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.

(Thorax 1999;54:420–422)

Keywords: cystic fibrosis; survival

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.1 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 complete 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.1 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 births2 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...
Survival estimates in cystic fibrosis

Results

Published annual births of patients with cystic fibrosis and UK live births between 1968 and 1979, 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 for three year birth cohorts from 1947 to 1967 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 age 24 years was 3% (95% CI 4% to 6%) and for the 1965–67 cohort the survival to eight years was 53% (95% CI 50% to 56%).

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 emigrants would be lower than amongst the immigrants, the UK having one of the largest incidences of cystic fibrosis in the world.

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 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, 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
time 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 expla-
nation is that these survivors have a higher than
usual number of cases with a historical diagno-
sis 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 recogni-
tion 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 differ-
ces. 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 fibro-
sis attending one large hospital between 1943
and 1964 showed 80% surviving to one year
and 25% surviving to 16 years of age.1 Interpo-
lation 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 formi-
dable challenges if they are to improve on this
historical mortality rate. The dramatic in-
creases 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 inter-
ested 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.

The UKCFS only succeeds due to the unstinting efforts of the
1700 clinicians and their staff who provide regular updates on
their patients. Mrs Morison is funded by a grant from the UK
Cystic Fibrosis Trust.

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