Trends in Cystic Fibrosis Related Diabetes Epidemiology between 2003-2018 from the USCFFPR

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Introduction

- Cystic fibrosis related diabetes (CFRD) is widely prevalent in the cystic fibrosis (CF) population and associated with greater morbidity and mortality.
- Between 2003-2018, median predicted survival in people with CF increased from 33 to 44 yrs [1], and greater gains are anticipated with more recent novel therapeutics.
- The US CFF Patient Registry (US CFFPR) includes data from ~30,000 individuals with CF.
- Our primary objective was to examine trends in screening, incidence, and prevalence of CFRD between 2003 and 2018.
- Secondly, we investigated relationships between demographic variables and risk factors for CFRD at different points in time.

Methods

Diagnoses of CFRD were reported by CF center into the USCFFPR.

People <10 years old were excluded

Definitions:

- *Prevalence* of CFRD is the percent of patients with CFRD in a given year.
- *Incidence* of CFRD is # of new diagnoses per 1,000 person-years.
- *Screening rates* for CFRD is the percent of individuals without CFRD who underwent an oral glucose tolerance test (OGTT).

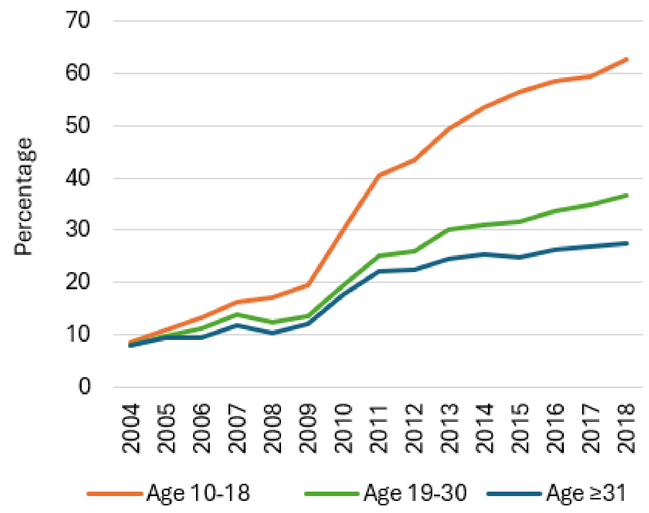
Risks for Developing CFRD Over Time:

- Multivariate logistic regression analyses were performed with CFRD as the dependent variable, and the following as independent variables:
  - Age
  - Sex
  - Race
  - Hispanic ethnicity
  - BMI Category
  - Mutation class
  - Pancreatic enzyme use
  - Enteric feedings
  - Liver Disease
  - FEV1 percent predicted
  - Number of admissions per year for pulmonary exacerbations
  - Use of corticosteroids
  - Use of CFTR modulator Vx770 (Ivacaftor)*
  - Use of CFTR modulator Vx809 combination (Lumacaftor-Ivacaftor / Tezacaftor-Ivacaftor) **

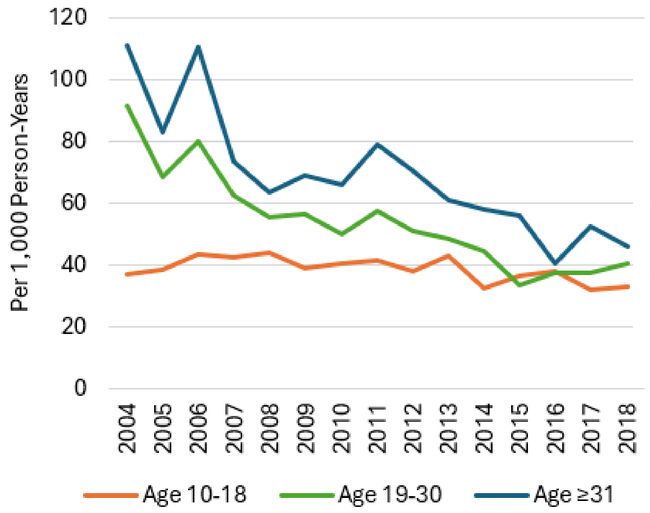
* Available 2012-2018
** Available 2015- 2018

Results

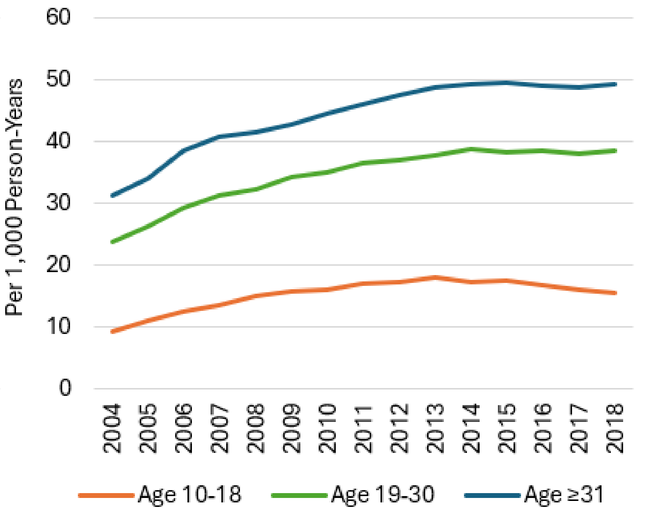
Screening Rates for CFRD



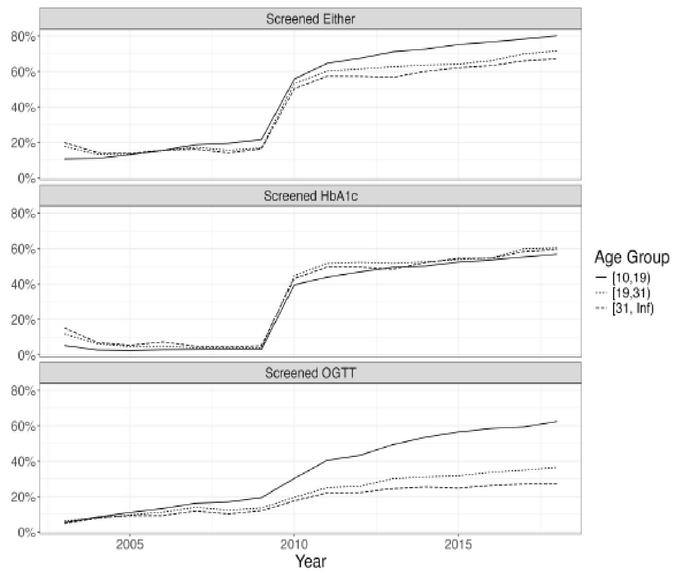
Incidence of CFRD



Prevalence of CFRD

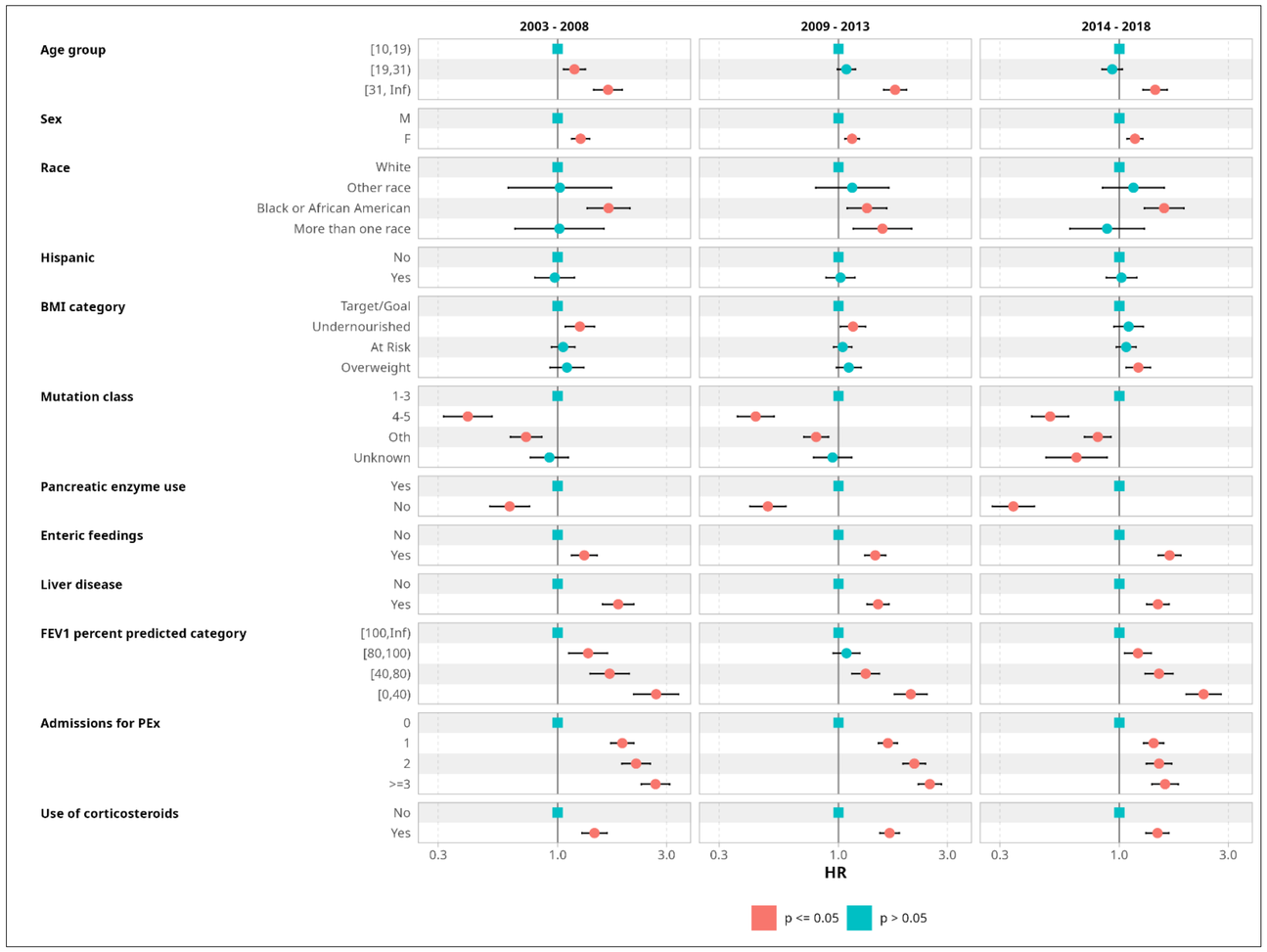


Screening Rates per age group



- Older age, female sex, Black or African American race, both low and high BMI percentiles (<10% and >85%), enteric feedings, liver disease, lower pulmonary function, increased hospitalizations, and use of corticosteroids were associated with increased hazard of CFRD. Residual function mutations and lack of pancreatic enzyme use were associated with decreased hazard of CFRD.
- Screening and prevalence of CFRD are increasing across time, and incidence is decreasing.
- Ivacaftor was associated with a lower hazard of CFRD (HR 0.7, 95% CI 0.66, 0.9, p<0.001), while lumacaftor-ivacaftor and/or tezacaftor-ivacaftor were not (HR 0.99, 95% CI 0.89, 1.09, p=0.8).

Time Varying Coefficients



Conclusions & Future Directions

- Strengths: largest study to date examining CFRD trends with national registry data from multiple CF centers across the United States.
- Limitations: Data were dependent on center report of CFRD; possibility of missing or incomplete data, given use of registry data; diagnoses may still be underrepresented, given overall low screening rates.
- Data show rising number of individuals with BMI >50%. Notably, BMI ≥85% in past decade is associated with greater odds of CFRD. Ongoing investigation is needed to determine if rising overweight and obesity in highly effective modulator therapy (HEMT) era will increase CFRD.
- Declining CFRD incidence over time may be due to increased detection and subsequent convergence towards previously reported rates of 2.4-4%[2].
- Risk of developing CFRD is decreasing over time, possibly related to earlier detection and improved therapies.
- Trends in prevalence support increased need for more specialists trained to care for growing population of adults with CFRD.
- Screening and incidence trends support need for revised, targeted screening algorithms CF patients at low- vs high-risk for developing CFRD.

References: [1] US CF Foundation Annual Patient Registry Data Report 2018; Knapp et al, The CFF Patient Registry: Design and Methods… AATS. 2016 / (2) Moran A, Dunitz J, Nathan B, Saeed A, Holme B, Thomas W. Cystic fibrosis-related diabetes: current trends in prevalence, incidence, and mortality. Diabetes Care. Sep 2009;32(9):1626-31. doi:dc09-0586

Regulatory Approval: Study was submitted to COMIRB and approved as non-human subjects research (IRB 20-1188). Additionally access to the data was granted and approved by the CF Foundation Patient Registry Committee.
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