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# Cystic Fibrosis

07

## Key Points

- Ireland has one of the highest global incidences of cystic fibrosis
- Cystic fibrosis remains a lethal inherited disease but is also now a chronic disease of both childhood and adulthood
- Seven mutations of the CFTR gene account for over 80% of cystic fibrosis cases in Ireland
- The F508del mutation, which causes severe or classic cystic fibrosis, is a more common cause of cystic fibrosis in Ireland than in many other countries
- Newborn screening for cystic fibrosis commenced in the Republic of Ireland in July 2011

## Background

Cystic fibrosis (CF) is a life-shortening, inherited disease that affects most body systems, especially the lungs and digestive system. Most of the morbidity and mortality from CF is due to respiratory disease but complications affecting other body systems are becoming more prominent as life expectancy increases. With improved diagnosis and improved therapies, CF is changing from primarily a disease of children to a disease of children and adults.

CF is an autosomal recessive condition. There are global and regional variations in gene frequency. It is the commonest lethal inherited disease of Caucasians, but no ethnic group is exempt, although prevalence varies. One in 25 people carry a CF gene in Ireland. The genetic condition is caused by mutations of the CFTR gene which regulates salt transport. Over 2000 mutations in CFTR have been identified that cause CF. The most common CFTR mutation that causes CF worldwide is the F508del which causes severe or classic CF. In Ireland, of those living with CF, 55.6% have two copies of F508del while 36.0% have one copy of it<sup>1</sup>. This mutation is a more common cause of CF in Ireland than in many other countries. The G551D is the second most common mutation. Within Europe, Ireland has the highest frequency of G551D mutations<sup>1,2</sup>.

In Ireland, seven mutations account for over 80% of CF cases<sup>5</sup>. The mutations are divided into different classes of severity which impact on survival. Comparisons of survival must take account of these genetic variations but within each class there is considerable individual variation<sup>3</sup>. This can relate to a variety of factors, including environmental factors, so predicting prognosis for an individual from their genotype is not possible. Mutation class also has implications for treatment development<sup>3</sup>.

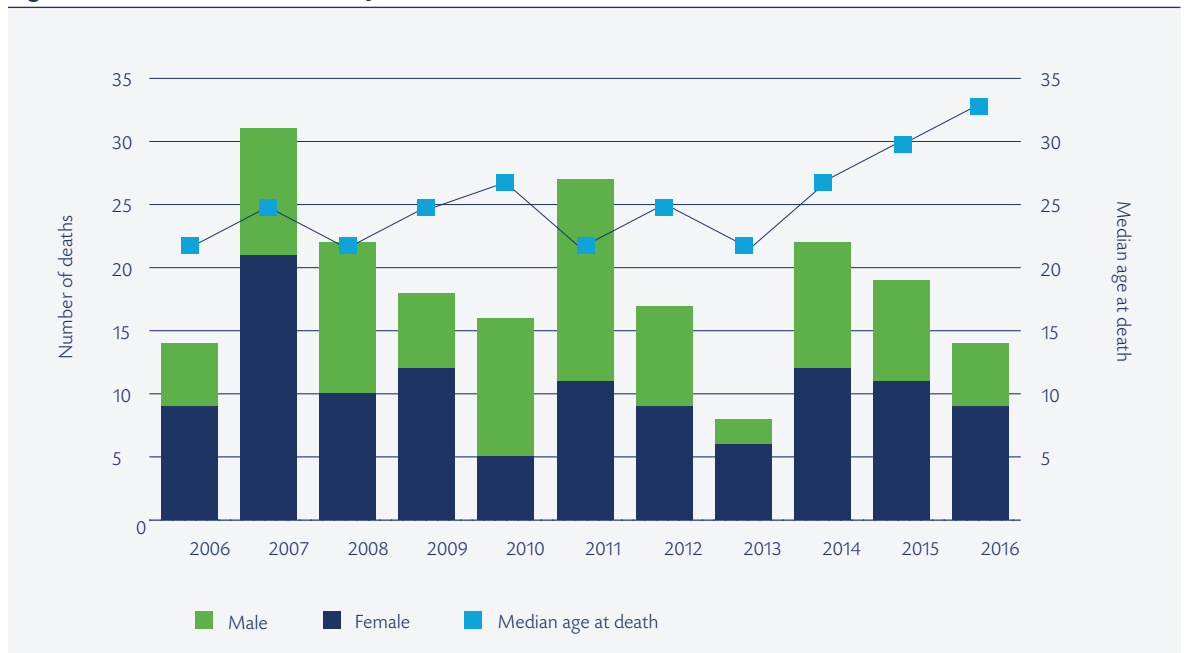
## Incidence and Prevalence

Between 2008 and 2016, on average 38 individuals were diagnosed with CF each year in Ireland (range 22-49). The median age of diagnosis was 0.33 years. Since the introduction of newborn screening in 2011, the numbers of new patients diagnosed following symptomatic presentation each year is approximately 25%<sup>1</sup>.

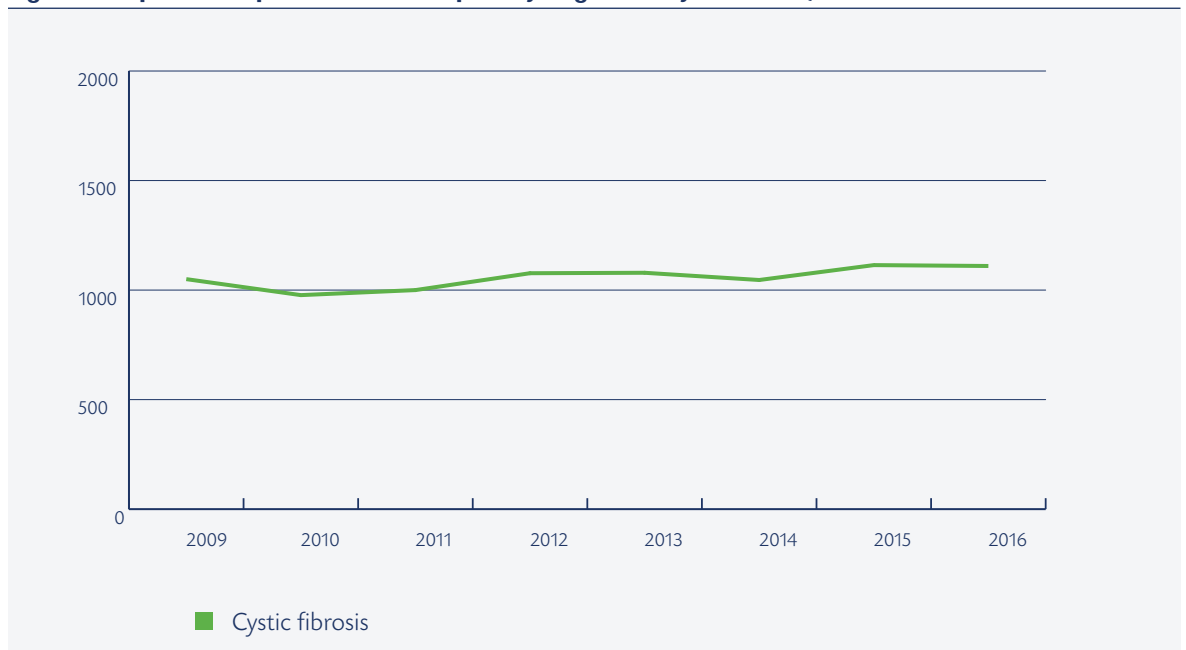
In 2016, there were 1,339 people living with CF in Ireland of whom 94.5% were on the (voluntary) Cystic Fibrosis Registry of Ireland.

## Mortality

Since 2000, an average of 18 people with CF died each year (range 7-31 years)<sup>1</sup>. Of the 13 people who died in 2016, (9 females, 4 males) they ranged in age from 11-59 years with a median age of death of 32.5 years (this differs to median life expectancy as the former only represents the 13 deaths which occurred in 2016)<sup>1</sup>. Figure 7.1 below shows deaths by gender and increasing median age of death for the years 2006-2016<sup>1</sup>. The estimated life expectancy in Ireland for those born today with CF is 37.5 years based on the assumption of no change in the mortality rate from any future changes in CF care<sup>1</sup>.

**Figure 7.1. Deaths associated with cystic fibrosis 2006-2016**

Source: *The Cystic Fibrosis Registry of Ireland Annual Report 2016*<sup>1</sup>.

**Figure 7.2. Inpatient hospitalisations with a primary diagnosis of cystic fibrosis, 2009-2016**

Source: *HIPE 2009-2016. All hospitals reporting data to HIPE.*

### Impact on health services

Neonatal screening for CF facilitates detection and intervention at an earlier age so numbers screened, numbers re-called and numbers detected should be included in consideration of impact on health services. Once diagnosed, impact on health services includes long term illness card resources, implications of co-morbidities, drug costs, provision and running costs of respiratory aids and appliances including oxygen and nebulisers, allied healthcare professional requirements

in addition to GP, Emergency Department, Outpatient Department and out of hours implications.

The number of inpatient hospitalisations for CF from HIPE reporting hospitals over the years 2009-2016 is shown in figure 7.2 above. In Ireland between the years 2011-2016 there were 60 lung transplants performed for people with CF. This included 7 bilateral lung transplants<sup>1</sup>.

There were almost six visits to out-patient settings for each person with CF in 2016<sup>1</sup>.

In 2016, there were 1,110 inpatient hospitalisations for CF (1.2% of respiratory inpatient hospitalisations, 0.2% of all inpatient hospitalisations) which used 14,081 inpatient bed days (2.4% of respiratory inpatient bed days, 0.4% of all inpatient bed days). Of these hospitalisations, 72% were emergencies. In addition there were 2,135 day cases.

Of the inpatients in 2016, 69% were classified as CF with major complexity with a mean and median length of stay (LOS) of 13.1 and 14 days respectively. For those inpatients with CF minor complexity, the mean and median LOS was 7.8 and 6 days respectively<sup>4</sup>.

Of those on the CF Registry in 2016, 16.1% were also on treatment for CF related Diabetes Mellitus, 11.7% for CF related liver disease, 1.0% were on CFTR modulation therapy, 5.9% on long term home oxygen (LTOT) and 5.4% on home non-invasive ventilation (NIV)<sup>1</sup>.

## Gender

Of those on the CF Registry from 2010 – 2016, approximately 58% were males and 42% females. As stated earlier, of those who died in 2016, 69% were females<sup>1</sup>.

## Age

With the introduction of neonatal screening in 2011, patients are increasingly diagnosed in the neonatal period. Of those on the registry in 2016, 44.6% were aged under 18 years of age, and 8.9% were aged 40 years or over<sup>1</sup>.

Of inpatient hospitalisations in 2016, 27% were aged 0-15 years and 73% aged 16-64 years. Within the 0-15 year old age group, 14.3% (43) were aged 0-4 years.

Comparing children (age < 18 years) with adults, 6.9% versus 17.1% were on treatment for CF related liver disease, 5.2% versus 26.1% for CF related Diabetes Mellitus, 18.2% versus 14.9% on CFTR modulators, 2.0% vs 9.1% on LTOT and 2.6% versus 16.1% on NIV<sup>1</sup>.

## Regional variation

In the South West of Ireland the G551 mutation accounts for 20% of cases compared with 15.2% nationally<sup>5</sup>.

## Socio-economic analysis

CF impacts on the education and employment opportunities of those affected as well as on carers/parents. There are also additional ancillary costs incurred such as heating, travel, electricity, nutrition, etc.

Environmental circumstances contribute to at least as much to the prognosis as CFTR gene class and modifier genes. Low socio-economic status is associated with an adverse outcome at all ages<sup>3</sup>.

## International Comparisons

Farrell in 2008 reported a mean prevalence of CF of 0.737/10,000 in 27 EU countries which was similar to the value of 0.797 in the United States. Ireland was an outlier at 2.98<sup>6</sup>.

In the USA, 24 CFTR mutations account for over 80% of all cases of CF. In Ireland, 7 mutations account for over 80% of CF cases. As mentioned in the Background, in Ireland, of those living with CF, 55.6% have two copies of F508del. This compares with 46.1% in the USA and 50.3% in the UK<sup>1</sup>. This is the mutation which causes severe or classic CF.

The European CF report of 2016 reflects data from 31 countries. Of those seen in 2016, the median age of diagnosis was 0.34 months (Ireland: 0.3 months) with a range of 0.2 months to 10 years<sup>2</sup>.

In the UK, one third of those hospitalised for CF are children<sup>7</sup>. In Ireland, 27% of the inpatient hospitalisations for CF in 2016 were in those aged 0-15 years.

1% of the Irish population with CF died in 2016 which is slightly lower than that of the USA and UK (1.3% and 1.5% respectively)<sup>1</sup>. The median age of death in Europe in 2016 was 30 years compared with a median age of 32.5 years in Ireland<sup>1,2</sup>.

## References

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