

# Survival estimates for adults with cystic fibrosis born in the United Kingdom between 1947 and 1967

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## Abstract

**Background**—The UK has published observed cohort survival figures for subjects with cystic fibrosis born since 1968. Prior to 1968 cohorts cannot be established directly from routine data as cystic fibrosis was classified with a number of unrelated conditions in ICD7. Reported here are interrupted survival curves from 1978 for patients with cystic fibrosis born before 1968.

**Methods**—Life tables for the three year cohorts born between 1947 and 1967 were constructed by firstly estimating the numbers of patients with cystic fibrosis born in each cohort from live birth data and the disease incidence. The number of the estimated cohort that had survived to 1978 is known, which enables the proportion surviving to 1978 to be calculated. The survival of these cohorts after 1978 can be calculated in the usual way.

**Results**—The survival for each successive cohort was better than that of the previous one, but most of the improvements appear to have taken place up to the age of about 20 years. Only 3% of the 1947-49 cohort survived to 30 years of age compared with 21% for the 1965-67 cohort, and 3% of the 1953-55 cohort survived to 40 years of age. For the later cohorts the mortality rate for those aged between 26 and 30 years appears to be about 50 per 1000 per year.

**Conclusions**—While the trend in the numbers surviving into later adulthood is upwards, the mortality rates for these ages does not appear to be improving. It is not possible to tell from these data whether the high mortality rates in adulthood will improve with better resourced adult clinics or with improved treatment during childhood.

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plete cohorts pass through adulthood, there have been no comparative data available from earlier cohorts to assess the effects of treatment.

Coded data on cause of death for patients with cystic fibrosis from the UK death registration authorities are thought to be too unreliable before 1968 because the 7th edition of the International Classification of Disease (ICD7) was used in which cystic fibrosis was classified with a number of unrelated conditions. The numbers of patients born with cystic fibrosis in the UK prior to 1968 are therefore not available from official data.

This paper estimates the sizes of the pre-1968 UK cystic fibrosis birth cohorts from live birth population data and the presumed incidence of cystic fibrosis. Survival of the pre-1968 cohorts after 1978 is calculated from observed data held by the United Kingdom Cystic Fibrosis Survey (UKCFS) and presented as interrupted survival curves for adults with cystic fibrosis in the UK.

## Methods

The UKCFS has been described elsewhere.<sup>1</sup> Briefly, it seeks to identify all those born with cystic fibrosis in the UK since 1968 and to identify any pre-1968 cystic fibrosis births who were still alive in 1978. This is achieved primarily by population surveillance backed up by reports from the death certification authorities.

The survival of the pre-1968 cohorts can be calculated for those who have survived to 1978 for their post-1978 survival. This method assumes that the 1978 survivors represent 100% of the population. In fact, these survivors represent only a proportion of the original cohort. The size of the original cohort was estimated by assuming that the incidence of one cystic fibrosis birth per 2416 live births<sup>1</sup> in the period 1968-87 applied to earlier births. The proportion surviving to 1978 could then be calculated directly. The life tables for the survivors were calculated from 1978 and these data were manually assembled into the graph. In addition, the complete survival for the 1968-70 cohort was calculated for comparison purposes. Data from the death certification authorities were available up to the end of 1996.

Three year cohorts are used to give a reasonably large initial sample size and to maintain consistency with other published data. Because the numbers surviving are small, particularly in the earlier cohorts, both sexes are given

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The UK is the only country in the world that has published observed cohort survival data for subjects with cystic fibrosis. These cohorts are only complete since 1968 so even the most recent results give virtually no data for adults over the age of 25 years.<sup>1</sup> Each successive cohort since 1968 shows an improved survival on the previous with, for example, the percentage surviving to age 10 increasing from about 65% to over 98%. As the survivors of the com-

Table 1 Published annual total UK live births and births of patients with cystic fibrosis (CF) and resultant incidence of cystic fibrosis (live births per case) per three years

Year	CF births	Total births	Three year CF incidence
1968	367	947.3	
1969	356	920.2	
1970	388	903.9	2.495
1971	407	901.8	
1972	326	834.9	
1973	309	779.6	2.415
1974	316	737.2	
1975	291	697.4	
1976	299	675.6	2.329
1977	278	657.0	
1978	292	686.9	
1979	302	734.6	2.384

Table 2 UK live births (thousands), estimated numbers of births with cystic fibrosis (CF) and survivors with cystic fibrosis to 1978 for three year birth cohorts from 1947 to 1967

Three year cohort	UK live births (1000s)	Estimated CF live births	CF survivors to 1978
1947-49	2760	1143	35
1950-52	2368	981	39
1953-55	2342	970	88
1956-58	2503	1036	188
1959-61	2711	1123	308
1962-64	2970	1230	490
1965-67	2942	1218	651

together and two year time increments are used in the survival calculations. The life table was calculated using SPSS<sup>2</sup> and the confidence intervals were calculated separately.<sup>3</sup>

## Results

Published annual births of patients with cystic fibrosis and UK live births between 1968 and 1979,<sup>1</sup> and the resultant incidence of cystic fibrosis (live births per case) per three years are shown in table 1.

UK live births, estimated births with cystic fibrosis between 1947 and 1967, and survivors with cystic fibrosis to 1978 are shown in table 2. The cohort survival curves are presented in fig 1. The extent of the differences between these curves is shown by the confidence intervals (CI). For the 1947-49 cohort the survival to 24 years was 3% (95% CI 4% to 6%) and for

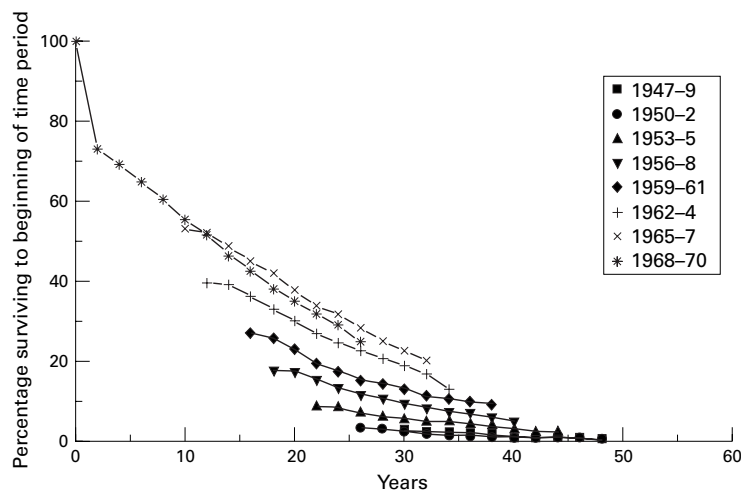


Figure 1 Percentage of three year cohorts of patients with cystic fibrosis born between 1947 and 1967 surviving to the beginning of two year time periods.

the 1965-67 cohort the survival to eight years was 53% (95% CI 50% to 56%).

Once past the age of about 20 years the mortality rates for all the cohorts averages about 50 per 1000 per year. Only 3% of the 1947-49 cohort survived to the age of 30 years compared with 21% of the 1965-67 cohort. Of the 1953-55 cohort, 3% survived to the age of 40.

## Discussion

Data are presented which, for the first time, give a reasonably accurate indication of the mortality of cohorts of subjects with cystic fibrosis born between 1947 and 1967. There are cases in the UK with cystic fibrosis who were born before 1947 but the numbers are so small that any survival calculations would be uninformative.

These calculations rely primarily on two related assumptions—the stability of disease incidence and a stable ethnic mix. Table 1 shows the UK data on disease incidence for the 12 years following the period when the cases reported were born. They show no important trend and thus there is no reason to suppose that there was a variation in the incidence in previous years. There are at least three possible mechanisms by which changes in ethnic mix could influence this study. During the relevant time period there was quite a large emigration from and immigration to the UK, the net result being to increase the ethnic mix. The available evidence suggests that the carrier frequency amongst the immigrants would be lower than amongst the emigrants, the UK having one of the largest incidences of cystic fibrosis in the world.<sup>4</sup>

The estimates of disease incidence have been virtually constant between 1967 and 1994, so any changes in disease incidence can only have occurred before 1967. The disease incidence would decrease with increasing ethnic mix, so estimates of the number of cystic fibrosis cases in the earlier cohorts would be too low and the estimated proportions surviving to 1978 would be too high. This would increase rather than decrease the contrasts. If the common genotypes of the immigrants led to less severe disease, this would tend to increase the contrasts. It has already been shown that social class is a strong determinant of survival<sup>5</sup> and, assuming that immigrants would tend to be in the lower classes, this would decrease the contrasts.

The problem of small numbers in the earlier cohorts reported here has necessitated combining the two sexes, even though there is no evidence that the mortality rate of the two sexes is the same. Indications of differences in mortality between adult men and women are best obtained from the complete cohorts,<sup>1</sup> even though they currently finish before 30 years of age.

The complete 1968-70 survival curve and the interrupted 1965-67 curve are similar. As each successive cohort shows a higher survival rate than the previous rate for all other years, this similarity requires investigation. The number of infants born with cystic fibrosis in

1965–67 could have been high by chance (the year on year variation is surprisingly large but still within the limits of random variation), leaving a larger than expected number (but not proportion) of survivors. An alternative explanation is that these survivors have a higher than usual number of cases with a historical diagnosis of cystic fibrosis which would not have been made using current criteria. This would imply that all of these interrupted curves overestimate survival among subjects with cystic fibrosis.

The survival curves are clearly very different, especially up to the age of about 25. However, what is much more important is the separation of the survival curves for the cohorts into a time order. This is encouraging on two counts. Firstly, this type of consistency suggests that the data are reasonably reliable in terms of the trend. Secondly, it provides a belated recognition of the advances made in the treatment of these patients 30–50 years ago which is enabling increasing numbers to survive into middle adulthood.

The extent of any improvements in the survival of those over the age of 25 is much harder to evaluate. The slopes of the curves look similar and an inspection of the hazard rates does not suggest any important differences. This observation would be consistent with the survivors of each cohort consisting of primarily mild cases, the moderately severe cases having had their survival extended for the later cohorts, but not as far as age 25.

Life table data for children with cystic fibrosis attending one large hospital between 1943 and 1964 showed 80% surviving to one year and 25% surviving to 16 years of age.<sup>6</sup> Interpolation of the data presented here suggests that these were optimistic estimates. It is plausible that the one year survival for the 1947–49 cohort was only 20%, while 25% survival to age 16 was only comfortably exceeded by the 1962–64 cohort.

These data show the trends in survival of cystic fibrosis cohorts in the adult age groups. While any extrapolation of these trends should be viewed with caution, the increasing percent-

age achieving, say, 30 years of age is further evidence that the adult population is set to continue growing for some time yet.

The number of adult survivors for each cohort is generally insufficient to quote any meaningful adult mortality rates. However, between the ages of 20 and 30 years the mortality rate appears to be similar in all the cohorts at about 50 per 1000 per year. The carers of adults with cystic fibrosis face formidable challenges if they are to improve on this historical mortality rate. The dramatic increases in survival to age 16 are leading to greater numbers of adult patients per year, many of whom had a phenotype that until recently would have been lethal in childhood.

These observations, based on the population of the UK, provide the basis for monitoring and interpreting future changes in the survival of adults with cystic fibrosis. They may also be useful in informing patients and other interested parties of the mortality rates experienced by adults with cystic fibrosis. While the trend in the numbers surviving into later adulthood is upwards, the mortality rate in adults shows no evidence of improvement. It is not possible to tell from these data whether the high mortality rates in adulthood will be improved with better resourced adult clinics or improved treatment for patients with cystic fibrosis during childhood.

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