

Report:

Deaths involving *Clostridium difficile*: England and Wales, 1999–2004

INTRODUCTION

This is the first report on deaths in England and Wales where *Clostridium difficile* was mentioned as a contributory factor. This report covers the period 1999 to 2004 and includes figures for those years for which ONS has coded all deaths to the tenth revision of the International Classification of Diseases (ICD-10). Since 2001, ONS has routinely coded deaths to ICD-10. Deaths registered in 1999 were coded to both ICD-9 and ICD-10, and are also included in the analysis. As deaths in 2000 were only coded to ICD-9, no figures are presented for that year.

BACKGROUND

This report examines trends in those deaths that involved *C. difficile* as a contributory factor between 1999 and 2004. *C. difficile* is a spore forming bacterium found naturally in the gut of a small proportion (around 3 per cent)¹ of the healthy adult population. *C. difficile* can cause diarrhoea, ranging from a mild disturbance to very severe illness with ulceration and bleeding from the colon (colitis), and perforation of the intestine leading to peritonitis, which can be fatal.² *C. difficile* disease occurs when normal, healthy intestinal bacteria are subdued by the use of antibiotics. This allows *C. difficile* to flourish in the gut and produce a toxin that causes diarrhoea.

Box One explains the terms used in this report.

C. difficile was first described in the 1930s,³ but it was not identified as the cause of pseudomembranous colitis following antibiotic therapy until the late 1970s.⁴⁻⁷ Patients who have been treated with broad spectrum antibiotics (those affecting a wide range of bacteria, including intestinal bacteria) are at the greatest risk of *C. difficile* infection. In addition to antibiotic exposure, the risk of contracting *C. difficile* is also raised for elderly patients, those who have recently had gastrointestinal surgery, those who have a long length of stay in healthcare settings, and those who have a serious underlying illness or a condition that compromises their immune system.^{8,9} Patients are also at risk of developing *C. difficile* disease when there are outbreaks in hospitals. Infection control is also an important risk factor.

A recent Department of Health report addresses actions that should be taken to reduce levels of hospital-acquired infections.¹⁰ A report on *C. difficile* and actions to reduce the chances of outbreaks was released by

the Health Protection Agency (HPA) in February 2003.¹¹ In January 2004, the HPA began to carry out a mandatory reporting scheme for all cases of *C. difficile* in persons 65 years and over.¹² Results from the first year's surveillance (January to December 2004) were published by the Department of Health.¹³

The number of deaths due to *C. difficile* is difficult to estimate. Trends in mortality are normally monitored using the underlying cause of death (the disease which initiated the train of events leading directly to death). *C. difficile*, and other hospital-acquired infections such as MRSA, are often not the underlying cause of death. Those who die with *C. difficile* are usually patients who were already very ill and it may be their existing illness, rather than *C. difficile*, which is designated as the underlying cause of death. There is therefore an interest in the number of deaths where *C. difficile* contributed to the death – only conditions which contribute directly to the death should be recorded on the medical certificate of cause of death (death certificate). Results presented in this report identify deaths where the underlying cause was *C. difficile* and those where it was mentioned on the death certificate as a contributory factor.

METHODS

Identification of deaths involving *Clostridium difficile*

All deaths are coded by the Office for National Statistics (ONS) according to the International Classification of Diseases (ICD) supplied by the World Health Organization. In the Tenth Revision (ICD-10), used by ONS from 2001 onwards, there is a specific code (A04.7) for 'Enterocolitis due to *Clostridium difficile*'. While this code identifies the vast majority of deaths involving *C. difficile*, a small number of *C. difficile*-related deaths are not captured by this code alone. Since 1993 ONS has stored the text of death certificates on a database in addition to all the ICD codes relating to causes identified on the death certificate. This means that it is possible to identify records where *C. difficile* is mentioned, but is not coded under the specific ICD-10 code. In addition to extracting all deaths related to the specific A04.7 ICD-10 code, deaths mentioning a number of other ICD categories to which diseases including *C. difficile* could be coded were also extracted. The text of these records was then searched manually for mentions of *Clostridium difficile*, *C. difficile* or pseudomembranous colitis. In the Ninth Revision of the ICD (ICD-9) there is no specific code for 'Enterocolitis due to *Clostridium*

difficile. Identifying deaths involving *C. difficile* would therefore require extensive text searching of very large numbers of death certificates.

The ICD-10 codes used to select deaths to search manually are shown in Table 1. ONS used ICD-10 coded data from 2001 onwards for this report. All deaths registered in 1999 in England and Wales were coded to both ICD-9 and ICD-10, to provide comparisons between the two ICD revisions. Deaths registered in 1999, identified from their ICD-10 codes as involving *C. difficile*, are also included in this report.

Since 1986 ONS has used the internationally recommended death certificate for neonatal deaths. This means that these deaths cannot be assigned an underlying cause of death.¹⁴ However, as the data for this report were based on all mentions of *C. difficile* or pseudomembranous colitis, neonates have been included. Neonatal deaths were extracted in the same way as described above for post-neonatal deaths.

Deaths with an underlying cause of death of *C. difficile* were identified by selecting those deaths with a mention of *C. difficile* or pseudomembranous colitis that also had one of the underlying causes of death noted in Table 1.

Derivation of place of death categories

The place of death categories used in this analysis have been derived from three items of information recorded by ONS (Table 2). First, the communal establishment code distinguishes between deaths in communal establishments (which are given a code specific to the particular institution) and those at home or occurring elsewhere. Second, the establishment type code classifies communal establishments into different types (e.g. hospital, hospice, local authority residential home). Lastly, the NHS Indicator code shows whether the establishment was NHS or non-NHS funded.

Methods of analysis

This report presents the number of *C. difficile* related deaths by sex, age and place of death. Both age-specific and age-standardised death rates for *C. difficile* are presented in this report. Age-standardised rates are explained in Box One.

Specific codes*	Non-specific codes*
A04.7 (Enterocolitis due to <i>Clostridium difficile</i>)	A05.8 (Other specified bacterial food borne intoxications)
	A41.4 (Septicaemia due to anaerobes (Excludes: gas gangrene))
	A48.0 (Gas gangrene: Clostridial; cellulites, myoncosis)
	A49.8 (Other bacterial infections of unspecified site)
	P36.5 (Sepsis of newborn due to anaerobes)

* Codes used to identify deaths where *C. difficile* was the underlying cause of death (on deaths where *C. difficile* was mentioned): A04.7, A09, A41.4, and A49.8.

RESULTS

Number of deaths where *Clostridium difficile* contributed to the death or was the underlying cause of death

The number of death certificates mentioning *C. difficile* increased each year in England and Wales between 1999 and 2004 (Table 3). Figure 1 shows the increasing number of death certificates where *C. difficile* was mentioned since 1999. Mentions of *C. difficile* on death certificates increased from 975 in 1999 to 2247 in 2004. Overall the number of deaths with a mention of *C. difficile* was 2.3 times higher in 2004 than it was in 1999. Among deaths with a mention of *C. difficile*, the percentage for which it was the underlying cause was similar (around 55 per cent) in each year (Table 3).

Mortality rates for all deaths mentioning *Clostridium difficile*

Age-standardised rates for deaths involving *C. difficile* in England and Wales have more than doubled since 1999, from 11.4 to 23.6 per million for males and from 10.7 per million to 23.4 per million for females (Table 4). Overall, rates for deaths involving *C. difficile* were very similar for both males and females in each year (Figure 2).

Most of the deaths involving *C. difficile* occurred among people aged 65 and over. Mortality rates in specific age groups for England and Wales are shown in Table 5. Between ages 75 and 84, there were 208.4 and 214.7 deaths per million population for males and females respectively in the period 2001 to 2004. This compares with 0.1 and 0.2 deaths per million population, for males and females respectively, in the under 45 age group (Table 5).

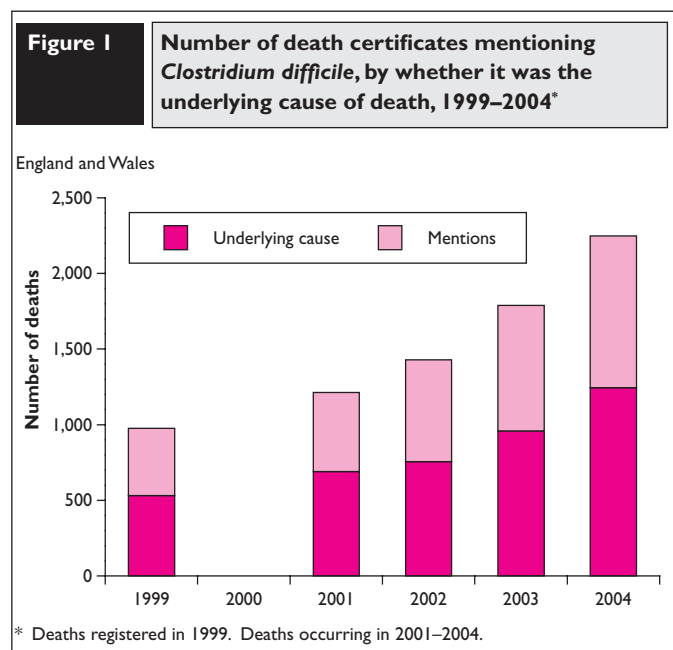


Table 2 Derivation of Place of Death Classification

Place of death classification	Communal Establishment	Establishment type	NHS Indicator
Own home	Home	N/A	N/A
NHS general hospital	Communal Establishment Code	General hospital or Multi-function site	NHS
Non-NHS general hospital		General hospital or Multi-function site	Non-NHS
Hospice		Hospice	
NHS nursing home		Homes for the chronic sick or Medical nursing home	NHS
Non-NHS nursing home		Homes for the chronic sick, Medical nursing home, Private nursing home or Private nursing home (aged)	
Private residential home		Residential home (private)	Non-NHS
Local Authority residential home		Residential home (Local Authority)	NHS
Other places	Elsewhere	All other codes	N/A

Table 3 Number of death certificates with *Clostridium difficile* mentioned and as the underlying cause, 1999–2004

England and Wales

	1999	2001	2002	2003	2004	% change 1999–2004
England and Wales*						
Certificates mentioning <i>C.difficile</i>	975	1,214	1,428	1,788	2,247	130
Certificates where <i>C.difficile</i> was the underlying cause of death†	531	691	756	958	1,245	134
Percentage of mentions selected as underlying cause	54	57	53	54	55	
England						
Certificates mentioning <i>C.difficile</i>	918	1,150	1,338	1,702	2,155	135
Certificates where <i>C.difficile</i> was the underlying cause of death†	499	661	709	912	1,187	138
Percentage of mentions selected as underlying cause	54	57	53	54	55	
Wales						
Certificates mentioning <i>C.difficile</i>	56	63	88	85	88	57
Certificates where <i>C.difficile</i> was the underlying cause of death†	31	29	46	46	55	77
Percentage of mentions selected as underlying cause	55	46	52	54	63	

* England and Wales data include non-residents who died in England and Wales. Data for England and Wales on their own exclude deaths of non-residents.

† Excludes neonatal deaths.

Table 4 Age-standardised mortality rates for *Clostridium difficile* by sex, 1999–2004

England and Wales

Rates per million population

	1999	2001	2002	2003	2004	% change 1999–2004
England and Wales*						
Males	11.4	13.1	15.5	18.6	23.6	106
Females	10.7	12.8	15.1	18.8	23.4	120
England						
Males	11.6	13.2	15.3	18.8	23.9	107
Females	10.6	12.9	15.1	19.0	23.9	126
Wales						
Males	9.5	11.9	17.9	13.7	16.7	76
Females	11.6	10.6	15.1	15.9	16.2	39

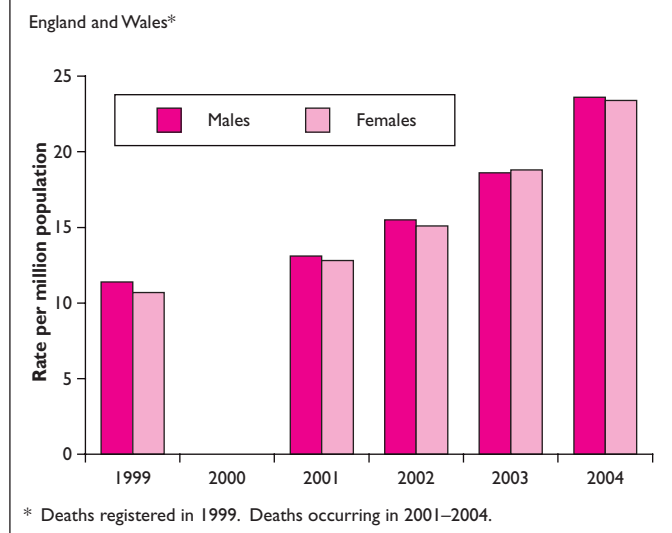
* England and Wales data include non-residents who died in England and Wales. Data for England and Wales on their own exclude deaths of non-residents.

Table 5 Age-specific mortality rates for *Clostridium difficile* by sex, 2001–2004

England and Wales		Rates per million population					
Age group	England and Wales*		England		Wales		
	Males	Females	Males	Females	Males	Females	
Under 45	0.1	0.2	0.1	0.2	0.0	0.9	
45-54	1.4	1.6	1.3	1.6	1.3	2.6	
55-64	5.2	7.5	5.2	7.8	4.3	2.8	
65-74	39.5	37.8	40.3	37.8	27.8	39.0	
75-84	208.4	214.7	212.0	218.3	154.2	152.7	
85 and over	832.0	789.8	832.6	798.0	806.7	647.1	

* England and Wales data includes non-residents who died in England and Wales. Data for England and Wales on their own exclude deaths of non-residents.

Figure 2 Age-standardised mortality rates for *Clostridium difficile* by sex, 1999–2004*



Place of death

Death certificates rarely specify the place where an infection was acquired. However, the place of death is recorded. Between 2001 and 2004, deaths involving *C. difficile* made up 0.32 per cent of all deaths in England and Wales. Among deaths that occurred in NHS general hospitals and NHS nursing homes deaths involving *C. difficile* made up 0.52 per cent and 0.45 per cent of the total in these institutions respectively, or almost 5 per thousand deaths.

Most deaths in England and Wales occur in hospital (56 per cent of all deaths between 2001 and 2004 occurred in NHS general hospitals). Over the period 2001 to 2004, 92.4 per cent of deaths that mentioned *C. difficile* occurred in NHS general hospitals. Many of these deaths in hospital will have been to patients who were admitted because they were already seriously ill with another condition.

Box One

Glossary of Terms

***Clostridium difficile* (*C. difficile*):** is a spore forming bacterium which is present as one of the 'normal' bacteria in the gut of up to 3 per cent of healthy adults. It is much more common in babies – up to two thirds of infants may have *C. difficile* in the gut, where it rarely causes problems. People over the age of 65 years are more susceptible to contracting infection.

Diarrhoea: Diarrhoea occurs when the lining of the small or large intestine is irritated. *C. difficile* toxins are a major cause of antibiotic-associated diarrhoea. This leads to increased water being passed in the stools. Acute diarrhoea is usually caused by a viral infection or a bacterial infection and affects almost everyone from time to time. It usually clears up in a couple of days and is not serious. However it can be serious in babies and the frail and elderly, because of the risk of dehydration.

Pseudomembranous colitis (PMC): is a complication of antibiotic therapy often caused by *C. difficile* infection. PMC causes severe inflammation in areas of the colon (large intestine). Almost any antibiotic can cause PMC by upsetting the balance of the bacteria in the gut and intestines.

Age-standardised rate: Directly age-standardised rates make allowances for differences in the age structure of the population, over time and between sexes. The age-standardised rate for a particular disease is that which would have occurred if the observed age-specific rates for the disease had applied in a given standard population. In this report we have used the **European Standard Population**. This is a hypothetical population standard, which is the same for both males and females allowing standardised rates to be compared over time, and between males and females.

Sources: Health Protection Agency/ NHS Direct Online/ Office for National Statistics

Table 6

Number of deaths mentioning *Clostridium difficile* by place of death, compared to all causes of death, 2001–2004

England and Wales

	All cause number of deaths	Number of deaths	Percentage of all <i>C.difficile</i> deaths	<i>C.difficile</i> as a percentage of all deaths in the establishment
England and Wales*				
Own home	387,529	48	0.7	0.01
NHS general hospital	1,178,776	6,168	92.4	0.52
Non-NHS general hospital	11,561	12	0.2	0.10
Hospice	92,116	13	0.2	0.01
NHS nursing home	11,077	50	0.7	0.45
Non-NHS nursing home	199,924	133	2.0	0.07
Private residential home	118,138	41	0.6	0.03
Local Authority residential home	30,586	16	0.2	0.05
Other places	84,988	196	2.9	0.23
Total	2,114,695	6,677	100.0	0.32
England				
Own home	362,252	47	0.7	0.01
NHS general hospital	1,097,719	5,864	92.4	0.53
Non-NHS general hospital	10,892	12	0.2	0.11
Hospice	89,363	12	0.2	0.01
NHS nursing home	10,923	50	0.8	0.46
Non-NHS nursing home	188,764	123	1.9	0.07
Private residential home	112,284	40	0.6	0.04
Local Authority residential home	28,720	16	0.3	0.06
Other places	76,922	181	2.9	0.24
Total	1,977,839	6,345	100.0	0.32
Wales				
Own home	25,226	1	0.3	0.00
NHS general hospital	77,885	296	91.4	0.38
Non-NHS general hospital	273	0	0.0	0.00
Hospice	2,641	1	0.3	0.04
NHS nursing home	147	0	0.0	0.00
Non-NHS nursing home	11,014	10	3.1	0.09
Private residential home	5,828	1	0.3	0.02
Local Authority residential home	1,861	0	0.0	0.00
Other places	7,065	15	4.6	0.21
Total	131,940	324	100.0	0.25

* England and Wales data include non-residents who died in England and Wales. Data for England and Wales on their own exclude deaths of non-residents.

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