

TWENTIETH ANNUAL REPORT 2011

CREUTZFELDT-JAKOB DISEASE SURVEILLANCE IN THE UK

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SUMMARY

The national surveillance programme for Creutzfeldt-Jakob disease (CJD) in the UK was initiated in May 1990. In 1999, the National CJD Research & Surveillance Unit (NCJDRSU) became a WHO Collaborative Centre for Reference and Research on the surveillance and epidemiology of human transmissible spongiform encephalopathies (TSEs). In September 2001, the National Care Team was formed in response to concerns regarding the care of CJD patients. The team currently comprises two care coordinators (who are senior nurses) with secretarial and clinical neurological support from within the NCJDRSU where it is based.

The information provided in this Twentieth Annual Report continues to indicate that the number of sporadic cases remains relatively stable (the data for 2011 may still be incomplete). Detailed clinical and epidemiological information has been obtained for the great majority of patients. Although the general autopsy rate in the UK is low, it remains relatively high in suspected cases of CJD (being around 60% of all referred cases to the NCJDRSU). The number of brain specimens examined for sporadic CJD in the neuropathology laboratory in 2011 was 36 (compared with 29 in each of 2009 and 2010).

In 1990-2011 average annual mortality rates from sporadic CJD in England, Wales, Scotland and Northern Ireland were, respectively, 0.99, 1.20, 1.08 and 0.70/million/year. The differences between these rates are not statistically significant ($p=0.5$). The mortality rates from sporadic CJD in the UK are comparable to those observed in most other European countries and elsewhere in the world, including countries that are free of BSE. The variation in the observed mortality rates between the different regions within the UK is not statistically significant ($p=0.4$).

Up to 31st December 2011, 176 cases of definite or probable vCJD had been identified in the UK (122 definite and 54 probable who did not undergo post mortem). All 176 cases have died. The clinical, neuropathological and epidemiological features of the cases of vCJD are remarkably uniform and consistent with previous descriptions. Risk factors for the development of vCJD include age, residence in the UK and methionine homozygosity at codon 129 of the prion protein gene - all 159 clinically affected definite and probable cases of vCJD with available genetic analysis have been methionine homozygotes. Analysis of vCJD diagnoses and deaths from January 1994 to December 2011 indicates that a peak has passed. While this is an encouraging finding, the incidence of vCJD may increase again, particularly if different genetic subgroups with longer incubation periods exist. The identification of an individual of the *PRNP*-129 MV genotype as a possible case of vCJD and, in a separate case, disease-related prion protein in the spleen of a clinically unaffected blood recipient (reported in 2004) is consistent with such a hypothesis. These cases, along with the report of the prevalence of abnormal prion protein in the large study of appendix and tonsil tissues (two of the positive specimens from VV individuals) suggests the possibility of a greater number of preclinical or subclinical cases in the population than might be indicated by the present numbers of confirmed clinical cases.

The NCJDRSU continues to collaborate with the Health Protection Agency Centre for Infections and Health Protection Scotland, in relation to a range of activities, including testing of pathological specimens from the National Anonymous Tonsil Archive study through to input into the development and implementation of public health policy, for example, in relation to the follow up of those identified as at increased risk of CJD.

The activities of the NCJDRSU are strengthened by collaboration with other surveillance projects, including the Transfusion Medicine Epidemiology Review and the study of Progressive Intellectual and Neurological Deterioration in Children. The collaboration of our colleagues in these projects is greatly appreciated; the effectiveness of this collaboration allowed the identification in 2003 of a case of vCJD associated with blood transfusion and the identification in 2004 of disease-related PrP in the spleen of a recipient of blood donated by someone incubating vCJD. No further cases of vCJD attributed to blood transfusion were identified in 2010. However, a case was identified in 2010 who had evidence of vCJD infection in the spleen (but no evidence of clinical vCJD), considered probably due to blood products (treatment for haemophilia). A study has also been undertaken to investigate dental treatment as a possible risk factor for vCJD and the findings submitted for publication.

The recently described form of prion disease originally termed Protease Sensitive Prionopathy and renamed Variably Protease Sensitive Prionopathy, is of uncertain nosological significance but is presently considered a form of sporadic prion disease, alongside sporadic CJD. The NCJDRSU has so far identified a total of 5 such cases in the UK and is continuing to monitor this form of disease.

The success of the National CJD Research & Surveillance Unit continues to depend on the extraordinary level of co-operation from the neurology and neuropathology communities and other medical and paramedical staff throughout the UK. Ongoing support is provided by the Infectious Disease Epidemiology Unit, London School of Hygiene and Tropical Medicine. We are also particularly grateful to the relatives of patients for their collaboration.

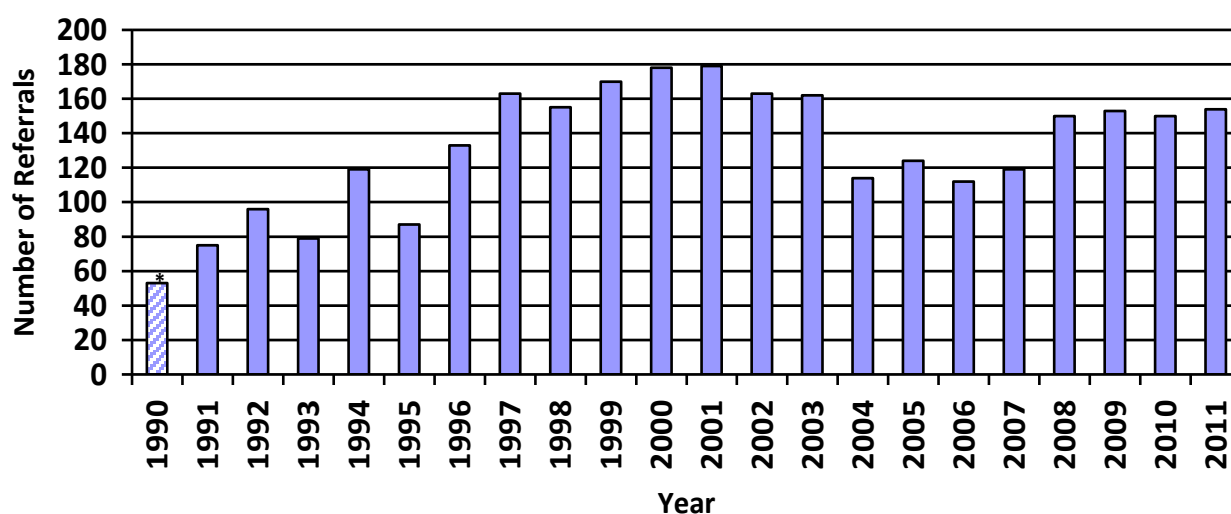
CLINICAL SURVEILLANCE

The national surveillance of CJD in the UK was initiated in May 1990. Surveillance is funded by the Department of Health, UK and by the Scottish Government Health Department. The NCJDRSU aims to monitor characteristics of CJD, specifically sporadic CJD and vCJD, to identify trends in incidence rates and to study risk factors for the development of disease. This report documents the findings in relation to UK cases of sporadic, genetic, iatrogenic and vCJD referred up to 31st December 2011 (with data ascertained up to 31st May 2012). Mortality data from England and Wales include retrospective data from 1970; for Scotland and Northern Ireland, retrospective mortality data are available from 1985. Case definitions for the various types of CJD can be found at www.cjd.ed.ac.uk/criteria.htm. Cases classified as definite or probable are included in all analyses.

2.1 Referrals to NCJDRSU

The NCJDRSU receives referrals of suspect cases of CJD and a proportion of these will turn out not to have CJD. Referrals of suspect cases increased after the present surveillance system began in 1990, particularly following the description of vCJD in 1996 (Figure 1). Numbers fluctuate from year to year, partly explained by changes in the number of non-CJD cases referred to the NCJDRSU. This would be consistent with year on year variation in referral and classification of suspect cases, particularly since the introduction of 14-3-3 as a routine test in 1999, having produced these changes.

Figure 1 Referrals to NCJDRSU : 1 May 1990 – 31st December 2011



*from 1 May 1990

2.2 Sporadic Creutzfeldt-Jakob Disease

Between 1st January 1970 and 31st December 2011, 1716 cases of sporadic CJD were identified in the UK, of which 15 cases were alive on 31st December 2011. Of these UK cases, 1255 (73%) were classified as definite cases with the remainder classed as probable. Four further cases have been identified (3 in Jersey and one in the Isle of Man) but they are not included in the following UK analyses.

Figure 2 shows the number of deaths each year from sporadic CJD for the UK between 1985 and 2011. The number of deaths identified each year has increased over time. A similar phenomenon has been observed in other European countries, and may reflect improved case ascertainment, particularly in those aged over 70 years.

Figure 2 Deaths from sporadic CJD, UK, 1985-2011

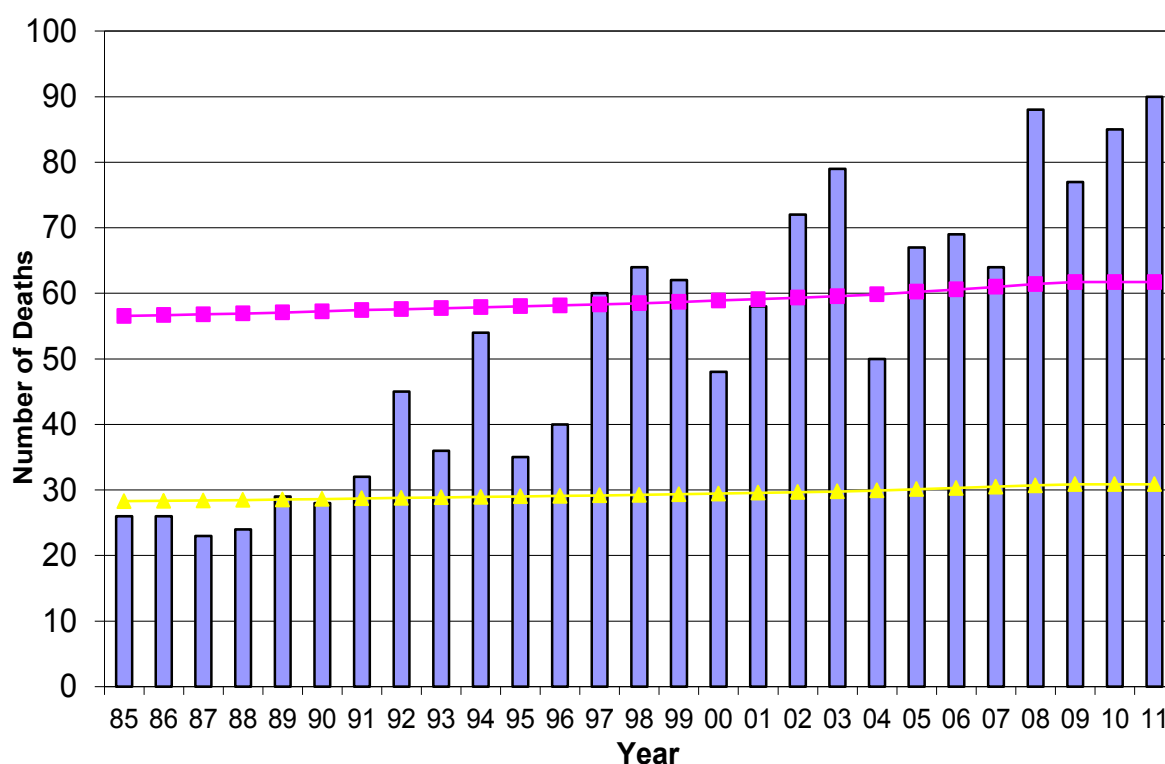
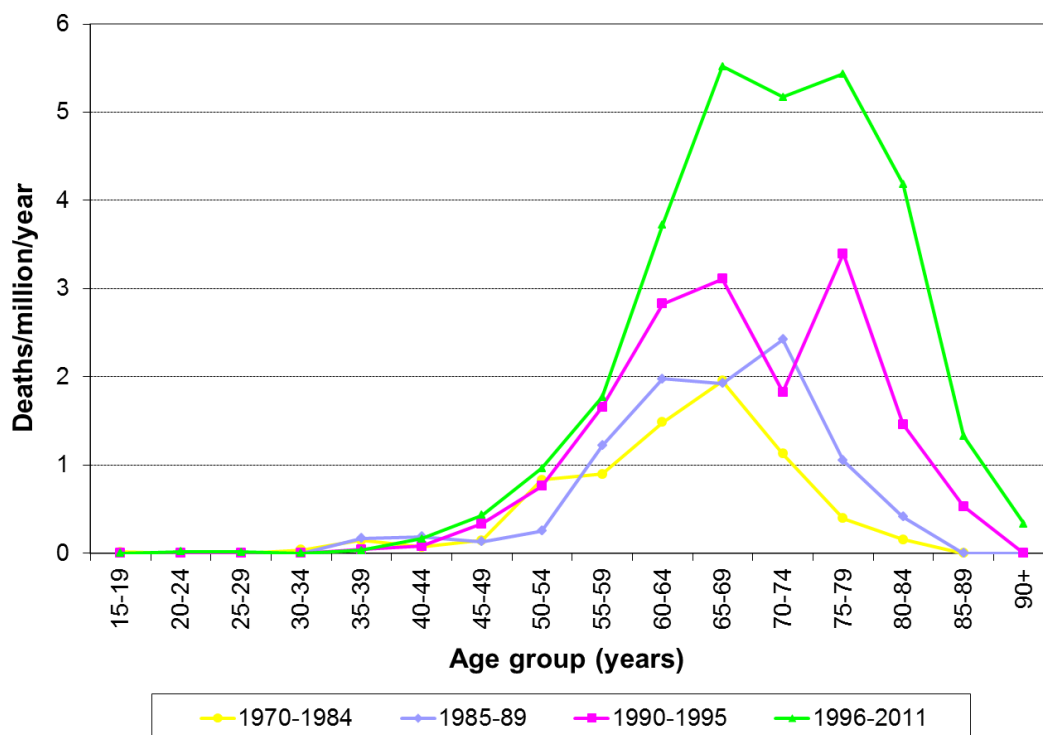


Figure 3 shows average annual age-specific mortality rates over the time periods 1970-84, 1985-89, 1990-95 and 1996-2011. These data also emphasise the very small numbers of cases of sporadic CJD occurring in individuals aged <50 years. The median ages of cases at death during these four time periods were 63, 65, 66 and 68 years, respectively. In all four time periods, the mortality rates below 40 years of age were extremely low (< 0.2/million/year). Thereafter, in all four periods, the mortality rates increased up to ages 65-79 years and then declined. This decline might be explained by an under-ascertainment in the most elderly. Comparison between the different time periods, indicate an increase in age-specific recorded mortality over time in all age groups over 50. These observations are consistent with improved case ascertainment in all ages over 50 years, but with the greatest increase occurring in the elderly.

Figure 3 Age-specific mortality rates from sporadic CJD in the UK 1970-2011
(note: from 1970-1984 only England and Wales, thereafter UK)



1970-84 Mortality rates calculated using mid-1981 England & Wales population estimates based on the 1981 Census
 1985-89 Mortality rates calculated using mid-1981 UK population estimates based on the 1981 Census
 1990-95 Mortality rates calculated using mid-1991 UK population estimates based on the 1991 Census
 1996-11 Mortality rates calculated using mid- 2001 UK population estimates based on the 2001 Census

Geographical distribution of sporadic CJD

Over the period 1990-2011 the average crude annual mortality rates from sporadic CJD per million population were 0.99 in England, 1.20 in Wales, 1.08 in Scotland and 0.70 in Northern Ireland (Tables 1a and 1b). When account is taken of age and sex, the variation in recorded mortality between the different countries is not statistically significant ($p=0.5$).

Age- and sex- standardised mortality ratios (SMRs) for the 12 government office regions of the UK for the period 1st January 1990 to 31st December 2011 were calculated (Figure 4). An SMR of 100 equates to the national average mortality rate; an SMR above or below this value reflects relative high or low mortality, respectively. After adjusting for the age/sex distribution of the population, the variation in mortality rates between the different regions is not statistically significant ($p=0.4$).

Table 1a Deaths from definite and probable sporadic CJD shown by region and local authority of residence at death: 1st January 1990 to 31st December 2011

ENGLAND	No. of cases	Mortality Rate*	ENGLAND	No. of cases	Mortality Rate*
North East	52	0.93	East	130	1.09
Darlington UA	2		Luton UA	3	
Hartlepool UA	3		Peterborough UA	2	
Middlesbrough UA	1		Southend-on-Sea UA	4	
Redcar & Cleveland UA	3		Thurrock UA	4	
Stockton-on-Tees UA	2		Bedfordshire	9	
Durham	8		Cambridgeshire	8	
Northumberland	7		Essex	40	
Tyne & Wear	26		Hertfordshire	18	
			Norfolk	22	
North West	148	0.99	Suffolk	20	
Blackburn with Darwen UA	6				
Blackpool UA	3		London	129	0.80
Halton UA	3		Inner London	41	
Warrington UA	5		Outer London	88	
Cheshire	13				
Cumbria	15		South East	182	1.03
Greater Manchester	44		Bracknell Forest UA	3	
Lancashire	26		Brighton and Hove UA	1	
Merseyside	33		Isle of Wight UA	3	
			Medway UA	2	
Yorkshire and the Humber	105	0.96	Milton Keynes UA	1	
East Riding of Yorkshire UA	6		Portsmouth UA	2	
Kingston Upon Hull, City of UA	4		Reading UA	3	
North East Lincolnshire UA	1		Slough UA	1	
North Lincolnshire UA	3		Southampton UA	3	
York UA	6		West Berkshire UA	5	
North Yorkshire	18		Windsor and Maidenhead UA	3	
South Yorkshire	32		Wokingham UA	3	
West Yorkshire	35		Buckinghamshire	9	
			East Sussex	14	
East Midlands	80	0.87	Hampshire	30	
Derby UA	5		Kent	35	
Leicester UA	5		Oxfordshire	16	
Nottingham UA	3		Surrey	22	
Rutland UA	1		West Sussex	26	
Derbyshire	16				
Leicestershire	14		South West	147	1.35
Lincolnshire	12		Bath & North East Somerset UA	4	
Northamptonshire	6		Bournemouth UA	7	
Nottinghamshire	18		Bristol, City of UA	10	
			North Somerset UA	8	
West Midlands	107	0.92	Plymouth UA	10	
Herefordshire, County of UA	3		Poole UA	3	
Stoke-on-Trent UA	2		South Gloucestershire UA	8	
Telford and Wrekin UA	2		Swindon UA	2	
Shropshire	6		Torbay UA	3	
Staffordshire	31		Cornwall and Isles of Scilly	18	
Warwickshire	7		Devon	17	
West Midlands (Met County)	41		Dorset	13	
Worcestershire	15		Gloucestershire	15	
			Somerset	19	
			Wiltshire	10	
TOTAL FOR ENGLAND	1080	0.99			

* number of deaths/million/annum based on mid-2001 population estimates in England (source: ONS) over the 22-year period of the study. Postcode of residence obtained from AFD Postcode Plus.

Table 1b Deaths from definite and probable sporadic CJD: Wales, Scotland and NI
1st January 1990 to 31st December 2011

WALES†	No. of cases	WALES†	No. of cases
Isle of Anglesey	4	Neath Port Talbot	0
Gwynedd	6	The Vale of Glamorgan	3
Conwy	5	Cardiff	5
Denbighshire	1	Bridgend	2
Flintshire	2	Rhondda, Cynon, Taff	6
Wrexham	5	Merthyr Tydfil	2
Powys	8	Caerphilly	6
Ceredigion	3	Blaenau Gwent	0
Pembrokeshire	1	Torfaen	3
Carmarthenshire	2	Monmouthshire	2
Swansea	7	Newport	4
TOTAL FOR WALES (MORTALITY RATE*)	77 (1.20)	†unitary authorities	

SCOTLAND†	No. of cases	SCOTLAND†	No. of cases
Aberdeen City	4	Highland	2
Aberdeenshire	7	Inverclyde	2
Angus	1	Midlothian	1
Argyll & Bute	3	Moray	3
Clackmannanshire	1	North Ayrshire	4
Dumfries & Galloway	3	North Lanarkshire	4
Dundee City	6	Orkney Islands	0
East Ayrshire	1	Perth & Kinross	1
East Dunbartonshire	3	Renfrewshire	4
East Lothian	3	Scottish Borders	3
East Renfrewshire	1	Shetland Islands	3
Edinburgh, City of	18	South Ayrshire	3
Eilean Siar	0	South Lanarkshire	6
Falkirk	4	Stirling	2
Fife	9	West Dunbartonshire	2
Glasgow City	12	West Lothian	4
TOTAL FOR SCOTLAND (MORTALITY RATE*)	120 (1.08)	†council areas	

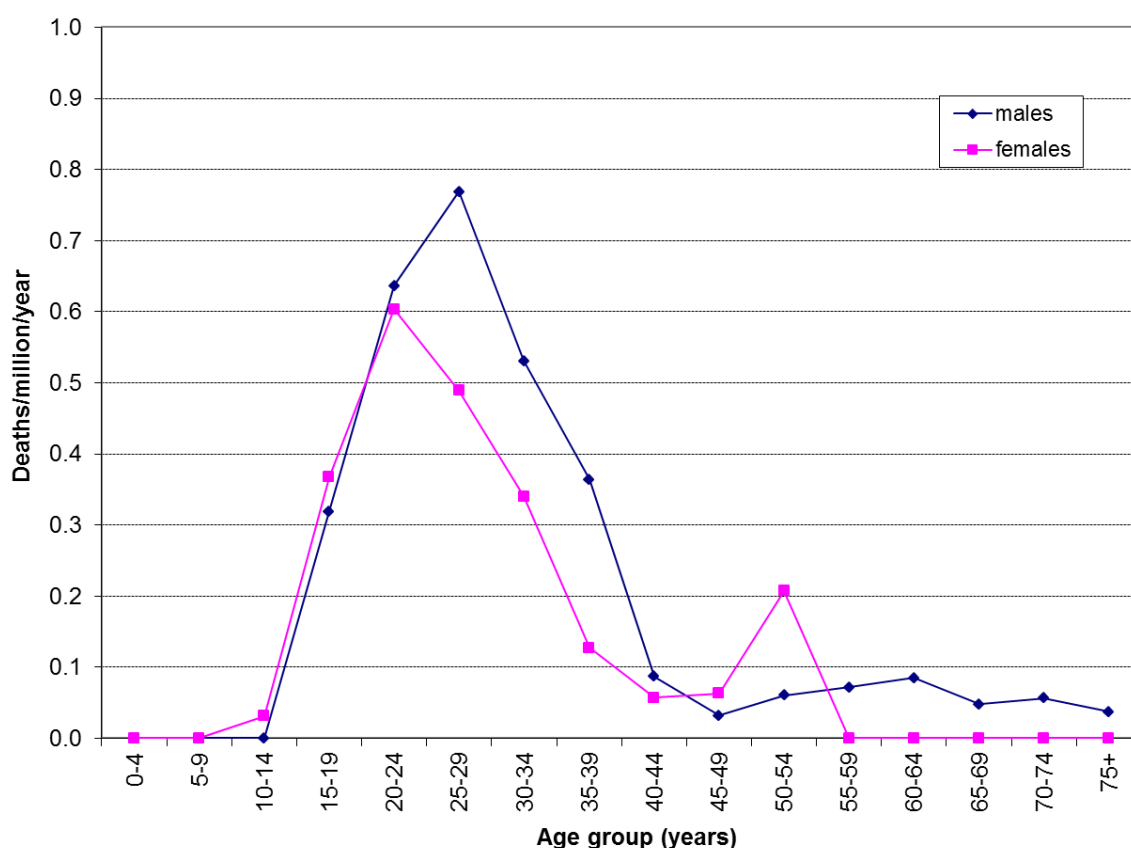
NORTHERN IRELAND†	No. of cases	NORTHERN IRELAND†	No. of cases
Antrim	1	Down	2
Ards	1	Dungannon	0
Armagh	1	Fermanagh	0
Ballymena	0	Larne	1
Ballymoney	1	Limavady	0
Banbridge	1	Lisburn	4
Belfast	8	Magherafelt	0
Carrickfergus	0	Moyle	0
Castlereagh	0	Newry & Mourne	0
Coleraine	1	Newtownabbey	0
Cookstown	0	North Down	0
Craigavon	3	Omagh	1
Derry	1	Strabane	0
TOTAL FOR N IRELAND (MORTALITY RATE*)	26 (0.70)	†district council areas	

* based on mid-2001 population estimates for unitary authorities in Wales, council areas within Scotland and district council areas in Northern Ireland (ONS) over the 22-year period of the study. Postcode of residence obtained from AFD Postcode Plus.

2.3 Variant Creutzfeldt-Jakob Disease

Up to 31st December 2011, 176 cases of definite or probable vCJD had been identified in the UK (122 definite and 54 probable cases who did not undergo post mortem; no cases still alive). Seventy-five (43%) of the 176 cases were women. The median age at onset of disease was 26 years and the median age at death 28 years (compared with 67 years for the median age at onset and 68 years for the median age at death for sporadic CJD). The youngest case was aged 12 years at onset while the oldest case was aged 74 years. The age- and sex-specific mortality rates for vCJD over the time period 1 May 1995 to 31 December 2011 are shown in Figure 5. The median duration of illness from the onset of first symptoms to death was 14 months (range 6-114) compared with a median duration of illness for cases of sporadic CJD of 4 months (range 1 to 80) during the period 1990-2011.

Figure 5 Age- and sex-specific mortality rates from vCJD in the UK
1 May 1995 - 31st December 2011



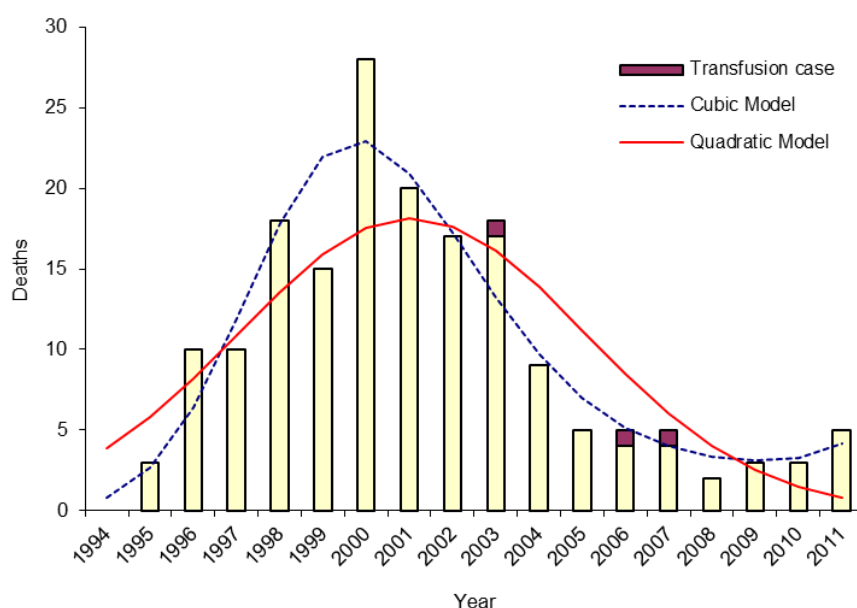
Mortality rates calculated using ONS mid-2001 population estimates

All definite and probable cases of vCJD with genetic analysis have been *PRNP*-129 MM individuals (a single case of possible vCJD with an MV genotype was described in the Seventeenth Annual Report 2008 (<http://www.cjd.ed.ac.uk/archive.htm>)). To date, no case of vCJD has been identified in the UK in individuals born after 1989.

Deaths from vCJD

Results from modelling the incidence of vCJD deaths indicate the epidemic peaked in about the year 2000 when there were 28 deaths and has since declined to a current incidence of about one to two deaths per year. There is evidence that the epidemic curve is skewed with an extended tail (see Figure 6). The shape of the epidemic differs significantly by birth cohort ($p < 0.001$, not shown), mainly due to the fact that deaths of individuals born in the 1980s were only seen from 1999; this is consistent with those born in the 1980s being infected towards the end of the BSE epidemic when they were older rather than at the beginning. This requires a lower exposure/susceptibility in the very young, which is compatible with no cases having been seen to date in individuals born in the 1990s¹.

Figure 6 vCJD deaths by year with fitted quadratic and cubic trend lines



It is important to note that although a peak has been passed, it is possible that there will be future peaks, possibly in other genetic subgroups. To date, however, there is no evidence of a second wave. There is also the possibility of ongoing person to person spread as seen with 4 cases of transfusion associated vCJD infection to date, who received blood in 1999 or earlier from donors who were later diagnosed with clinical vCJD.

Geographical distribution of vCJD

Tables 2a and 2b present data on the geographical distribution by residence at onset (for all 176 vCJD cases) and residence at death (for 173 vCJD cases who had died by 31st December 2011 and were resident in the UK at death), along with the crude mortality rate per million population per annum of each standard region.

¹ Analysis undertaken by N J Andrews, Senior Statistician, Statistics Unit, Centre for Infections, Health Protection Agency. Further detail is available at <http://www.cjd.ed.ac.uk/cjdq72b.pdf>

Table 2a Cases of definite and probable variant CJD shown by residence at onset (n=141) and residence at death (n=142†) in England (region & local authority)

	No. resident at onset	No. resident at death	Mortality rate*		No. resident at onset	No. resident at death	Mortality rate*
North East	11	11	0.26	East	13	13	0.14
Darlington UA	0	0		Luton UA	0	0	
Hartlepool UA	0	0		Peterborough UA	0	0	
Middlesbrough UA	1	1		Southend-on-Sea UA	1	1	
Redcar & Cleveland UA	1	1		Thurrock UA	0	0	
Stockton-on-Tees UA	1	1		Bedfordshire	0	0	
Durham	0	1		Cambridgeshire	1	1	
Northumberland	3	4		Essex	2	2	
Tyne & Wear	5	3		Hertfordshire	3	3	
				Norfolk	3	3	
North West	27	27	0.24	Suffolk	3	3	
Blackburn with Darwen UA	0	0					
Blackpool UA	1	1		London	19	17	0.14
Halton UA	0	0		Inner London	7	7	
Warrington UA	2	2		Outer London	12	10	
Cheshire	5	6					
Cumbria	1	1		South East	23	20	0.15
Greater Manchester	10	9		Bracknell Forest UA	1	1	
Lancashire	4	4		Brighton and Hove UA	0	0	
Merseyside	4	4		Isle of Wight UA	0	1	
				Medway UA	0	1	
Yorkshire and the Humber	17	18	0.22	Milton Keynes UA	0	0	
East Riding of Yorkshire UA	1	1		Portsmouth UA	1	2	
Kingston Upon Hull, UA	0	0		Reading UA	0	0	
North East Lincolnshire UA	1	1		Slough UA	0	0	
North Lincolnshire UA	0	0		Southampton UA	1	0	
York UA	0	0		West Berkshire UA	0	0	
North Yorkshire	4	4		Windsor & Maidenhead UA	0	0	
South Yorkshire	5	5		Wokingham UA	0	0	
West Yorkshire	6	7		Buckinghamshire	0	1	
				East Sussex	2	2	
East Midlands	8	10	0.14	Hampshire	5	2	
Derby UA	0	0		Kent	5	4	
Leicester UA	0	0		Oxfordshire	1	1	
Nottingham UA	0	0		Surrey	6	4	
Rutland UA	0	0		West Sussex	1	1	
Derbyshire	0	1					
Leicestershire	4	5		South West	17	16	0.19
Lincolnshire	2	2		Bath & NE Somerset UA	0	0	
Northamptonshire	1	1		Bournemouth UA	1	1	
Nottinghamshire	1	1		Bristol, City of UA	1	1	
				North Somerset UA	0	0	
West Midlands	6	10	0.11	Plymouth UA	0	0	
Herefordshire, County of UA	0	0		Poole UA	0	0	
Stoke-on-Trent UA	0	0		South Gloucestershire UA	1	0	
Telford and Wrekin UA	0	0		Swindon UA	0	0	
Shropshire	1	1		Torbay UA	0	1	
Staffordshire	0	0		Cornwall and Isles of Scilly	2	1	
Warwickshire	2	3		Devon	3	3	
West Midlands (Met County)	3	5		Dorset	0	0	
Worcestershire	0	1		Gloucestershire	1	1	
				Somerset	4	5	
				Wiltshire	4	3	
TOTAL FOR ENGLAND	141	142	0.17				

* number of deaths/million/annum based on mid 2001 population estimates (source: ONS): 1 May 1995 to 31 Dec 2011. Postcode of residence obtained from AFD Postcode Plus.

† excludes 3 cases who died abroad.

Table 2b Cases of definite and probable variant CJD shown by residence at onset (n=35) and residence at death (n=31): Wales, Scotland and NI

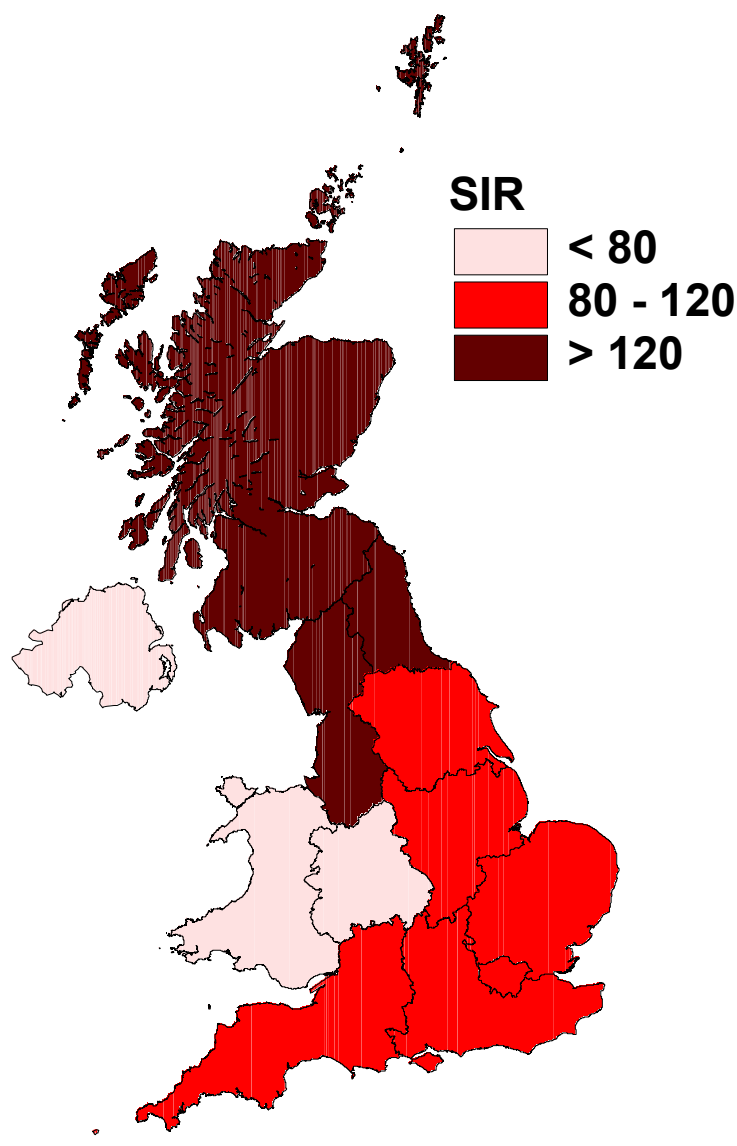
WALES†	No. resident at onset	No. resident at death	WALES†	No. resident at onset	No. resident at death
Isle of Anglesey	0	0	Neath Port Talbot	0	0
Gwynedd	1	1	The Vale of Glamorgan	1	1
Conwy	0	0	Cardiff	0	0
Denbighshire	1	0	Bridgend	0	0
Flintshire	0	0	Rhondda, Cynon, Taff	0	0
Wrexham	0	0	Merthyr Tydfil	0	0
Powys	1	1	Caerphilly	0	0
Ceredigion	0	0	Blaenau Gwent	0	0
Pembrokeshire	2	2	Torfaen	0	0
Carmarthenshire	1	1	Monmouthshire	0	0
Swansea	1	0	Newport	0	0
TOTAL (MORTALITY RATE*)	8	6 (0.12)	†unitary authorities		
SCOTLAND†	No. resident at onset	No. resident at death	SCOTLAND†	No. resident at onset	No. resident at death
Aberdeen City	1	1	Highland	3	2
Aberdeenshire	0	0	Inverclyde	0	0
Angus	0	0	Midlothian	0	0
Argyll & Bute	0	0	Moray	0	0
Clackmannanshire	0	0	North Ayrshire	0	0
Dumfries & Galloway	0	0	North Lanarkshire	3	3
Dundee City	0	0	Orkney Islands	1	0
East Ayrshire	1	1	Perth & Kinross	0	0
East Dunbartonshire	1	1	Renfrewshire	1	1
East Lothian	0	0	Scottish Borders	0	0
East Renfrewshire	1	1	Shetland Islands	0	0
Edinburgh, City of	2	2	South Ayrshire	1	1
Eilean Siar	0	0	South Lanarkshire	1	1
Falkirk	1	1	Stirling	0	0
Fife	2	2	West Dunbartonshire	0	0
Glasgow, City of	3	3	West Lothian	2	2
TOTAL (MORTALITY RATE*)	24	22 (0.26)	†council areas		
N IRELAND†	No. resident at onset	No. resident at death	N IRELAND†	No. resident at onset	No. resident at death
Antrim	0	0	Down	0	0
Ards	0	0	Dungannon	0	0
Armagh	0	0	Fermanagh	0	0
Ballymena	0	0	Larne	0	0
Ballymoney	0	0	Limavady	0	0
Banbridge	0	0	Lisburn	1	1
Belfast	1	1	Magherafelt	0	0
Carrickfergus	0	0	Moyle	0	0
Castlereagh	0	0	Newry & Mourne	0	0
Coleraine	0	0	Newtownabbey	1	1
Cookstown	0	0	North Down	0	0
Craigavon	0	0	Omagh	0	0
Derry	0	0	Strabane	0	0
TOTAL (MORTALITY RATE*)	3	3 (0.11)	†district council areas		

* number of deaths/million/annum based on mid-2001 population estimates (source: ONS): 1 May 1995-31 Dec 2011. Postcode of residence obtained from AFD Postcode Plus.

Cases have been widely spread throughout the UK, although there remains a relatively high incidence amongst those who lived in the north (Scotland, North East, North West, Yorkshire & Humberside; 16.9 million people, 74 vCJD cases) compared to the south (Wales, East Midlands, West Midlands, South West, South East, London, East of England; 31.7 million people, 98 vCJD cases) of Great Britain in 1991.² The rate ratio controlling for age and sex is now 1.42 (95% CI 1.05-1.92), ie individuals living in the “North” in 1991 are about one and a half times more likely to have developed vCJD than individuals who were living in the “South” in 1991. Age- and sex- standardised incidence ratios (SIRs) based on cases' place of residence in 1991 (shortly after the time when exposure to the BSE agent is assumed to have peaked) are shown in Figure 7.

Investigations into geographically associated cases of vCJD (either through proximity of residence or through an occupational, educational or social/recreational link with the same location) have found no convincing evidence of factors that may have augmented local risks for vCJD³

Figure 7 Standardised vCJD incidence ratios (SIRs) up to 31st December 2011, by region of residence on 1st January 1991



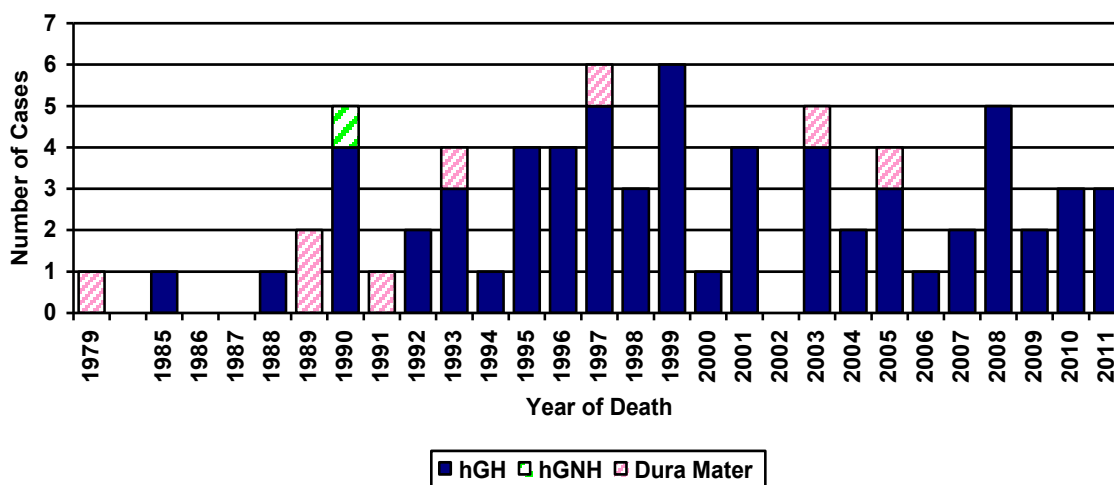
² Cousens S, Smith PG, Ward H, Everington D, Knight RSG, Zeidler M, Stewart G, Smith-Bathgate EAB, Macleod MA, Mackenzie J, Will RG. Geographical distribution of variant Creutzfeldt-Jakob disease in Great Britain, 1994-2000. *Lancet* 2001; 357: 1002-1007.

³ Molesworth AM, Cousens SN, Gill ON, Ward HJT on behalf of the local investigation teams. Variant Creutzfeldt-Jakob disease in the United Kingdom: a countrywide or local risk? *J Epid Comm Health* 2010; 64: 616-621.

2.4 Iatrogenic Creutzfeldt-Jakob disease

Since 1970, up to 31st December 2011, 74 cases of CJD attributable to iatrogenic exposure have been identified, 8 in individuals receiving dura mater implants, 65 in individuals who had received human-derived growth hormone (hGH) and one in a recipient of human gonadotrophin (hGN) who was treated in Australia. Seventy-three of these individuals have died (Figure 8) and one was still alive as at 31st December 2011. The mean age at death of the hGH/hGN group was 33 years (with a range of 20-51 years) and for the dura mater cases 46½ years (range 27-78 years).

Figure 8 Deaths from iatrogenic CJD, 1979-2011



The first identified iatrogenic case was a dura mater recipient who died in 1979. The first hGH-related death occurred in 1985. Since 1985 in the UK, human pituitary-derived hormones have been replaced by synthetic preparations. Details of the UK human pituitary-derived hormone cases, with a discussion of the incubation periods, were published in 2003.⁴ A study of the accumulated UK experience with dura mater-related CJD, including incubation periods, was undertaken and the results published in 2006.⁵

2.5 Transfusion Medicine Epidemiology Review

The Transfusion Medicine Epidemiology Review (TMER) is a collaborative project between the UK NCJDRSU and UK Blood Services (UKBS). The main purpose is to investigate whether there is any evidence that CJD or vCJD may have been transmitted via the blood supply. Cases (definite and probable) are notified to the UKBS by NCJDRSU; a search establishes whether any have acted as donors or received blood transfusions. Donation/transfusion records are checked and all components traced through hospital records. Details of all identified recipients/donors are forwarded to NCJDRSU for subsequent checking to ensure none appear on the NCJDRSU database as a case of CJD. Further details are given in the 19th Annual Report (see <http://www.cjd.ed.ac.uk>)

Four instances of probable transfusion transmitted infection have been identified. The first recipient (Case 1) developed symptoms of vCJD 6½ years after receiving a transfusion of red cells donated 3½

⁴ Swerdlow AJ, Higgins CD, Adlard P, Jones ME, Preece MA. Creutzfeldt-Jakob disease in United Kingdom patients treated with human pituitary growth hormone. *Neurology* 2003; 61: 783-91.

⁵ Heath CA, Barker RA, Esmonde TFG, Harvey P, Trend P, Head MW, Smith C, Bell JE, Ironside JW, Will RG, Knight RSG. Dura mater-associated Creutzfeldt-Jakob disease: experience from surveillance in the UK. *JNNP* 2006; 77: 880-2.

years before the donor (Donor 1) developed symptoms of vCJD⁶. The second recipient (Case 2) died from a non-neurological disorder 5 years after receiving blood from a donor (Donor 2) who subsequently developed vCJD⁷; at post mortem protease-resistant prion protein (PrP^{res}) was detected in the spleen but not in the brain. This was the first recorded case in the UK of autopsy detection of presumed pre- or sub-clinical vCJD infection. The third recipient (Case 3) developed symptoms of vCJD 7 years, 10 months after receiving a transfusion of red cells donated about 21 months before the donor (Donor 3) developed symptoms of vCJD⁸. The fourth recipient (Case 4), who received a transfusion from the same donor as Case 3, developed symptoms of vCJD 8 years, 4 months after receiving a transfusion of red cells donated about 17 months before the donor (Donor 3) developed symptoms of vCJD⁹.

The identification of 3 cases of vCJD in the small cohort of known recipients of blood from persons incubating vCJD, together with the fact that 2 of the cases were associated with a common blood donor, establishes beyond reasonable doubt that blood transfusion is a transmission route for vCJD.

(Collaborators on this project: Dr P.E. Hewitt, Dr C.A. Llewelyn, Ms M Malfroy).

2.6 Study of Progressive Intellectual & Neurological Deterioration (PIND)

The aim of this project is to use the mechanism of the British Paediatric Surveillance Unit to identify all cases of progressive intellectual and neurological deterioration in children in the UK, particularly those with features suggestive of vCJD. All cases are discussed by an Expert Neurological Advisory Group of eight paediatric neurologists and one geneticist which allocates the cases to a diagnostic category¹⁰⁻¹¹.

As of 31st December 2011, after nearly 15 years of surveillance, 3187 patients with suspected PIND had been reported and the Expert Group had discussed 2157 of these. 1335 cases had a confirmed underlying cause other than vCJD, being categorised into over 150 known neurodegenerative diseases¹². There have been six cases of vCJD; four definite and two probable. Three were reported in 1999, one in 2000 and 2 in mid-2001. One girl was aged 12 at onset - the youngest UK case of vCJD identified to date.

(Collaborators on this project: Dr C. Verity, Prof A. Nicoll, Ms L. Stellitano, Ms AM Winstone)

⁶ Llewelyn CA, Hewitt PA, Knight RSG, Amar K, Cousens S, Mackenzie J, Will RG. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. *Lancet* 2004; 363: 417-421.

⁷ Peden AH, Head MW, Ritchie DL, Bell JE, Ironside JW. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient. *Lancet* 2004 364: 527-529.

⁸ Wroe SJ, Pal S, Siddique D, Hyare H, Macfarlane R, Joiner S, Linehan JM, Brandner S, Wadsworth JD, Hewitt P, Collinge J. Clinical presentation and pre-mortem diagnosis of variant Creutzfeldt-Jakob disease associated with blood transfusion: a case report. *Lancet* 2006; 368: 2061-2067.

⁹ Health Protection Agency. Fourth case of transfusion-associated variant-CJD. *Health Protection Report* 2007;1(3):

¹⁰ Verity CM, Nicoll A, Will RG, Devereux G, Stellitano L. Variant Creutzfeldt-Jakob disease in UK children: a national surveillance study. *Lancet* 2000; 356: 1224-1227.

¹¹ Devereux G, Stellitano L, Verity CM, Nicoll A, Will RG, Rogers P. Variations in neurodegenerative disease across the UK: findings from the national study of Progressive Intellectual and Neurological Deterioration (PIND). *Arch Dis Child* 2004; 89: 8-12.

¹² Verity C, Winstone AM, Stellitano L, Will R, Nicoll A. The epidemiology of progressive intellectual and neurological deterioration in childhood. *Arch Dis Child* 2010; 95: 361-364.

CASE-CONTROL STUDY

Between 1998 and 2008 a case-control study of CJD was funded in the UK, courtesy of the Department of Health and Scottish Government, to investigate potential risk factors for variant and sporadic CJD.

Patients themselves are usually too unwell to answer questions when they are seen by members of the Unit. Therefore, relatives of patients with suspected CJD are approached and, with informed consent, interviewed about the patient using a standard questionnaire relating to possible risk factors for CJD, including residential, occupational, dietary and medical histories. This interview takes place as early as possible after a person is suspected of having CJD. We are indebted to the families of those with suspected CJD, who agree to be interviewed at what is an extremely difficult time in their lives.

A general population control group, recruited in 2002-2003, has been used in analyses comparing risk factors of the control group with cases of vCJD and sCJD, based on information provided by the families of cases and controls at interview (for details of the findings please see below). The methodology of the recruitment of this control group can be found in Ward et al, 2006, *Annals of Neurology*¹³

Results from the case-control study of reported risk factors for variant CJD are consistent with dietary exposure to contaminated beef products being the main route of infection of vCJD, but recall bias cannot be excluded as an explanation¹³. For sporadic CJD, an analysis of reported medical risk factors, found that it was unlikely that a high proportion of UK sCJD cases are the result of transmission during surgery, but we cannot exclude the possibility that such transmission occurs occasionally¹⁴.

Although funding for the case-control study has now ceased, the Unit continues to collect risk factor information for all suspect cases of human prion diseases referred to the Unit as part of its core work. In addition, analysis continues to be undertaken on data gathered already, such as the ongoing examination of medical risk factor data obtained directly from primary care records. *Ad hoc* studies that may require extra funding (for example the dental study¹⁵, funded by Department of Health, UK) have been and will continue to be undertaken as necessary. If in the future it is thought necessary, funding will be sought to recruit further controls.

¹³ Ward HJT et al. Risk factors for variant Creutzfeldt-Jakob disease: a case-control study. *Ann Neurol* 2006; 59: 111-120.

¹⁴ Ward HJT et al. Risk factors for sporadic Creutzfeldt-Jakob disease. *Ann Neurol* 2008; 63: 347-354.

¹⁵ A manuscript has been submitted detailing a study to investigate dental treatment as a possible risk factor for vCJD using data acquired directly from the examination by dental professionals of dental records.

LABORATORY ACTIVITIES

Laboratory investigations are part of the internationally-agreed diagnostic criteria for CJD, both during life (CSF protein analysis, PrP genetic studies, brain biopsy neuropathology and prion protein studies) and post-mortem (autopsy neuropathology and prion protein studies). The NCJDRSU has facilities to perform all of these investigations, which aid the timely and accurate diagnosis of all forms of CJD and are essential for surveillance purposes.

4.1 Neuropathology – Statement of Progress and Surveillance Activities

The neuropathology laboratory in the NCJDRSU continues to maintain its diagnostic and research activities, with most of the cases investigated referred from other centres across the UK (see Table 3). The laboratory maintains close links with other neuropathology centres across the UK and overseas with scientific, medical, technical and student visitors over the past year for specialist training purposes. The laboratory has continued to maintain an active research programme both in-house and by collaboration with other research centres in UK, Europe and across the world.

The number of cases of vCJD have declined in the UK, with 2 cases being examined in 2011. In contrast, we received more cases of sporadic CJD in 2011 than in the previous year, and there was also an increase in the number of cases referred in which sporadic CJD was suspected, but not confirmed on the results of the investigations performed in our laboratory. Fewer cases of CJD have been referred from outside the UK, reflecting the decline in suspect cases of vCJD overseas.

In addition to the UK CJD surveillance work, the neuropathology laboratory is involved in vCJD screening studies in three groups of patients identified as being at increased risk of vCJD through exposure to blood products or plasma products (Table 3). The laboratory is also involved as a reference centre for a HPA study on the prevalence of vCJD infection in appendix tissue samples from the UK, and in a series of international collaborative studies in relation to neuropathological diagnosis of CJD and other human prion diseases.

The laboratory and its staff continue to participate in a range of EQA activities related to both technical and diagnostic neuropathology. As before, the laboratory continues to act as a source of information to a wide range of professionals involved in health and safety issues relating to CJD. We are most grateful to all neuropathologists, general pathologists and their technical, secretarial and autopsy room staff for their continuing support of the NCJDRSU. We are also grateful to the relatives of patients with CJD for allowing us to study this group of devastating disorders.

**Table 3 Breakdown of Laboratory Activities:
Period 1st January 2010– 31st December 2011**

	CURRENT YEAR	PREVIOUS YEAR
REFERRED CASES (UK)		
Sporadic CJD	36	29
Genetic CJD	2	1
Variant CJD	2	2
Iatrogenic CJD (GHT)	2	1
Gerstmann-Straussler-Scheinker Syndrome	0	1
Fatal Familial Insomnia	0	0
No evidence of CJD (no alternative pathological diagnosis)	23	11
Alzheimer's disease	1	1
Dementia with Lewy Bodies	3	2
Motor neurone disease	0	2
Other forms of brain disease†	6	10
REFERRED CASES (EU)		
Sporadic CJD	2	3
Genetic CJD	0	0
Variant CJD	0	0
Gerstmann-Straussler-Scheinker Syndrome	0	0
Other forms of brain disease	0	1
UK PRION SCREENING STUDIES		
Haemophilia cases - UKHCDO	1	2
Primary immunodeficiency cases – PIDSUK	2	6
Enhanced Surveillance of “at risk” individuals (HPA)	4	1
OTHER REFERRALS AND STUDIES		
European Collaborative Study	5	0
TOTAL NUMBER OF CASES	89	73

Notes

†Other:

Chronic Encephalitis	1
Extra Pontine Myelinolysis	1
Diffuse Large B-cell Lymphoma	1
Hypoxic Brain Damage/Arteriosclerosis	3

Abbreviations:

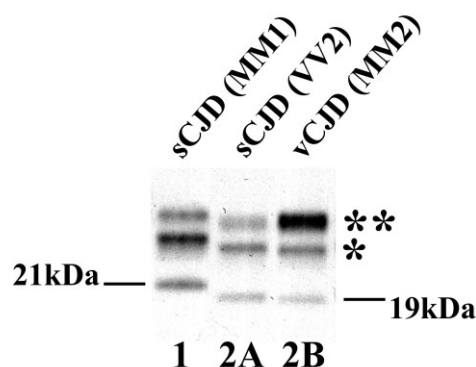
GHT	Growth Hormone Therapy
EU	European Union
ROW	Rest of World

4.2 Prion Protein Laboratory

Prion protein detection and typing

Prion protein typing is carried out as a routine diagnostic test on all suspected cases of CJD from which frozen brain tissue is received by the NCJDRSU. Small quantities of cerebral cortex or cerebellum are homogenised, treated with protease and the size and relative abundance of the three PrP^{res} glycoforms determined by Western blot analysis. The prion protein isotype is classified as type 1 if the nonglycosylated form has a molecular weight of ~21kDa or type 2 if the nonglycosylated form has a molecular weight of ~19kDa. The suffix B is used to denote a PrP^{res} type 2 in which the diglycosylated band predominates. The remaining type 2 cases where the diglycosylated band does not predominate are termed type 2A. The type 2B isotype has previously found to be characteristic of variant CJD. A typical result is shown in Figure 9. Low molecular weight (<10kDa) PrP^{res} fragments have also been recognised to characterise certain cases of Gerstmann-Straussler-Scheinker (GSS) disease, and the more recently described Variably Protease Sensitive Prionopathy (VPSPr). Although one PrP^{res} type usually predominates, mixtures of types (1, 2 and/or the <10kDa PrP^{res}) are found in some cases.

Figure 9: PrP^{res} types in sporadic and variant CJD



Western blot analysis of protease-resistant prion protein (PrP^{res}) in two cases of sporadic CJD (sCJD) of the MM1 and VV2 subtypes and in a case of variant CJD (vCJD (MM2)). The size of the nonglycosylated (bottom band) is either 21kDa (termed type 1) or 19kDa (termed type 2). Diglycosylated PrP^{res} (***) predominates in the vCJD and the pattern is termed type 2B to distinguish it from type 2 cases in which the monoglycosylated form (*) predominates (type 2A).

In cases from which only peripheral tissues are available (such as those in which diagnostic tonsil biopsy is performed), or in cases in which the patient is thought to have been at risk of developing CJD due to potential iatrogenic exposure and is enrolled in a UK prion screening study, a modified Western blot procedure is used which employs centrifugal concentration or sodium phosphotungstic acid precipitation to enrich for PrP^{res} and increase the sensitivity of the test.

UK Referrals

A total of 50 UK cases with frozen tissue were received and analysed in 2011, representing a 39% increase in the number of cases with frozen tissue referred to the NCJDRSU for analysis compared with the previous year. The results of the analysis were as follows:

Table 4 Breakdown of cases analysed in 2011

Diagnosis	Type	PrP ^{res} +ve CNS
CJD (n=36)	Sporadic	30
	Variant	2 ¹
	Iatrogenic	2
	Genetic	2
Alternative final diagnosis or not determined (n=14)		0/14 ²⁻⁵

¹ brain tissue in one case was received having been fixed prior to freezing and was therefore unsuitable for further biochemical analysis

² includes one growth hormone recipient

³ includes one brain biopsy

⁴ includes four enhanced surveillance at risk individuals (HPA)

⁵ includes one haemophilic patient from the UKHCDO Study

Further sub-classification by PrP^{res} type and *PRNP* genotype yields the following results:

Table 5 PrP^{res} type / *PRNP* genotype breakdown of CJD cases analysed in 2011

Diagnosis	<i>PRNP</i> genotype	Type 1	Type 2A	Type 1+2	Type1 + <10 kDA	Type 1+2 + <10kDA	Type 2B	Total
Sporadic CJD	M/M	18 ¹	3	3		1		25
	M/V	3						3
	V/V		2					2
Variant CJD	M/M						1	1
Iatrogenic CJD	M/V			1 ²	1 ²			2
Genetic CJD	E211Q-MM	1						1
	7X1NS-MM	1						1

¹ includes one case of the panencephalopathic type

² growth hormone recipient

Non-UK referrals

Western blot analysis was performed on frozen tissue from five non-UK cases. One was from Sweden and was found to be a case of sporadic CJD of the VV2 subtype. The other four were cases of fatal familial insomnia and thalamic degeneration from Austria received as part of a European collaborative study.

4.3 Brain banking activities

The bank of fixed and frozen tissues in the Surveillance Unit was used extensively in 2011 for diagnostic and collaborative research purposes with colleagues in the UK and overseas. Funding from MRC was renewed in 2009 to support the activities of the Bank for a further 2 years. The Bank is a member of the MRC Network of UK Brain Banks, under the Directorship of Professor JW Ironside. This network will strengthen banking activities and ensure uniform high standards of operation. The Bank has a website, on which further details are available including instructions on how to request tissue samples for research (<http://www.edinburghbrainbanks.ed.ac.uk/CJD/indexcjd.htm>). The activities of the Bank comply with current guidelines from the Royal College of Pathologists, the Human Tissue (Scotland) Act 2006 and the Human Tissue Act 2004.

4.4 Molecular Genetics

Genetic CJD

One hundred and twenty-four cases of genetic CJD (excluding cases of GSS) have been identified since 1970 by the NCJDRSU (these data are incomplete as formal investigation of genetic CJD in the UK is undertaken by the National Prion Clinic in London). Of the 124 cases, 109 were resident in England, 9 were resident in Wales, 3 were resident in Northern Ireland and 3 were resident in Scotland. Twenty cases were still alive as at 31st December 2011. Sixty of the cases had insertions in the coding region of the PrP gene, 34 carried the mutation at codon E200K, 12 at codon D178N, 3 at codon V210I, one at codon D167G, 2 at codon V163STOP, one at codon G54S and one at codon E211Q. The remaining 10 were identified as familial on the basis of relatives known to have had CJD. The mean age at death was 55 years (range 31-77 years).

PRNP Codon 129 distribution in sporadic CJD

The distribution of PRNP codon 129 genotypes in sporadic CJD has been analysed since the inception of the Unit in 1990. The overall distribution of PRNP codon 129 genotypes in sporadic CJD is 63% MM, 19% MV, 18% VV (see Table 6). There appears to be evidence ($p=0.005$) of a change in the PRNP codon 129 distribution in sporadic CJD between the periods 1990-1995 and 1996-2010. The explanation for this remains unclear and is being investigated further. It should be noted that not all cases are genotyped (data available on 62%) and, therefore, changes in PRNP codon 129 distribution may reflect changes in the way in which cases are selected for analysis.

Table 6 PRNP codon 129 genotypes of cases of sporadic CJD in the UK, 1990-2011

Deaths from sporadic CJD	MM(%)	MV(%)	VV(%)
Deaths from 1 January 1990 – 31 December 1995	101 (75)	16 (12)	17 (13)
Deaths from 1 January 1996 – 31 December 2011	398 (61)	134 (20)	127 (19)
Total	499 (63)	150 (19)	144 (18)
Genotype distribution for the normal population	(39)	(50)	(11)
Pooling data from five studies			

PRNP codon 129 distribution in vCJD

All clinical cases for whom genetic data are available ($n=159$, 90%) were methionine homozygotes at PRNP codon 129 of the PrP gene.

The genetic laboratory undertakes genetic analysis on a national and international basis.

4.5 CSF 14-3-3 and other brain specific proteins

Introduction

The laboratory received 315 cerebrospinal fluid (CSF) samples from January 2011 – December 2011, from patients residing in the United Kingdom (UK) and from patients in non-UK countries. One CSF sample was blood-stained and as such unsuitable for analysis. The origin and numbers of these samples are given in Table 7.

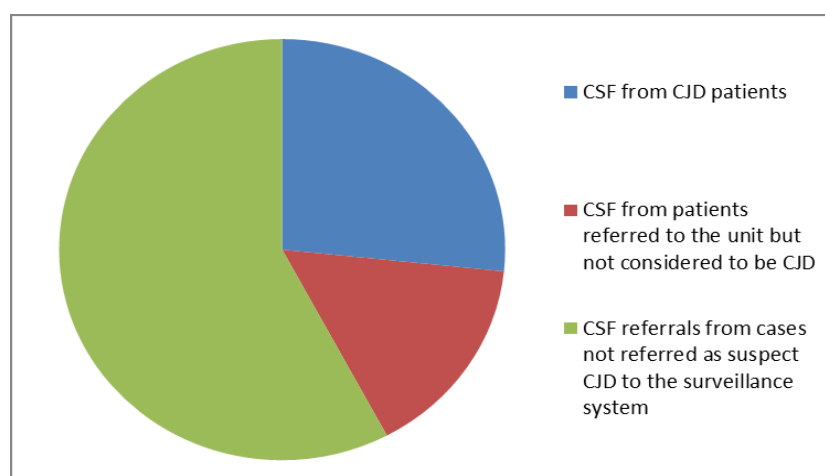
Table 7 Origin of CSF samples sent to the NCJDRSU for CSF 14-3-3 analysis from January 2011 – December 2011

<i>Origin of CSF samples</i>	<i>Total number CSF samples (%)</i>
CSF from UK patients	270* (86%)
CSF from non-UK countries	45 (14%)
Total number	315 (100%)

* One CSF sample was blood-stained and as such unsuitable for analysis.

Of the 269 analysable CSF samples received from patients within the United Kingdom, 102 samples were from patients who were finally referred to the NCJDRSU as a suspected case of CJD. Of these, 77 patients were finally diagnosed as having definite, probable or possible CJD (Table 8). The remaining 25 patients were diagnosed as not having CJD. The remaining 167 CSF samples were sent to the NCJDRSU for the analysis of CSF 14-3-3 and S-100b but in none of these cases did the requesting clinician refer the patient to the NCJDRSU as a suspected case of CJD. Many requests for CSF 14-3-3 and S-100b analysis are on patients where the clinical suspicion of CJD is low and the request is made to exclude the diagnosis. However, if a CSF 14-3-3 request is made for a patient where CJD is reasonably suspected the referring clinician is encouraged to formally refer the patient to the NCJDRSU.

Figure 10 Source of CSF samples received from the UK for CSF 14-3-3 analysis



The final diagnosis of the 77 patients referred to the NCJDRSU who were diagnosed with some form of CJD is given in Table 8.

Table 8 The CSF 14-3-3 results in patients diagnosed with CJD or prion disease

<i>Diagnosis</i>	<i>Number of cases</i>	<i>Number of positive CSF 14-3-3</i>
Definite sporadic CJD	39	36
Probable sporadic CJD	30	28
Possible sporadic CJD	1	0
Definite variant CJD	1	0
Definite Genetic CJD	2 (E200K mutations)	2
	1 (V210I mutation)	1
Probable Genetic CJD	1 (E200K mutation)	1
	1 (insert mutation)	0
Probable Iatrogenic CJD*	1	0

* Secondary to administration of human cadaveric growth hormone.

Of the patients with probable sCJD, 15 died without undergoing a post-mortem, 8 have died and neuropathological confirmation of sCJD is awaited. Of the remaining 7 patients, 5 have died and it is unclear whether a post-mortem has been performed and 2 patients are still alive. Of the 15 patients who died without post-mortem examination, 12 had EEG traces that were considered typical for sCJD and/or MRI appearances considered typical for sCJD whilst 3 had EEG traces or MRI appearances that were not considered typical. Therefore 3 of the 15 patients with probable sCJD who died without neuropathological confirmation have been classified as probable on the basis of the 14-3-3 result without independent EEG or MRI support.

Of the 167 CSF samples sent from patients who were not formally referred to the NCJDRSU, 2 were positive for CSF 14-3-3. One patient was diagnosed as having Wernicke's encephalopathy and the other patient had intra-cerebral haemorrhages secondary to head injury.

NATIONAL CJD CARE TEAM

Established by the Department of Health, the National CJD Care Team is based within the National CJD Research & Surveillance Unit and was formed in order to optimise the care of patients suffering from all forms of CJD. The national care coordinator post was established in February 2000 and in September 2001 the National CJD Care Team was formed. The present team consists of 2 care coordinators who are senior nurses with secretarial and clinical neurological support from within the Unit.

When a referral is made to the NCJDRSU the research registrar will take that referral and, if appropriate, ask the Care Co-ordinator to attend that first visit to meet with the family. Once a diagnosis of probable or possible CJD is made, if the co-ordinator has not already met the family, the coordinator makes direct contact with the family and offers the opportunity to meet and to assist with care planning. Referrals are also made to the Care Team from Leah Davidson (who coordinates the care of iatrogenic CJD cases) and the National Prion Clinic in London. Once contact is made, the coordinator can meet on a regular basis with the patient, family and professionals involved in care. This will depend on need and will provide support and assist with coordination of local health and social care professionals. The coordinators provide valuable expertise in nursing patients with CJD and can anticipate and prevent some problems that may arise by offering skilled advice and education. The care team enables local teams to provide high standards of care and continues to be involved as long as needed. This does not always involve a visit in person. Contact by telephone, text or email is just as important and may be preferred by families and other professionals involved. Post bereavement support is offered to the family after the patient dies and assistance is given in accessing more specialised counselling.

The National CJD Care Team works in close liaison with the Department of Health and provides access to the CJD Care Package. This is a sum of money from The Department of Health which provides funding to assist local authorities with the care of patients suffering from all forms of CJD. The Care Fund is available to supplement local care and equipment provision. Health and Social Services will provide the basic elements of the individual patient's care package. The Care package involves an individual assessment of need and will vary accordingly. It is essential that care packages are flexible and can change quickly to meet the rapidly changing needs of the patient. The aim is to provide a package of care that will meet the needs both for the patient and their family in a timely manner.

In addition to collaborations with national organisations in the United Kingdom, the Care Team liaises closely with international organisations, including the Australian and American CJD Support Groups and is an Official Friend of the CJD International Support Alliance.

The National Care Coordinators undertook 251 patient visits, case conferences and teaching sessions during 2011 (Table 10). Care Fund payments from 1st January to 31st December 2011 are shown in Table 11.

**Table 10 Patient Visits, Case Conferences and Teaching Sessions
1st January to 31st December 2011**

Month	Patient Visits/Case Conferences/Teaching Sessions
January	23
February	17
March	33
April	22
May	21
June	14
July	17
August	21
September	29
October	16
November	24
December	14

**Table 11 Care Fund Payments
1st January to 31st December 2011**

Description	£
Adaptations	22,616.92
Alternative Therapy	400.00
Counselling	4,900.00
Equipment	6,483.86
Nursing	121,604.40
Other	1,795.00
Physiotherapy	1,632.00
Social Care	3,920.00
Transport	36,270.40
TOTAL	199,622.58

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