Incidence, population, and survival of cystic fibrosis in the UK, 1968–95

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Abstract

The UK Cystic Fibrosis Survey holds data on all people resident in the UK who were diagnosed as having cystic fibrosis and born either since 1968 or before 1968 and alive in 1977. Thus, incidence may be reported from 1968 and prevalence from 1977.The previous estimates are updated to the end of 1995 from data held in the database on 23 August 1996.

The incidence is now calculated as one in 2415 live births. The 1992 mid-year population was 6500 people with 65% aged under 16 years. Births outnumber deaths by 160 per year, which suggests a population of 7750 by the year 2000, with all the increase being in the adult age range.

The survival of successive cohorts continues to be better than earlier cohorts, the linear descent of the curves is still evident. The infant mortality rate for cystic fibrosis is now under 20 per thousand per year and early childhood mortality is under five per thousand per year.

The crude mortality rate for 1995 was 21 per thousand per year, but the standardised mortality ratio was about 3300.

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The UK Cystic Fibrosis Survey (UKCFS) has described the basic epidemiology of cystic fibrosis in the UK from 1968 to 1988.[1] The UKCFS is one of four total population registers of people with cystic fibrosis, the others being in the Netherlands,[2] Sweden,[3] and Czechoslovakia.[4]

The data from the survey are widely used in health service planning, research on cystic fibrosis and in placing the UK experience within an international context.[5]

This paper updates estimates[1] and adds additional years of data up to 1995. All results are presented in a manner consistent with the previous reports.

Methods and analysis

The data collection methods and analysis are effectively the same as in the previous report.[1] Three additional surveys have taken place, at the end of 1990 and 1992 and mid-year 1995. Some 1700 clinicians have contributed to the UKCFS; all death certificates for UK residents since 1968 and up to the end of 1995, on which cystic fibrosis or any of its synonyms were mentioned, have been obtained. The UKCFS now holds data on all people who have been resident in the UK with a diagnosis of cystic fibrosis and were born either since 1968 or before 1968 and still alive in 1977. All patients who were alive at any time since 1977 had their diagnosis confirmed by a named consultant. Those who were born and died between 1968 and 1977 were reported by the death certification authorities only. Cases who died before 1968 would have had their cause of death coded using the *International Classification of Diseases*, eighth revision, which would not always have properly distinguished cystic fibrosis from other conditions. Many patients enjoy shared care between local and regional or national clinics, and great care has been taken to avoid duplicate reporting. Ascertainment is inevitably incomplete for patients born in recent years, either because they are not yet diagnosed or because of delays inherent in the data collection methods used. Experience has shown that there is a delay of about five years before the population estimates become reliable.

The data analysed were those held in the database on 23 August 1996, and the statistical

Table 1 Year of birth for UK cystic fibrosis cases, incidence, and estimated births based on data held up to 1995

Year	*Cases*	*UK births (1000)*	*Births/case*	*Estimated cystic fibrosis births**
68	367	947.3	2581	392
69	356	920.2	2585	381
70	388	903.9	2330	374
71	407	901.8	2216	373
72	326	834.9	2561	346
73	309	779.6	2523	323
74	316	737.2	2333	305
75	291	697.4	2397	289
76	299	675.6	2260	280
77	278	657.0	2363	272
78	292	686.9	2352	284
79	302	734.6	2432	304
80	302	753.7	2496	312
81	302	730.9	2420	303
82	356	719.1	2020	298
83	301	724.5	2407	300
84	310	729.6	2354	302
85	311	750.7	2414	311
86	276	754.9	2735	313
87	294	775.6	2638	321
88	326	787.6	2416	326
89	290	777.3	2680	322
90	295	798.6	2707	331
91	259	792.5	3060	328
92	239	781.0	3268	323
93	202	761.3	3769	315
94	205	750.3	3660	311
Aggregated incidence				
Time period				
1968–87	6383	15415	2415	
1968–77	3337	8055	2414	
1978–87	3046	7360	2416	

*Calculated as UK births/2424.

Table 2 Mid-year UK cystic fibrosis population by year, age, and sex based on data held to 1995

	Age (years)									
Year	*0–< 1*	*1–< 5*	*5–< 15*	*15*	*16*	*17–< 25*	*25–< 35*	*35+*	*45+*	*Total*
1986										
Male	135	642	1223	140	106	579	162	28		3015
Female	132	564	1057	114	76	442	129	33		2547
Total	267	1206	2280	254	182	1021	291	61		5562
%	4.8	21.7	41.0	4.6	3.3	18.4	5.2	1.1		100.0
1987										
Male	148	601	1291	91	140	596	207	28		3102
Female	147	560	1083	81	112	478	141	34		2636
Total	295	1161	2374	172	252	1074	348	62		5738
%	5.1	20.2	41.4	3.0	4.4	18.7	6.1	1.1		100.0
1988										
Male	160	582	1328	103	88	663	244	30		3198
Female	140	570	1101	100	74	528	166	39		2718
Total	300	1152	2429	203	162	1191	410	69		5916
%	5.1	19.5	41.1	3.4	2.7	20.1	6.9	1.2		100.0
1989										
Male	161	608	1332	108	101	672	276	34		3292
Female	147	566	1131	95	94	514	207	48		2802
Total	308	1174	2463	203	195	1186	483	82		6094
%	5.1	19.3	40.4	3.3	3.2	19.5	7.9	1.3		100.0
1990										
Male	158	596	1371	116	103	692	317	36		3389
Female	118	562	1179	85	92	538	227	54		2855
Total	276	1157	2550	201	195	1230	544	90		6244
%	4.4	18.5	40.8	3.2	3.1	19.7	8.7	1.4		100.0
1991										
Male	147	619	1371	118	113	687	366	44		3465
Female	131	549	1201	86	83	557	253	59		2919
Total	278	1168	2572	204	196	1244	619	103		6384
%	4.4	18.3	40.3	3.2	3.1	19.5	9.7	1.6		100.0
1992										
Male	126*	620	1410	96	117	710	399	51		3529*
Female	120*	531	1245	86	83	558	286	61		2970*
Total	246*	1151	2655	182	200	1268	685	112		6499*
1993										
Male	121*	585*	1436	118	93	732	425	67		3577*
Female	94*	512*	1280	83	83	555	311	68		2986*
Total	215*	1097*	2716	201	176	1287	736	135		6563*
1994										
Male	96*	549*	1453	129	116	729	451	81		3604*
Female	93*	458*	1290	114	79	564	324	74		2996*
Total	189*	1007*	2743	243	195	1293	775	155		6600*
1995										
Male	90*	487*	1473	126	125	742	487	89	14	3633
Female	86*	436*	1275	115	108	575	346	62	21	3024
Total	176*	923*	2748	241	233	1317	833	151	35	6657

Notes: (1) The experience of UKCFS is that population estimates are subject to systematic bias and are continually revised upwards due to problems of ascertainment.[1] The data items marked * are likely to be serious time related underestimates and thus give a false picture of trends in the data. (2) Data for those aged over 45 years are not given before 1995 as the UKCFS does not publish any aggregate results involving fewer than 10 persons for reasons of confidentiality.[11]

package SPSS-X was used as before.[6] For the current life table calculation we employed a purpose written program using the methods described by Bradford Hill.[7]

The 1992 age/sex specific death rates for England and Wales,[8] which are very close to the UK rates given the relative sizes of the population, were applied to the 1992 UK population given in table 2 to calculate a standardised mortality ratio (SMR). The number of those aged under 1 year were adjusted to that expected from table 1 in the calculation of the SMR.

Results

Table 1 gives the number of people with cystic fibrosis born in the UK per year and the calculated incidence. The average proportion of cystic fibrosis births between 1968 and 1987 is 1/2415, slightly greater than the 1/2475 reported previously.

Table 2 gives the new recorded mid-year UK cystic fibrosis population from 1986 to 1988 and adds the years to 1995. The age group 25+ years has been split into 25 to 34 years and 35+ years except for 1995 which has a 35 to 45 years and 45+ years groups.

The survival of three year cohorts for the two sexes is given in fig 1 with the corresponding hazard rates in table 3. The last two years of each cohort contain censored data and are therefore less reliable than the earlier parts of the curve. The 'current survival', based on hazard rates for 1994 is given in fig 2.

The number of patients dying each year in the decade up to the end of 1995 averaged 138, range 115 to 164. This is some 160 less than the numbers born per year.

Our extrapolation of the population size for the year 2000 is the 1990 population (6244) plus 1500 giving 7750.

The expected deaths in 1992 were 4.4, while the actual deaths were 144, giving an approximate SMR of 3300.

Discussion

The method used to collect data for the UKCFS adds an additional delay to the delays in diagnosis. Experience shows that reliable population estimates for the younger ages only become available after a delay of five years. However, some more recent data are given here to help answer health service planning problems.

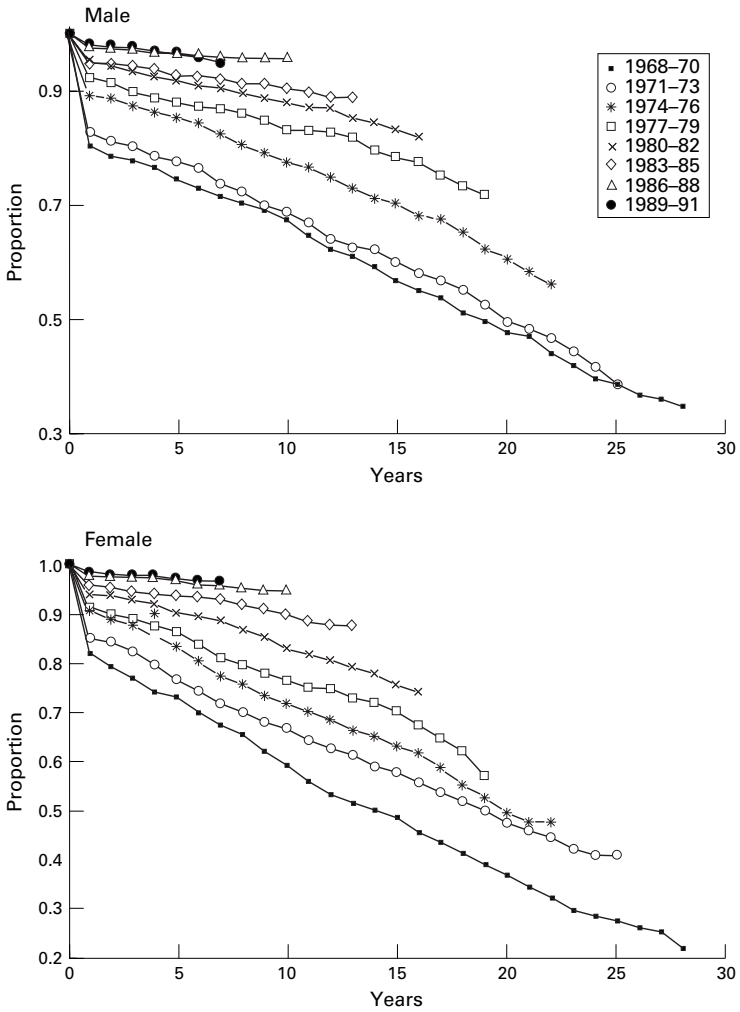

Figure 1 Proportion of males and females surviving of each successive three year cohort of UK residents with cystic fibrosis.

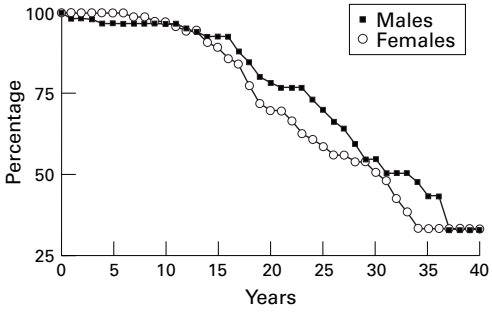

Figure 2 Current survival of UK residents with cystic fibrosis for 1994 for both sexes.

The slight increase in the average incidence over the period 1968 to 1985 is due to both an original under ascertainment in the later years, due to delays in diagnosis, together with small numbers of cases being diagnosed in later adult life. For planning purposes the incidence may be assumed as constant at 1/2500, which implies a gene frequency of 1:25.

The 1992 population is already recorded as 6499 people, showing that a previous extrapolation,[1] which predicted 6000, was conservative.

Paediatric practice in the UK traditionally continues to age 16; therefore the usual World Health Organisation age groups have been adapted to show the numbers of patients who were eligible for transfer from paediatric to adult care.

The pattern of linear descent of the survival curves continues unbroken after the addition of data up to 1995. The mortality rates for children with cystic fibrosis have now been reduced to such a low level that the prime determinant of the size of the child cystic fibrosis population is the number born. Given

Table 3 Cohort survival of UK cystic fibrosis population: number in population, and hazard rate per thousand by sex (number in parentheses) based on data held to 1995

	Year of birth								
	1968–70	*1971–73*	*1974–76*	*1977–79*	*1980–82*	*1983–85*	*1986–88*	*1989–91*	*1992–94*
Males									
Population of cystic fibrosis births	588	535	479	457	527	467	457	459	342
Age (years)									
0–< 1	216.8 (115)	185.9 (91)	112.5 (51)	79.6 (35)	48.6 (25)	52.7 (24)	24.4 (11)	19.8 (9)	2.1 (7)
1–< 5	18.6 (34)	15.7 (27)	10.7 (18)	11.5 (19)	8.6 (17)	5.7 (10)	2.8 (5)	3.9* (6)	†
5–< 10	19.6 (41)	24.4 (48)	18.9 (37)	11.2 (22)	8.4 (20)	4.7 (10)	2.7* (3)	2.6* (2)	
10–< 15	34.4 (63)	26.6 (46)	19.7 (35)	11.9 (22)	13.3* (20)	3.8* (4)			
15–< 20	34.4 (53)	38.0 (56)	33.8* (45)	18.9* (17)	2.9* (1)				
20–< 25	41.5 (53)	55.4* (37)	14.4* (7)						
25–< 30	21.0* (12)								
Females									
Population of cystic fibrosis births	523	507	427	415	433	455	439	385	304
Age (years)									
0–< 1	195.2 (93)	157.4 (74)	95.7 (39)	90.7 (36)	61.9 (26)	42.6 (19)	25.4 (11)	15.7 (6)	13.3 (4)
1–< 5	28.9 (47)	26.1 (43)	20.8 (31)	13.6 (20)	10.0 (16)	5.8 (10)	1.8 (3)	3.9* (5)	†
5–< 10	42.1 (73)	28.0 (51)	30.1 (50)	24.2 (41)	16.5 (31)	8.1 (17)	7.5* (8)	1.6* (1)	
10–< 15	39.7 (56)	28.4 (45)	25.7 (37)	17.0 (26)	22.1 (26)	6.8* (7)			
15–< 20	54.6 (61)	39.6 (53)	55.2* (56)	39.7* (29)	3.6* (1)				
20–< 25	56.8 (48)	46.5* (28)							
25–< 30	30.3* (11)								

Notes: (1) Data subject to censoring marked by * (see footnote). (2) Previously censored data based on fewer than 10 deaths have not been reported. However, the five year age group specific mortality rates are now so low that in some cases there are fewer than 10 deaths reported in uncensored groups. Hence only censored groups with more than 100 life years of observation are included. (3) The 1983–85 cohort overestimates the hazard rate due to reduced ascertainment of the cases (see text). (4) The standard error of all the 0–1 year age group hazard rates is approximately 10 per thousand, for the 1–5 year group it is approximately four per thousand rising to six per thousand for the 25–30 year group. (5) Entry marked † has no deaths reported at the time of analysis so no rate can be calculated.

the projected cystic fibrosis births based on total UK births and the most recent incidence estimates (table 1), the child population has stabilised at around 4500 cases. All future increase in the population will be in adults and is currently 2600 increasing by about 150 per year.

The final size of the adult population is a matter of conjecture, there being no reliable mortality rates for those aged over 30. We assume that, as is the case for children, adult mortality rates are much lower than they were in 1968–70. Consequently, estimates of continued improvement in median survival[9] are now beginning to look realistic. Of course, there is no experience of how cystic fibrosis interacts with the normal aging process, but clinical experience indicates that potentially life shortening complications of cystic fibrosis such as diabetes mellitus and liver disease may become more frequent with advancing age, so projections based on our previous experience of younger people could be erroneous.

Nevertheless, the survival of each successive cohort continues to be more favourable than the previous cohorts. Improvements in mortality may still be possible. However, when compared with the cohorts born since 1983 the margin for improvement is now relatively small and will be difficult to detect given the cohort sizes.

There is still no evidence of a particular age being a crisis point at which the mortality rises sharply. A comparison of the sexes illustrates that, except for the first year of life, the mortality of females is generally greater than that of males. This is consistent with reports from other countries.[10]

There is no indication that prenatal diagnosis, which has been available in some form for a decade, has had any impact on numbers of cystic fibrosis births but this is not unexpected as most cases are born into families without a history of cystic fibrosis. However, if we have overestimated the number of births since 1991, and if there is any substantial trend towards decreasing incidence, this should become apparent within the next five years.

The numbers dying each year have remained constant at some 160 fewer than those born. This is consistent with improving survival, and the first evidence that improvements in survival are diminishing will be an increase in deaths. As deaths are reported to us promptly by the death certification authorities a worsening of survival would become evident within a couple of years of it occurring. The crude death rate for people with cystic fibrosis has fallen from 40 per thousand per year in 1977 to 21 per thousand per year in 1995. This apparently compares well with the 10.9 per thousand for the general population. However, an SMR for people with cystic fibrosis in 1995 is about 3300, due to the preponderance of young people in the cystic fibrosis population.

To date the UKCFS has found no important systematic differences in either the incidence of cystic fibrosis or the survival of people with cystic fibrosis by region of residence.

These basic epidemiological data provide evidence which should help ensure that planning health care for people with cystic fibrosis is equitable, by reassuring health care purchasers that the levels of provision are not too high and by reassuring patients, their families, and carers that the level of provision is not too low.

The UKCFS only succeeds due to the unstinting efforts of the 1700 clinicians and their staff who provide regular updates on their patients.

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1 Dodge JA, Morison S, Lewis PA, *et al.* Cystic fibrosis in the United Kingdom, 1968-1988: incidence, population and survival. *Paediatr Perinat Epidemiol* 1993;**7**:157-66.
2 Ten Kate LP. Cystic fibrosis in the Netherlands. *Int J Epidemiol* 1977;**6**:23-34.
3 Selander P. The frequency of cystic fibrosis of the pancreas in Sweden. *Acta Paediatrica* 1962;**51**:65-7.
4 Brunechy Z. The incidence and genetics of cystic fibrosis. *J Med Genet* 1972;**9**: 33-7.
5 Lewis PA. The epidemiology of cystic fibrosis. In: Hodson ME, Geddes DM, eds. *Cystic fibrosis*. London: Chapman Hall, 1995:1-13.
6 SPSS Inc. *SPSS-X users guide*. 3rd Ed. Chicago: SPSS Inc, 1988.
7 Hill AB, Hill ID. *Bradford Hill's principles of medical statistics*. 12th Ed. London: Edward Arnold 1991:188-203, 257.
8 Office of Population Censuses and Surveys. *Mortality statistics—area, England and Wales 1992*. Series DH5 No 19. London: HMSO, 1994.
9 Elborn JS, Shale DJ, Britton JR. Cystic fibrosis: current survival and population estimates to the year 2,000. *Thorax* 1991;**46**:881-5.
10 Rosenfeld M, Davis R, FitzSimmons S, Pepe M, Ramsey B. Gender gap in cystic fibrosis mortality. *Am J Epidemiol* 1997;**145**:794-803.
11 Coles EC. *UK Cystic Fibrosis Survey: policy statement on confidentiality of the data held.* Cardiff: University of Wales College of Medicine, 1994.