rhage are at a threefold to fivefold increased risk of having a subarachnoid haemorrhage.

Contributors: DG, KC, and HTS initiated the study. DG was principal investigator and study coordinator, contributed to the design of the study, the collection and the analysis of the data, and wrote the initial draft; he will act as guarantor for the paper. MV contributed to the design of the study and did the statistical analyses. IT contributed to the design of the validation part of the study, which he also conducted. KC, EC, JO, and HTS participated in the design and discussed core ideas. All authors contributed to the interpretation of the data and the writing of the paper.

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Extent of misclassification of death from Creutzfeldt-Jakob disease in England 1979-96: retrospective examination of clinical records

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Abstract

Objective To investigate the extent to which deaths from Creutzfeldt-Jakob disease were misclassified during 1979-96.

Design Structured review of clinical records based on predetermined criteria to determine whether death could have been due to sporadic or variant Creutzfeldt-Jakob disease.

Setting 100 health authorities and 275 NHS trusts in England.

Subjects 1485 people who died aged 15-44 years from selected neurological disorders in England during 1979-96.

Main outcome measure Cause of death.

Results The clinical records of 705 (48%) subjects were successfully traced. Tracing of clinical records was highest in subjects who died during 1990-6. There was sufficient information in the records of 640 (91%) of the 705 subjects to exclude Creutzfeldt-Jakob disease as a cause of death. In 61 (9%) subjects, there was insufficient information to reach any conclusion about the validity of the cause of death recorded on the death certificate. The clinical records of four subjects were examined further by the National Creutzfeldt-Jakob Disease Surveillance Unit; none was thought to have died from Creutzfeldt-Jakob disease.

Conclusions No new cases of sporadic or variant Creutzfeldt-Jakob disease were detected in a sample of deaths most likely to have included misclassified cases. This suggests that the surveillance system is unlikely to have missed a significant number of cases among people aged 15-44 years. Hence, any rapid increase in the number of cases of variant Creutzfeldt-Jakob disease in this age group is likely to be real not artefactual.

Introduction

A national surveillance programme for Creutzfeldt-Jakob disease was started in the United Kingdom in May 1990. The primary aim of the programme was to detect any change in the epidemiology of the disease that might be attributable to bovine spongiform encephalopathy.[1] In 1996, Will and colleagues reported 10 cases of a variant of Creutzfeldt-Jakob disease that was possibly associated with bovine spongiform encephalopathy.[2] Speculation that bovine spongiform encephalopathy and Creutzfeldt-Jakob

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disease might be linked led to fears that the United Kingdom could face a substantial epidemic of variant Creutzfeldt-Jakob disease because of the large number of people who were exposed to meat infected with bovine spongiform encephalopathy before the bovine offal ban was introduced in 1989.[3–6]

Table 1 Demographic and clinical details of study subjects

	No (%) of records obtained (n=705)	No (%) of records not obtained (n=780)	Total (n=1485)
Sex:			
Male	389 (55.2)	434 (55.6)	823 (55.4)
Female	316 (44.8)	346 (44.4)	662 (44.6)
Age group (years):			
15-19	93 (13.2)	129 (16.5)	222 (14.9)
20-24	92 (13.0)	105 (13.5)	197 (13.3)
25-29	113 (16.0)	101 (12.9)	214 (14.4)
30-34	114 (16.2)	118 (15.1)	232 (15.6)
35-39	122 (17.3)	133 (17.1)	255 (17.2)
40-44	171 (24.3)	194 (24.9)	365 (24.6)
Disease group:			
Cerebral degenerations usually manifest in childhood	58 (8.2)	62 (7.9)	120 (8.1)
Encephalitis, myelitis, and encephalomyelitis	140 (19.9)	102 (13.1)	242 (16.3)
Other cerebral degenerations	128 (18.2)	177 (22.7)	305 (20.5)
Other extrapyramidal disease and abnormal movement disorder	160 (22.7)	218 (27.9)	378 (25.5)
Other non-organic psychoses	8 (1.1)	14 (1.8)	22 (1.5)
Senile and presenile organic psychotic conditions	15 (2.1)	17 (2.2)	32 (2.2)
Slow virus infection of central nervous system	82 (11.6)	50 (6.4)	132 (8.9)
Spinocerebellar disease	114 (16.2)	140 (17.9)	254 (17.1)
Period of death:			
1979-84	77 (10.9)	337 (43.2)	414 (27.9)
1985-9	123 (17.4)	292 (37.4)	415 (27.9)
1990-6	505 (71.6)	151 (19.4)	656 (44.2)

Table 2 Classification of cause of death according to demographic and clinical details of subjects

	No (%) in each classification		
	CJD excluded (n=640)	Insufficient information (n=61)	Referred to surveillance unit* (n=4)
Sex:			
Female	357 (55.8)	30 (49.2)	2
Male	283 (44.2)	31 (50.8)	2
Age group (years):			
15-19	90 (14.1)	3 (4.9)	
20-24	87 (13.6)	5 (8.2)	
25-29	105 (16.4)	8 (13.1)	
30-34	103 (16.1)	9 (14.8)	2
35-39	111 (17.3)	11 (18.0)	
40-44	144 (22.5)	25 (41.0)	2
Disease group:			
Cerebral degenerations usually manifest in childhood	56 (8.8)	2 (3.3)	
Encephalitis, myelitis, and encephalomyelitis	117 (18.3)	23 (37.7)	
Other cerebral degenerations	107 (16.7)	18 (29.5)	3
Other extrapyramidal disease and abnormal movement disorder	156 (24.4)	4 (6.6)	
Other non-organic psychoses	4 (0.6)	3 (4.9)	1
Senile and presenile organic psychotic conditions	12 (1.9)	3 (4.9)	
Slow virus infection of central nervous system	79 (12.3)	3 (4.9)	
Spinocerebellar disease	109 (17.0)	5 (8.2)	
Period of death:			
1979-84	68 (10.6)	8 (13.1)	1
1985-9	109 (17.0)	14 (23.0)	
1990-6	463 (72.3)	39 (63.9)	3

CJD=Creutzfeldt-Jakob disease. *Referred to CJD Surveillance Unit for further assessment.

After the first report of variant Creutzfeldt-Jakob disease in 1996, the number of deaths remained fairly constant until early 1999, when Will and colleagues reported that there had been an increase in deaths in the last quarter of 1998.[7] However, without knowing the extent of past underascertainment of Creutzfeldt-Jakob disease, it is not possible to say whether any increase in deaths from variant Creutzfeldt-Jakob disease is due to a real increase in incidence or to better ascertainment.[8] We investigated whether deaths from Creutzfeldt-Jakob disease were misclassified during 1979-96 in people who died aged 15-44 years from selected neurological disorders with which Creutzfeldt-Jakob disease could have been confused.

Subjects and methods

We identified all deaths from selected neurological disorders in people aged 15-44 years in England during 1979-96. The list of conditions was based on a study published by Will and Matthews in 1984 and was expanded after discussion with specialists at the National Creutzfeldt-Jakob Disease Surveillance Unit.[8 9] The data extracted on each subject included name, date and place of death, and last known address. Information on place of death and last known address was used to trace hospital and general practice records.

A structured data collection form was used to extract information from clinical records on clinical history, risk factors for Creutzfeldt-Jakob disease, findings on examination, results of investigations, and postmortem findings. AM and RK reviewed the information extracted on each subject. Deaths that clearly were not from Creutzfeldt-Jakob disease were not examined further. The clinical details of remaining cases were examined further by AM and RK using a clinical profile agreed with the Creutzfeldt-Jakob disease surveillance unit. After assessment, cases were placed into three categories: cause of death not Creutzfeldt-Jakob disease; insufficient information to determine cause of death; and subject referred to surveillance unit for further assessment.

Ethical approval was obtained from the South Thames multicentre research ethics committee and from 149 local ethics committees.

Results

The selected diagnoses are relatively rare causes of death and resulted in 1537 deaths during 1979-96. Fifty two subjects were excluded because they had been investigated previously by the surveillance unit. A further 12 subjects were excluded because four health authorities and seven NHS trusts refused to take part in the study. Of the remaining 1473 subjects, 768 (52%) had had their records destroyed, leaving the records of 705 (48%) for further examination. The percentage of records obtained was low for 1979-89 (range 13-33%) because many records had been destroyed. From 1990 onwards, the percentage of records obtained increased from 55% in 1990 to 88% in 1996. There were some diagnostic differences in the certified cause of death between

subjects for whom clinical notes were and were not obtained (table 1).

In 640 (91%) of the 705 subjects whose records were examined, either the underlying cause of death on the death certificate was consistent with the clinical information in the medical records or there was sufficient information to exclude Creutzfeldt-Jakob disease as a cause of death. In 61 (9%) there was insufficient information in the clinical records to determine the underlying cause of death (table 2). The records of four subjects were examined further by the surveillance unit. No case of sporadic or variant disease was identified among this group.

Discussion

We did not identify any previously undetected cases of Creutzfeldt-Jakob disease in people aged 15-44 years who died during 1979-96 from selected neurological disorders with which Creutzfeldt-Jakob disease might have been confused. With any surveillance system an important concern is that not all cases may be identified. Furthermore, the implementation of a surveillance system may artefactually increase the incidence of a disease.[10] Our findings suggest that the national surveillance system for Creutzfeldt-Jakob disease that started in 1990 and the earlier surveillance for possible cases are unlikely to have missed a significant number of cases among people aged 15-44 years. Underascertainment of variant Creutzfeldt-Jakob disease in this age group is therefore unlikely during the early years of the bovine spongiform encephalopathy epidemic. Consequently, any rapid increase in the number of cases of variant Creutzfeldt-Jakob disease among people aged 15-44 years is likely to be real rather than an artefact due to better awareness and detection.

The main limitation of this study is that medical records were available for only 48% of subjects. However, the study still provides important information as from 1990 onwards, the period during which cases of variant Creutzfeldt-Jakob disease were most likely to occur, the percentage of case notes retrieved was high. There is also no reason to assume that people who were more likely to have the disease were also more likely to have had their notes destroyed. A second limitation is that in 61 subjects there was insufficient information in the clinical records to draw any firm conclusions about the cause of death.

A third limitation is that only patients aged 15-44 were included. This age group is suitable for detecting cases of variant Creutzfeldt-Jakob disease but less so for sporadic disease. A definitive diagnosis of Creutzfeldt-Jakob disease also requires histological examination of brain tissue, and the likelihood of a postmortem examination in patients dying from dementia decreases with age.[11] Hence, it is possible that cases of sporadic disease may be missed in elderly people.[12] Finally, any people with Creutzfeldt-Jakob disease who were certified as dying from non-neurological disorders such as bronchopneumonia would not have been included in the sample of deaths investigated.

What is already known on this topic

A major concern of any surveillance system is that not all cases of a disease may be identified

Implementation of a surveillance system may also increase the apparent incidence of a disease, particularly if clinicians are encouraged to refer suspected cases

What this study adds

No previously unsuspected cases of Creutzfeldt-Jakob disease were found in patients aged 15-44 years who died during 1979-96 from neurological disorders with which Creutzfeldt-Jakob disease could be confused

This suggests that the national surveillance system, which started in 1990, is unlikely to have missed a significant number of cases

Any rapid increase in the number of cases of variant Creutzfeldt-Jakob disease among this age group is likely to be real rather than artefactual

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Contributors: AM and MC planned the study with help from staff at the National CJD Surveillance Unit. AM, PL, and LK produced the data collection form with help from RK. PL and LK visited health authorities and NHS trusts, extracted information from clinical records, and carried out the data analysis. AM wrote the paper and received comments from the other authors. AM and MC are the guarantors for the study.

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