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ESTIMATING THE SIZE OF THE HIV EPIDEMIC BY USING MORTALITY DATA

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Evidence that more people are dying as a result of HIV infection than is reflected by the number of deaths among reported cases meeting the WHO definition of AIDS is derived from mortality data. Ninety-five causes of death likely to be associated with HIV infection were selected. Standardized mortality ratios due to these causes increased for single men aged 15–54 years from 100 in 1984 to 118 in 1987. The age, sex, marital status, temporal and geographic distribution of these excess deaths suggest that they are HIV-associated. It is estimated that 58 % of excess deaths due to HIV-related causes were among cases reported to the CDSC AIDS Surveillance Programme in 1987. Some of these deaths may have been among HIV-positive people who did not meet the WHO definition at the time of death. There is a need for surveillance to be extended to include HIV-positive people who die before meeting the WHO definition if the full extent of the HIV epidemic is to be identified.

1. Introduction

The epidemic of human immune deficiency virus type 1 (HIV-1) infection in England and Wales is monitored by using data from sources described in this volume and elsewhere (McCormick 1987). Identification of cases depends upon voluntary reporting of positive laboratory tests for HIV and on people with acquired immune deficiency syndrome (AIDS) meeting the World Health Organisation (WHO) definition (Centres for Disease Control 1987). Additional cases are identified from death entries on which AIDS or HIV infection is certified as a cause of death. It is uncertain how many of these fulfil the WHO definition of AIDS unless the doctor signing the medical certificate of cause of death subsequently responds to an invitation to report the case to the PHLS Communicable Disease Surveillance Centre (CDSC).

Data published monthly by the Department of Health presenting the number of deaths include only those deaths known to have occurred among people meeting the WHO definition who have been reported to the CDSC aids surveillance programme. Universal use of the standard WHO definition allows comparison with data collected in other countries. There is evidence, however, that there may be nearly as many deaths again among people who are infected with hiv, who have developed aids but have not been reported to the CDSC programme, or who have died as a result of their hiv infection without developing aids.

Reported causes of death among people who are HIV-positive but do not fulfil the WHO definition of AIDS include bacterial pneumonia (Selwyn et al. 1988; Stoneburner et al. 1988; Wilkes et al. 1988), pulmonary embolus (Selwyn et al. 1988; Wilkes et al. 1988), bacteraemia (Krumholz et al. 1988), various cardiac conditions (Wilkes et al. 1988) including endocarditis (Afessa et al. 1988; Galli et al. 1988), myocarditis and pericarditis (Marche et al. 1988;

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Anderson et al. 1988), myocardial infarction (Galli et al. 1988) and cardiomyopathy (Zasso et al. 1988), febrile episodes (Periman et al. 1988), metabolic problems (Chirgwin et al. 1988), cerebral haemorrhage (Selwyn et al. 1988), suicide (Afessa et al. 1988; Rajs et al. 1988; Marzuk et al. 1988) and drug overdose (Selwyn et al. 1988; Afessa et al. 1988; Galli et al. 1988), gastrointestinal haemorrhage (Selwyn et al. 1988; Afessa et al. 1988), peptic ulcer (Wilkes et al. 1988), gastroenteritis (Moreno et al. 1988), pancreatitis (Wilkes et al. 1988), acute renal tubular necrosis (Wilkes et al. 1988) and many cancers (Galli et al. 1988; Kahn et al. 1988; Tirelli et al. 1988; Holtzman et al. 1988). For some deaths due to these and other causes, though occurring in people with AIDS, the stated cause(s) of death on the medical certificate may not have included AIDS or HIV infection. Most studies of mortality have been carried out on cohorts of men known to have been HIV-positive. Other than in England and Wales (McCormick 1988) no studies have been published that attempt to identify trends in the general or selected groups of the population for causes other than AIDS that were likely to be associated with HIV infection.

This paper describes how mortality data for England and Wales have been used to estimate the full extent of HIV infection severe enough to cause death, and the possible short fall in the number of cases identified when the WHO definition of AIDs is used as the criterion for acceptance.

2. EVIDENCE FOR MORE DEATHS DUE TO HIV INFECTION THAN REFLECTED IN REPORTED NUMBER OF DEATHS AMONG CASES OF AIDS

2.1. Standardized mortality ratios (SMRS)

SMRs for all causes of death for both men and women aged 15-54 years in England and Wales have fallen from 100 in 1980 to 83.3 for men and 84.7 for women in 1987 (figure 1).

Every death entry in which AIDS OF HIV is mentioned is coded ICD 279.1 (deficiency of cell-mediated immunity) unless an underlying cause of death unlikely to be associated with HIV infection is stated. To study the possible effect of HIV infection, 95 causes of death were selected because they are included in the WHO definition of AIDS, or because they have been mentioned on the certificates of persons known to have had AIDS. These causes, which include ICD 279.1, were considered to be possibly HIV-related. SMRS for these causes alone for men who never married aged 15–54 years have increased from 100 in 1984 to 109 in 1985, 113 in 1986 and 118 in 1987 (figure 2, table 1).

Comparable figures for women who never married are 99 in 1985, 103 in 1986 and 101 in 1987. For men of all marital states other than those who never married, smrs are 100 in 1985, 102 in 1986 and 99 in 1987 (table 2). The baseline was taken as 1984 because a change at the beginning of 1984 in the method of coding underlying cause of death makes comparison with previous years by selected causes invalid. smrs for men who never married aged 15–54 years due to the same hiv-related icd codes indicate however that death rates fell between 1980 and 1983 (table 3). No data on marital status was recorded on death entries during 1981.

2.2. Rates by 5-year age groups

For men who never married aged 15–49 years, mortality rates due to HIV related causes have increased in each 5-year age group since 1984 (table 4). The increase between 1984 and 1987 was greatest in 30–34 year olds (43%) but also high for 35–39 year olds (38%) and 40–44

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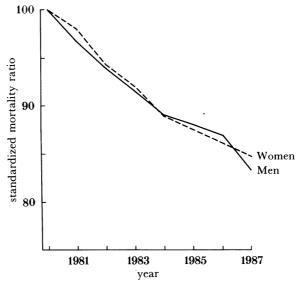


FIGURE 1. Standardized mortality ratios, all causes, all marital states, aged 15-54 years.

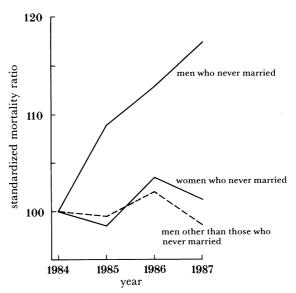


FIGURE 2. Standardized mortality ratios, HIV-related causes, marital state, aged 15-54 years.

year olds (39%). There was no similar increase among men of all marital states other than those who never married (table 4).

The age distribution at the time of death is similar to that among men with AIDS reported to CDSC who are known to have died; among these there are more deaths among 35–39 and 40–44 year olds than any other five-year age group.

2.3. Geographical distribution

The greatest increase in death rates, among men who never married aged 15–54 years, due to hiv-related causes between 1984 and 1987 was in North West Thames, North East Thames, South East Thames and North Western Regional Health Authorities (figure 3, table 5).

This is still true for HIV-related causes excluding deaths coded ICD 279.1, although in two of

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TABLE 1. STANDARDIZED MORTALITY RATIOS DUE TO HIV-RELATED CAUSES: MEN WHO NEVER MARRIED AGED 15-54 YEARS, (1984-1987)

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(Obs., observed; pop., population in thousands; exp., expected; 1984 = 100.)

		1984			1985		
age	obs.	pop.	exp.	obs.	pop.	exp.	
15-19	282	2064.6		264	2021.5	276	
20-24	370	1671.5		417	1747.2	387	
25 – 29	232	707.1		272	769.5	252	
30-34	166	329.3		211	339.5	171	
35 – 39	146	223.0		197	231.6	152	
40-44	134	143.5		157	148.7	139	
45 – 49	175	120.3		195	121.0	176	
50 - 54	285	119.6		275	115.6	275	
total	1790	5378.9		1988	5494.6	1828	
	smr = 100			smr = 108.8			
		1986			1987		
15-19	310	1994.6	272	309	1948.1	266	
20-24	420	1794.2	397	492	1811.1	401	
25 – 29	310	840.8	276	307	922.1	303	
30-34	232	356.4	180	272	376.8	190	
35 – 39	228	240.4	157	215	238.1	156	
40-44	179	156.1	146	223	172.2	161	
45-49	189	120.2	175	203	121.3	176	
50 - 54	242	112.2	267	230	110.1	262	
total	2112	5614.9	1870	2251	5699.8	1915	
		smr = 112.9			smr = 117.54		

Table 2. Standardized mortality ratios for 95 hiv-related causes for persons AGED 15-54 YEARS BY SEX AND MARITAL STATUS

(1985-1987; 1984 = 100.)

	1984	1985	1986	1987
men who never married	100	108.9	112.9	117.5
women who never married	100	98.5	103.5	101.2
men (other than those who never married)	100	99.5	102.0	98.6

Table 3. Standardized mortality ratios due to hiv-related causes: MEN WHO NEVER MARRIED AGED 15-54

(1980-1983; (1980 = 100); Obs., observed; pop. population in thousands; exp., expected.)

1980				1982			1983		
age	obs.	pop.	obs.	pop.	exp.	obs.	pop.	exp.	
15-19	321	2069.6	334	2117.8	328.5	346	2108.2	327.0	
20-24	338	1352.9	372	1492.0	372.8	378	1578.4	394.3	
25 - 29	269	566.8	280	615.2	292.0	265	654.6	310.7	
30 – 34	195	306.5	206	314.0	199.8	180	318.8	202.8	
35 - 39	158	172.6	153	200.7	183.7	186	213.4	195.3	
40–44	164	133.4	153	134.2	165.0	140	137.7	169.3	
45-49	195	126.5	216	120.8	186.2	194	120.2	185.3	
50 - 54	351	132.8	295	127.8	337.8	261	124.3	328.5	
total	1991	4861.1	2009	5122.5	2065.7	1951	5255.6	2113.3	
	SMR	= 100		smr = 97.3			smr = 92.3		

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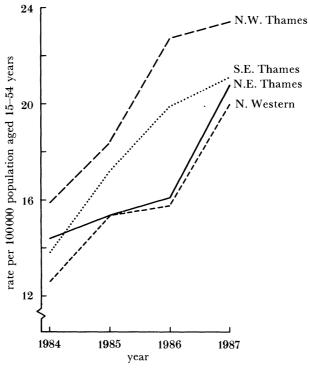


Figure 3. Deaths due to hiv-related causes, regional health authority of usual residence, men who never married aged 15–54 years.

Table 4. Death rates per million population for 95 hiv-related causes:

MEN AGED 15-54 YEARS, 1984-1987

						all marita	l states oth	ier than	
	nev	er marriec	ł			never l	having ma	rried	
age	1984	1985	1986	1987	age	1984	1985	1986	1987
15-19	137	131	155	159	15-19	320	901	909	826
20 – 24	221	239	234	272	20 – 24	193	195	265	255
25 - 29	328	353	369	333	25 – 29	215	208	181	209
30 - 34	504	622	651	$\bf 722$	30 – 34	272	249	256	261
35 – 39	654	851	948	903	35 – 39	292	306	287	309
40 – 44	934	1056	1147	1295	40-44	424	413	429	384
45 – 49	1455	1612	1572	1674	45 – 49	592	590	616	596
50 - 54	2383	2379	2157	2089	50 – 54	878	878	921	857

the three Thames regions there was a decrease between 1986 and 1987, suggesting that for a higher proportion of hiv-related deaths than previously, aids or hiv infection was stated as the cause (figure 4). Among patients with aids reported to CDSC, more people who died were reported from each of the four regions mentioned above than from any other regional health authority (table 5).

2.4. Temporal distribution

The number of deaths among men of all marital states, and men who never married, aged 15–54 years, due to HIV-related causes has increased steadily each quarter year from the beginning of 1984 to the end of 1987 (table 6). This increase is similar to that of cases reported to CDSC by month of diagnosis (figure 5). The number of deaths among women who never

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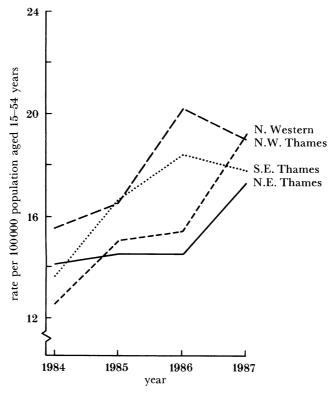


FIGURE 4. Deaths due to HIV-related causes excluding ICD 279.1, regional health authority of usual residence, never-marred men aged 15-54 years.

married also increased slightly between 1984 and 1987 but for all men except those who never married there was little change.

2.5. Comparison of observed and expected deaths

The number of excess deaths due to HIV-related causes in 1985, 1986 and 1987 compared with 1984 was obtained by adjusting for population changes such that

excess deaths = (observed deaths_i-observed deaths₀) × population_i/population₀, where 0 = 1984 and i = 1985, 1986, or 1987.

Compared with 1984, among men who never married aged 15–54 years, there was an estimated excess of 159 deaths in 1985, 243 in 1986 and 354 in 1987 (table 7). There was no similar excess among men of marital states, other than those who never married, between 1985 and 1987. Among women who never married there was an estimated deficit of 11 in 1985, and an excess of 19 in 1986 and 11 in 1987, compared with 1984.

2.6. Patients reported to CDSC who did not fulfil the WHO definition at the time of death

Doctors are asked to report to CDSC only those patients who meet the WHO definition of AIDS. Nevertheless, by the end of June 1988, 28 patients who had died as a result of HIV infection had been reported to CDSC but have not been included in the surveillance scheme because they did not meet the WHO definition. This may be the tip of the iceberg because doctors would not be expected to report cases that they did not believe fulfilled the definition.

Deaths due to HIV-related causes 200 Reports to CDSC 1984 1985 1986 1987

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FIGURE 5. Deaths due to HIV-related causes, quarter year of registration, men who never married aged 15–54 years. Reports of AIDS cases to CDSC, quarter year of diagnosis.

year

Table 5. Death rates per 100000 population due to 95 hiv-related causes by regional health authority (rha) of usual residence, never-married men. Deaths among cases of aids reported to cdsc by regional health authority of reporter, all ages, men and women

					deaths by end 1987
		нıv-relat	ed causes		among cases reported
RHA	1984	1985	1986	1987	to CDSC
Northern	10.3	13.7	14.4	13.9	22
Yorkshire	13.4	16.1	13.5	14.1	13
Trent	11.6	12.1	11.0	11.6	8
East Anglia	9.1	11.5	12.8	12.9	12
N.W. Thames	15.9	18.4	22.7	23.4	275
N.E. Thames	14.4	15.4	16.1	20.8	137
S.E. Thames	13.8	17.2	19.9	21.1	66
S.W. Thames	17.7	16.1	15.8	17.2	27
Wessex	10.9	12.2	11.7	13.4	13
Oxford	11.5	12.3	11.4	9.8	12
South Western	12.2	13.1	13.3	13.1	18
West Midlands	11.7	11.8	14.5	12.9	15
Mersey	14.5	14.8	18.5	15.4	12
North Western	12.6	15.4	15.8	20.0	29
Wales	12.7	12.8	13.7	15.3	14

2.7. Medical certificates stating AIDs as cause of death for persons not reported to CDSC

Doctors who mention AIDS or HIV on the medical certificate of cause of death for a person who has not been reported to CDSC are invited to report him or her. However, despite this active follow-up in 1985 to 1987, 31 death entries mentioning AIDS or HIV for people never reported to CDSC also mentioned lymphoma, Kaposi's sarcoma, encephalopathy or an opportunistic infection, suggesting that the case would meet the WHO definition. For a further 67

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Table 6. Deaths due to 95 hiv-related causes by quarter year of registration (Persons aged 15-54 years by sex, 1984-1987.)

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	me	n who never ma	arried	
	1984	1985	1986	1987
1	453	522	506	496
2	464	485	512	580
3	430	478	507	547
4	443	503	587	628
total	1790	1988	2112	2251
	wom	ien who never n	narried	
	1984	1985	1986	1987
1	158	166	159	160
2	148	132	159	157
3	120	131	161	164
4	158	159	155	154
total	584	588	634	635
	men (exce	pt those who ne	ver married)	
	1984	1985	1986	1987
1	914	902	913	926
2	859	902	894	924
3	880	866	849	784
4	903	864	957	893
total	3556	3534	3613	3527

Table 7. Observed and expected excess deaths due to 95 hiv-related causes for PERSONS AGED 15-54 YEARS BY SEX AND MARITAL STATUS 1985-1987 COMPARED WITH 1984

(observed, o; expected, E)

		never married mer	1		
	population (thousands)	observed, o	expected, E	ex	cess, o-E
1984	5378.9	1790			
1985	5494.6	1988	1829		159
1986	5614.9	2112	1869		243
1987	5699.8	2251	1897		354
				total	756
	all me	en except never-ma	arried		
1984	8280.7	3556	_		
1985	8273.7	3534	3553		-19
1986	8252.5	3613	3544		69
1987	8253.1	3527	3544		-17
				total	33
	ne	ever-married wome	en		
1984	4105.8	584	_		_
1985	4209.8	588	599		-11
1986	4325.1	634	615		19
1987	4390.4	635	624		11
				total	19

unreported cases, AIDS or HIV was mentioned on the death entry, either alone or with some other condition that is not included in the current WHO definition.

3. Estimation of completeness of reporting

Comparison between the number of deaths identified from death entries and deaths among cases reported to CDSC is more likely to be accurate for men who never married than for all men. Men who never married form the largest group of AIDS cases. They are a minority among men in the population aged 15–54 years and trends are therefore less biased for this group by deaths due to the 95 selected causes that are unrelated to HIV infection.

Between 1985 and 1987, there was an excess of deaths among men who never married aged 15–54 years of 756 compared with 1984. Over the same period there was an excess of deaths to men reported to be single or for whom the marital status was not known aged 15–54 years of 408 among patients with AIDS reported to CDSC compared with 1984. This suggests that only 54% of deaths due to HIV-related causes were among people with AIDS meeting the WHO definition reported to CDSC (table 8). However, during 1987 alone the proportion of cases reported to CDSC was 58%. The figure of 65% for all marital states between 1985 and 1987 compares favourably with the results of an earlier study (McCormick 1988) that suggested that only 42% of men dying from HIV infection were reported to CDSC. The improvement in reporting is largely due to active follow-up of death entries on which AIDS or HIV is mentioned, for patients not reported to CDSC at the time of death. Although this started in May 1987, retrospective follow-up increased the number of cases reported who had died in previous years.

Table 8. Excess deaths as a percentage of excess deaths reported to CDSC for men aged 15–54 years by marital status 1985–1987 compared with 1984

(Among cases reported to CDSC, (a); from 95 HIV-related causes on death entries, (b).)

	all marital states			never-married			
	(a)	(b)	% reported	(a)	(b)	% reported	
1985	55	136	40.4	53	159	33.3	
1986	179	298	60.1	150	243	61.7	
1987	253	317	79.8	205	354	57.9	
total	487	751	64.8	408	756	54.0	

4. Conclusion

There is evidence from abroad and in England and Wales that deaths have occurred due to hiv infection to persons who have not developed aids meeting the WHO definition. This is apparent from reports from clinicians and pathologists, and from mortality data. The temporal, geographic, age, sex and marital status distribution of increasing mortality rates due to possible hiv-related causes of death is similar to that among cases of aids reported to CDSC, and suggests that the trend is associated with hiv infection. The trend in mortality data derived from death certification is more marked than in deaths among people with aids reported to CDSC.

It is possible that only 54% of the excess deaths due to HIV-related causes in 1985-1987 identified from death certification are among cases reported to CDSC who are known to have

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died. This is likely to be an underestimate because it has been assumed that the 1984 baseline would remain the same in subsequent years. However, between 1980 and 1983 the standardized mortality rate for hiv-related causes fell from 100 to 92 for men who never married aged 15–54 years. It could be expected that the downward trend in deaths due to hiv-related causes but unrelated to hiv infection would have continued beyond 1983. The difference therefore between the observed and expected number of deaths in 1984–1987 is almost certainly greater than that estimated. Forward extrapolation of smrs beyond 1983 by using 1980 as the baseline is not possible owing to the change in coding policy that resulted in approximately 11 % of deaths that would have been coded to hiv-related causes before 1984, being assigned to codes other than hiv-related causes after the beginning of 1984.

The shortfall in the number of cases reported to CDSC may be (a) because not all diagnosed AIDS cases have been reported to CDSC, (b) AIDS cases have died without being diagnosed, or (c) HIV-positive persons have died before developing AIDS. If the size of the predicted epidemic is based only on the number of cases of AIDS reported to CDSC, the result may be an appreciable underestimate of the true picture.

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