1. Background

Individuals and groups were formerly identified as at increased risk of Creutzfeldt - Jakob Disease (CJD) by the CJD Incidents Panel (The Panel) on the basis of risk assessments and mathematical modelling of the different exposure risks. The Panel was dissolved on the 31st March 2013; as a result new guidance was introduced to enable local teams to manage their own surgical incidents. New notifications following a surgical incident would be made at a local level and reported to the Public Health England (PHE) CJD Team.

Individuals at increased risk of CJD as a consequence of their medical care are informed of their exposure and asked to follow public health precautions to avoid transmitting the infection to others. They are also followed-up to help determine the risks of CJD transmission to patients through different routes and to ascertain whether any people who may have been exposed to increased CJD risks go on to develop CJD.

Public Health follow-up activities include clinical monitoring, General Practitioner (GP) updates, and carrying out post mortem investigations to determine whether asymptomatic individuals in these groups have been infected with the CJD agent. Some individuals also provide blood or tissue specimens for research purposes. A number of different organisations are involved in these activities: Public Health England (PHE) formerly the Health Protection Agency (HPA), Health Protection Scotland (HPS), Institute of Child Health (ICH), NHS Blood and Transplant (NHSBT), National CJD Research and Surveillance Unit (NCJDRSU), National Prion Clinic (NPC), and UK Haemophilia Centre Doctors' Organisation (UKHCDO).

2. Identification and notification of patients at increased risk of CJD

All 'at risk' patients are first identified through one of the following routes:

- Incident management (blood recipients, blood donors, 'other' blood recipients, plasma product recipients (non-bleeding disorder patients) and surgical 'at risk')
- Pre-surgical assessment (highly transfused, dura mater graft recipients)
- Large-scale notifications (human growth hormone recipients, human gonadotrophin hormone recipients, and bleeding disorder patients who received UK-sourced plasma products)

The Panel advised that all living patients at increased risk of CJD should be notified. In a small number of cases, local teams have decided that if serious emotional harm to the patient is considered likely to be caused by the notification, the decision not to notify the patient should be made on these grounds. In some cases, local teams may be unable to locate a patient and therefore are unable to confirm that the patient has been notified. Therefore, a small number of patients at an increased risk will be recorded as 'alive but not notified'. These patients are not managed as at increased risk for the purposes of risk management and enhanced surveillance.

In addition, patients may be classified as 'notified by proxy', whereby relatives/carers are informed instead of the patient because the patient is thought unable to understand the information; for example, children and patients with dementia. These patients should be managed as 'at risk'.

Patients identified as being at increased risk of CJD may have died before they were notified. In this case they will be recorded as having 'died before notification'.

3. Data collection

The PHE CJD Section collects data on individuals identified as at increased risk of CJD, and who have been informed of this. These individuals are followed up through public health monitoring and research activities by different organisations (Table 1).

The PHE CJD Section currently holds data on the following groups of 'at risk' patients:

1. Recipients of blood components from vCJD cases
2. Blood donors to vCJD cases
3. Other recipients of blood components from blood donors to vCJD cases
4. Recipients of plasma products linked to vCJD cases (non-bleeding disorder patients)
5. Surgical contacts of CJD cases
6. Highly transfused recipients

Data on the following risk groups are not held by PHE, but are held by other organisations:

1. Bleeding disorder patients (UKHCDO)
2. Human derived growth hormone recipients (ICH)
3. Patients who could have received a dura mater graft[1] (data not currently collected)
4. Family risk of genetic prion disease (NPC)[2].

The data from the UKHCDO are likely to be an underestimate of the true number of 'at risk' patients with bleeding disorders who received UK-sourced clotting factors, as there was incomplete reporting of identified 'at risk' patients by haemophilia centres to the UKHCDO database. Notified 'at risk' patients are given the option of removing their details from the UKHCDO database, and are then removed from the 'at risk' totals.

The data on 'at risk' patients who received human-derived human growth hormone held by the ICH is a slight underestimate of the total as a small number of these patients are not included in the ICH follow-up.

---

[1] Some dura mater grafts have transmitted CJD. Confirmation of whether a patient has been treated with a dura mater graft is difficult. The Advisory Committee on Dangerous Pathogens (ACDP) Transmissible Spongiform Encephalopathy (TSE) Risk Management Subgroup has defined which patients should be considered to have an increased CJD risk on the basis of their surgical history.

[2] This group may receive clinical care from the NPC and are eligible to join the National Prion Monitoring Cohort (NPMC). Follow up activities relating to this group are not included in this paper.

Table 1: Patient follow-up – organisations and activities

Risk Category	Organisation	Activities						
		Flag deaths	Cross check cases	Genotype	Post mortem consent	Blood samples	Tissue samples	GP changes
Recipients of blood components from donors	NCJDRSU/NHSBT	TMER	TMER					
	PHE[a]	PH	PH	ES	ES	ES	ES	PH
	NPC			NPMC/CC	NPMC/CC	NPMC/CC	NPMC/CC	
Donors of blood components to people who develop vCJD	NCJDRSU/NHSBT	TMER	TMER					
	PHE[a]	PH	PH	ES	ES	ES	ES	PH
	NPC[b]			NPMC	NPMC	NPMC	NPMC	
Other recipients who received blood from donors to vCJD cases	PHE[a]	PH	PH	ES[c]	ES		ES	PH
Plasma recipients (non-bleeding disorder patients)	PHE[a]	PH	PH	ES[c]	ES		ES	PH
Surgical contacts of CJD cases	PHE[a]	PH	PH	ES[c]	ES		ES	PH
Highly Transfused	PHE[a]	PH	PH	ES[c]	ES		ES	PH
Bleeding disorders who received UK sourced clotting factors	UKHCDO	NHD	NHD	TBVS[d]	TBVS[d]		TBVS[d]	
Inherited Prion Disease	NPC			NPMC/CC	NPMC/CC	NPMC/CC		
Human derived growth hormone recipients	ICH	CS	CS					
Dura mater graft[e]								

[a] PHE activities are only conducted on those 'at risk' patients alive at the time of notification.

[b] The NPMC protocol was amended to include those donors to vCJD cases, where a small number of people donated blood to each case.

[c] The study protocol specifies that these patients would not be asked for additional invasive samples. Genotyping could be carried out on any spare tissues/blood samples.

[d] Joint study between UKHCDO and NCJDRSU.

[e] Data not currently collected.

Key

CS -Cohort study
CC- Clinical Care
ES-Enhanced Surveillance
ICH-Institute Child Health
NCJDRSU- National CJD Research and Surveillance Unit
NHD-National Haemophilia Database
NHSBT- NHS Blood and Transplant
NPC- National Prion Clinic
NPMC-National Prion Monitoring Cohort
PH-Public Health activities
PHE-Public Health England
TBVS-Tissue based vCJD Surveillance
TMER-Transfusion Medicine Epidemiological Review
UKHCDO- UK Haemophilia Centres Doctor's Organisation

4. 'At risk' patient data

Data are compiled from the different organisations every 6 months. Here, we present data correct as at 30th June 2013. Table 2, 3 and 4 presents a summary of all 'at risk' groups on which data are collected.

Key points are:

- The overall numbers of people identified as at risk have only slightly changed since the last biannual report. Of note are two further cases in recipients of human derived growth hormone.

- One surgical incident, which may result in further surgical notifications, is being considered by the health board and the NCJDRSU. The surgical contacts from this incident will not be not included in these figures until a final decision is made.

- There is currently a denotification exercise of recipients of UK sourced plasma products who received these products only in the 1980s. The exercise is expected to be completed by late autumn 2013. The at risk plasma recipient numbers in this report still include those who will be denotified during this exercise. It is anticipated this will affect around 600 people and this will be reflected in the next biannual report.

- Since January 2013 there have been seven deaths in the enhanced surveillance cohort. One was in a Scottish patient who was in the "other blood" category. The remaining six deaths were in residents of England. Four were in the surgical at risk group and two were blood recipients.

- No post mortems were conducted among the seven individuals who died this year. PHE has received cause of death information from the Health and Social Care Information Service and the NCJDRSU are in the process of undertaking medical notes review of the cases where possible.

- Surgical incidents were formerly notified through the CJD Incidents Panel. The Panel was dissolved on the 31st March 2013 and responsibility for managing incidents was transferred to local teams. Local teams are also asked to make the CJD Unit at PHE aware of surgical incidents and the details of any subsequently notified persons in order to continue national surveillance and monitoring. An audit is planned to estimate if notifications fall following the dissolution of the CJDIP.

- Of those identified at risk, 5078 (83%) are still alive. Of those still alive 80% are aged between 20 and 59. 15 blood recipients, who are considered at higher risk of vCJD, have donated blood samples to the enhanced surveillance (research) study and there are currently five blood recipients who have provided in life consent to post mortem.

Table 2: Summary of groups identified as at increased risk of CJD on which data are collected (Data correct as at 30th June 2013)

'At risk' Group	Identified as 'at risk'	Number notified as being 'at risk'		Cases	Asymptomatic infections [b]
		All	Alive		
Recipients of blood from vCJD cases	67	27	15	3	1
Blood donors to vCJD cases	112	107	104	0	0
Other recipients of blood donors to vCJD cases	34	32[c]	20[c]	0	0
Plasma product recipients (all except one are non-bleeding disorders)	11	10	4	0	0
Surgical contacts of all CJD cases	154	129 [d]	115[e]	0	0
Highly transfused patients (recipients of blood from over 80 donors identified at pre-surgical assessment)	11	10	7	0	0
Total for 'at risk' groups where PHE holds data	**389**	**315[f]**	**265[f]**	**3**	**1**
Patients with bleeding disorders who received UK sourced plasma products [a]	3,862	National information incomplete	National information incomplete	0	1
Recipients of human derived growth hormone [a]	1,883	1,883	1,505	73	0
Total for all 'at risk' groups [a]	**6,134**	**>2,198**	**>1,770**	**76**	**2**

[a] These are minimum figures. Central reporting for bleeding disorder patients is incomplete, and seven patients have opted out of the central UKHCDO database. A small number of 'at risk' growth hormone recipients are not included in the Institute of Child Health study. Not all of 'at risk' growth hormone recipients have been notified. There is no central record of who has been informed.

[b] An asymptomatic infection is when an individual does not exhibit any of the signs and symptoms of CJD in life but abnormal prion protein indicative of CJD infection has been found in tissue obtained from them. In these cases the abnormal prion protein was identified during post mortem after the individuals had died of other causes.

[c] One patient was notified by proxy.

[d] Four of these were notified by proxy.

[e] Two of these were notified by proxy.

[f] Includes patients who were notified by proxy.

Table 3: Current status of 'at risk' groups (Data correct as at 30th June 2013)

Summary of 'at risk' groups		Recipients	Donors	Other Blood	Highly Transfused	Plasma Bleeding	Plasma non bleeding	Surgical	Growth Hormone	Total
Current status of 'at risk' patients	Alive	15	107	22	7	3301	4	117	1505	5078
	Dead	52	5	12	4	561	7	37	378	1056
	Total	67	112	34	11	3862	11	154	1883	6134
'At risk' patient notifications	Notified	27	107	32	10	National Information Incomplete	10	125	1883	2194
	Alive and notified	15	104	20	7		4	113	1505	1768
Genotype	MM	11	-	-	-	5	-	-	-	16
	MV	7	-	-	-	4	-	-	-	11
	VV	-	-	-	-	1	-	-	-	1
	Not known	49	112	34	11	3852	11	154	1883	6106
Sex [a]	Male	19	53	16	4	3283	8	75	987	4445
	Female	20	58	18	7	579	2	79	518	1281
	Not known	28	1	0	0	0	1	0	0	30
Current age band of living 'at risk' patients	0-19	0	0	1	0	94	0	2	0	97
	20-39	1	8	5	1	1233	2	16	268	1534
	40-59	6	53	3	3	1253	0	30	1184	2532
	60-79	5	42	6	3	607	1	52	53	769
	80+	3	4	7	0	112	0	17	0	143
	Not known	0	0	0	0	2	1	0	0	3
Number of surgical incidents reported involving 'at risk' patients		23	0	4	2	80	0	6	3	118

[a] Sex is all identified at risk (alive and dead) with the exception of recipients of human derived growth hormone where the sex of the 378 people who have died is not included.

Table 4: Potential tissues for investigation from 'at risk' patient groups

Group	Living patients who have given in-life post mortem consent	Post mortems conducted	Blood samples	Spare tissue samples (not from post-mortem)
Recipients	5[a]	8[b]	15[c]	7[d]
Donors	0	2[e]	0	0
Other recipients	0	2[f]	0	0
Plasma product recipients	0	1[g]	0	0
Surgical contacts	0	4[h]	0	0
Highly transfused	0	0	0	0
Bleeding disorders	N/A	16	0	11 (9)
Growth hormone recipients	0	0	0	0

[a] These are patients: 0301, 0314, 0504, 0507, 0509.
[b] These are patients: 0302 (NPC), 0317 (NPC), 0502 (NPC), 0303 (NPC), 0307 (NPC), 0318 (NCJDRSU), 0321 (NCJDRSU), 0515 (NPC).
[c] These are patients: 0301, 0302, 0304, 0306, 0308, 0310, 0314, 0317, 0502, 0504, 0311, 0312, 0507, 0509, 0515.
[d] These are patients: 0302 (dead), 0304, 0306, 0314, 0317 (dead), 0502 (dead), 0507.
[e] These are patients: 290 (coroner's PM), 327 (informed from Medical Notes Review report 20/01/12).
[f] These are patients: 420/S34 (informed from National Health Service Central Register (NHSCR)), 420/S27 (informed from NHSCR).
[g] This is patient 2340 (informed from Medical Notes Review).
[h] These are patients: 143.11 (by The James Cook University Hospital Pathology, Dr David Scoones), 143.26, 513.02 (informed from Medical Notes Review, don't know who did it), 530.19.

5. Contributors

We would like to thank the following organisations and individuals who have contributed data for this report:

- HPS: Oliver Blatchford, Caroline Creasey and Annette Rankin
- ICH: Peter Adlard and Leah Davidson
- NCJDRSU: James Ironside, Linda McCardle and Jan Mackenzie
- NPC: Simon Mead
- NHSBT: Pat Hewitt
- UKHCDO: Lynne Dewhurst, Charles Hay, Mike Makris, and Ben Palmer