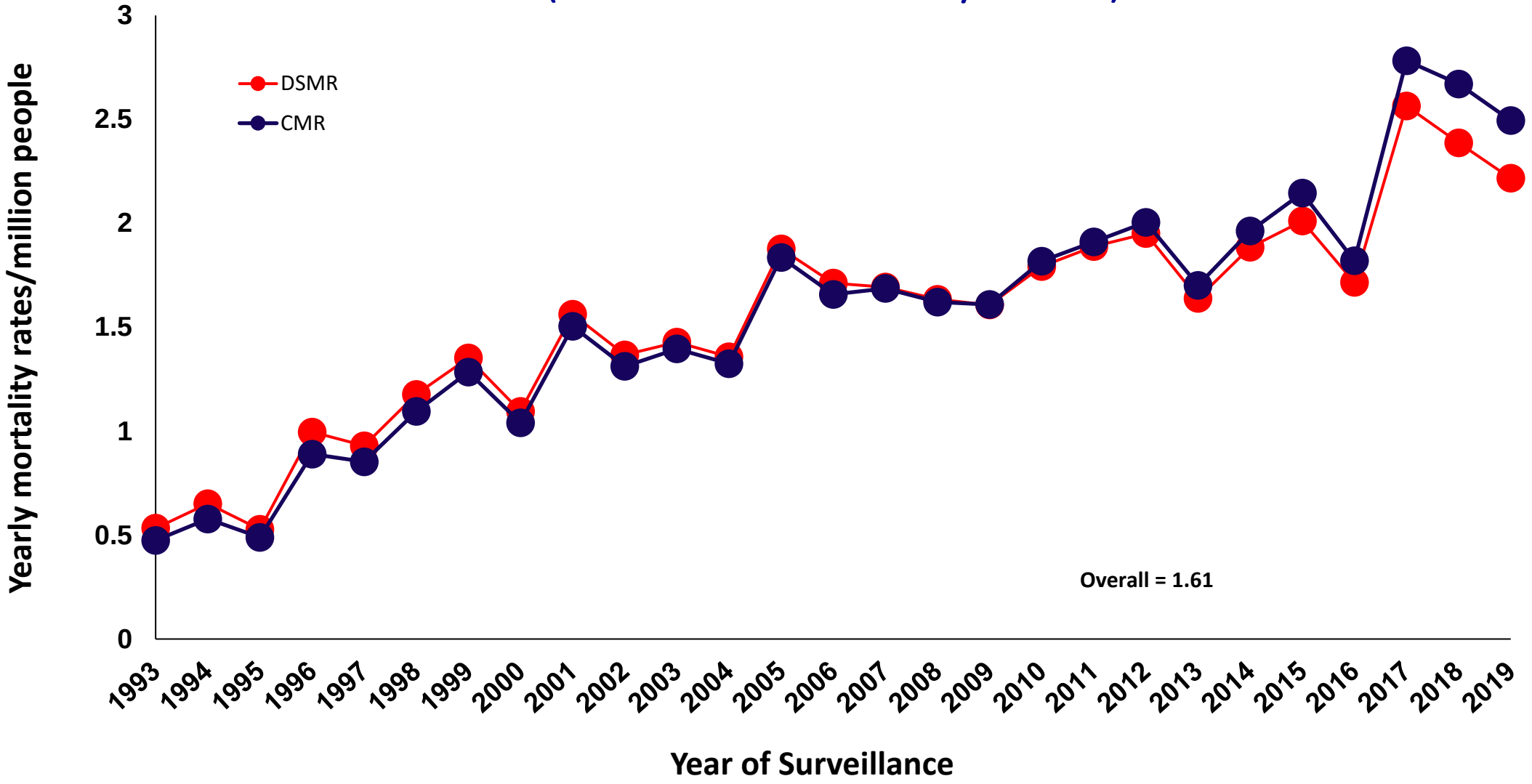
Data from ECDC, 2021

Crude mortality rates from sporadic CJD in European countries (1993-2019)



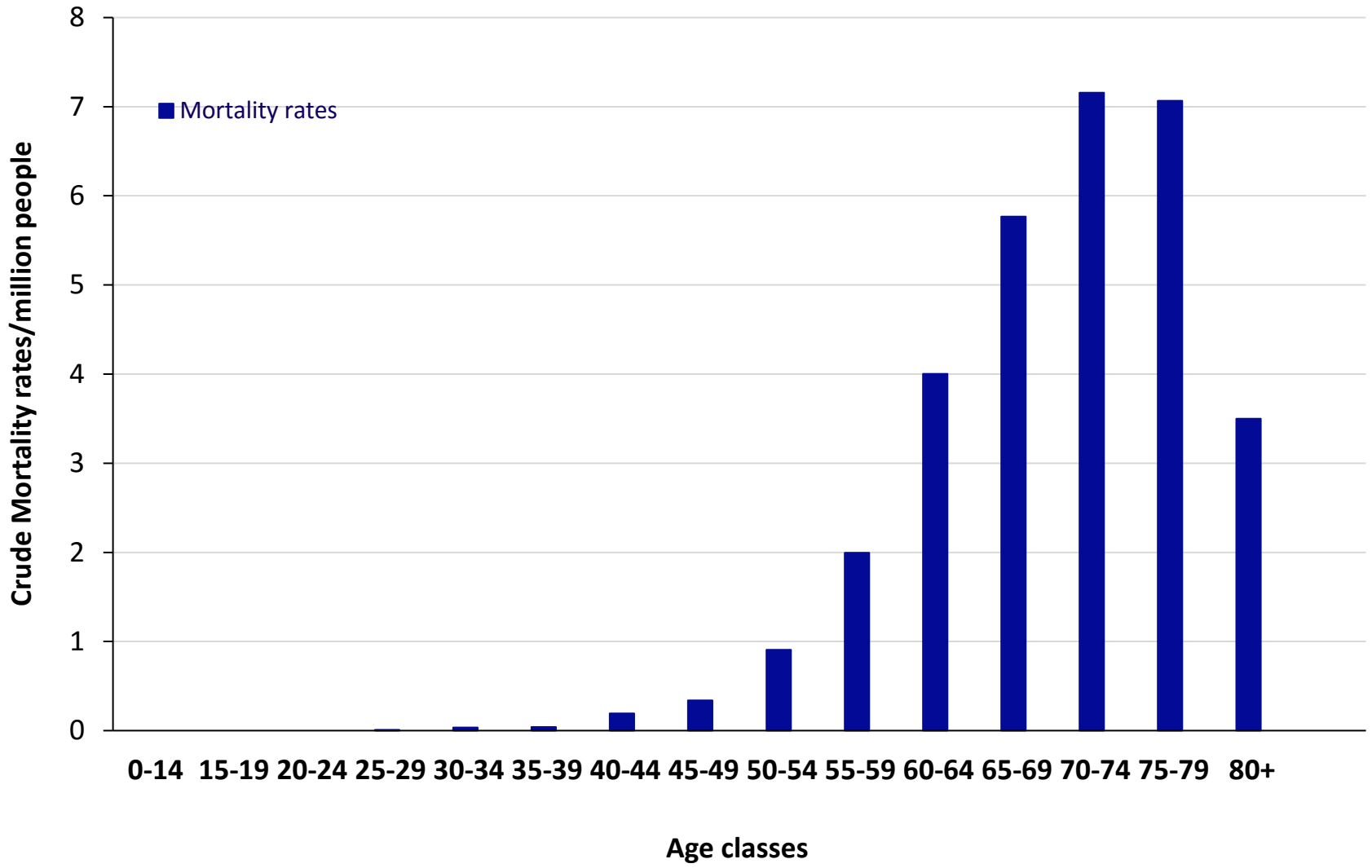
Data from ECDC, 2021

Epidemiological trends of sporadic CJD 1993-2019 (Standardized Mortality Rates*)

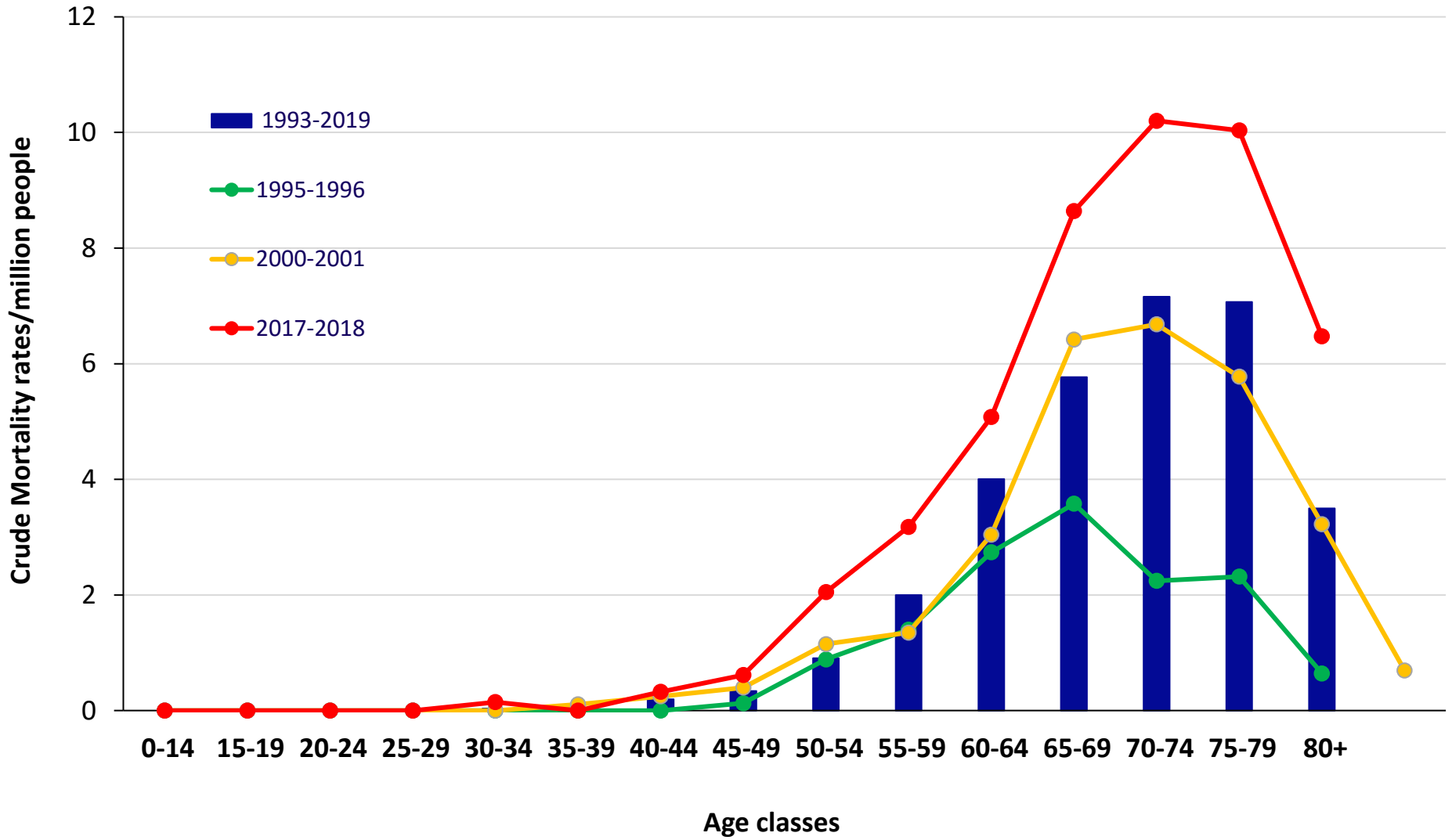


*Direct standardization, using 2013 European Reference Population, EUROSAT,

Mortality Rates from Sporadic CJD by Age Groups (1993-2019)



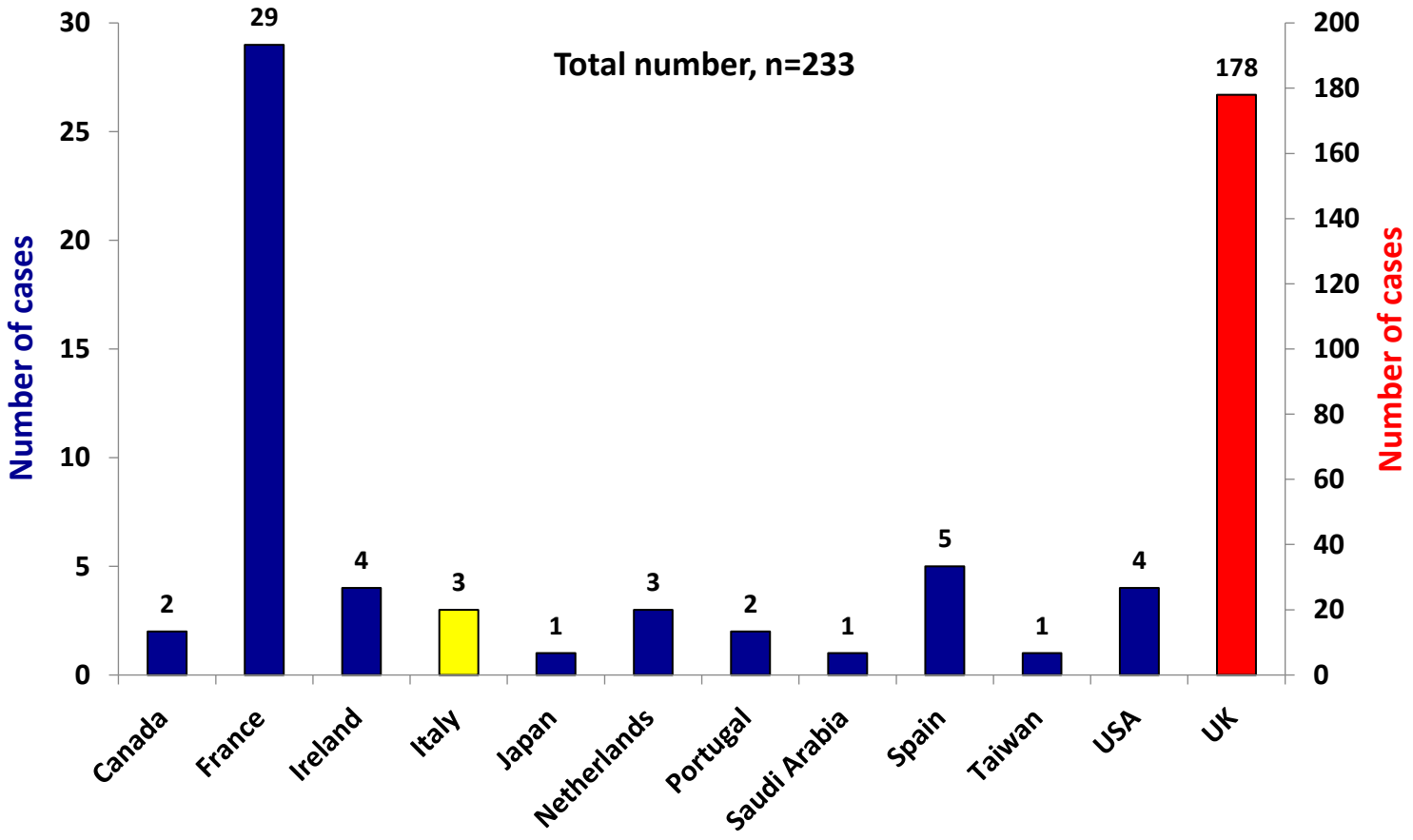
MORTALITY RATES FROM sCJD BY AGE GROUPS (1993-2019)



Increase in figures for sporadic CJD

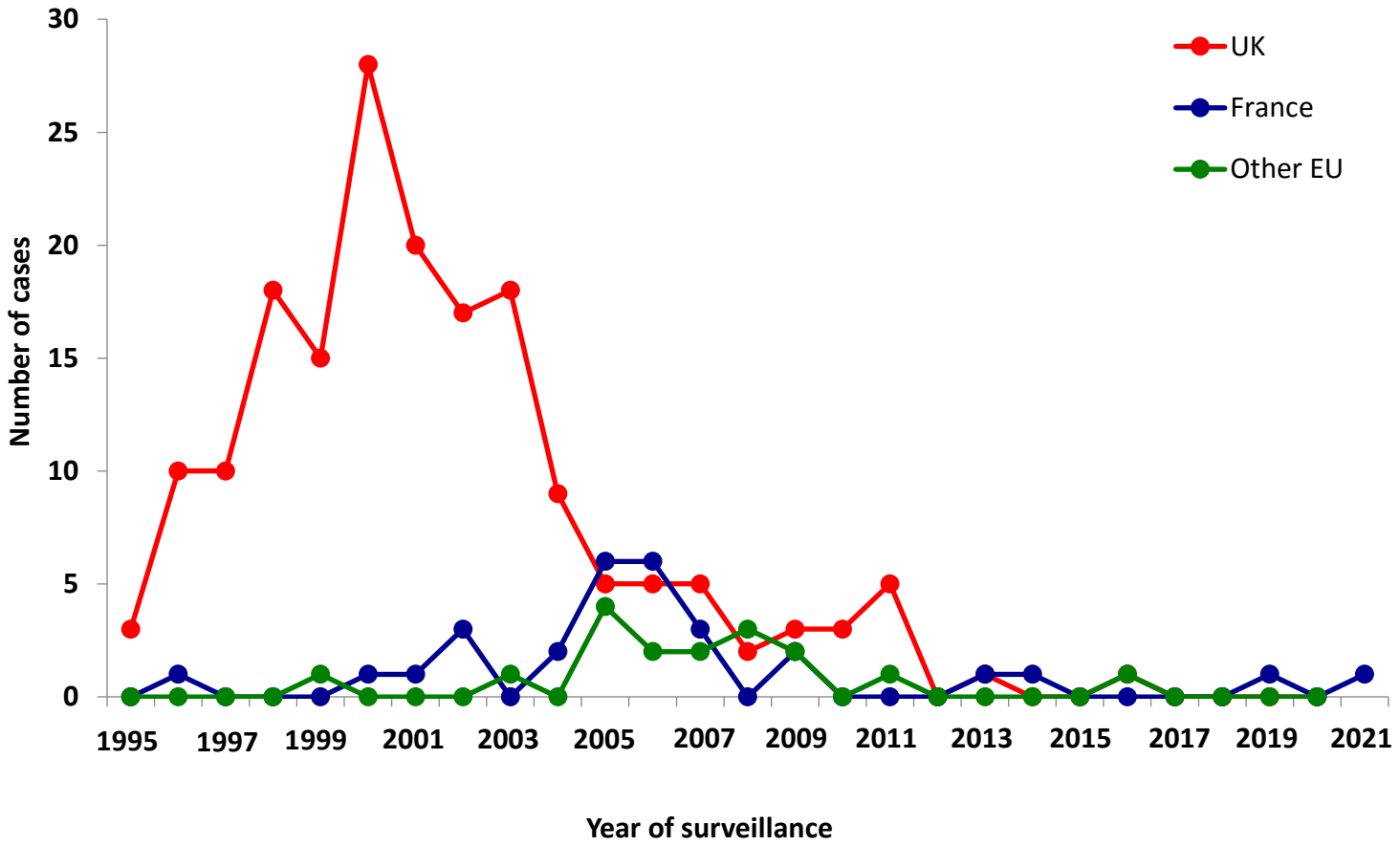
- **Numbers of referrals (Clinical suspicion)**
- **Sensitivity of diagnostic test (RT-QuIC)**
- **Age classes**

VARIANT CREUTZFELDT-JAKOB IN THE WORLD



All tested patients were M/M but one, who was heterpzigous, M/V (UK)

VARIANT CJD IN UK, FRANCE AND IN OTHER EU COUNTRIES



UK, n=178; France, n=29; Other EU (Ireland, Italy, Netherlands, Portugal, Spain), n=17

VARIANT CJD

INFECTION NOT LINKED TO BSE-INFECTED MEAT CONSUMPTION

Risk factors	Numbers	Year
Transfusion with red cells w/o leucodepletion	3 + 1 (no clinical disease)	2003-2005 (2004)
Therapy with VIII factor concentrated	1 (no clinical disease)	2008
Working in Prion Laboratories	3	2016, 2019, 2021

Acknowledgements

- **CJD and related Disorder Registry, Istituto Superiore di Sanità, Rome:**
    - **Elisa Colaizzo, clinical consultant**
    - **Dorina Tiple, clinical consultant**
    - **Luana Vaianella, clinical consultant**
    - **Anna Poleggi, molecular biology geneticand RT-QuIC analyses**
    - **Franco Cardone, Biochemistry**
    - **Marco Sbriccoli Biochemistry**
    - **Michele Equestre, RT-QuIC analyses**
    - **Alessandra Garozzo e Cinzia Gasparrini, administrative and secretary**
    - **Maurizio Pocchiari, former CJD Scientific Responsible**
- **Neuroscience Departement**
    - **Maria Puopolo statistic**
- **Network di sorveglianza:**
    - **Bologna, Piero Parchi**
    - **Milano, Giorgio Giaccone**
    - **Torino, Daniele Imperiale**
    - **Verona, Gianluigi Zanusso**
    - **Cagliari, Sara Vascellari, laboratory tests**
- **Neurologists, neuroradiologists, neuropatologists at hospital and University**
- **Patient families**