exclusion of patients who transferred to a different adult center, and missing outcome data.

Acknowledgements: The authors would like to thank the Cystic Fibrosis Foundation for the use of Cystic Fibrosis Foundation Patient Registry data to conduct this study, and we would like to thank the patients, care providers, and clinic coordinators at CF centers throughout the United States for their contributions to the Cystic Fibrosis Foundation Patient Registry. This work was supported by the National Institute of Nursing Research [1F31NR020141–01].

40

An update from Minnesota on the seroprevalence of COVID-19 immunoglobulin G in our adult population

K. Mahan[1], J. Billings[2], S. Kiel[2], J. Dunitz[3]. *[1]Pulmonology, University of Minnesota Cystic Fibrosis Center, Minneapolis, MN; [2]Pulmonary, Allergy, Critical Care and Sleep Medicine, Department of Medicine, University of Minnesota, Minneapolis, MN; [3]Internal Medicine, University of Minnesota, Minneapolis, MN*

Background: Since the onset of the COVID-19 global pandemic in 2019, much has been learned about the clinical course and epidemiology of SARS-CoV-2 in the cystic fibrosis (CF) population. Because of the severity of illness seen in this population during the H1N1 pandemic, people with CF were initially thought to be at greater risk of severe disease [1], but this community has shown significant resilience without clear evidence of more-severe COVID pneumonia [2]. The reasons for this are probably multifactorial, including younger age and long-standing infectious risk-mitigation practices such as social distancing and handwashing.

Methods: Individuals aged 12 and older who receive care at the Minnesota CF Center provided virtual consent and completed a brief online survey detailing possible exposures, symptoms of COVID-19, and behavioral data (e.g., handwashing, remote work opportunities, social-distancing practices). We extracted additional data from the electronic medical record to further risk stratify our patient cohort, including age, body mass index, sex, forced expiratory volume in 1 second, CF transmembrane conductance regulator modulator use, and diabetes. Participants were evaluated for COVID-19 immunoglobulin G (IgG) at the time of enrollment (0 months) and 6 and 12 months after enrollment.

Results: Data were obtained 120 enrollees with an average age of 37; 50% were female. Preliminary data show that 25 (20.1%) of those tested had evidence of a natural COVID infection (IgG+ pre-vaccination or nucleocapsid Ab+). Two of these were hospitalized with COVID pneumonia between December 2020 and October 2021. Induced IgG ranged between 0 and 12 months' duration. At this time, 85% of the enrolled participants have been vaccinated against SARS-CoV-2: 67% with Pfizer-BioNTech, 25% with Moderna, and 9% with Johnson & Johnson. This is significantly higher than the vaccination rate of the general population in Minnesota, currently 66%.

Conclusions: As SARS-CoV-2 evolves, so too must our understanding of its natural history in people with CF. Our study shows that induced immunity through vaccination results in prolonged (12 months) IgG production in a subset of patients. The higher vaccination rate in the CF population along with infection risk-reduction practices have all helped reduce disease severity from COVID-19.

Acknowledgements: University of Minnesota Medical School COVID-19 Rapid Response Grant Initiative, With One Breath Foundation. We thank our patients and their caregivers for participating in this study.

References

[1] Viviani L, Assael BM, Kerem E; ECFS (A) H1N1 study group. Impact of the A (H1N1) pandemic influenza (season 2009–2010) on patients with cystic fibrosis. *J Cyst Fibros* 2011;10(5):370–6.

[2] Cosgriff R, Ahern S, Bell SC, *et al.* A multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis. *J Cyst Fibros* 2020;19:355–8.

41

Association between *Pseudomonas aeruginosa* infection stage and lung function trajectory in children with cystic fibrosis

M. Rosenfeld[1,2], A. Faino[3], P. Qu[4], F. Onchiri[4], E. Blue[5], J. Collaco[6], W. Gordon[7], Y. Zhou[8,9], M. Bamshad[1,10,11], R. Gibson[12,13]. *[1]Department of Pediatrics, University of Washington School of Medicine, Seattle, WA; [2]Department of Epidemiology, University of Washington School of Medicine, Seattle, WA; [3]Children's Core for Biostatistics, Epidemiology and Analytics in Research, Seattle Children's Research Institute, Seattle, WA; [4]Seattle Children's Research Institute, Seattle, WA, USA; [5]Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, WA; [6]Pediatric Pulmonology, Johns Hopkins University School of Medicine, Baltimore, MD; [7]Pediatrics, University of Washington, Seattle, WA; [8]Bioinformatics Research Center, North Carolina State University, Raleigh, NC; [9]Department of Biological Sciences, North Carolina State University, Raleigh, NC; [10]Department of Genome Sciences, University of Washington, Seattle Children's Hospital, Seattle, WA; [11]Brotman-Baty Institute, Seattle, WA; [12]Center for Clinical and Translational Research, Seattle Children's Research Institute, Seattle, WA; [13]Division of Pulmonary & Sleep Medicine, Department of Pediatrics, University of Washington, Seattle, WA*

Background: The effect of chronic *Pseudomonas aeruginosa* infection on lung function trajectory in people with cystic fibrosis (CF) is not known. We aimed to evaluate the association between longitudinal lung function (percentage predicted forced expiratory volume in 1 second (FEV_1pp) with different stages of *P. aeruginosa* infection (never, incident, chronic) using four definitions of chronic *P. aeruginosa* in a U.S. national cohort of children with CF.

Methods: Participants in the Early Pseudomonas Infection Control Observational Study diagnosed with CF before age 3 contributed encounter-based data through the U.S. CF Patient Registry 1992–2017. Follow-up was censored at the time of solid organ transplant or gaps of more than 2 years in culture or FEV_1 data. Cubic spline linear mixed-effects models were used to evaluate the association between *P. aeruginosa* stage and longitudinal FEV_1pp. Participants contributed to the *P. aeruginosa* never FEV_1 curve until they acquired incident *P. aeruginosa*, at which point they began contributing to the incident *P. aeruginosa* FEV_1 curve. If they developed chronic *P. aeruginosa*, they then began contributing to the chronic *P. aeruginosa* FEV_1 curve. Models contained interaction terms between age and *P. aeruginosa* stage (never, incident, chronic) and were adjusted for birth cohort, diagnosis after a positive newborn screen, sex at birth, race, ethnicity, insurance at first FEV_1, *CFTR* genotype (minimal vs. residual function), and the following time-varying covariates: CF-related diabetes, modulator use (ivacaftor, lumacaftor/ivacaftor), and respiratory culture positive for other individual CF pathogens. We used four chronic *P. aeruginosa* definitions [1]: 2 *P. aeruginosa*+ years over 3 years, 3 *P. aeruginosa*+ years over 4 years, 3 *P. aeruginosa*+ age-quarters over 2 years, 2 *P. aeruginosa*+ age-quarters over 1 year.

Results: Of 1,264 subjects born between 1992 and 2006 that provided a median 9.5 years (interquartile range 0.25–15.75 years) of follow-up, 89% developed incident *P. aeruginosa,* and 39% to 58% developed chronic *P. aeruginosa* depending on the definition. Model estimates were similar for all chronic *P. aeruginosa* definitions, so we show results using the second definition (3 *P. aeruginosa*+ years over 4 years) in Figure 1. The top panel shows the model estimates of FEV_1 (mean and 95% confidence intervals) according to age and *P. aeruginosa* stage. The bottom panel shows the number of FEV_1 values available at each age for each *P. aeruginosa* stage. The estimated mean FEV_1pp is lower after initial *P. aeruginosa* acquisition and lower still after chronic *P. aeruginosa* infection at all ages; this effect increases with age. Similarly, the slope of FEV_1pp decline is greater in those with chronic *P. aeruginosa*, particularly after age 12.

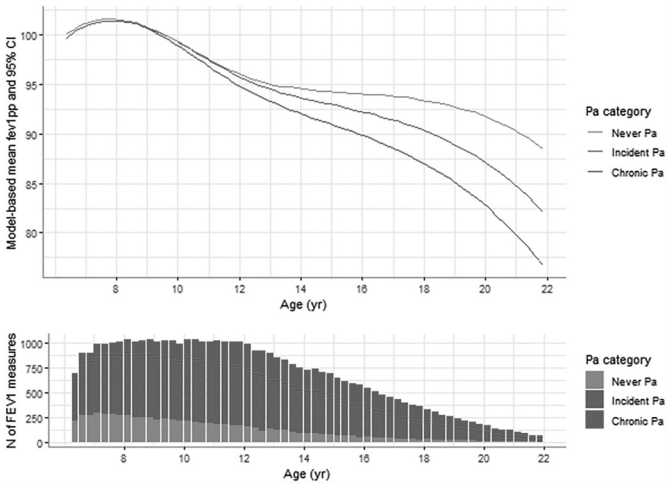

Figure 1. The top panel shows the model estimates of mean percentage predicted forced expiratory volume in 1 second (FEV_1pp) according to age and *Pseudomonas aeruginosa* stage for the reference value of all covariates. The bottom panel shows the number of FEV_1 values available at each age for each *P. aeruginosa* stage

Conclusions: Chronic *P. aeruginosa* infection is associated with lower FEV_1pp and more-rapid decline, particularly after age 12, in children with CF, even after adjustment for relevant covariates and regardless of chronic *P. aeruginosa* definition. Measures to prevent chronic *P. aeruginosa* infection could slow FEV_1 decline and improve long-term outcomes.

Acknowledgements: This work was supported by Cystic Fibrosis Foundation OBSERV13K0 and CUTTIN18XX1, BAMSHA18XX0, and KNOWLE18XX0. We thank all the people with CF who participated in the Early Pseudomonas Infection Control Observational Study and all the site primary investigators and research coordinators.

Reference

[1] Rosenfeld M, Faino A, Onchiri F, Aksit MA, Blackman SM, Blue EE, *et al.* Comparing encounter-based and annualized chronic Pseudomonas infection definitions in cystic fibrosis. *J Cyst Fibros* 2022;21(1):40–4.

42

Cystic fibrosis–specific reference equations for lung function adjusted for mortality attrition for people with cystic fibrosis in the United States

J. He[1], H. Cheng[2], D. Polineni[3]. *[1]Biostatistics and Data Science, University of Kansas Medical Center, Kansas City, KS; [2]Department of Biostatistics and Data Science, University of Kansas Medical Center, Kansas City, KS; [3]Pulmonary and Critical Care Medicine, University of Kansas Medical Center, Kansas City, KS*

Background: Percentage predicted forced expiratory volume in 1 second (FEV_1pp) has been widely used as the primary marker of lung health in a variety of pulmonary diseases, but it compares people with cystic fibrosis (PwCF) with healthy people without CF. In clinical care, patients and providers may benefit from generally understanding the health of a person with CF relative to that of other PwCF of similar age, sex, height, and CF transmembrane conductance regulator *(CFTR)* mutations. Using U.S. CFF Patient Registry (CFFPR) data from 1994 to 2001, reference equations of CF-specific FEV_1 percentiles have been calculated for U.S. CF populations [1]. Data from the Canadian CF Data Registry (CFDR) as of 2002 allowed modified CF-specific FEV_1 percentiles according to mortality to afford comparison of an individual with CF with all PwCF (alive and deceased) of the same birth cohort [2,3]. There has been an unmet need to update these health measures using recent lung health and mortality data from the U.S. CF population.

Methods: Based on recent U.S. CF registry data (CFFPR 2010–2017), we built reference equations generating CF-specific FEV_1 percentiles for the U.S. population using quantile regression. Yearly mortality for every 2-year birth cohort (1950–2010) was estimated based on the Kaplan-Meier survival curve or modified crude estimates. Rshiny software was used to develop a user-friendly online application to provide CF-specific reference equations for lung function with or without adjustment for mortality attrition for PwCF in the United States.

Results: The estimated U.S. CF-specific FEV_1 percentiles showed similar trends as previous estimates. Women and girls had lower scores than men and boys (Figure 1). Women and girls born between 1960 and 2000 also had lower survivor probability in recent years but not those born before 1960 or after 2000. The Rshiny application provides a tool that can automatically generate U.S. CF-specific FEV_1 percentiles with or without modification according to mortality, as well as previous versions of these measures.

Conclusions: These analyses yield a user-friendly online resource that may benefit patients, clinicians, and CF researchers.

Acknowledgements: This work was supported by the Cystic Fibrosis Foundation Statistical Expertise and Network (StatNet) Award (POLINE18Y7).

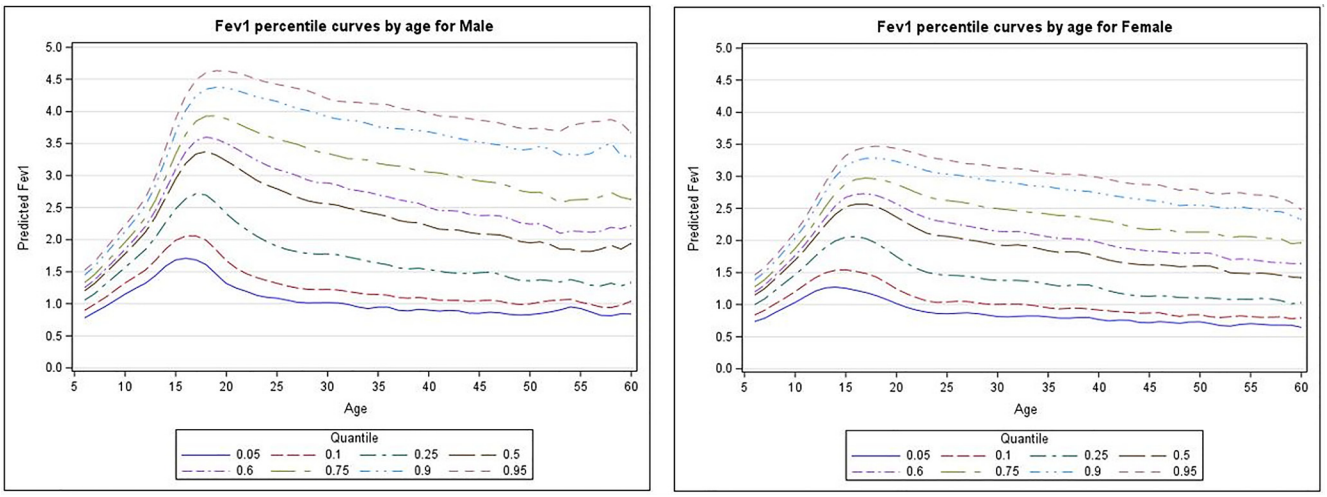

Figure 1 (abstract 42): Estimated reference equations for lung function for individuals with cystic fibrosis in the United States according to sex