Changing incidence of CF in Ireland?

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Ireland has the world’s highest incidence of Cystic Fibrosis at approximately 1 in 1400 [1,2]. CF was integrated into the newborn bloodspot screening programme in July 2011 using an IRT/DNA analysis strategy. Babies with a blood IRT above the 99th percentile and with one or two CFTR mutations detected are referred for sweat testing. The anticipated number of CF cases (54) and carriers (94), were calculated based on the birth rates from the 2008 census and assuming a 2.5-fold enrichment of carriers within the top IRT percentile.

During the first 6 months of the programme, 37,435 babies were screened and 391 (1.0%) were referred for DNA testing. 16 CF cases (all with 2 mutations and confirmed by sweat testing) and 35 unaffected carriers were detected, giving an annualised CF incidence of 1 in 2340. Just 59% of the predicted number of CF cases (p = 0.038) and 74% of the predicted number of unaffected carriers (p = 0.014) were detected. Data from 2010 indicates that 25% of newborns in Ireland had non-Irish mothers. When the expected numbers were recalculated, based on the CF incidence in the nationality of the mother (and assuming the father has the same nationality), 72% of expected cases (p = 0.187) and 100% of expected unaffected carriers were detected. The apparent reduction in the number of cases and the changing incidence of CF in Ireland may reflect the significant increase in immigration (particularly from Eastern Europe) since 2004, and 100% of expected unaffected carriers were detected. The current figures are 59% of the predicted number of CF cases (p = 0.038) and 74% of the predicted number of unaffected carriers (p = 0.014).

Reference(s)

Who is reported in the Belgian, Dutch and French CF registries?

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Inclusion criteria of subjects in CF registries can vary over time and between countries which may introduce bias when data are used for benchmarking. We explored whether the subjects included in 2009 in 3 national CF registries [Belgium (BE), The Netherlands (NL), France (FR)] fulfilled strict diagnostic criteria: sweat test (ST) chloride >60 mEq/L and/or 2 disease causing CFTR mutations identified as specified in the CFTR2 project (access via courtesy of P Sosnay and G Cutting). The dataset includes around 46,000 measures of %FEV1 on 8,000 patients seen between 1999 and 2010, and captures 1000 deaths. In our preliminary analysis stratified by birth cohort: For people born in 1975 to 1979, all other things being equal, a 10% higher level of %FEV1 is associated with a halving of the concurrent hazard for death (HR 0.44 CI 0.38 to 0.50).

Conclusions: We apply a novel modelling approach to quantify how longitudinal changes in lung function are related to survival. Both an increased rate of decline in lung function, and a decreased absolute level of lung function are associated with an increased risk of death.

Determinants of lung disease progression in children with CF

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Although many risk factors are postulated as important in the progression of CF lung disease, their relative impact over time has been uncertain. The epidemiologic component of the 27 year old Wisconsin Newborn Screening Project afforded us the opportunity to evaluate the significance of 18 potential determinants. For this study, we combined the 132 enrolled subjects of the Screened and Control cohorts to increase power since group comparisons revealed no differences in pulmonary outcomes after adjustment for confounders. Prospective, systematic assessments were performed longitudinally beginning at diagnosis and continuing throughout childhood, including 1579 chest radiographs, scored by the Wisconsin chest xray (WCXR) method, and 1792 pulmonary function tests. Examining 6 intrinsic and 12 extrinsic risk factors and using mainly GEE analysis with adjustments for age, we found that the strongest associations with worsening WCXR scores were genotype, mucoid Pseudomonas aeruginosa (MPa) and its presence and duration, malnutrition (using height percentile <10th), and hospitalizations (reflecting exacerbations). The longitudinal comparisons with FEV1 values generally confirmed the significance of these four factors but the decreases over time were relatively modest compared to the lung disease progression evident in the chest radiographs. In contrast to MPa, neither Staphylococcus aureus nor non-mucoid Pa showed a significant association. In addition, meconium ileus and gender were not significant. Our observations support the view that aside from genotype extrinsic factors that can be modified are the major determinants of lung disease progression in children with CF.